Curing Tuberculosis

a manual for developing communities

by

Sok Thim and Anne Goldfeld

with

Eunice Tsai and Steve Miles

Curing Tuberculosis

a manual for developing communities

By

Sok Thim and Anne Goldfeld

with

Eunice Tsai and Steve Miles

We dedicate this book to the
memory of our colleagues,
Thang Chouy and Joyce Quinn, M.M.

"He who saves a single life is as
though he saved the entire world
—*Pirke Avoth*

ACKNOWLEDGEMENTS

THIS MANUAL HAS EVOLVED over a decade, and although in the end it was assembled by a few of us, this book has many authors. This is, in fact, a work in progress and it is impossible to fairly name all who have contributed an idea, a criticism, or an insight.

The medical assistants, expatriate workers and program staff of the American Refugee Committee TB program on the Thai-Cambodian border and of the Cambodian Health Committee program in Cambodia built the programs, which are the basis of this manual. These workers, who include Thang Chouy, Tan Bun-Leng, Bernadette Gliese, Sam Sopheap, Choeut Saroen, Map Phouern, Lori Dostal, Arlys Herem, Corinne Bowmaker, Debbie Webber, Jean Jachman, Sun Sath, Sa Rom and Brian Heidel, preserved and added to the wisdom of this experience from 1981 to the present. But it is to Bob Maat in particular, that this effort owes a great debt. It was his vision and persistence that allowed the TB program on the Thai-Cambodian border to exist and to flourish in the 1980s. Many of the ideas and approaches that are outlined in this manual were first pioneered by him.

There are all those who served on the boards and the administrative staff of organizations who have given financial, strategic, and moral support over the years—first and foremost, the Cambodian Health Committee. We are also indebted to the American Refugee Committee, the Christopher Reynolds Foundation, Oxfam America, Partners in Health, the Blue Oak Foundation, and the Jeanne and Joseph P. Sullivan Foundation for the resources which have allowed the Cambodian Health Committee to exist.

We are also grateful to Paul Farmer, whose belief in this manual and whose moral support was critical as we began. Partners in Health and the Center for Blood Research provided important support, as did Kristin Nelson, Barbara Pesavento, and Ann Corbett, whose editorial assistance at different times made this project feasible. We also thank Lisa Albers for her assistance on the Pediatric TB chapter.

The approach outlined in this manual has been built by our patients. They have often been underestimated by many, but they have

eloquently expressed through their actions that are, no matter their economic or educational level, can choose a common to be well and to cure their families and communities of tuberculosis.

There have also been innumerable experts in tuberculosis, refugee relief, and development, who have spoken in praise and in criticism of what this program was doing or trying to do since 1981—they have all challenged us to be the very best.

To all these people, we owe a debt of gratitude.

This mother in Svay Rieng with pulmonary TB is undergoing treatment. Her treatment may prevent her child from becoming infected and will help eradicate TB from the community.

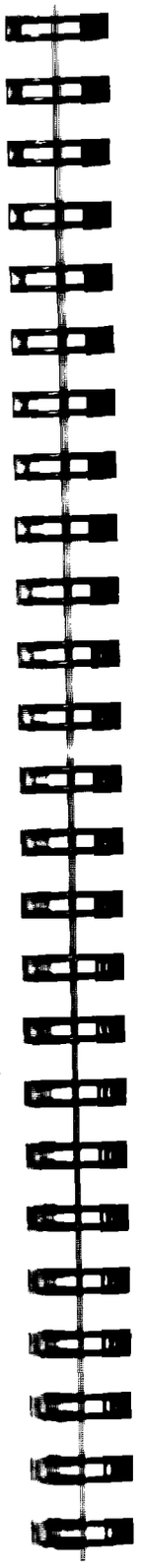
CONTENTS

People live far from cities in the developing world and TB programs must be able to reach into the communities and villages where TB infection lies.

One Hot Afternoon

IT IS A HOT AFTERNOON *in a small village in Cambodia. Aun, the mother of the house, has tuberculosis and is coughing. Her diagnosis is no surprise. She had been losing weight and coughing up blood for several months. Sophy, Aun's adult daughter, has agreed to be her mother's supporter during therapy. Sophy and the rest of the family listen carefully as Thim reviews in detail exactly what Aun and her family must do to cure Aun and prevent her from spreading TB to those she loves. She will remain in the hospital for two months according to the Cambodian TB Ministry's policy. Then, for six months, Aun will return to the clinic every month to refill the TB medicines she will take as an outpatient. In addition to taking medicine and coming to the clinic, Aun must agree to eat good food, even if she does not feel like eating, so that she can regain weight and strength to fight the infection.*

Thim, the Cambodian Health Committee's tuberculosis program director, has brought a treatment contract for Aun. The contract explains what tuberculosis is, what the treatment program involves, und what Aun is required to do to cure her TB. In the treatment contract, Aun and Sophy pledge that Aun will take her medicine and keep her appointments at the clinic. Sophy, Aun, and Thim solemnly sign two copies of the contract. Since Aun does not know how to write, she places her thumb print in red ink on the paper. Aun and her daughter make a serious, respectful, and informed commitment. A partnership and a promise has been made. Now, the drug phase of Aun's treatment can begin.



PART I

Building a TB treatment program through partnership

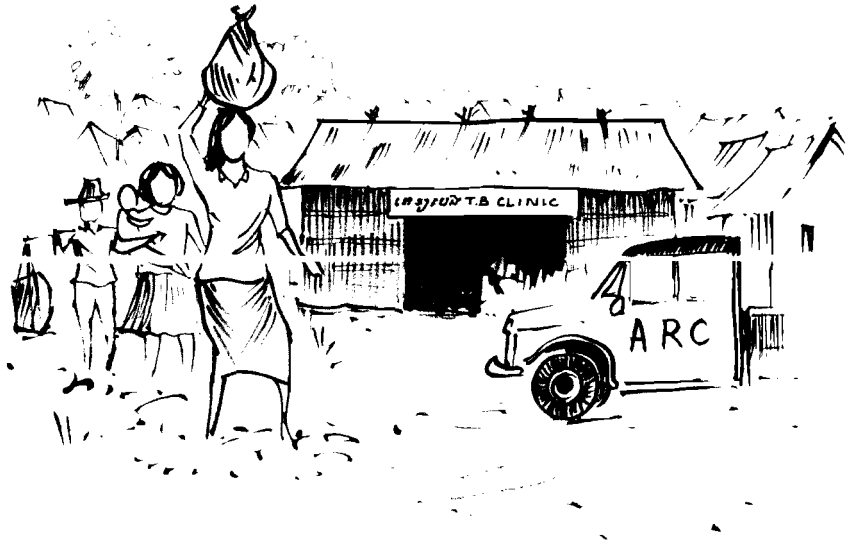
A HISTORY OF THE TB PROGRAM ON THE THAI-CAMBODIAN BORDER

The authors

The authors of this book are enthusiastic proponents of tuberculosis treatment programs in developing nations. Treatment programs can play a significant role in reducing the suffering and death tuberculosis causes and are a necessary part of any health system's public health strategy. This book's approach comes from experience with a program created on the Thai-Cambodian border in 1981. This program pioneered daily observed therapy (D.O.T.) and cured TB in over 3000 people with a daily compliance rate of over 99% by the time the refugee camps closed on the Thai-Cambodian border in 1993. This book has been further informed by new community-based treatment approaches developed by the Cambodian Health Committee (CHC) since 1994 in Svay Rieng, a province in southeastern Cambodia.

The Thai-Cambodian border program's treatment approach

Refugee camps have among the highest tuberculosis rates in the world. Poverty, malnutrition, exhaustion, and overcrowding have long made tuberculosis an overwhelming problem in refugee camps. In 1981, the idea that tuberculosis treatment in refugee camps could be successful was deemed unthinkably naive. Treating tuberculosis in camps was also politically taboo, though few would say so openly. Refugee camps were supposed to be emergency, temporary operations (though the reality in Thailand, Afghanistan, Palestine, Nepal,



The ARC TB program successfully treated thousands of patients and pioneered daily observed therapy (DOT) beginning in 1981

Sudan, and the former Yugoslavia has proved otherwise). Refugees were considered a transient and uneducable population unable to comply with a treatment regimen that could take up to a year. Racism, cynicism, political ideology and more "pressing" emergency priorities made the treatment of a lethal but curable infectious disease a low priority in refugee relief.

This view began to change in Thailand's Cambodian refugee camps in 1980. The Swiss Red Cross introduced a short course, six-month treatment protocol to a major refugee camp with controlled borders. It treated only those who agreed to be detained for a full six months. Tuberculosis treatment was strictly forbidden in open border encampments.

The American Refugee Committee (ARC) was the lead non-governmental organization responsible for medical care at the Nong-Samet camp in the early 1980s. Nong-Samet was a sprawling village of 50,000 refugees straddling the Thai-Cambodian border. Its Cambodian side was open and people could move freely to and from Cambodia through the camp. ARC operated a program in which American and European staff educated Cambodian medics who became the front line personnel for an 80-bed hospital and a clinic with 1000 patient visits per week. The medical operation was organized according to protocol manuals into a highly developed set of courses used to educate the Cambodian staff in diagnosis and treatment. ARC's Nong-Samet clinical medical education was the most extensively organized and best run program of refugee medical care in Thailand. It was widely emulated

ARC staff believed that its approach would work equally well for tuberculosis. Before it could be implemented, however, the ARC proposal's feasibility was debated by the International Committee of the

Red Cross (ICRC). Several major issues were raised. First, some doubted that refugee compliance could be high in a camp with an open border to Cambodia with uncontrolled refugee movement. Second, if compliance rates were low, resistance would be induced to this powerful new and expensive rifampin-based therapy. Third, initiating tuberculosis treatment would implicitly acknowledge that these temporary refugee camps were in fact permanent or at least long term. (In the end, these camps existed for more than a decade.) In late 1981, ARC won tentative approval for a trial of its novel and controversial approach of daily observed therapy.

The ARC approach contended that informed refugees, treated with dignity by clinic staff and supported by educated familirs and communities, would he successful partners in a six or nine month course of treatment, depending upon whether patients had pulmonary or extrapulmonary TB, respectively. The program ensured compliance through education, mutual respect and engagement of patients, their families, and their communities and was characterized by scientific integrity, discipline, and compassion. It operated even during shelling and an emergency evacuation and proved strikingly successful with a daily compliance rate of almost 100%.

In keeping with its philosophy, the ARC program trained Cambodian refugees to diagnose and treat tuberculosis as well as to manage the program. Expatriate staff were skeptical at first that Cambodians could in fact supervise the program. In order to test this approach, a one year study was initiated which randomized patients to either an expatriate coordinator or a Cambodian medic. The study demonstrated no difference in outcome between the expatriate and Cambodian program management and therefore the program was turned over to a Cambodian medic, Sok Thim, who subsequently became the tuberculosis coordinator of the entire border region (encompassing 11

camps). In this capacity Thim trained medics at five border camps in the diagnosis and treatment of tuberculosis and how to establish a successful treatment program. In 1990, Thim began to compile the lessons learned during the course of his tuberculosis training and program experience. These lessons were the beginning of this book.

Sok Thim and other Cambodian refugees were repatriated to Cambodia in 1992. Afterthree decades of war, the Cambodian medical and economic infrastructures were in shambles. As a result, Cambodia continues to have one of the highest rates of tuberculosis in the world. In 1994, international health experts estimated that there were 40,000 new cases and 13,000 deaths per year due to tuberculosis in a Cambodian population of approximately 10 million. As well, tuberculosis was cited as the leading cause of death for men between ages 15 and 45 (the working population of the country). Furthermore, in the early 1990s, only 30% of persons starting TB therapy completed their course. Thus, chronic war, poverty, and the lack of an organized TB program all contributed to the lethality of TB in Cambodia. Interestingly, recent studies have also indicated that genetic factors may contribute to the high rate of TB in Cambodia.

In 1993, Sok Thim and others began to envision a Cambodian-run nongovernmental organization (NGO) devoted to curing TB. The concept initially met with much resistance from many different directions. Critics wondered whether a border-trained medic who was not a physician could contribute to TB treatment in Cambodia. Furthermore, they doubted the efficacy of a community-based approach to TB treatment. Nonetheless, the Cambodian Health Committee (CHC) was formed and CHC's first board of directors meeting took place in Pursat, Cambodia, in March 1994. Shortly thereafter, with a modest grant from ARC, and the Christopher Reynolds Foundation, work began in Svay Rieng Province, one of the poorest

Red Cross (ICRC). Several major issues were raised. First, some doubted that refugee compliance could be high in a camp with an open border to Cambodia with uncontrolled refugee movement. Second, if compliance rates were low, resistance would be induced to this powerful new and expensive rifampin-based therapy. Third, initiating tuberculosis treatment would implicitly acknowledge that these temporary refugee camps were in fact permanent or at least long term. (In the end, these camps existed for more than a decade.) In late 1981, ARC won tentative approval for a trial of its novel and controversial approach of daily observed therapy.

The ARC approach contended that informed refugees, treated with dignity by clinic staff and supported by educated families and communities, would be successful partners in a six or nine month course of treatment, depending upon whether patients had pulmonary or extrapulmonary TB, respectively. The program ensured compliance through education, mutual respect and engagement of patients, their families, and their communities and was characterizetl by scientific integrity, discipline, and compassion. It operated even during shelling and an emergency evacuation and proved strikingly successful with a daily compliance rate of almost 100%.

In keeping with its philosophy, the ARC program trained Cambodian refugees to diagnose and treat tuberculosis as well as to manage the program. Expatriate staffwere skeptical at first that Cambodians could in fact supervise the program. In order to test this approach, a one year study was initiated which randomized patients to either an expatriate coordinator or a Cambodian medic. The study demonstrated no difference in outcome between the expatriate and Cambodian program management and therefore the program was turned over to a Cambodian medic, Sok Thim, who subsequently became the tuberculosis coordinator of the entire border region (encompassing 11

camps). In this capacity Thim trained medics at five border camps in the diagnosis and treatment of tuberculosis and how to establish a successful treatment program. In 1990, Thim began to compile the lessons learned during the course of his tuberculosis training and program experience. These lessons were the beginning of this book.

Sok Thim and other Cambodian refugees were repatriated to Cambodia in 1992. After three decades of war, the Cambodian medical and economic infrastructures were in shambles. As a result, Cambodia continues to have one of the highest rates of tuberculosis in the world. In 1994, international health experts estimated that there were 40,000 new cases and 13,000 deaths per year due to tuberculosis in a Cambodian population of approximately 10 million. As well, tuberculosis was cited as the leading cause of death for men between ages 15 and 45 (the working population of the country). Furthermore, in the early 1990s, only 30% of persons starting TB therapy completed their course. Thus, chronic war, poverty, and the lack of an organized TB program all contributed to the lethality of TB in Cambodia. Interestingly, recent studies have also indicated that genetic factors may contribute to the high rate of TB in Cambodia.

In 1993, Sok Thim and others began to envision a Cambodian-run nongovernmental organization (NGO) devoted to curing TB. The concept initially met with much resistance from many different directions. Critics wondered whether a border-trained medic who was not a physician could contribute to TB treatment in Cambodia. Furthermore, they doubted the efficacy of a community-based approach to TB treatment. Nonetheless, the Cambodian Health Committee (CHC) was formed and CHC's first board of directors meeting took place in Pursat, Cambodia, in March 1994. Shortly thereafter, with a modest grant from ARC, and the Christopher Reynolds Foundation, work began in Svay Rieng Province, one of the poorest

regions of Cambodia with the highest prevalence of TB in the country in 1994 (186 cases per 100,000 people).

At that time, the general daily compliance with TB therapy in Svay Rieng Province as a whole was approximately 30%. Using the approaches outlined in this manual, the CHC began to work in three district hospitals of Svay Rieng and achieved a daily compliance rate of over 80% within the first year. By the end of 1995, a daily compliance rate of over 99% was accomplished. CHC uses an innovative community-based program to treat tuberculosis, working in conjunction with the Cambodian Ministry of Health and the World Health Organization. The CHC program takes account of the links between TB and poverty by treating TB in conjunction with attempting to improve economic conditions for the patients and their communities. By the end of 1999, 1682 people had been successfully cured of their TB by the CHC program, with a daily compliance rate of 99.9%.

A PERSON-AND-COMMUNITY-CENTEREI) APPROACH TO TB TREATMENT

This book is written for:

- those who view tuberculosis as a human tragedy and believe that TB can be fought by people through programs that see and respond to its human dimensions by using their personal energies and the tools of medical science;

- those who work in developing communities where money is short and people's education, dignity, and respect have yet to be fully utilized. Developing communities can be found in all parts of the world, including the industrialized west;

- medical assistants, nurses or medical directors working in tuberculosis clinics or control programs in developing nations where there is little money and tuberculosis is common. This book will provide information about tuberculosis and about how to make programs more effective;

- those responsible for funding or organizing tuberculosis clinics or control programs in refugee camps or in developing countries. This book will assist in understanding, evaluating, monitoring, and advising tuberculosis programs.

Why we need another book on TB

TB is both an ancient and modern plague. Archeologists have found TB in ancient skeletons and some of the oldest medical books describe its symptoms. Sadly, despite the discovery of adequate chemotherapy against TB with streptomycin in 1945 and isoniazid (INH) in 1956, tuberculosis remains the largest single cause of death in the world from an infectious disease and kills approximately three million people every year. This figure does not include the number of people who are disabled by TB or the immense loss to the world economy of their productivity.

In the 19th century, science found and characterized the tuberculosis bacteria. 111 the 20th century, medical science gave us a series of drugs and ways to use them to cure tuberculosis. To stop the plague of tuberculosis, however, we must move beyond these scientific accomplishments to address TB as it strikes people's homes and communities. We must move from scientific insight to partnerships in order to conquer tuberculosis.

This book is about forming the kinds of partnership between experts. patients, families, and communities necessary to conquer tuberculosis. This book will take scientific knowledge as a point of departure to build tuberculosis programs sensitive to the human dimensions of this tragic disease.

Successful tuberculosis treatment requires a person-centered approach

Given the availability of effective medications for tuberculosis, human failure, not bad medical science, accounts for the dismal outcomes of many tuberculosis treatment programs. Patients are inherently motivated to be well, *so they will seek and complete therapy;* their lack of compliance is due to a number of other factors.

A biomedical model of treatment gives patients only scientific facts about tuberculosis. Health care workers will tell patients they have tuberculosis and must take medicines for six to twelve months to cure it. The biomedical model often fails because it makes patients passive recipients of medicine rather than partners in their own care. This approach may also fail because it does not take into account the competing social pressures and cultural beliefs that affect patients' compliance.

A coercive model of treatment requires patients to be detained or hospitalized in order to get treatment. These programs are often implemented due to poor compliance with other types of treatment programs. This approach often fails because few patients will agree to have their family and economic lives completely disrupted. Even if this model is effective for a small number of individuals, it will not reach large numbers of patients because the high costs of prolonged inpatient care will consume resources that would be better spent on

drugs, outpatient care, and serving more people. Also, in a country like Cambodia, where losing work may mean that a family will not eat, patients will often wait until they are deathly ill before submitting to inpatient hospitalization.

A person-centered approach to tuberculosis treatment assumes that people have an interest in being treated and can be mobilized to participate actively in that treatment. Respecting patients' dignity fosters high compliance. Tuberculosis treatment programs must be responsive to local understandings of the social context of the disease while tailoring themselves to how the community uses available health care services. A person-centered view moves beyond a biomedical view of tuberculosis to a broader view that is both scientific and responsive to the social realities and individual circumstances that affect compliance. A person-centered approach engages how human beings live in society to create successful tuberculosis treatment and control.

The foundations of a person-centered approach to tuberculosis

Empathy and compassion of the health care worker for the impact of TB upon the lives of those affected by it bring about respect for patients as persons, which is the key to compliance. TB is a lethal, debilitating disease that dismembers families, imposes economic hardship, and amplifies the cycle of poverty so that the sick get poor and the poor get sick. Empathy must shape the health care worker's personal commitment to the program.

Respect assumes that patients, families, and communities are fundamentally well motivated and, given the opportunity, will choose to drive tuberculosis from their lives. Respect for persons means that tuberculosis treatment is an opportunity for patients to better

themselves. help their families, and safeguard their communities. Respectful treatment has four elements: compassion and empathy on the part of clinic staff; education; clear and informed choices; and measured accountability. Thus, new patients are students who spend a short time in on-site education programs at the start of therapy. They do not need to be locked up to secure their cooperation.

Insight into the patients' society is critical because the treatment of tuberculosis cannot be separated from how people live. Treatment programs must build from a local understanding of how the circumstances of people's lives may negatively affect compliance with TB treatment. For example, poverty makes it difficult for patients to be diagnosed and treated because they may find it financially impossible to travel to a clinic. Their need to earn a daily income to feed their family may prevent them from losing a day's work to go to a clinic. The stigma associated with tuberculosis and the fear of being driven from their work or family are also barriers to seeking help. This fear thus actually endangers the community.

Awareness that patients' loved ones are an important resource in TB treatment. Most people, including those being treated for tuberculosis, live with people whom they love and who love them. Family members are a valuable resource. They can care for patients who are ill and encourage patients to continue with therapy when they are discouraged. They are the people in the world whom an infected person wants to protect most. They can give patients a reason to live — to watch a baby grow or to support a loving husband or wife. It is wasteful for tuberculosis treatment programs not to work with family members of patients and to use these incentives to help patients to complete therapy.

Health workers must respect the privacy and dignity of the patient. To cure TB, a successful partnership must be established.

Elements of a person-centered program

Education. Education brings people knowledge about their illness and helps them change their behaviors. It allows people to understand the effects of the disease and the benefit treatment can have on their lives. Education clarifies choices and provides the information allowing people to make responsible choices. Education helps patients support their community, understand how to help themselves, and act responsibly toward people they care about.

Enlisting family support. *A* person-centered understanding of tuberculosis recognizes the critical role of family in patients' lives. A partnership-centered approach will not simply define tuberculosis in terms of doctor-patient relationships but will understand it as a partnership between the program and the patients' families. Clinic staff should know patients' families. Families should be present in the TB education program and patients should identify a family partner to learn about TB who will support the patient and the other family members throughout treatment.

Building community cooperation. Tuberculosis changes patients' relationships with their communities. They may lose their jobs, be shunned by neighbors, be exiled from adoptive families, or be forced from communal housing. Fear of such events may discourage people from seeking help, ultimately harming the entire community. In order for a program to succeed in treating tuberculosis, it must address these issues. Once it does so, the community can be a very helpful partner—it can help identify cases, assist people in getting to a clinic and help reinforce the idea that tuberculosis is a community problem that can be cured.

Data collection. A program must measure and publicly disclose its successes and failures in completing therapies. No program is too

small to maintain records of its successes and failures. Records ensure that program staff are honest with themselves and with the community and therefore improve treatment practices.

Clinically, legible medical records are essential for communication between professionals in order to properly select drug therapy, to understand side effects, and to respond to changing patterns of resistance of TB bacteria to drugs.

Data collection is also needed to continuously improve the program's quality. Data can identify treatment drop-outs so that the problem of non-compliance can be investigated, understood, and addressed. The reasons for patients' non-compliance often reveal inadequacies in program design.

Finally, data collection is needed because it is the only way to improve the world's efforts against TB. Data collection allows different approaches to be tested, highlights the reality of tuberculosis, and demonstrates the feasibility of successfully solving this problem. Successful tuberculosis treatment programs will continue to evolve as the effects of drug resistance, new drugs, and the HIV epidemic change the spectrum and treatment of this disease. Data collection will guide this evolution.

Tuberculosis treatment and social justice.

Every case of tuberculosis is a misfortune, but misfortune can become injustice due to the way the disease affects the poor to a greater degree than the rich. Because of the social forces that exist at the beginning of the 21st century, TB most often affects people who are poor, neglected, and without power more than those who are respected, cared for, or with resources. Tuberculosis treatment is costly, and access is not available to all on a fair basis. Tuberculosis

is most common in nations and communities with many serious needs that compete for limited resources. Tuberculosis goes hand in hand with social disruption in war zones, the urban slums of cities in developed and underdevelopecl nations, in homeless shelters, and among drug addicts and alcoholics.

The most basic questions of justice ask us who we are as moral beings. How do we remedy the injustice of who gets tuberculosis'.' How do we remedy the injustice of who has the best access to tuberculosis treatment? This book cannot answer these large questions of justice, but we hope it will enable broader access to TB treatment and cure.

CAMBODIA: A CASE EXAMPLE

Although the Cambodian context is specific, the lessons learned can be applied to other countries and programs. We will use the Cambodia case as an example for building a successful TB program under very difficult conditions. In Cambodia, the current national policy (as it is in 1994–2000) designed by the WHO is to hospitalize patients in district hospitals for the first two months of treatment with four drugs followed by treatment for six months with two drugs (total of eight months). Upon diagnosis, patients are hospitalized and, if not previously treated, are begun on INH, pyrazinamide, rifampin, and ethambutol. Unless drug resistance is suspected, streptomycin and rifampin are avoided. Streptomycin is avoided because of the difficulty in ensuring clean needles lor injection and rifampin because of its high cost.

This enforced hospitalization program was developed in response to the poor compliance rate (before 1994, less than 30% of patients who began therapy completed therapy) found under a centrally based

TB and poverty are closely intertwined. Poor patients without resources often wait until the last stages of their disease to seek treatment, such as the case of this Cambodian grandmother who was carried to the border camps by her children seeking treatment.

Svay Rieng Province, where the Cambodian Health Committee works, is highlighted on the map

program designed and run by the French Red Cross in the 1980s and early 1990s. The reasoning behind this policy is that if patients take their drugs correctly during the first two months, the proportion of people who are actively spreading TB will be decreased and thus the spread of TB will be decreased. This type of hospitalization also allows for intensive daily education of patients about TB. After the two months of hospitalization, patients are discharged and are expected to return to the district hospital on a monthly basis to obtain TB medicines to complete another six months of therapy.

The Cambodian Health Committee (CHC)

The CHC is an independently funded, Cambodian-run non-governmental organization that works to support TB diagnosis, compliance, and care in cooperation with the Cambodian government TB staff. Thus, it helps to support the Cambodian national TB policy. This is accomplished through human resource and program development, strengthening the technical ability of the Cambodian government TB staff through on-site teaching, continuing patient education, and monitoring of medicines and case management. The CHC method is outlined below.

Case Identification

In Cambodia, TB cases are defined by the following criteria:

- Pulmonary TB is diagnosed by a positive sputum smear (usually three) and must be supported by the signs and symptoms of TB. The diagnosis of smear negative pulmonary TB is made on clinical signs and symptoms consistent with TB, such as persistent cough, wasting, night sweats, and chest

x-ray findings demonstrating granuloma or cavities, and confirmed by a positive response to treatment.

- Extrapulmonary TB is diagnosed based on clear clinical syndromes such as scrofula, characterized by enlarged lymph nodes; Pott's disease, characterized by gibbus formation on physical examination or by x-ray demonstration of vertebral disc destruction; or various other symptoms such as those described in Part II of this book (TB of the joints and bones, TB of the GI tract or peritonitis, TB of the urinary tract, TB of the reproductive organs, TB meningitis, etc.)

TB New Case Finding

To decrease the number of infective TB patients in the community new cases of open pulmonary TB must be aggressively identified and treated.

- Active case finding involves the survey of villages and households to identify any individuals with symptoms suggestive of TB who are then evaluated in the health center

- Passive case finding involves screening patients who have come to the health center for a different reason for symptoms suggestive of TB.

Patient and Family Education

Immediately upon diagnosis of TB, the TB staff begin informal and formal teaching sessions with the patient. Informal teaching is carried out on a one-to-one basis to give the patient knowledge about his or her disease and to educate the patient to be a resource in the community about TB. For example, after patients are taught the signs and

The Cambodian Health Committee (CHC) goes into the villages and into the homes to find new cases of TB and to make sure that patients under treatment are making progress towards a cure of their TB.

Where there is one TB patient in a family, often there is another, such as this mother and daughter who both had pulmonary TB. Two members of the same family provide support to one another through the long process of TB treatment.

symptoms of TB plus the side-effects of the TB medications that they will take, they can help identify other cases of TB in their village or explain to another patient what to expect when taking the medicines. Formal teaching sessions occur during the first three days of hospitalization for one hour each day. All other TB patients are invited to participate to reinforce their own learning and to share their experiences of the disease and treatment process with the new patients.

Topics covered in the teaching sessions are:

What is TB? (day 1)

The nature of TB

- how many people throughout the world are affected
- how TB spreads
  - that it is caused by a bacteria
  - that it is contagious
- how TB is curable

People's cultural beliefs

- traditional Cambodian views about TB and people who get TB

Orientation to the different kinds of TB

- education about the particular type of TB the patient has (for example, pulmonary TB or TB of the spine, etc.)

Signs and symptoms of TB (day 2)

- Treatment and prevention
- side-effects of drugs

Patient responsibilities during treatment (day 3)

- the responsibility of the patient to him or herself, the family, the TB program, and to the community to be a partner in his or her own treatment

- the responsibilities of the support person
- the responsibilities of the program to the patient to provide excellent clinical treatment, follow-up and support to enable the patient to finish the long and often difficult course of TB treatment

Home Visit

When a new patient is accepted into therapy, the TB staff visits the patient's home as soon as possible. The home visit is important for many reasons.

- It allows the TB staff to confirm that the patient's history is true through interviews with the family. For example, verifying that the patient never received TB therapy before is important before choosing particular medicines to treat the patient.
- It allows the staff to see and learn about the general living conditions of the patient and his or her family and to help identify a support person who will be the patient's partner in the treatment.
- It continues the process of teaching that was begun at the hospital. The support person is identified and informally taught about TB, the disease, and the commitment that treatment entails. At the Thai-Cambodian border outpatient TB program and in the recently initiated CHC TB Home Care Project in Svay Rieng, the patient teaches this information to the support person so that his or her own learning can be reinforced by the process of teaching. The TB staff then test the support person's knowledge and thereby also test the understanding of the patient. This has proved to be an outstanding teaching approach

Upon entry into the TB treatment program, patients undergo education about their disease, its impact on their families and communities, and the long course of therapy in front of them.

Hospitalization for TB treatment is a difficult process. This patient's husband, who serves as the patient supporter, emotionally supports his wife and helps ensure that she takes medicines properly and has adequate nutrition and care during the long course of treatment

- It allows for new case identification in the household.
- The visit of the TB staff is noticed by neighbors and helps to increase the community education process about TR.

To be educated is to be responsible: patient accountability

The patient is educated about patient responsibilities should he or she choose TB treatment. These responsibilities include:

- remaining in the hospital for the first two months of treatment in accordance with the current protocol in Cambodia
- taking medicines correctly and only as prescribed–medicines are not to be sold or given to others
- honestly reporting symptoms, side effects, and all other health issues to the TB staff
- maintaining good nutrition throughout treatment
- coming to refill medicines on a monthly basis after discharge from the hospital
- reporting to the TB staff if any family member has signs or symptoms of TB.

Support person accountability

The support person is taught his or her responsibilities after agreeing to be a partner in TB treatment. These responsibilities include:

- checking that the patient is taking medicines correctly and that the patient refills the medicines on a monthly basis

- ensuring that the patient eats well, even when the patient has side effects such as nausea and vomiting which can commonly occur secondary to INH and rifampin
- bringing the patient to the clinic or hospital if the patient is unable to get there on his or her own
- serving as a messenger between the patient and the health team when necessary

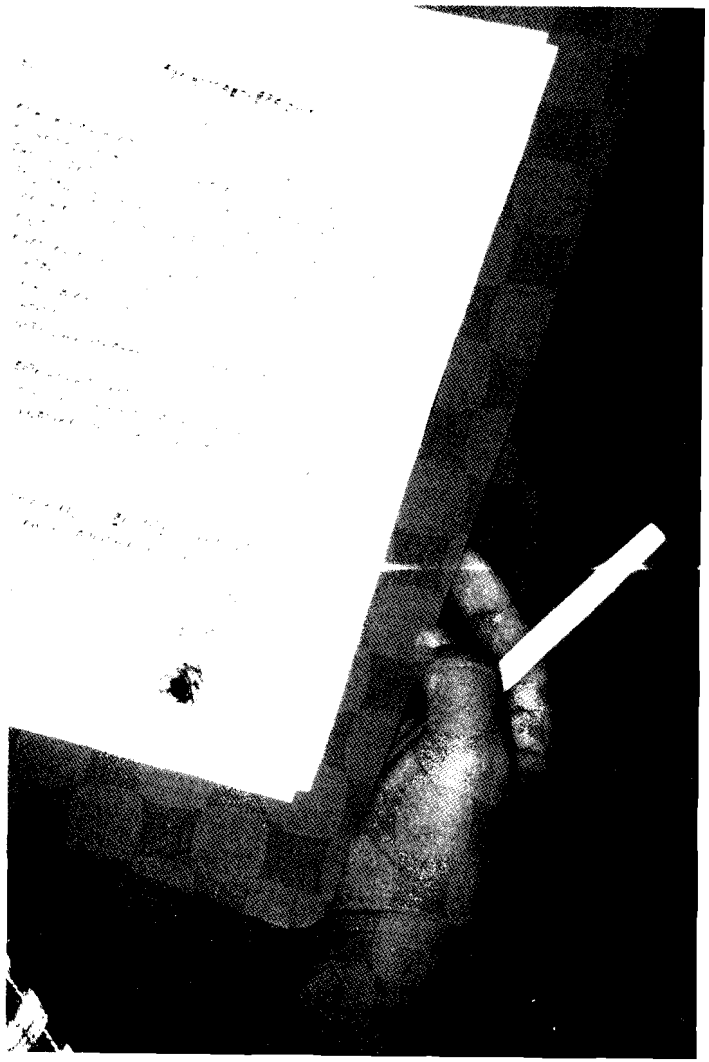
The patient TB treatment contract

The TB treatment contract informs patients of the seriousness of the commitment being asked of them. In it, patients acknowledge that they are ill with TB, that they can die of TB, and that they can spread this deadly yet curable disease to other people. We have found that a key motivation for people to make and honor a commitment to treatment involves their concern for others, both family and neighbors. and a desire not to infect them.

When a TB patient understands the facts about TB, its treatment and side effects, and the impact of the disease upon their own bodies, family, and community, they can make an educated decision about undergoing treatment. The patient signs or places his/her thumb print on a contract, which is also signed by the patient's support person and the TB staff member. Two copies of the contract are made, one for the patient and one for the TB staff.

The CHC TB Patient's Contract Form reads:

I know I have TB and that I can die of this disease.
I know that I will need to take TB medicine every day for 8 months to cure my TB



The TB contract is a solemn commitment to complete TB treatment among the patient, the patient supporter, and the health care worker. The contract is signed by all three or, if the patient cannot read or write, it is thumbprinted

I know that my family and other people in my community can catch TB from me if I don't take my medicines.
I want my TB cured.
I am asking you to give me TB medicines.
I promise to eat good food and drink enough fluids to keep my body strong.
I promise to do mild exercise to keep my body strong.
In case of an emergency that prevents me from picking up my medicine, I promise that I or my support person will contact the TB staff and arrange for my medicine to be picked up.
I promise to comply with the TB program policies and take my medicine every day for 8 months.
These statements are all made of my own fret. will.

Signatures or thumb prints of:

Patient: _____
Patient supporter: _____
TB staff: _____
Date _____

Why does a contract work?

The contract formalizes the commitment between patient, support person and medical staff. It is a declaration that all parties understand the important points taught during the education process and that a firm promise is being made to complete the long and difficult therapy in the effort to cure the patient's TB.

A commitment to treatment can be very powerful, as evidenced by the continuation of TB treatment during a military attack on the Nong Samet refugee camp at the Thai Cambodian border. That TB program was for many years conducted in an active war zone and attack and

evacuation of the camp was an ongoing threat. Thus, the daily observed TB therapy was under constant threat of disruption. Each patient was therefore given three days of medicine to be saved in case of attack. On Christmas morning, 1984, the camp was attacked and patients fled, taking their emergency medicines with them. They faithfully took these medicines in the following days until a makeshift TB clinic could be organized at the evacuation site, where they all resumed treatment.

The vitamin protocol

An effective compliance tool developed and used at the Thai-Cambodian border was called the "vitamin protocol." It works best in a clinic or outpatient setting where patients are not extremely ill and hospitalization of TB patients is not enforced. The protocol involves the oral administration of vitamins (B-complex, iron and folic acid) to patients on a daily basis under observation at the TB clinic. The duration of the vitamin protocol varied from two to four weeks, depending on the patient's diagnosis and disease severity.

Taking vitamins helped orient patients to taking medicines under daily supervision and, more importantly, was a way for health staff to screen for potentially non-compliant patients. That is, if patients were not motivated enough to take vitamins on a daily basis, they were not prepared for the long-term commitment required for completing TB treatment. The vitamin protocol proved extremely useful in building and testing compliance in the clinic setting, as evidenced by the high rate of compliance (greater than 99%) at the Thai-Cambodian border program.

The vitamin protocol was useful in other ways. For example, the two to four weeks of vitamin treatment provided an extended opportunity

When TB patients come to refill their TB medications, they receive food rations, which serve to motivate them to return to the clinic on a monthly basis to refill medicines and receive a medical checkup.

for teaching by the TB staff and for sharing of information between new patients and those already on therapy. In addition, while patients took the vitamins, repeat sputum smears were done to confirm the diagnosis of pulmonary TB. For those who were suspected of having TB but who were initially AFB-negative, repeat sputum smears often became AFB-positive, again confirming the diagnosis of TB.

Food Supplements

For the patient

After the first two months of inpatient therapy, the patients receive a one month supply of medicine and are instructed to return to the hospital on a monthly basis for refills. In the districts where CHC works, a program of food supplementation has been instituted in collaboration with the World Food Program (WFP). When the patients return to the hospital to receive next month's medicine supply, they receive this footl ration, which includes fifteen kilograms of rice, six cans of sardines, and 750 grams of vegetable oil.

TB patients are among the poorest patients in Cambodian society. For example, in Svay Kieng Province, 90% of the TB patients were found to have less than the average annual per capita income (approximately $90–$220 per year) and to have less ability to generate income. That is, among TB patients there is a greater proportion of illiterates, fewer means of transportation, fewer skilled laborers, and fewer land and animal owners. Those who do own land own relatively less productive land. All these factors result in a lack of food for the majority of patients for three to six months of the year. Thus, food supplementation provided in conjunction with TB therapy is an important benefit to the TB patient and his or her family. Food supplements serve not only as a way to increase the nutritional status of patients, but also as an important compliance motivator. Supplements also motivate

neighbors in the community to find out whether they have TB and may qualify for extra food. The importance of food supplementation concretely illustrates to villagers the link between TB and poverty.

Monthly check-up, monitoring, and patient tracking

All patients are expected to appear monthly in person at the district hospital with their personal medical history notebooks. At this visit, patients pick up next month's medicines and food supplements then undergo a brief examination to assess their progress and to look for side effects of any medicines. If a patient is unable to go to the clinic, his or her support person must go instead to explain why the patient is absent. If neither the patient nor support person shows up, TB staff must make a home visit to locate the patient and ensure that outpatient TB treatment continues. CHC has set up a patient tracking system within each district that maintains a list of the names and addresses of all patients under treatment. If a patient does not show up, the TB staff finds him or her and identifies the factor(s) preventing proper compliance.

Surprise home visits

Surprise home visits are used to verify that patients are taking their medicines correctly. Once a month, a CHC staff member makes an unannounced home visit to every TB patient receiving outpatient medicine. During the visit, pills are counted to verify that the correct amount has been taken and to check on the general well being of the patient. In addition, the staff interview each patient's support person to confirm that the patient is following the prescribed regimen and eating nutritious food.

CHC staff make surprise visits to TB outpatients to count their pills to make sure that they are taking their medicines properly. These visits also reinforce education about the importance of taking medicines and show patients, their families. and the community the TB program's commitment to curing its patients.

Working with the TB staff: quality management

Successful TB programs rely on quality staff management. Quality can be directly measured. The CHC for example, strives continually to improve care delivery and compliance of TB patients. As part of this process, CHC staff reviews the records of inpatients on an ongoing basis. They also check the government TB staff's diagnoses and the dosage of prescribed medicines. Such cross checking is a useful informal educational tool to improve the quality of TB care delivery. It also allows the detection of corruption among underpaid staff who may steal TB medicines and sell them for their own profit. Training the patient to know what pills and how many pills they need to take also helps fight this type of corruption.

CHC keens its own records on each natirnt which include the patient's history and physical exam, laboratory tests, and assessment and plan. Statistics should also be kept on death rate, cure rate, and default rate. These statistics are used to track improvements in the treatment of TB and in the quality of the program.

COMPLIANCE

Compliance and the TB treatment program

Compliance is the most important, most serious problem of any TB program. The CHC philosophy is based on the concept that it is better to have no treatment program at all than to have a poorly run program because such a program will contribute to drug resistant TB strains.

Non-compliance includes:

1. Never taking the medicine;
2. Not taking the full course;
3. Not taking medicine as ordered;
4. Wrong dosage by staff and/or patients;
5. Wrong purpose (taking medicine for the wrong reason);
6. Adding medications not prescribed.

Who is non-compliant?

Based on our experience, compliance problems exist among: soldiers, elderly people abandoned by their families, alcoholics/gamblers, the homeless, the extremely poor, beggars, migrant workers, and those without close family supporters. Men seemed to nave more compliance problems than women. In children, some reasons for non-compliance were difficulty swallowing the medicine or dislike for the way the medicine tasted. Children's compliance depends upon the parents' cooperation and sometimes on the parents' educational level. With less-educated parents, clear and careful instructions, sometimes with drawings, need to be given.

However, the individual who is non-compliant can be *anyone*. There is no stereotype.

Many factors affect patients' compliance with TB treatment

- Patients often feel much better after one month of taking TB medicines and if they don't understand the life cycle of the

TB bacteria and the necessity of taking medicines for the entire course, they may stop taking the drugs.

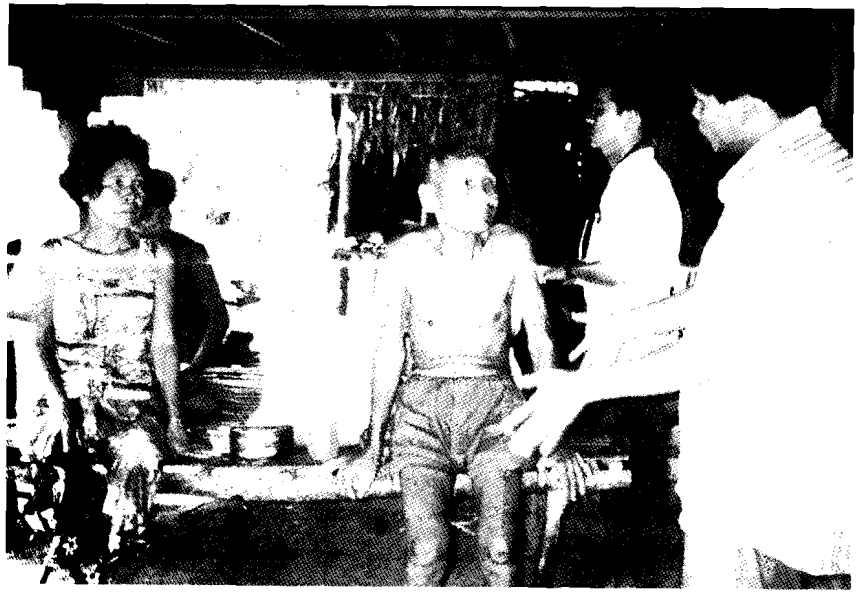
2. It may be difficult to return to the clinic to get a refill of medicines because of the need to work or because of the cost of transportation to the health facility.
3. Many TB medicines have unpleasant side effects and if patients do not understand the importance of taking the medicines for a long time they may quit because of these side effects.
4. Since TB treatment involves multiple medicines, patients who are improperly educated may not take these multiple medications correctly.

Results of non-compliance

Non-compliance contributes to the development of drug resistant strains of TB. This undermines efforts to treat the TB epidemic in the community as a whole. On an individual level, not taking prescribed drugs deprives patients of cure and may result in recurrence or worsening of illness. Also, if symptoms do not improve because patients are not taking the medicines, health staff may be misled into prescribing larger doses or using a more potent drug that could be more toxic to patients. Most importantly, over-utilization (i.e., the patient forgets one dose so he or she doubles the next dose) may increase the risk of severe side effects.

Remember:

The non-compliant patient is not an easily identifiable individual. There is no "defaulting type" of patient. Compliance can never be assumed. If a patient defaults, it is better that he or she defaults on the vitamin protocol than on TB therapy. Patients who fail to show up



When a patient does not show up to refill medicines, the CHC staff goes to the patient's home to find out why. This patient had bad sciatica and was unable to get to the clinic. The CHC staff brought his food supplements and medicine refills. The staff educated the patient and his support person (his wife) about how important it is for the patient or supporter to return to the clinic monthly to obtain medicine throughout the course of therapy.

This gentleman, who is in the outpatient phase of his TB treatment, collects his medicines for the next month. He is carrying the food supplements he has just received

for treatment or who fail to pick up their monthly supply of medicines must be found immediately. The importance of taking daily medicines must be constantly reinforced.

FORCES THAT UNDERMINE A PROGRAM

There are many reasons why a TB program fails, including:

- ***Drug diversion*** – selling of medicines by patients or stealing of medicines by staff. Sometimes false records are created by staff of non-existent so-called "ghost" patients so that medicines can be ordered, diverted and sold.

- ***Interruption in drug provisions.*** For example, in Cambodia at various times, streptomycin and rifampin were unavailable due to political instability and and/or due to an unreliable supply of medicines to Cambodia from outside countries.

- ***Lack of drug accountability.*** A steady and reliable source of medicines must always be available. Daily medicine orders must be checked and the existence of patients verified. Ideally, two people should check all medicine orders, perform a daily pill count at the end of the day, and compare the numbers of the pills dispensed with the number of pills ordered.

- ***Poor training of TB staff.*** Monitoring of care provided by the TB staff is crucial. Verification of physical exam findings, interpretation of laboratory data, and diagnostic accuracy

needs to be done on a routine basis. Upgrading of skills and educational opportunities should be incorporated into a TB program.

- ***Not involving the community and family.*** The community and patient's family can be great assets in the treatment of tuberculosis. The treatment of TB is long and difficult and patients will need the support and care of both their family and their community.

- ***Racism.*** The belief that people who have not had the privilege of education or who are members of certain ethnic groups are not capable of completing a course of TB therapy. Every individual given the proper education and support is capable of completing TB treatment. Another bias can be against programs that focus on a community based approach to TB treatment. For example, some individuals and agencies believe that only centrally based approaches are appropriate to fight TB, even if they yield poor compliance results. That is, they place confidence in programs that are managed by government ministries and filter down to villages through provincial and district hospitals rather than in community-based approaches that involve local/indigenous health care providers to create and carry out their own TB program at the community/village level.

- ***Poverty.*** If patients are too poor to eat properly, their immune systems are weakened. If patients are so poor that they have no transportation to a health facility, they will not be able to pick up their medicines or be seen by a health worker. Furthermore, poverty leads to both patients and providers selling TB medicines for a profit. Therefore, treatment of TB must also address issues of poverty if a program is to be successful.

- ***Geographical isolation of villages.*** A program will not be successful if many people cannot be reached because they live too far from a district center. A program must find ways to reach villagers who are in outlying areas.

- ***Poor motivation among health care staff.*** A program can be difficult to run if staff are poorly or irregularly paid. These issues can create irregular working schedules from clay to day because staff may take a second job to supplement their income to support their families. These conditions can lead to corruption.

PUTTING IT ALL TOGETHER: TREATMENT ORGANIZATION

The first two months:

In Cambodia, after patients are diagnosed with TB, they are hospitalized and begin daily observed therapy with the standard regimen of isoniazid, rifampin, ethambutol, and pyrazinamide. Hospital staff continually monitor the patients for improvement in their clinical symptoms. Patients attend general formal and informal teaching sessions on TB throughout the early stages of treatment.

At the end of the two months, pulmonary TB patients are again screened for AFB positivity in their sputum. If the smear is negative, they are discharged to continue their treatment as outpatients. Patients receive monthly food supplements throughout the eight months of therapy.

Enforced hospitalization

There are many problems with enforced hospitalization in district hospitals, such as is currently practiced in Cambodia. Patients are separated from their families and are unable to work even when they feel better. Furthermore, there are often not enough beds in district hospitals for TB patients, limiting the number of patients on TB therapy at one time.

Outpatient therapy: the next 6 months

The patients with negative sputum smears after two months are discharged to outpatient therapy for the following six months. The outpatient phase of therapy is a two drug regimen of isoniazitl and ethambutol. When rney are discharged, patients are given a one month supply of medicines and food supplements and are instructed to return to the hospital each month to refill their medicines and receive additional food supplements. In addition, the staff give the patient a medical record book containing the patient's diagnosis and descriptions of the completed and current therapy. This record helps the patient and future care-givers know which drugs were used and whether they were effective.

At the end of therapy:

After eight months of therapy, pulmonary TR patients are once again given a sputum smear test to check for AFB+ organisms. If the smear is negative, a discharge summary is prepared and entered into the patient's medical notebook. The patient is given this notebook along with an extra month of rice, fish and oil to augment nutritional status. During this visit, the CHC staff checks for new symptoms and verifies that the patient has been cured. This visit allows the CHC staff to assess the patient's family members to see if any have developed TB

In countries where there is forced hospitalization for TB therapy, many poor patients will not come to be treated until they are very ill because they cannot afford to stop working because their families may not eat. These patients often have many complications and can be a source of infection for the community.

symptoms in the intervening months. If the patient still has a positive AFB of their sputum or if there is no improvement, the patient likely has resistant TB and a regimen for drug resistant TB should be considered.

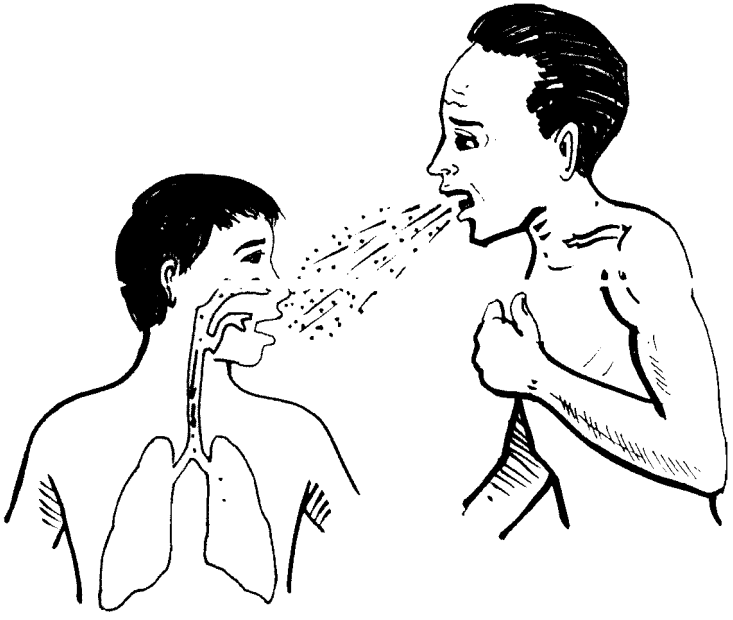
In summary, the person-centered approach to TB treatment that we have outlined above combines respectful treatment of patients that recognizes their dignity through education, clear and informed choices, and measured accountability with compassion and empathy on the part of the health care staff. These programs understand that successful TB treatment and control must engage how human beings live as people, which is in a family, and in a society. A successful program acknowledges the dignity of the TB patient and creates partnerships between the patient, the family, the community, and the health care provider. This is done by:

- ***Respecting*** ancl involving the patient in the decision to begin and continue treatment through education and the commitment of signing a contract.
- ***Learning*** about the patient and their family, home, economic and community situation to anticipate any compliance problems in advance.
- ***Seeing*** the many forces that can undermine a TB program, particularly in a poor developing country and finding strategies to overcome them.
- ***Recognizing*** that in most countries, TB patients are among the poorest in the community and that poverty is directly related to non-compliance. Thus, efforts should be made to improve the patients' economic and nutritional status and to improve the general economic situation of the community

- ***Educating*** the patient and a key support person from the patient's family as well as the community and its leaders about TB.
- ***Passionately caring*** and doing our utmost to make sure that each patient successfully completes therapy through home visits, surprise medicine counts, and locating any patients who fail to show up for refills of their TB medicines.
- ***Accounting*** and documenting the success of a program, as measured in decreased cases of sickness and death due to TB and in increased case identification.

PART II

Clinical presentation, diagnosis, and treatment of tuberculosis



The most common route of TB infection is via inhalation of invisible infectious respiratory droplets from a person who has active pulmonary TB.

UNDERSTANDING TB

Introduction

In 1882, Robert Koch discovered the causative agent of tuberculosis, a bacillus called *Mycobacterium tuberculosis*, or Mtb. Once the bacillus is breathed into tne lungs, it establishes a primary infection and can multiply to become the focus of later disease. Bacilli can subsequently spread to other parts of the body via the lymphatic system or via the bloodstream. The infection is usually contained successfully by the individual's immune system. However, one in ten people infected will progress to clinical TB.

How TB spreads

TB is spread from a person with active pulmonary disease to others when he or she coughs, spits, sneezes, or does anything else that may spray infected droplets into the air. Many millions of bacteria are carried in the spray of one cough or sneeze. The bacilli travel in the air and are inhaled by another person, who can then develop the disease and infect others. This deadly chain of infection can threaten the health status of a whole community.

Factors causing reactivation of TB

Factors that weaken the immune system can cause reactivation of TB:

1. Malnutrition;
2. Diseases such as lymphoma, leukemia or AIDS;
3. Drugs such as steroids or cancer chemotherapy that suppress the immune system;
4. Stress or depression;
5. Intercurrent infections (measles, chicken pox, mumps, etc)

Patients who are more susceptible to TB reactivation are:

1. Patients with any of the above conditions;
2. Gastrectomy patients who are malnourished;
3. Pregnant women;
4. Babies and young children.

PRIMARY TB INFECTION

Epidemiology

Primary TB infection is traditionally known as a childhood disease. Children who live in close contact with adult pulmonary TB patients are most susceptible. However, within the last few decades, primary TB has decreased in frequency in children and increased in frequency among adults.

Pathogenesis

Bacilli can multiply rapidly because there is no immunity at this stage. There is an exudative inflammatory response in which neutrophils and monocytes are predominant. TB bacteria spread (in hours to days) through bloodstream and lymphatic system and disseminate to other parts of the lung and body, particularly to the lymph nodes, bones or kidneys. Within 4 to 8 weeks of the infection, the body's immune response to the TB bacteria will develop, causing a reaction to the tuberculin skin test. This is called delayed type hypersensitivity. If the host's immune response is strong enough, it will force the bacilli to lay dormant, usually in areas where oxygen and nutrients are highly supplied (i.e., the apices of the lungs or in the kidneys).

Tuberculosis is commonly contracted in childhood from family members with open pulmonary TB.

Transmission

In the primary stage, children and others who become infected do not pass the infection to others.

Signs and symptoms

1. Mild fever
2. Flu-like illness
3. Cough
4. Poor appetite
5. Respiratory distress

Diagnosis

1. PPD test;
2. Gastric aspirate in children;
3. Chest x-ray, which may show:
   a. Hilar adenopathy
   b. Pleural effusion
   c. Pulmonary infiltrate

Treatment and patient care

1. Patients or parents attend education classes;
2. Home visits (check household contacts for active TB);
3. Family interview;
4. Sign TB contract form;
5. Begin drug therapy with appropriate treatment regimen;
6. Offer supplementary feeding;
7. Follow up weights and physical examination every month

Prevention

1. Administration of BCG to children at birth;

2. Avoiding unnecessary use of steroids;
3. Good nutrition;
4. Improvement of family economy;
5. Early seeking of medical advice if TB is suspected;
6. Isolation of small children from infected adults.

PULMONARY TB

Introduction

Pulmonary TB is a form of tuberculosis which affects the lungs. It has two different forms:

> ***AFB positive or open pulmonary TB:*** TB in the lung with acid fast bacilli in the sputum smear.
>
> ***AFB negative pulmonary TB:*** Sputum smear is negative in the adult, but chest x-ray is positive and there are positive clinical signs.

Epidemiology

TB of the lung is the most common form of TB. In Cambodia, for example, ~80% of clinical TB cases are pulmonary TB. Pulmonary TB can affect any age group.

Transmission

Open pulmonary TB is the major source of infection in the community. TB bacteria can be spread through coughing, spitting, speaking, sneezing, screaming, shouting, kissing, or other respiratory secretions.

Signs and symptoms

Symptoms include:

1. Hemoptysis (coughing up blood)
2. Sputum production;
3. Persistent cough;
4. Chest pain;
5. Dyspnea;
6. Feeling of fullness in the chest.

onstitutional symptoms of TB infection in general include:

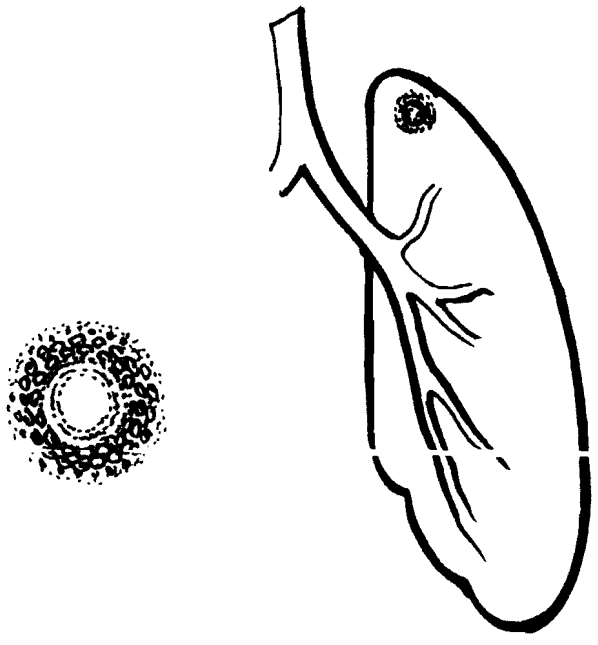
1. Fever and chills;
2. Night sweats;
3. Weight loss;
4. Poor appetite;
5. Weakness or fatigue.
6. Chronic ill health, inexplicable.

xamination may reveal:

1. Rales, commonly heard at the apex of the lung;
2. Rhonchi;
3. Wheezing;
4. Tubular breath sounds;
5. Consolidation;
6. Increased respiratory rate;
7. Tracheal deviation.

Diagnosis

1. Careful health history;
2. Complete physical examination;
3. Sputum smear for AFB;



TB reactivation usually occurs in the upper lobes of the lungs because of the high oxygen tension in this region. Millions of infectious mycobacteria can live in a single cavity.

4. In children, if sputum is not obtainable, gastric aspirate for AFB should be performed in the early morning before the child has eaten;
5. Sputum for culture (if possible);
6. Laryngeal swab if patient is not producing sputum;
7. Chest x-ray (in situations where resources are limited, such as in Cambodia, this should be sparingly used since physical exam and AFB of sputum is sufficient for the majority of cases);

This may reveal:

a. nodular or patchy shadows in the upper lobe (posterior and apex);
b. cavitation;
c. calcification;
d. mediastinal lymphadenopathy.

Treatment and patient care

When the diagnosis is confirmed, patient care can begin following the 5 Rs: (Right route, Right time, Right dose, Right medicine, and Right patient):

1. Patients and/or supporters attend education classes;
2. Home visits (check household contacts for active TB);
3. Family interview;
4. Sign TB contract form;
5. Begin drug therapy with appropriate treatment regimen (see part III, "Therapeutic regimens lor pulmonary and extrapulmonary TB");
6. Offer supplementary feeding if possible;
7. Follow-up examinations, including following the patient's weight, sputum smear, and signs of drug toxicity;
8. Encourage pulmonary exercises to promote lung expansion

Complications of pulmonary TB

While the patient is affected by TB, there are many secondary complications. These complications are often closely related to one another. Some of the more typical complications are pleural effusion, emphysema, empyema, massive hemoptysis, TB of the bronchi/larynx, TB otitis, bronchiectasis, respiratory distress, asthma, pneumothorax, rniliary TB, and TB meningitis.

Prevention

The best prevention of TB is to treat those who have open pulmonary TB with effective multi-drug therapy. The following are other means by which transmission can be minimized:

1. Teach patient to cover mouth when coughing.
2. Family members and clinic workers should use masks in known cases.
3. Give BCG vaccination to newborns and children <5 years who did not receive BCG vaccination at birth.
4. Improve lamily economy.
5. Avoid use of steroids because they can suppress the body's immune system.

PLEURAL TB

Introduction

Pleural TB is a form of pulmonary tuberculosis that manifests itself in the pleural space. It is usually secondary to pulmonary TB. There are two forms of pleural TB, a wet form, which refers to the presence of

fluid in the pleural space, and a dry form without fluid in the pleural space.

Epidemiology

Pleural TB probably represents a relatively "active" form of pulmonary tuberculosis. Untreated patients usually develop active pulmonary or extra pulmonary tuberculosis within **2–3** years. Tuberculosis of the pleura can happen in any age group. In the population treated at the Thai-Cambodian border, the highest incidence was among young adults. Men were more frequently afflicted than women.

Transmission

Pleural TB is not infectious unless the patient also has open pulmonary TB

Signs and symptoms

1. Difficulty breathing/shortness of breath;
2. Chest pain/pleuritic chest pain;
3. Cough with or without sputum;
4. Hemoptysis;
5. Orthopnea (shortness of breath while lying down);
6. Asymmetrical chest wall movement;
7. Dullness to percussion of chest;
8. Pleural effusion, usually unilateral and small;
9. Heart displacement by the effusion;
10. Tracheal deviation;
11. Decreased breath sounds;
12. Egophony;
13. Constitutional symptoms similar to those found in pulmonary TB (fever, chills, weight loss, loss of appetite, weakness/fatigue)

Diagnosis

1. Careful health history;
2. Complete physical examination;
3. PPD test;
4. Chest x-ray:
   a. Unilateral effusion;
   b. Heart displacement;
   c. Pulmonary lesions can be obscured by the pleural effusion;
   d. When effusion resolves, chest x-ray may appear normal.
5. Sputum for AFB if possible;
6. Pleural biopsy (not possible in some third world health care facilities):
   a. AFB stain of pleural biopsy,
   b. Culture of pleural biopsy.
7. Thoracentesis:
   Pleural fluid should be sent for AFB stain, culture, and chemical and hematologic analysis. The fluid typically manifests a lymphocytic exudate (>80% lymphocytes). The pH falls within a wide range (7.05 to 7.50). Pleural glucose may be low, normal, or near normal. Protein is usually high.

Treatment and patient care

1. TB contract, home visits, family interview, patient education, and follow-up examinations same as for all cases of TB;
2. Begin drug therapy with appropriate regimen (see part III);
3. Encourage the patient to increase lung exercises to promote lung expansion,

4. For massive pleural effusion patients may need therapeutic thoracentesis to relieve respiratory symptoms.

Prevention

There is no specific means to prevent TB pleural effusion.The most effective prevention strategy is to detect and treat pulmonary TB as early as possible.

MILIARY OR DISSEMINATED TB

Introduction

The term 'miliary' comes from the word "millet," a fine-grainctl seed which bears a likeness to the TB lesions distributed through the body, especially in the lung. These fine-grained lesions can be seen on chest x-rays.

Epidemiology

Miliary or disseminated TB occurs in two types of patients:

1. Among babies, children, or other immunologically naive subjects, shortly after primary pulmonary TB infection.
2. Late or delayed spread of TB found in old age, during inter current infection, with immuno-suppressive diseases such as AIDS or cancer, or during immuno-suppressive treatment

Transmission

Miliary TB is not contagious unless the patient also has pulmonary TB with sputum that is smear positive for AFB. Patients with both miliary

TR and open pulmonary TB can be a great source of infection to others.

Signs and symptoms

1. Persistent cough;
2. Chest pain/chest tightness;
3. Shortness of breath;
4. Hemoptysis;
5. Severe unexplained debilitating illness (patient may have night sweats, fever of unknown origin, headaches, abdominal pain, etc.);
6. Constitutional symptoms similar to those found in pulmonary TB.

Diagnosis

The diagnosis of miliary TB can be complicated and requires a careful diagnostic approach. In addition to a complete health history and physical examination, the following are helpful:

1. PPD test, although this may be negative;
2. Sputum for AFB;
3. Gastric aspirate in children for AFB;
4. Chest x-ray, which may show:
   a. Diffuse, finely nodular shadows, which appear equal on both sides;
   b. Enlarged hilar lymph nodes;
   c. Enlarged mediastinal nodes;
   d. Pleural effusion;
   e. Localized parenchymal lesions;
   f. Occasionally, the x ray pattern will appear normal, especially in immunosuppressed patients or in children;

5. Neurologic exam;
6. Lumbar puncture if patient has neurological signs;
7. If effusion is present, thoracentesis for gram stain and AFB.

Additional procedures may also be helpful. These procedures require a high degree of technology and expertise which are not normally available in developing countries. The following procedures may be performed for AFB staining and culture to evaluate a patient in whom the suspicion of miliary TB is high but the above procedures failed to establish a diagnosis of TB.

1. Pericardiocentesis if pericardial effusion is present.
2. Bone marrow biopsy.
3. Liver biopsy.

Treatment and patient care

Treatment should be provided as soon as possible when the diagnosis is confirmed. The delay of treatment may lead to loss of the patient's life.

1. TB contract, home visits, family interview, patient education, and follow-up examinations sanie as for all cases of TB
2. Begin drug therapy with appropriate regimen (see part III)
3. Control fever.
4. Supplementary feeding.

Prevention

As for other forms of TB.

TB MENINGITIS

Epidemiology

TB meningitis can occur in any age group. The TB meningitis cases in our patient series from the Thai-Cambodian border tended to occur among young adults and small children under the age of 10.

Transmission

TB meningitis alone is not infectious to others unless the patient also shows signs of open pulmonary TB.

Pathogenesis

TR meningitis is an inflammation of the meninges caused by mycobacterial infection, which may be secondary to blood borne or lymphatic spread of organisms or due to direct extension secondary to TB arachnoiditis, or secondary to a tuherculoma in the brain.

Signs and symptoms

TB meningitis occurs in three stages:

Stage I (early): symptoms are mild and nonspecific

a. Vague ill health (particularly in children);
b. Fever;
c. Exhaustion;
d. Apathy;
e. Anorexia;

f. Vomiting;
g. Abdominal pain;
h. Constipation;
i. Mild headache;
j. Constitutional symptoms similar to those found in pulmonary TB.

Stage II (intermediate)

a. Moderate to severe headache;
b. Stiff neck;
c. Photophobia;
d. Positive Kernig's sign and Babinski sign;
e. Drowsiness, lethargy;
g. Cranial nerve palsies (VI most common, also III, IV, VII);
k. Seizure.

Stage III (advanced)

a. Generalized cerebral edema;
b. Papilledema;
c. Change in mental status: confusion, psychosis stupor, coma;
d. Seizure;
e. Athetoid limb movements;
f. Gross paresis or paralysis.

Diagnosis

1. PPD test;
2. Check sputum for AFB/gastric aspirate in small children;
3. Chest x-ray, head x-ray, or spine x-ray looking for evidence of pulmonary TB or a TB focus in the brain or spine;

4. Lumbar puncture:
   The spun sediment of the cerebral spinal fluid (CSF) should be stained for AFB. The characteristics of CSF in TB meningitis are:
   a. Clear to slightly cloudy;
   b. Polymorphonuclear (PMN) leukocytes are seen in the early stages of infection; however, as disease progresses the percentage of lymphocytes increases;
   c. Moderately elevated protein;
   d. Moderately low glucose;
   e. AFB rarely positive on direct smear exam.

Treatment and patient care

Treatment should begin promptly; delay will increase the fatality rate.

1. Treat immediately with a regimen that includes INH and Rifampin because these two drugs have good CSF penetration (see part III);
2. TB contract, home visits, family interview, patient education, and follow-up examinations same as for all cases of TB
3. Look for signs of dehydration;
4. Look for signs of secondary bacterial infection;
5. Teach family about responsibilities and discuss the prognosis, which may be poor.

For unconscious patients:

1. Nasogastric tube placement;
2. Urine catheter placement;
3. Good skin care to prevent skin breakdown and pressure ulcers (bed sores) by changing the patient's position frequently, patients may be mobilized as tolerated.

4. If the patient is unable to swallow or is unconscious, drugs must be given intravenously, intramuscularly, or grountl, mixed with water and given through the NG tube.

TUBERCULOSIS OF THE EAR (TB OTITIS MEDIA)

Transmission

TB otitis alone is not infectious to others unless it occurs with open pulmonary TB.

Pathogenesis

Otitis media caused by TB is usually secondary to open pulmonary TB. When a patient coughs, some bacilli may hnd their way into the eustachian tube, where they multiply. Bacilli then spread from eustachian tube to the middle ear.

Signs and symptoms

1. Ear pain;
2. Chronic purulent discharge from the ear, usually unilateral;
3. Impaired hearing;
4. Perforation of ear drum;
5. Constitutional symptoms similar to those found in pulmonary TB.

Diagnosis

1. Check discharge from ear for gram stain and AFB;
2. Check sputum for acid fast bacilli;
3. PPD test;

Tuberculosis of the middle ear with chronic drainage is usually associated with enlarged regional lymph nodes.

4. If a sputum sample is not available, a chest x-ray may be helpful to support the diagnosis of pulmonary TB.

Treatment and patient care

1. Pre-treatment and treatment procedures same as for all cases of TB.
2. Control fever.
3. Usually discharge will clear after two months of treatment.

Complications

1. Mastoiditis;
2. Meningitis;
3. Hearing loss or deafness.

TB SINUSITIS

Transmission

This form of TB is not infectious to others.

Pathogenesis

Sinusitis due to TB is the result of blood borne or lymphatic spread of TB, which lodge in the sinuses.

Signs and symptoms

1. Headache;
2. Chronic sinusitis unresponsive to antibiotics;
3. Nasal discharge that may be green in color or malodorous.

4. Sinus tenderness to percussion;
5. Signs of meningitis may be present if the organism has invaded the meninges;
6. Constitutional symptoms similar to those found in pulmonary TB.

Diagnosis

1. PPD test;
2. Check sputum for AFB;
3. Check other organs for evidence of TB;
4. Skull x-ray, which may reveal:
   a. Air fluid levels in sinus space, usually unilateral;
   b. Destruction of sinus bone with possible calcification;
5. Chest x-ray to look for pulmonary TB;
6. Lumbar puncture is indicated if signs of meningitis are present.

Treatment and patient care

1. TB contract, home visits, family interview, patient education, and follow-up examinations same as for all cases of TB.
2. Begin drug therapy with appropriate regimen (see part III).

TUBERCULOSIS OF THE LARYNX AND ORAL CAVITY

Epidemiology

Laryngeal TB is rare in advanced countries but is still common in developing countries, especially in Cambodia.

Transmission

TB of the larynx is a serious source of the infection to others. When it is associated with open pulmonary TB, the danger of disease transmission is even greater.

Pathogenesis

Laryngeal TB is usually associated with open pulmonary TB. Direct bronchogenic spread to the larynx and oral cavity can occur as well as hematogenous or lymphatic spread.

Signs and symptoms

1. Hoarseness:
2. Coughing;
3. Painless lesions on the voice box with typical caseating necrosis may be seen;
4. Gums may become red and swollen with non-painful ulcer with caseating necrosis;
5. Constitutional symptoms similar to those found in pulmonary TB.

Treatment and patient care

1. TB contract, home visits, family interview, patient education and follow-up examinations same as for all cases of TB;
2. Begin drug therapy with appropriate regimen (see part III);
3. Check airway for any signs of obstruction.

Complications and management

1. Hoarseness may slowly lessen but may never disappear even with successful TB therapy.

2. Airway obstruction is a serious concern. The airway should be checked regularly. In serious cases, surgery may be necessary.
3. The patient may experience difficulty swallowing certain hard foods and should avoid them to prevent choking.

TB LYMPHADENITIS (SCROFULA)

Introduction

Tuberculosis lymphadenitis is a form of TB known in different parts of the world by different names. In Cambodia for example, this form of TB is called "maring." It also commonly known as "scrofula."

Epidemiology

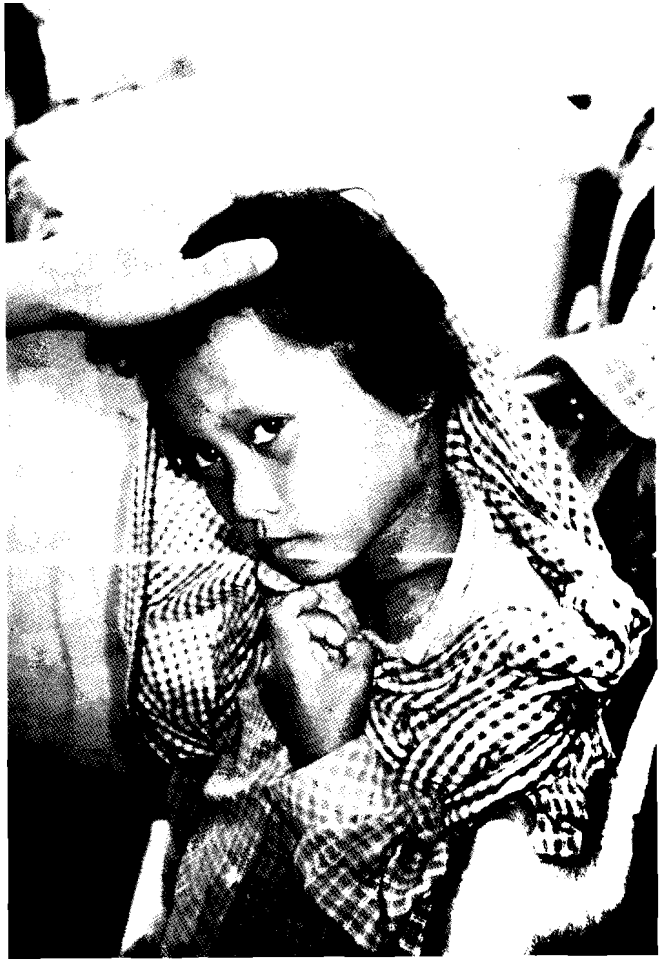
TB lymphadenitis is the most common form of extra pulmonary TB in our clinical experience in Cambodia. The most common site of TB lymphadenitis is in the cervical chain of lymph nodes in the neck, although it may occur in any lymph node.

Transmission

TB lymphadenitis alone is not infectious to others.

Pathogenesis

After primary infection, TB bacilli spread via the blood or lymphatic system. TB lymphadenitis results from proliferation of the bacilli within the lymph nodes.



TR of the lymph nodes, or scrofula, is one of the most common forms of pediatric TB. This eleven year-old girl presented to the clinic with painless swelling in her neck for several months and was found to have matted cervical lymph nodes with drainage which was AFB positive. The lymphadenopathy disappeared completely and she had no further symptoms of TB after completing a successful course of therapy.

Signs and symptoms

1. Slowly enlarging movable lymph nodes that are painless or only mildly tender to palpation, and not associated with skin warmth or erythema;
2. In advanced disease, there is typically a caseous-like discharge;
3. Usually presents unilaterally, but can present bilaterally. (Lymph node enlargement at multiple sites generally indicates another diagnosis);
4. If multiple adjacent nodes are affected, these are sometimes palpated as a matted, fixed mass.

Diagnosis

1. A complete medical history and physical examination;
2. A PPD test;
3. If the diagnosis of TB lymphadenitis is in doubt, a biopsy is required;
4. Take sample of drainage for AFB, gram-stain and culture;
5. Check the sputum for AFB;
6. Check elsewhere in the body for supporting evidence of TB.

Treatment and patient care

1. TB contract, home visits, family interview, patient education, and follow-up examinations same as for all cases of TB.
2. Begin drug therapy with appropriate regimen (see part III) only when the diagnosis of TB is clear. If there is any doubt, delay the treatment and repeat the biopsy.
3. Measure lymph node size precisely in centimeters at every examination to determine response to treatment.

Note: Patients with TB lymphadenitis usually do not experience it as serious, may live with it for many years without concern, and may not seek treatment. Patients on treatment often default, so education and understanding are particularly important.

PERICARDITIS OR PERICARDIAL EFFUSION DUE TO TB

Introduction

Tuberculosis of the pericardium is an uncommon but ominous disease and must be recognized early in order to save the patient's life.

Transmission

TB pericarditis is not infectious to others unless the patient also has open pulmonary TB.

Pathogenesis

TB pericarditis develops most often via direct spread from an infected mediastinal lymph node into the pericardial sac. The bacilli can also invade the heart muscle directly, resulting in severe heart dysfunction that can be fatal.

Signs and symptoms of TB pericarditis.

1. Cough;
2. Dyspnea;
3. Orthopnea;

4. Chest pain that may increase with rotation of the trunk and may decrease with bending forward;
5. Tachycardia;
6. Hepatomegaly;
7. Jugular vein distention;
8. Diminished heart sounds;
9. Pericardial friction rub;
10. Pleural effusion;
11. Constitutional symptoms similar to those found in pulmonary TB.

Diagnosis

1. A complete medical history and physical examination;
2. PPD test;
3. Chest x-ray;
4. Sputum for AFB;
5. Pericardiocentesis and pericardial biopsy may be done in severe cases to establish diagnosis and should be performed by a competent, experienced doctor. Send pericardial fluid or tissue for gram stain, AFB, and culture.

Treatment and patient care

1. Pre-treatment and treatment procedures same as for pulmonary TB. This is a life-threatening condition and thus timely diagnosis is critical;
2. Steroids are recommended to prevent scarring of the pericardial sac and right sided heart failure;

TUBERCULOSIS OF THE BREASTS

Introduction

TB of the breast is rare. We have not observed cases in males or in young children.

Pathogenesis

TB of the breast is secondary to lymphatic or hematogenous spread after primary infection.

Transmission

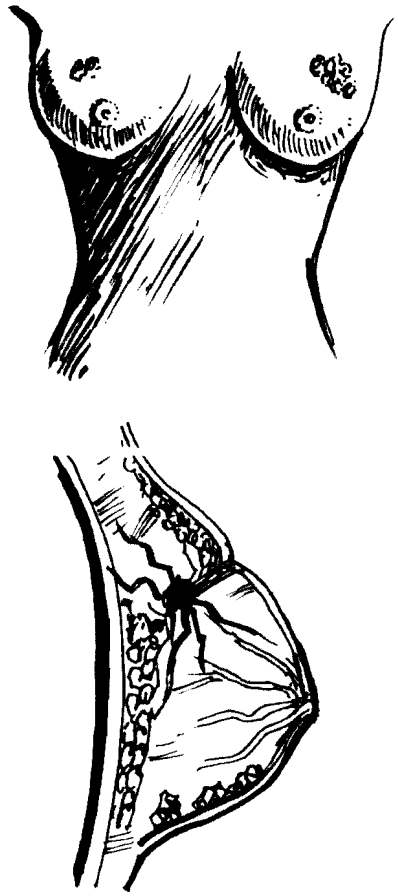
TB of the breast alone is not infectious to others.

Signs and symptoms

1. A breast lump, usually unilateral, which slowly increases in size;
2. The breast is usually tender and may have associated redness;
3. Nearby lymph nodes may show swelling/tenderness;
4. Breast abscess;
5. Constitutional symptoms similar to those found in pulmonary TB.

Diagnosis

1. A complete medical history and physical examination;
2. PPD test;
3. Fine needle aspiration (FNA) of breast lump. Send the aspirate for gram stain, AFB, and culture;



TB can cause a painless breast abcess which can destroy the mammary glands and ducts.

4. If FNA is non-diagnostic, then breast lump may be biopsied. Histology reveals granulomas with caseating necrosis.

Treatment and patient care

NOTE: In some cultures, women are embarrassed to report symptoms involving the breasts. Reassure the patient that she need not be ashamed and can confide in you. The presence of a spouse or relative may be helpful.

1. TB contract, home visits, family interview, patient education, and follow-up examinations, as for all cases of TB;
2. Begin drug therapy with appropriate regimen (see part 111);
3. Monthly follow-up exam should include measurement of size of breast lump tn document any improvement;
4. If patient is a lactating mother, see that the baby is examined and fed properly. Encourage the mother to continue breastfeeding from the unaffected breast but not from the affected breast. Instruct patient to report any difficulty in breastfeeding;
5. If mother also has pulmonary TB, evaluate her baby for active TB.

Complications and management

1. If the lump does not decrease in size, the lesion may have become calcified. Surgery may be effective in removing the mass.
2. Chronic sinus tract drainage may occur, even after full term TB therapy. Surgery may be helpful.
3. Problem with breastfeeding: encourage mother to continue feeding from the unaffected breast

TUBERCULOSIS OF THE PERITONEUM/TB ASCITES

Introduction

Although peritonitis and ascites due to TB are common, they are often difficult to diagnose. Liver cirrhosis and secondary ascites is a risk factor for TB peritonitis and ascites, particularly in patients with a history of alcoholism.

Epidemiology

TB peritonitis is an uncommon form of TB disease occurring with approximately the same frequency as TB of the intestine.

Transmission

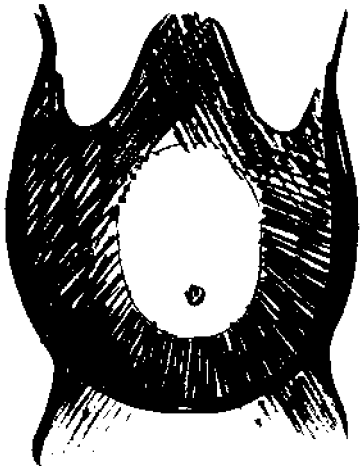
TH peritonitis is not infectious to others unless the patient also has open pulmonary TB.

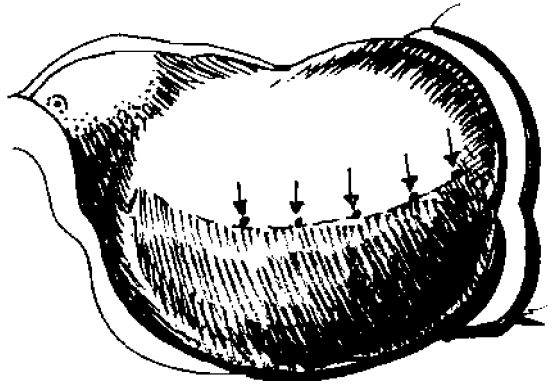
Pathogenesis

TB peritonitis and/or TB ascites generally develops via hematogenous spread from a primary source of infection. However, there are several other ways peritonitis and ascites can occur. In women with TB salpingitis, intratubal spread can occur to the peritoneal cavity. Bacilli in the GI tract lymph nodes or in the liver can directly spread to the peritoneal cavity. Urinary tract TB can, rarely, spread to the peritoneal cavity.

Signs and symptoms

1. Abdominal pain, discomfort, and abdominal distension;





Ascites is usually associated with TB peritonitis, TB of the GI tract, or pelvic TB. On physical examination, ascites can be detected by a shifting dullness to percussion or a positive fluid wave.

2. Difficulty breathing when lying down flat if ascites is substantial;
3. Positive fluid wave/shifting dullness to percussion of abdomen;
4. Bulging flank;
5. Bowel mass may be palpable;
6. Pleural effusion;
7. Pericarditis (very rare);
8. Vaginal discharge in females with TB salpingitis;
9. Constitutional symptoms similar to those found in pulmonary TB.

Diagnosis

1. A complete medical history and physical examination;
2. PPD test;
3. Sputum for AFB;
4. Paracentesis for gram-stain, AFB, and culture (one liter of fluid is recommended); characteristics of the ascitic fluid include:
    a. Straw colored
    b. WBC ranges from 150–4000 cell/mm3 with lymphocytic predominance
    c. Exudative levels of protein
5. A pelvic exam in a female patient is often helpful;
6. Peritoneoscopy (if facilities and trained personnel are available);
7. Peritoneal biopsy for AFB stain and culture (if facilities and trained personnel are available).

Remarks

In patients who also have cirrhosis, fluid may be dilute and appear to be a transudate due to ascites secondary to portal vein hypertension. The characteristics of peritoneal fluid in patients with both TB and cirrhosis include a low protein and a low number of white blood cells. This can obscure the inflammatory process and confuse the diagnosis.

Treatment and patient care

1. TB contract, home visits, family interview, patient education, and follow-up examinations same as for all cases of TB;
2. Begin drug therapy with appropriate regimen (see part III);
3. Monthly follow-up exam should include patient weight and measurement of abdominal girth;
4. If respiratory symptoms or distress persist, consider performing a therapeutic paracentesis. However, do not remove all of the ascitic fluid at one time.

TB OF THE GASTRO-INTESTINAL TRACT

Epidemiology

TB of the GI tract is rare. In our patient series of 1,298, we saw 26 cases of abdominal and intestinal TB in individuals between 15–70 years of age, and more frequently among males.

Transmission

TB of the GI tract alone is not infectious to other

Pathogenesis

TB of the GI tract commonly occurs through blood or lymphatic spread from the primary source of infection, usually from pulmonary TB.

Signs and symptoms

1. Chronic diarrhea (months to years);
2. Change in bowel habits, e.g. constipation or diarrhea;
3. Abdominal pain;
4. Abdominal mass;
5. Bleeding from anus or blood in stool;
6. Anemia;
7. Thickening of the mesenteric omentum, which has a sand [illegible] on abdominal exam;
8. Peritoneal signs;
9. Ascites;
10. Constitutional symptoms similar to those found in pulmonary TB

Diagnosis

1. A complete medical history and physical examination;
2. PPD test;
3. Stool exam for parasites and stool culture to rule out other causes of GI complaint;
4. Laparotomy done in the setting of an acute abdomen usually shows
   a. Lesion in the ileum, with thickening,
   b. Regional mesenteric lymph node enlargement,
   c. Acid fast bacilli on histologic exam of biopsy specimen or ascitic fluid

Treatment and patient care

1. TB contract, home visits, family interview, patient education, and follow-up examinations same as for all cases of TB;
2. Begin drug therapy with appropriate regimen (see part III);
3. Monitor for malnutrition or dehydration:
   a. Evaluate appetite and food intake daily;
   b. Evaluate fluid intake, output, and weight daily.

TUBERCULOSIS OF THE LIVER

Introduction

TB of the liver is rare and is difficult to document, particularly where facilities and expertise are limited.

Transmission

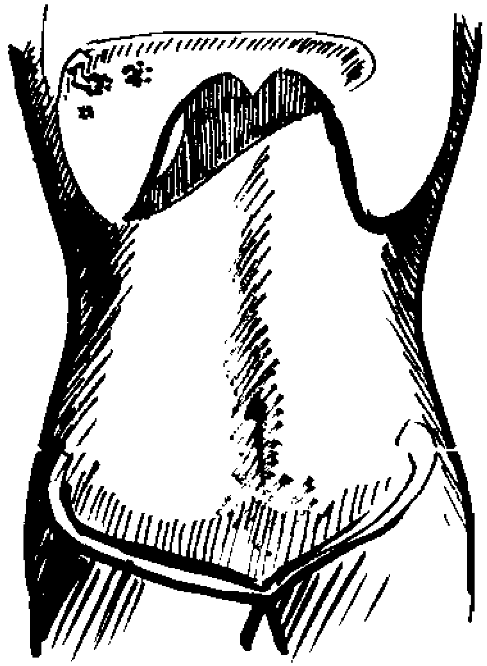
TB of the liver is not infectious.

Pathogenesis

TB of the liver develops via hematogenous or lymphatic spread

Signs and symptoms

1. Hepatomegaly;
2. Jaundice;
3. Right upper quadrant pain and tenderness;
4. Fever with other constitutional symptoms.



TB of the liver presents as hepatosplenomegaly. Granuloma formation with AFB positive organisms are found on biopsy.

Diagnosis

1. PPD test;
2. Liver biopsy if facilities and expertise are available. Caution must be exercised as procedure can cause severe bleeding;
3. Rule out other causes of liver infection such as amoeba, liver fluke or malaria if in endemic areas;
4. Abdominal x-ray to look for masses or calcification of the liver;
5. Check sputum for AFB if pulmonary symptoms are associated.

Patient care and treatment

1. TB contract, home visits, family interview, patient education, and follow-up examinations same as for all cases of TB;
2. Begin drug therapy with appropriate regimen (see part III);
3. Monitor for drug side effects;
4. Consider hospital admittance for optimal treatment and patient care;
5. High protein diet.

Complications and management

1. Pleural effusion and ascites:
   a. Should disappear within 2-3 months of starting TB chemotherapy;
   b. Thoracentesis or paracentesis to relieve respiratory symptoms;
2. Check liver function tests often, if possible. If not, follow patient closely for risk of drug toxicity. If toxicity occurs:
   a. Reduce or stop drugs which are the likely cause;

   b. NEVER use maximum dose of drugs for TB of the liver as complications are common.

TUBERCULOSIS OF THE URINARY TRACT

Introduction

TB of the urinary tract was rare in our experience in the Thai-Cambodian border camps. The true incidence and prevalence of TB in the urinary tract is difficult to estimate because the majority of patients remain asymptomatic.

Transmission

TB of the urinary tract is not infectious.

Pathogenesis

Urinary tract TB develops via hematogenous spread to the kidneys. Kidneys are a preferred site for TB because of the high oxygen content in the nephrons. Bacilli in the kidneys may remain dormant; however, granulomas may rupture, allowing spread of TB to the lower urinary tract. The most common affected sites are the kidney, ureter, or the bladder.

Signs and symptoms

1. Pain in the back, flank, groin, or abdomen;
2. Changes in urination, i.e., nocturia, dysuria, urgency or increased frequency;

3. Hematuria;
4. Epididymitis that does not improve with antibiotics;
5. Cystitis that does not improve with antibiotics;
6. Recurrent urinary tract infection (UTI);
7. Sterile pyuria (WBC's detected in the urine, but no bacteria seen on gram stain or in culture);
8. Constitutional symptoms similar to those in pulmonary TB.

Diagnosis

1. A complete medical history and physical examination;
2. PPD test;
3. Take urine spun sediment for gram-stain, AFB, and culture (take first voided urine specimen in the early morning);
4. Kidney, ureter, and bladder (KUB) x-ray may show calcifications in the renal cortex;
5. Intravenous pyelogram (IVP) x-ray (if facilities available) is abnormal with erosions of nephron or necrotic areas of the kidney cortex;
6. Biopsy and cystogram if technology and expertise is available.

Treatment and patient care

1. TB contract, home visits, family interview, patient education, and follow-up examinations same as for all cases of TB;
2. Begin drug therapy with appropriate regimen (see part III);
3. Look for signs of kidney failure and drug toxicity. Since kidney function may be impaired and excretion of TB medicine therefore compromised, the amount of drug in the serum may be toxic;
4. Look for signs of TB of the male reproductive organs (see below).

TB OF THE FEMALE REPRODUCTIVE ORGANS

Introduction

We treated 52 cases of pelvic TB in our patient series from the Thai-Cambodian border refugee camps. TB of the female reproductive organs is one of the important causes of infertility in countries of the developing world like Cambodia.

Epidemiology

Pelvic TB is most commonly diagnosed in women of child bearing age who have never been pregnant. It is also diagnosed among older women.

Transmission

Pelvic TB is not likely transmitted via sexual contact; however, this mode of transmission cannot be completely ruled out. At the Thai-Cambodian border, we had one case of a female partner of a male with TB epididymitis who had pelvic TB, suggesting the possibility of transmission via sexual contact. It is unknown whether a female with TB of their cervix can transmit TB to her male partner through sexual contact. Of the **30** cases we studied, none of the male partners of the affected patients had TB of the testes or epidydimis.

Pathogenesis

TB of the female reproductive organs usually develops via hematogenous spread from primary infection. Pelvic TB can spread endogenously from the fallopian tubes to the peritoneum, causing inflammation and ascites. The sites of infection in our 52 cases (20 cases

proven by biopsy and 32 cases diagnosed based upon clinical signs and symptoms) of female genital TB were: the fallopian tubes (21). uterus (20), ovaries (6), cervix (3), and vagina (2).

Diagnosis

1. A complete medical history and physical examination including a pelvic exam; send vaginal smear for AFB and gram stain;
2. PPD test;
3. Check sputum for AFB;
4. Chest x-ray to look for evidence of primary TB infection;
5. Biopsy of the infected organs. Histology would reveal caseous necrosis or granulomas;
6. If ascites is involved, check the fluid for AFB, gram stain, routine culture, protein and WBC.

Treatment and patient care

1. TB contract, home visits, family interview, patient education, and follow-up examinations same as for all cases of TB;
2. Begin drug therapy with appropriate regimen (see part III);
3. Monthly pelvic exam, checking patient response to medication;
4. Check husband or partner for TB Epididymitis.

Tuberculosis of the Fallopian Tubes

Fallopian tubes are the preferred site of TB in the female reproductive organs because of the high concentration of oxygen located there.

Signs and symptoms

a. Tubo ovarian (adnexal) mass;

b. Unexplained vaginal discharge;
c. Mild to moderate abdominal pain;
d. Abdominal distention;
e. Abdominal mass;
f. Infertility.

TB of the fallopian tubes should be considered in:

a. Women who are not yet sexually active who have salpingitis;
b. Post-menopausal females with salpingitis;
c. Women with infertility problems or an ectopic pregnancy;
d. Women who have salpingitis that is not responsive to antibiotics;
[illegible]

Complications

a. Tubal scarring leading to infertility;
b. Peritonitis;
c. Sterility.

TB of the Endometrium

Usually develops secondary to TB of the fallopian tubes.

Signs and symptoms

a. Amenorrhea;
b. Infertility;
c. Rigid and fixed uterus;
d. Vaginal discharge;
e. Mild abdominal pain

Endometrial TB should be suspected in women of childbearing age with:

a. Menstrual irregularity;
b. Prolonged amenorrhea;
c. Endometritis unresponsive to antibiotics;
e. Post-menopausal women with vaginal bleeding.

TB of the Ovaries

Ovarian TB is almost always secondary to fallopian tube TB.

Signs and symptoms

a. Abdominal pain;
b. Premature menopause;
c. Prolonged amenorrhea;
d. Unilateral palpable mass;
e. Ovarian tenderness.

TB of the Cervix

Tuberculosis of the cervix is usually secondary to uterine TB.

Signs and symptoms

a. Dyspareunia (pain during sexual intercourse);
b. Vaginal discharge;
c. Ulcerating lesion on cervix that may resemble carcinoma;
d. Cauliflower-tike growth on the cervix;
e. Cervical mucosa may bleed easily when probed during examination.

Differential diagnosis

a. Cervical carcinoma (check Pap smear if possible);
b. Bacterial endocervicitis;
c. Bacterial endometritis;
d. Cervical ulcer;
e. Chancroid;
f. Syphilis;
g. Herpes;
h. Papillomavirus.

TB of the Vagina

Vaginal TB is usually secondary to TB of the cervix or uterus

Signs and symptoms

a. Dyspareunia;
b. Vaginal discharge;
c. On examination, the vagina is rigid and narrowed;
tl. Painless ulcerative lesion and/or hypertrophic lesions may be seen on the vaginal wall mucosa.

CONGENITAL TUBERCULOSIS/ PERINATAL TUBERCULOSIS

Congenital tuberculosis occurs very rarely. TB in newborn infants can be due to congenital TB infection or secondary to pulmonary infection after birth, most often from a mother with open pulmonary TB. This second route of infection results in perinatal TB. Perinatal TB is more common than congenital TB and has a lower mortality rate.

Perinatal TB is particularly dangerous if newborns subsequently develop meningitis or miliary TB.

Pathogenesis

Infection of the fetus can occur by spread of TB bacteria from the mother to the baby via the placenta; via maternal endometritis. placentitis or both; or via fetal ingestion of infected amniotic fluid at the time of delivery.

Signs and symptoms (usually begin in second to third week of life)

1. Poor feeding;
2. Poor weight gain;
3. Jaundice;
4. Hepatosplenomagaly;
5. Abdominal distention;
6. Coughing;
7. Tachypnea.

Diagnosis

1. PPD test (usually negative within first 6–8 weeks of life);
2. Gastric aspirate to check for AFB and culture;
3. Chest x-ray with miliary pattern;
4. Lumbar puncture: send CSF for AFB, gram stain, and culture.

Treatment and patient care

1. Pre-treatment and treatment procedures same as for pulmonary TB, with doses adjusted according to child's weight,

2. Encourage mother to breast feed as often as possible to improve nutritional status of the baby;
3. The mother should be checked for pulmonary TB and, if negative, then checked for pelvic TB.

TUBERCULOSIS OF THE TESTES

Introduction

This is an unusual form of TB. In our patient series at the Thai-Cambodian border, this occurred most frequently in men between the ages of 20–30 but was also reported in men age 33–60 years. It was rarely seen among prepubescent boys.

Transmission

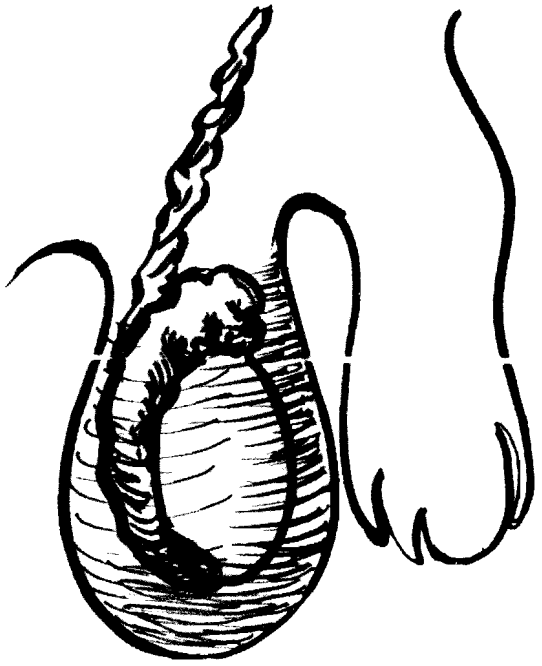
Testicular TB is generally not infectious. However, there is the possibility of spread to the female partner through sexual activity.

Pathogenesis

Testicular TB develops via henlatogenous or lymphatic spread from primary TB or is secondary to miliary spread. Testicular TB can spread directly from the infected testes to nearby organs, such as the prostate gland, the urinary tract, seminal vesicles, and epididymis.

Signs and symptoms

1. Scrotal swelling;
2. Epididymal pain that may radiate to spermatic cord, thigh, testes, and groin,



TB of the testicle results in painless swelling and involves the epididymis and vas deferens. This is usually secondary to TB of the urinary tract. Sexual partners of these patients should also be checked for TB of the cervix.

3. Dysuria;
4. Hematuria;
5. Urinary frequency;
6. Hematospermia;
7. Back, flank, or abdominal pain if the urinary tract is involved;
8. Palpable nodules on testes;
9. lrregular nodularity of epididymis;
10. Enlarged epididymis in later stages;
11. Epididymal abscess with purulent drainage;
12. Palpable nodules on vas deferens;
13. Enlarged prostate in advanced stages of disease (on examination, prostate is irregular, firm, nodular).

Examination of urine

1. Sterile pyuria;
2. Proteinuria;
3. AFB may be seen on direct smear of spun urine sediment;
4. Culture of urine is usually positive for AFR.

Diagnosis

1. PPD test;
2. Urine sample for AFB, gram-stain, and bacterial plus mycobacterial culture;
3. Sputum lor AFB if the patient has associated symptoms;
1. Test discharge lor gram-stain and AFB.

Treatment and patient care

1. TB contract, home visits, family interview, patient education, and follow up examinations same as lor all cases of TB;

2. Begin drug therapy with appropriate regimen (see part 111);
3. Follow up measurement of testes size monthly to document improvement with treatment;
4. Check sexual partner for TB of the cervix;
5. Instruct patient to wear loose underwear to avoid irritation to the infected testes.

Complications and management

1. The patient may become infertile if both testes are affected and vas deferens are obstructed. However, sexual function should not be affected;
2. Educate the patient and wife to understand that TB of the testicle is not a venereal disease. The wife should participate in the care of the patient;
3. Monitor for direct extension of infection to the urethra, prostate, rectum and peritoneum

TUBERCULOSIS OF THE SPINE (POTT'S DISEASE)

Introduction

Pott's disease, which is named after a British surgeon who lived between 1713–1788, is a tuberculous abscess of the vertebral bodies.

Pathogenesis

TB of the spine is caused by hematogenous or lymphatic spread from primary infection. It may be spread from an infected lymph node which has eroded into the vertebra. The destruction and compression of the affected vertebrae often result in a "gibbus formation," a kyphotic or scoliotic deformity of the spine. Infection often spreads to paravertebral tissues, giving rise to paravertebral abscesses

Spinal TB usually presents as a combination of arthritis and osteomyelitis, typically involving an intervertebral disc and vertebral body. In adults, spinal TB most commonly affects the lumbar vertebrae. In children, spinal TB most commonly affects the upper spine (the thoracic and cervical vertebrae).

Transmission

Pott's disease alone is not infectious.

Signs and symptoms

1. Limited range of motion of spine;
2. Local pain over infected vertebrae with radicular distribution of pain or sensory changes from the nerve roots originating at the affected spinal levels;
3. An abscess may form around the infected vertebrae and may drain into adjacent structures such as the pleural space, the inguinal area and psoas muscles, or the cervical area and supporting ligaments of the spine;
4. Meningitis;
5. Neurological impairment leading to paraplegia;
6. Curved or kyphotic spine (gibbus formation);
8. Abnormal gait;
9. Incontinence of urine and stool;

Diagnosis

1. Spine x-ray, which may show:
   a. Evidence of abscess;
   b. Calcification in the surrounding muscle due to abscesses

c. Complete bony fusion of affected vertebral bodies;
d. Anterior wedging or triangular shadow because of vertebral collapse and deformity.

2. PPD test;
3. If there is a draining abscess, examine drainage for AFB and gram-stain;
4. If meningitis occurs, perform lumbar puncture and send CSF for AFB, gram-stain, WBC, protein, and glucose. Usually the spinal fluid will show elevated protein, low glucose (but never as low as in bacterial meningitis) and the presence of lymphocytes.

Treatment and patient care

1. TB contract, home visits, family interview, patient education, and follow-up examinations same as for all cases of TB;
2. Begin drug therapy with appropriate regimen (see part III);
3. If the patient can still walk, advise against lifting heavy objects or other activities that can compromise a weakened spine;
4. If the patient cannot walk, admit to a hospital or TB clinic:
   a. If the patient has urinary incontinence, insert a bladder catheter and change often using sterile technique to prevent infection;
   b. Physical therapy such as range of motion exercises should be performed to maintain flexibility and function;
   c. In an immobile patient, his or her position should be changed often to prevent development of pressure ulcers (patient's family can be taught to do this). If ulcers are present, clean regularly and monitor for signs of infection.

TUBERCULOSIS OF BONES AND JOINTS (other than the spine)

Introduction

TB of the joints was commonly seen in our patient series from the Thai-Cambodian border. Joints commonly affected were hip, knee, ankle, followed by shoulder, elbow, wrist, and hand.

Epidemiology

TB of the bones and joints occurs in all age groups. There is increased incidence among the elderly.

Transmission

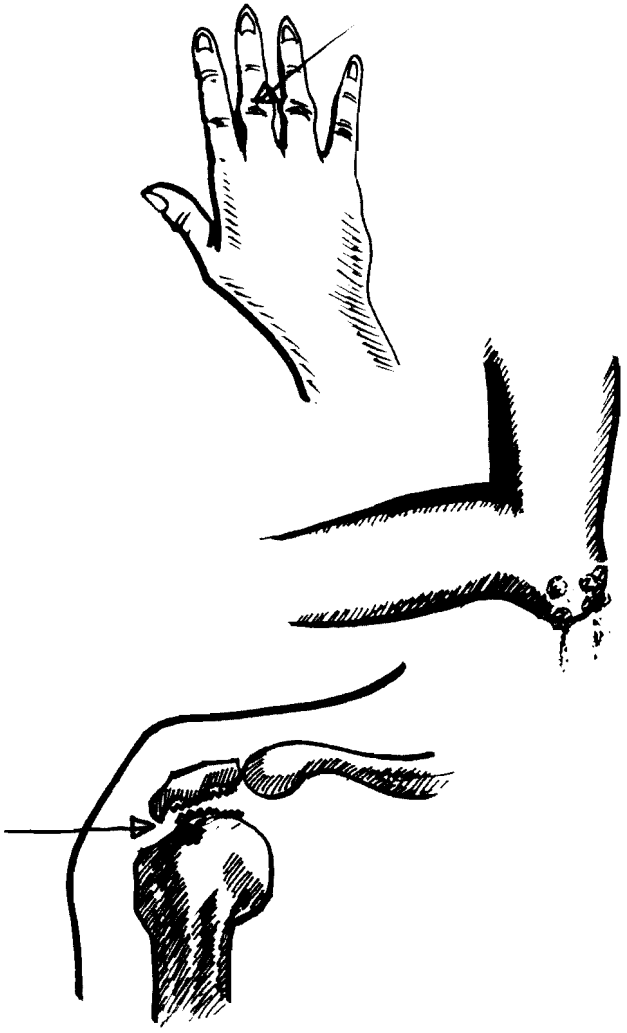
TB of the bones and joints is not infectious.

Pathogenesis

The disease can be spread through the bloodstream or through the lymphatic system during primary infection or occur in association with joint trauma or the intra-articular administration of steroids and secondary reactivation of dormant TB in the joint capsule.

Signs and symptoms

1. Monoarticular arthritis;
2. Painless swelling of joints;
3. Purulent drainage from joint (there is often no redness or warmth over the affected joint, except when secondary bacterial infection occurs);



TB of the joints is usually unilateral and can involve any joint of the body.

I. Joint stiffening.

Diagnosis

1. Complete medical history and physical examination;
2. PPD test;
3. X-ray of affected joint or joints;
I. If drainage is present, send for AFB, gram-stain, and culture;
5. Synovial fluid for AFB and gram-stain and culture;
6. Synovial biopsy, if available, should reveal granulomatous changes.

Treatment and patient care

1. TB contract, home visits, family interview, patient education, and follow up examinations same as for all cases of TB;
2. Begin drug therapy with appropriate regimen (see part 111);
3. Physical therapy and exercises to maintain range of motion and flexibility, as needed;
4. Encourage exercise after condition of joint has improved;
5. Avoid activities that may result in trauma or injury to the diseased bone and joints.

CUTANEOUS TUBERCULOSIS

Introduction

TB of the skin is very rare.

Pathogenesis

TB of the skin occurs via skin inoculations or viii hematogenous or lymphatic spread from primary infection.

Transmission

TB of the skin is not infectious.

Signs and symptoms

Painless, wartlike lesion of the skin that may be small or large, may grow very slowly, and may be covered with silver scales. Often there is no evidence of inflammatory changes.

Diagnosis

1. PPD test;
2. Smear of skin lesion for AFB;
3. Biopsy is very helpful. Histology reveals caseating or granulomatous tissue compatible with TB.

Treatment and patient care

1. TB contract, home visits, family interview, patient education, and follow-up examinations same as for all cases of TB;
2. Begin drug therapy with appropriate regimen (see part 111).

ERYTHEMA NODOSUM

This is an inflammatory reaction to the presence of Mtb in the blood stream.

Signs and symptoms

Tender nodules (2–5 cm) on the skin which may remain for weeks or months. The most common sites are the shin, thigh, and arm. After the lesion disappears, a brownish macule may remain in its place

Diagnosis

Biopsy of the lesion reveals inflammatory cells in the blood vessels of the dermis and subcutaneous tissue. TB bacilli are not seen.

TB AND HIV/AIDS

AIDS is an incurable infectious disease caused by the virus HIV-1. AIDS usually develops on average 10 years after HIV-1 infection although it can develop rapidly (1–2 years after infection) or be very delayed (in rare cases individuals have been infected with HIV-1 for up to 20 years and have not yet developed AIDS). AIDS develops as the HIV-1 virus destroys the infected person's immune system, making him or her susceptible to many other infections that lead to death if not treated. From the moment of infection with HIV-1 a person is infectious and can pass this deadly virus to others through unprotected sexual contact and through exposure to infected blood.

Because HIV-1 impairs the immune system which is critical for containment of the primary TB infection, TB reactivation is common in HIV-1 infected and AIDS patients. In fact, worldwide, the most common infection associated with AIDS is TB. In the early days of the AIDS epidemic in the early 1980's, the first presentations of AIDS in Africa and Haiti were noticed because there was a dramatic increase in severe cases of TB in these populations.

Individuals who have AIDS and are infected with TB are more likely to progress to symptomatic TB at a rate of 10% per year as compared to a rate of 1% per year in non-HIV-1 infected individuals. TB progression commonly occurs early in AIDS and often precedes the diagnosis of AIDS. If extrapulmonary TB develops in an HIV-1 positive patient, this is a criteria for reclassifying the patient as an AIDS patient. Therefore, extrapulmonary TB is an AIDS defining illness.

In the developing world: the example of Cambodia

In Cambodia, it is estimated that by the end of 1999 there were 180,000 to 200,000 people infected with HIV out of an estimated total population of approximately 12 million. Every day there are 100 new Cambodians infected with HIV. The high risk groups in Camboclia as elsewhere are:

1. Commercial sex workers
2. Policemen and military personnel who visit commercial sex-workers
3. Migrant workers including construction workers, taxi drivers, and truck drivers who visit brothels, bars, and commercial sex workers
4. IV drug users
5. Homosexual men
6. Recipients of blood transfusions
7. Anyone who practices unsafe sex (without use of a condom)
8. Anyone who uses unsterile needles in medical or dental procedures or in traditional medicine practices
9. An infant is at risk who was delivered from an infected mother (vaginal delivery is of significantly higher risk than Caesarean delivery)
10. Sexual partners and children of HIV-1 infected indivicluals
11. Health personnel and laboratory workers through needle sticks and exposure to infected blood.

Clinical presentation of TB in HIV/AIDS patients

1. Pulmonary symptoms (see pulmonary TB), however cavities are rarer and AFB+ sputum is comparatively rarer in HIV+ patients;

2. Chest x-ray often lacks typical apical infiltrates but may reveal:
   a. focal infiltration;
   b single or multiple cavities;
   c. hilar lymphadenopathy;
   d. miliary pattern;
   e. pleural effusion.
3. Extrapulnionary TB presentations occur commonly, including brain abscess, tuberculoma, meningitis, pericarditis, gastric, peritoneal or bone, or skin abscesses;
I. PPD is not a useful diagnostic aid since it is often negative once TB develops in HIV-1 positive patients.

Treatment of TB patients with HIV/AIDS

Treatment: See sections on pulmonary and extrapulmonary TB

Special considerations

HIV-1 positive TB patients should be treated with INH, rifampin, PZA and Ethambutol for 2 months then continue with INH and rifampin for at least I atlclitional months. Although current guidelines from the Center for Disease Control (CDC) in the US is for standard short course therapy for TB in HIV-1 infected patients, therapy should be individualized based on the extent and response to disease. For patients who are not taking protease inhibitors to inhibit HIV-1, it is recommended that the initiation of protease inhibitors be delayed until TB chemotherapy with rifampin is completed since the protease inhibitors can slow the metabolism of rifampin and lead to rifampin toxicity.

Prophylactic treatment

Although PPD screening is not useful once a patient has AIDS or disseminated TB in the setting of AIDS, it is useful in HIV-1 infected

individuals before they develop TB or the immunocompromise associated with AIDS.

Note that it is critical that active TB is excluded before starting INH prophylaxis in an HIV+ patient since only one drug (INH) is given for prophylaxis and therefore the active TB would only be treated with one drug and resistance to INH will develop.

It is recommended that all patients with HIV infection and a positive PPD skin test (>5mm) in whom active TB has been excluded should receive 9 months of INH 300mg/day with vitamin B6 (25 mg/day) to prevent the development of active TB. It is also recommended that if a person who is HIV+ who has been exposed to someone with active pulmonary TB should be given INH (same doses above) for 9 months regardless of PPD status. Another recommendation from the CDC in the U.S. is that an HIV infected person who had a negative PPD test on initial screening should be retested after 3 months.

PEDIATRIC TB

TB is not always recognized as a major cause of mortality and morbidity in children because it is difficult to diagnose pediatric TB, which is often confused with or complicated by pneumonia, malnutrition or failure to thrive.

Issues related to childhood TB

1. In children, it is essential to diagnose TB as early as possible because children die from disseminated TB or meningeal TB more frequently than adults. However, because many children have disseminated TB rather than

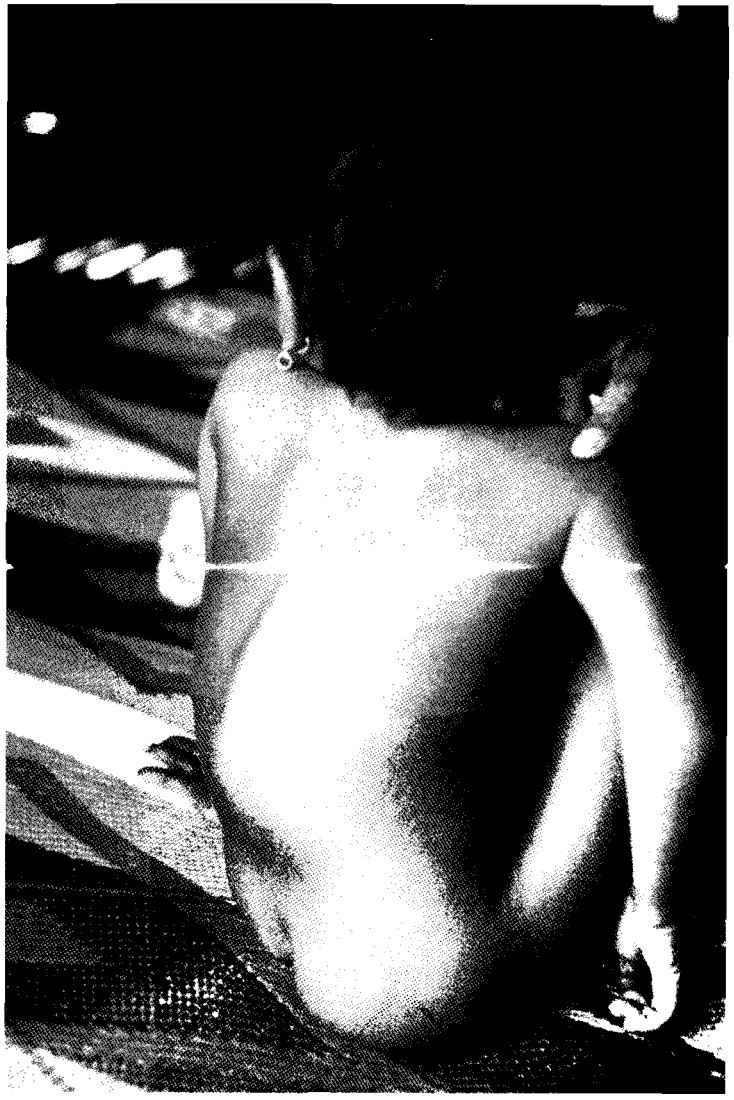
pulmonary TB, diagnosis cannot be based on sputum AFB alone; no simple test rules out the diagnosis of TB in children;
2. Children are almost always surrounded by adults with pulmonary TB who have infected them;
3. Children who are infected with TB are more likely than adults to develop active TB sometime in their lives (especially if they are under 2 when primary infection occurs) and will therefore serve as the source of infection to others.

The difficultyin diagnosing pediatric TB

1. Children have a smaller number of infectious TB organisms even when they have pulmonary TB
2. Children less than 10 years old have difficulty producing a sputum sample
3. Children frequently present with extrapulmonary TB, which is difficult to diagnose

Prevention of childhood TB

1. A very small number of adults with infectious pulmonary TB can expose a large number of children to infection. Therefore, every effort must be made to treat all cases of pulmonary TB in the community.
2. BCG vaccination has been reported to decrease spread of TB through the bloodstream or through the lymphatic system in children and therefore reduces the risk of a child developing extrapulmonary TB, including TB meningitis, and bone or joint TB. The use of BCG has not been proven to change the proportion of children in a population who are infected with TB



This five year-old girl has the typical gibbus formation of TB of the spine, or Pott's disease. Left untreated, Pott's disease can cause severe disability, including paralysis.

Common presentations of TB in children

In our patient series on the Thai-Cambodian border, we treated **136** cases of pediatric TB. Fifty three of these cases were pulmonary and 69 were extrapulmonary (see appendix) of which **14** presented with miliary TB. About half of these children presented as outpatients with a history of multiple pneumonias which had not responded to standard antibiotic treatment. The other half presented with failure to thrive or unexplained illness. Most of these children were younger than 10 years old and most had received BCG vaccination. One **3** month old child was brought to the clinic by his mother with fever and severe shortness of breath and was found to have a miliary pattern on chest x-ray. The mother reported that the child was spit on by a traditional healer soon after birth. When we went to investigate, we found that the traditional healer had symptoms of TB and had 4+ AFB in his sputum.

TB evaluation in children

1. PPD test
2. Xray:

   Chest xray findings in children commonly do not show typical cavities (except in adolescents) but may show:

   a. Hilar adenopathy
   b. Segmental atelectasis
   c. Infiltrates
   d. Calcification and scarring
   e. Miliary pattern
3. Gastric aspirate

   It is difficult for young children to produce sputum. Since they often swallow their sputum, a gastric aspirate can be a useful technique in the diagnosis of TB in children.

However, even if the gastric aspirate test is negative for acid fast bacilli, TB cannot be ruled out.

The following suggestions are useful for performing a gastric aspirate in young children:

a. The procedure is performed first thing in the morning prior to the child eating or breastfeeding. The evening before the procedure is to be done, instruct parents not to feed or breastfeed the child from midnight onwards;
b. Place NG tube into stomach, making sure that the tube is inserted carefully and properly;
c. Use a 10cc syringe to obtain gastric fluid from the stomach and examine the fluid fnr AFR (see below);
d. Perform this procedure for at least three mornings in row.

To aid in diagnosis of TB in children, assess the following characteristics:

1. Illness lasting 4 weeks or more
2. Malnourished: < 60 percentile weight for age
3. Contact with person (family or neighbors) who have active TB or who have history of TB
4. Not improved after 4 weeks of adequate feeding
5. History of recurrent pneumonia not responsive to antibiotics
6. Clinical findings suggestive of TB, e.g., chest x-ray with primary Ghon complex, enlarged lymph nodes, pleural effusion, bone lesion with cold abscess, meningitis, etc

The source of primary infection to children is usually a parent or other close adult with open pulmonary TB. It is important to examine all children of TB patients to look for signs and symptoms of pediatric TB.

7. PPD > 5mm

8. AFB +

Characteristics	*Diagnosis*
• If 1–4 of the above are positive: Additional close follow-up is needed.	TB less likely
• 5–6 positive:	TB likely
• 7–8 positive:	TB definite
• If AFB + with or without other characteristics: *The child requires TB treatment.*	TB definite

PART III

Practical guidelines

The diagnosis of TB is based on the microscopic detection of AFB positive organisms in sputum or other bodily fluids by experienced staff.

PREPARATION OF A SPUTUM SMEAR (ZIEHL NIELSEN TECHNIQUE)

Process for sputum collection

Three sputum specimens should be collected over the course of three days. Give the patient small, sealable containers for collection of the samples. Collection should be done first thing in the morning on three consecutive mornings. Instruct the patient to cough vigorously to produce a sputum sample (not a saliva sample) and deposit the sputum into a clean container each morning.

Basic lab supplies needed:

1. Sputum containers;
2. Wooden or bamboo sticks;
3. Sputum referral slips and record books;
4. Respiratory mask for the laboratory technician processing samples;
5. Indelible markers/pens;
6. Lamp;
7. Microscope;
8. Slides and basin with good drainage system to wash the stained slides;
9. Laboratory chemicals:
    a. fuchsin solution;
    b. 3% acid alcohol;
    c. Methylene blue;
    d. Methanol;

10. A trash container to put waste products and contaminated glass slides;
11. Face mask and latex laboratory gloves.

Making the sputum smear

Gloves and face mask should be worn to protect the laboratory technician from TB infection.

1. Use a clean glass slide. With an indelible pen, record the number or name of the patient on the slide and on the container;
2. Use stick to mix sputum sample and place a small amount of the sample on the central area of a clean slide;
3. Spread the sputum gently around the slide to make a thin and even layer;
5. Let the slide dry (about 15 minutes). Do not put it in sunlight or over flame;
6. Dispose of the stick and sputum container in the trash bin and burn or dispose of it as infectious medical waste as soon as possible. Use the stick and container oniy once.

Fixing the slide

Using forceps, pass the slide slowly (3 to 5 seconds) through the flame. Or. immerse in absolute methanol for one minute.

Staining and decolorization

1. Place the slide with the fixed sputum on top of the sink;
2. Cover the whole surface of slide with carbol fuchsin solution:

3. Heat the slide over a flame until sample begins steaming;
4. Let the slide cool for 5 minutes;
5. Kinse slide in a gentle stream of running water then drain excess from slide;
6. Cover each slide with 3% acid-alcohol until color no longer runs from slide;
7. Rinse gently with water and drain excess from slide;
8. Counter-stain with methylene blue: cover each slide with methylene blue for 30–60 seconds;
9. Rinse slide gently with water and allow slide to air dry. Do not blot slide.

Examination by microscopy

The slide should be read by trained personnel. Examine the stained slide under an oil immersion lens at 100X magnification. Look for the presence of mycobacteria, which appear as small red/pink rods.

Recording results

# of acid-fast bacilli seen	*Result*
0	negative
1–2/slide	+
3–9/slide	++
10/slide	+++
1/high power field	++++

NOTE Microscopist must keep a sputum examination notebook (sputum register) to record the date and results of smears from each patient

TUBERCULIN/PPD TEST

The PPD or Mantoux test is used for diagnostic purposes only. This test involves intradermal injection of PPD solution into the inner aspect of the forearm. The patient must be told beforehand that the test may cause redness, itching, and (rarely) blisters at the injection area. A standard antihistamine such as Benadryl (diphenhydramine) or steroid cream can be used to treat these symptoms.

The tuberculin skin test provides valuable information about whether a person has been infected with TB and also gives information about:

1. Prevalence of TB in the community;
2. Effectiveness of control measures against the spread of TB;
3. Those who may require chemoprophylaxis, for example:
   a. HIV+ patients who are PPD +;
   b. In the developed world, patients under the age of 35 who have been newly infected with TB;
   c. Children exposed to open pulmonary TB patients.

Remember: Always keep PPD refrigerated at 4 degrees centigrade, not frozen. It should not be exposed to direct sunlight.

Applying the PPD test

1. Use a tuberculin (1cc) syringe and a small bore needle (27 gauge);
2. Draw 0.1cc (5TU dose) of PPD solution into syringe;
3. Have patient extend his or her right forearm. The injection site should be in the upper 1/3 of the forearm. Clean the skin with alcohol in an area where there is no scarring or wound and allow alcohol to dry before proceeding with injection;

4. Orient syringe so that the bevel of the needle points upward. Stretch the skin of the forearm, enter the skin at a very shallow angle with the needle (needle should be almost horizontal and parallel to skin), and inject the full 0.1cc into the intradermal area. This should produce a wheal of about 5–8 mm in diameter. If a wheal of this size is not produced, the injection was probably too deep and the test may need to be repeated;
5. Do not put alcohol or a bandage over the injection site;
6. Instruct the patients that it is normal for the site of injection to become red, itchy, or indurated. Advise the patient not to scratch or put soap on the injection site. Instruct the patient to return to the clinic in approximately 48 hours (two days) for measurement of the PPD reaction.

Measuring the induration

1. Intluration should be located under good lighting;
2. Use a small ruler to measure the first diameter of the induration and record this in millimeters (mm). Measure the second diameter in a line perpendicular to the first recording and record this in mm;
3. Another option is to use a ball point pen to mark the borders of induration. Place the pen lightly on the patient's skin at a point 1–2 cm away from induration then drag the pen centrally toward the induration until it meets resistance (this should be the edge of the induration). Make another mark on the side directly opposite the first mark. The space between these two marks is measured as one diameter of the induration. Repeat this procedure on a line approximately 90 degrees to the first set of marks and measure this as the second diameter of the induration.

NOTE: Be sure to measure the induration, not the erythema.

The standard way of detecting previous exposure to TB is by the intradermal injection of PPD in the forearm of the patient. This causes an immune reaction in the skin which can be measured 48 hours later as an induration. If the reaction is greater than 10mm in diameter, the patient can be assumed to have been previously infected with TB. A negative reaction does not rule out TB

Interpretation of the induration size

0–4 mm	negative
5–10	may be positive
10 mm or greater	positive

If the PPD is positive, the possibilities are:

1. Previous infection with TB that is not active;
2. Active TB;
3. Previous TB infection that has been treated.

If the test is negative, the possibilities are:

1. Patient has not been infected with TB;
2. Patient has TB but has a negative reaction because:
   a. the test was not administered properly;
   b. the PPD is expired and no longer effective;
   c. the patient is malnourished or the patient's immunity is weakened by some other factor, such as use of steroids or other immunosuppressant drugs, cancer (particularly lymphoma), or HIV;
   d. the patient may be anergic to PPD, meaning he or she does not not have a delayed type hypersensitivity (DTH) reaction to PPD. (In our experience in Cambodia, approximately 20% of pulmonary TB patients are anergic to PPD during the initial phase of treatment. After completion of treatment, the majority of these patients become PPD+. It is unknown why some people are anergic to PPD when they are acutely ill with TB. Thus, a negative PPD never rules out active TB disease.)

3. Years after primary infection with TB, an individual's immune response to TB may weaken and although they still harbor inycobacteria they do not respond to PPD. It has been observed that reapplication of the PPD 2–4 weeks later may serve to "boost" this weakened immune response, resulting in a positive response to the second injection with PPD. Therefore, if previous TB infection is highly suspected and it is important to document that a patient has been previously infected,another PPD should be placed 2–4 weeks after the first PPD injection to look for DTH.

BCG VACCINATION

Introduction

BCC vaccination has been one of the most important components of tuberculosis control programs. It is recommended for newborns in countries with a high prevalence of TB according to the WHO policy. The purpose of BCC vaccination is to replace virulent natural infection with non-virulent BCC and thus to educate the immune system so that it will be resistant to disseminated tuberculosis disease. Studies about the effectivenessof RCC suggest that BCC cloes not prevent primary infection with TB but rather prevents the uncontrolled replication of mycobacteria and dissemination from the primary focus of infection to the other parts of the lung and body. Immunization is a valuable and cost-effective method of combating TB, particularly in countries where TB is endemic and where children are immunized at a sufficientlyearly age. Therefore, BCC vaccination does not prevent infection, hut makes TK disease less severe in children who have been vaccinated.

The vaccine

BCG is a safe live vaccine, but it can produce progressive disease in immunosuppressed people such as those with HIV-1 infection and should he avoided in children with a suspicion of HIV-1 infection. BCG vaccine should be kept cold.

Vaccination technique

The vaccine is usually administered by intradermal injection of 0.1cc of the vaccine using a 27 gauge needle in the upper layers of the skin. After 24 to 48 hours a papule appears at the injection site, which usually subsides. Within 6–12 weeks most lesions heal, leaving a scar. Occasionally, the scar can be slightly raised or forma keloid. A minority (less than 5%) heal without scar. In people who are already infected by natural means, the lesion can develop more quickly and be larger in size. The parent's anxiety should be allayed by explaining the normal evolution of the vaccinal lesion. Lymphadenitis or a secondary bacterial infection can occur. These symptoms usually resolve spontaneously and require no treatment. However, it is important to keep the lesion clean and dry. Antibiotic ointment may be used if necessary.

THERAPEUTIC REGIMENS FOR PULMONARY AND EXTRAPULMONARY TB

Although extrapulmonary TB and pulmonary TB can be treated identically, uncomplicated pulmonary TB is usually treated for a shorter duration than extrapulmonary TB. This is because the concentration of TB drugs may be lower in TB infected tissues as compared to the lungs, and therefore treatment is extended.

Introduction

There are many drugs and regimens available worldwide. The challenge lies in choosing an effective drug combination and treatment length to cure the TB that is feasible according to resources in each particular country and that is based on scientifically and medically accepted protocol.

TB drugs which are available worldwide

First line drugs:

Streptomycin (SM or S);
lsoniazid (lNH or H);
Rifamnin (R);
Pyrazinamide (PZA or Z);
Ethambutol (EMB or E).

Second line drugs.

Kanamycin (KANA);
Thioacetazon (Th);
Capreomycin (CM);
Viomycin (VN);
Ethionamide (ETA);
Para-amino salicylic acid (PAS);
Cycloserine (Cyclo);
Fluoroquinolones;
Clavulanate;
Macrolides;
Amikacin;
Ciprofloxacin (cipro).

Short (six to eight month) course chemotherapy (SCC)

Many patients failed to complete an adequate course of long term (12 months) TB therapy. In the 1960's, a short course chemotherapy (SCC) regimen of 6–8 months of multiple drugs including rifampin was introduced and found to be adequate to treat TB and to result in improved patient compliance with therapy.

Our experience using the 6 month SCC to treat pulmonary TB or the 8 rnonth course to treat extrapulmonary TB at the Thai-Cambodian border refugee camps (see appendix and below) resulted in a cure rate of 90% and a relapse rate of less than 2% within 2–4 years post lrcatinent.

TB treatment regimen at the Thai-Cambodian border program

1. *Pulmonary TB* (including primary TB and sputum smear negative pulmonary TB)

   2 months SRHZ (given daily) + 4 months RH (daily)

2. *Extrapulmonary TB:*

   2 months SRHZ (daily) + 6 months RH (daily)

TB treatment regimen in Cambodia (Current National TB Treatment Protocol)

Category I

2 months inpatient ERHZ (given daily) + 6 months EH (given daily)

- new cases of AFB positive pulmonary TB;
- serious cases of AFB negative pulmonary TB;
- serious cases of extrapulmonary TB.

New cases of AFB positive pulmonary TB are those patients who have never been treated with any kind of TB regimen in the past.

Serious cases of AFB negative pulmonary TB are those patients who present with severe debilitation such as malnutrition, severe weakness, inability to walk, or severe shortness of breath with or without hemoptysis.

Serious cases of extrapulmonary TB include those patients who present with miliary TB, TB of the spine, meningitis, or pericarditis.

Category 2:

2 months SHRZE (given daily) + 5 months HRZ (given 3 x /week)

- cases of relapse
- cases of treatment failure
- for defaulters who return for further treatment

Category 3:

2 months HRE (daily) + 2 months HR (daily)

- uncomplicated cases of AFB negative pulmonary TB
- Less serious cases of extrapulmonary TB

Uncomplicated cases of AFB negative pulmonary TB include the patients whose diagnosis was confirmed by clinical signs and symptoms and who do not have serious conditions as described in category 1.

Less serious cases of extrapulmonary TB include those patients who present with forms other than miliary TB, TB

of the spine, meningitis, or pericarditis and are not debilitated.

Note: Injections of TB medicines (including streptomycin) should be limited because of the difficulty of ensuring clean needles in many developing countries in this era of HIV-1 infection and AIDS.

Choice of treatment regimen

Decisions should be based upon:

1. Success, cure rate, and compliance rate of a regimen;
2. The incidence of multi drug-resistant tuberculosis (MDR TB) in the region:
3. The availability of an assured supply of specific TB drugs;
1. Cost of the different regimens.

GUIDELINES FOR TREATING DRUG RESISTANT TB

Introduction:

There are two types of drug resistance, primary and acquired. When a patient is infected with bacteria that is already resistant to specific drugs, this is known as primary drug resistance. Acquired drug resistance occurs when TB medicines are improperly taken and bacteria that were sensitive to particular drugs become resistant in a patient during a course of treatment. The actions of patients and medical staff therefore directly contribute to the development of acquired drug resistant bacteria. For example, staff should not use a single drug to treat TB because the susceptible bacteria will be killed while the drug

resistant mutants will remain, free to multiply and take over the infection. Patients, on the other hand, must be committed to taking all drugs on a regular basis until the end of the long course of treatment is achieved. Staff must be sure that a compliance problem is not the basis of an unfavorable response to treatment and carefully investigate any potential compliance problems before changing the regimen.

Factors contributing to drug resistance

1. Non-compliance;
2. Inadequate doses of drugs;
3. Irregular drug intake;
4. Treatment with a single drug.

Suspect drug resistance if

1. A patient has previously taken drugs irregularly;
2. A patient was treated with only one TB drug;
3. A patient comes from an area with a high rate of drug resistance;
4. Sputum smear is positive after 3 months of documented chemotherapy with 2SRHZ/4RH (90% of our patients had negative sputum smear at 2 months of therapy);
5. There is an unexplained clinical worsening of the patient's condition.

Prevention

1. Treat TR patients with multiple drugs;
2. Take measures to assure patient compliance;
3. Vitamin Protocol before initiating treatment to ensure compliance (see Part 1).

Avoid compounding the problem

1. Never add a single drug to a failing regimen. This is equivalent to treating the patient with one drug;
2. If a drug must be discontinued because of an adverse drug reaction and the patient was improving, i.e. smear negative, gaining weight, symptomatically improved, continue regimen without substituting for the discontinued drug and monitor closely;
3. If a drug must be discontinued because of an adverse drug reaction and the patient was not improving, i.e. smear persistently AFB+, symptomatically worse or not improved, not gaining weight, substitute two new drugs for the discontinued drug.

Relapse

Relapse refers to cases in which patients experience a recurrence of symptoms months or years after being treated successfully for TB. Some of these cases may also represent new TB infections in patients who were previously cured.

Treatment failure

Cases in which symptoms fail to improve in response to a drug regimen are always associated with drug resistance.

Indications of a treatment failure:

1. Patient's condition does not improve after approximately 45 days of treatment;
2. patient still has an AFB-positive sputum smear after three months of a presumably effective TR regimen.

Reasons For Failure or relapse

1. Patient never actually received or took drugs;
2. Regimen ineffective;
3. Drug dosage inadequate;
4. Only one new drug was added to a failing regimen;
5. Adverse drug reaction;
6. Psychological, cultural, or environmental factors contributing to non-compliance;
7. Drug interactions resulting in lower dosages than anticipated.

Criteria For choosing a treatment regimen

1. Best results are obtained with an effective three drug regimen (organism sensitive to all three drugs). INH and rifampin are drugs of choice because of their superior penetration into all body fluids. Treatment regimen should contain at least two oral drugs which the patient has never taken before. If the patient is severely ill or had numerous (++++) bacteria on sputum smear, four to five drugs are recommended.
2. If two drugs have been used before in a failed regimen but the TB bacteria still show susceptibility to these drugs, consider these two drugs as one and add at least two more drugs to the regimen.

Guidelines For changes in the regimen

It may be necessary to change drugs during therapy because of adverse reactions, particularly hepatitis (see appendix). Changes should only be made because of toxic reactions to drugs, not because of mild symptoms such as nausea, joint aches, and other tolerable

side effects. If there is no choice (the patient cannot tolerate a drug) the regimen may be carefully changed according to the length of time the patient has been on the treatment regimen.

1. Early (within three weeks of start): It is safe to exchange one effective drug for another effective drug;
2. Late (near completion of therapy): After the patient clearly shows response to therapy (i.e. follow-up sputum smear is repeatedly negative, the patient gains weight, and signs or symptoms improve), it is safe to substitute one effective drug for another effective drug;
3. After the first few weeks of therapy, but before a clinical response to drugs is clear, the regimen may be failing or the patient may have drug resistant organisms. In this case, it is important not to add a single new drug to a possibly failing regimen. Instead, two drugs should be added for the one drug discontinued and, after a positive response to therapy becomes clear, one of the newly added drugs may be dropped.

Treatment for rnultidrug-resistant (MDR) TB

In Cambodia and in other parts of the world there is a growing problem with MDR TB that is resistant to first line TB drugs. In our experience in Cambodia since 1994 we have successfully treated two patients with pulmonary TB resistant to four first line drugs (INH, streptomycin, PZA and rifampin). In the 1980s on the Thai-Cambodian border, we treated twelve patients with resistance to these same four drugs. We developed a new approach to these patients based on necessity. We added five new drugs (capreomycin, ethambutol, PAS, ethionamide, and ciprofloxacin). In addition we continued with INH, rifampin, PZA to kill the bacteria that were still sensitive to these drugs.

(A modification of this approach is called DOTS PLUS and has been used successfully in Peru on over twenty patients.) All patients treated on the Thai-Cambodian border or in Cambodia were on daily observed therapy for 12 months and have had subsequent AFB-negative sputum and resolution of their symptoms since completion of therapy. We believe the key to success in these patients was:

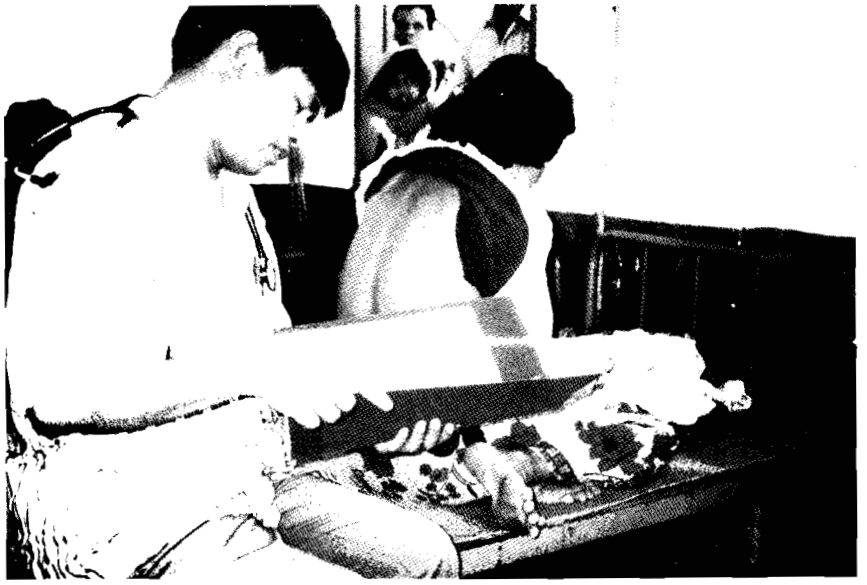
1. the addition of at least three (ideally four) drugs to which the TB bacteria were sensitive, which meant having knowledge about the resistance patterns of TB in Cambodia;

2. 100% compliance with therapy; patients were observed on a daily basis (daily observed therapy or DOT, for the course of their treatment);

3. patient education about the life-threatening nature of their disease to themselves, to their families, and to their communities;

4. the continuation of this eight drug regimen for at least eight months after sputum smears became negative in all patients.

This approach should absolutely not be used unless compliance can be guaranteed with a strong TB program that is committed to making sure that patients do not miss even one dose of medicines, since TB bacteria develop resistance to drugs when sub-optimal or irregular doses of medicine are taken and resistance to these second line drugs could then develop.



Patients are followed-up on a daily basis in the hospital to make sure they are improving and tolerating their medicines. This is documented in the patient's medical record.

PART IV

Pharmacology of anti-TB drugs

ISONIAZID (INH)

Other names	Rimifon
Activity	lsoniazid is bactericidal against actively dividing Mtb and is bacteriostatic against dormant TB. It is also effective against some atypical mycobacteria.
Absorption	lsoniazid is absorbed very well, both orally and parenterally.
Distribution	It is well distributed into all fluids and tissues including CSF and infected tissues. The latter retains the drug at levels well above those required for bacteriostasis.
Metabolism	By the liver
Excretion	75–95% of a dose of INH is excreted in the urine within 24 hours mostly as metabolites. The half-life of the drug may be prolonged in patients with hepatic insufficiency. In addition, there is heterogeneity in the human population regarding the rate of metabolism (via acetylation) of isoniazid. Thus, the half life may also depend on whether the patient happens to acetylate the drug at a faster or slower rate.
Peak time	1–2 hours after an oral dose
Half life	Depends on rate of acetylation and is longer in patient with hepatic insufficiency.

Indications For actively dividing Mtb in combination with other TB drugs and for prophylactic treatment for active TB after PPD conversion. It is also used to treat some diseases caused by atypical mycobacteria. To prevent peripheral neuropathy symptoms caused by INH, pyridoxine (10–50 mg/day) should also be given. Pyridoxine should not be given at a dosage higher than 50 mg because it may neutralize the effectiveness of INH.

Contraindications Isoniazid must not be given to patients with concurrent jaundice or liver disease. It also must not be given to patients who have a history of severe allergic reaction to INH in the past.

Precautions In patients with a history of liver disease, hepatic insufficiency or seizures, INH should be cautiously given.

Side effects Most common: skin rash, fever, jaundice, peripheral neuritis
(peripheral neuritis if pyridoxine not given concurrently)
Hepatitis
Precipitation of seizure in patients with seizure disorder
Phenytoin toxicity
Hematologic reactions (agranulocytosis, eosinophilia, thromhocytopenia, anemia, methemoglobinemia)
Arthralgias
Vasculitis

Neurotoxicity: (optic neuritis, muscle twitching, dizziness, ataxia, paresthesias, stupor, toxic encephalopathy)
Mental disturbances
Epigastric distress
Dryness of the rnouth
Tinnitus
Urinary retention

Drug interactions When used with high doses of pyridoxine, the effectiveness of INH can be neutralized. When INH is used with Rifampin, these two drug can increase the chance of hepatotoxicity. Isoniazid is known to inhibit the metabolism of phenytoin.

Dosage Adults: 5–8 mg/kg/day. Maximum 300mg/day.
Children: 10–20mg/kg/day.
Oral and parenteral doses are the same.

KIFAMPIN (R)

Other names Rifampicin, Rifadin, Rimactane.

NOTE: Rifamate is a capsule containing Rifampin and INH.

Activity This drug is bactericidal against against *M. tuberculosis, M. leprae* and other mycobacteria. It is also effective against gram positive organisms (particularly *N. meningitidis*) and gram negative organisms (particularly *H. influenzae*).

Absorption Rifampin is well absorbed by the GI tract. Absorption is delayed if taken after the patient eats; it is better to take the drug 1 hour before or 2 hours after eating a meal.

Distribution The drug easily distributes into many body organs and fluids, including the CSF.

Metabolism By the liver

Excretion 60–65% is excreted in feces. Up to 30% is excreted in urine; it may cause red-colored urine (patients should be warned about this).

Peak time 2–4 hours after oral dose.

Half life 1.5–5 hours; increased in presence of hepatic dysfunction.

Indications For the treatment of active TB. It is also used for prophylactic treatment in meningococcal disease and for meningitis due to H. influenzae.

Contraindications History of allergic reaction to rifampin, active hepatitis, or active internal bleeding. Because the drug can cross the placenta, it is best to avoid its use during pregnancy.

Precautions Use carefully in patients taking other hepatotoxic drugs and in patients with liver disease, alcoholism, thrombocytopenia or other bleeding disorders.

Side effects Most common: rash, fever, nausea/vomiting
Red color to bodily fluids such as urine
GI: jaundice, abdominal cramps, anorexia, heartburn, epigastric distress, diarrhea
CNS: headache, drowsiness, ataxia, dizziness, confusion, general numbness, fatigue, muscular weakness
Skin: rash, pruritis, urticaria
Arthralgias and myalgias
Hematologic: thrombocytopenia, anemia, temporary leukopenia
Hypersensitivity

Drug interactions Rifampin induces hepatic microsomal enzymes, resulting in decreased half life of the following drugs: steroids, oral contraceptives, digoxin, diabinase, cyclosporin, quinidine, ketoconazole, fluconazole, sulfonylureas, propranolol, metoprolol, clofibrate, verapamil, methadone, oral anticoagulants, theophylline, barbiturates, halothane, dapsone. Taking rifarnpin concurrently with alcohol or INH can increase hepatotoxicity.

Dosage Adults: 10–15 mg/kg/day.
Children under 5 years: 10 mg/kg.
Maximurn: 600 mg daily.
Give drug one hour before or two hours after meal.

ETHAMBUTOL (EMB)

Other names Myambutol

Activity Ethambutol is a bacteriostatic agent that works against actively dividing MTB and some atypical rnycobacteria.

Absorption About 70–80% of orally administrated dose is absorbed from the GI tract.

Distribution Ethambutol is well distributed in the plasma

Metabolism Partially by the liver

Excretion Mainly excreted in the urine.

Peak time 2–4 hours after an oral dose.

Ha If-life *3–4* hours

Indications Used to treat actively dividing Mtb and to treat some infections caused by atypical mycobacteria.

Contraindications History of severe allergic reaction to EMB. Not indicated in children less than 5 years of age.

Precautions Ethambutol should he used with precaution and closely monitored among those with impaired renal function or optic neuritis.

Side effects Optic neuritis:

This is the most important side effect. It can result in decreased visual acuity and inability to differentiate between red and green colors. Tests of visual acuity and retl-green discrimination before and during therapy are recommended.

Skin rash
Fever
Pruritis
Joint pain
Abdominal pain
Gastrointestinal upset
Malaise
Headache
Dizziness
Mental disorientation and confusion
Peripheral neuritis (infrequent)
Anaphylactic shock (rare)
Leukopenia (rare)
Decreased renal excretion of uric acid

Drug interactions When used with Pyrazinamide (PZA) the patient may experience severe joint pain.

Dosage Adults:

1. 25 mg/kg/day for first 2 months of therapy then reduce to 15 mg/kg/day for remainder of treatment.
2. Alternatively, use15 mg/kg/day throughout therapy.

Children: 10–15 mg/kg/day.

STREPTOMYCIN (SM)

Other name Strepto

Drug Class Aminoglycoside

Activity Bactericidal against MTB. Also effective against gram-negative aerobic bacteria and against most gram-positive bacteria. Not effective against anaerobic bacteria.

Absorption Poorly absorbed orally. 100% absorbed via intramuscular (IM) injection.

Distribution Poor penetration into central nervous system and eyes. High levels of the drug are found in the renal cortex and in the inner ear. Inflammation increases the penetration of the drug into tissues, including the peritoneum and meninges

Excretion Excreted unchanged in the urine.

Peak time Usually 0.5–1.5 hours after IM dose.

Half life Half life is 1.5–3 hours with normal kidney function. Half life can increase to 27–80 hours with decreased kidney function.

Indications Use streptomycin to treat active TB disease. Also effective in treating tularemia and plague.

Contraindications History of allergy to aminoglycosides and in women during pregnancy. Unless sterility of needles and syringes used for injection can be assured, streptomycin should not be used

Precautions Streptomycin should be used cautiously in patients with pre-existing kidney disease or patients taking other nephrotoxic drugs. Dehydration and advanced age make patients more likely to suffer kidney damage while taking streptomycin or other aminoglycoside drugs. In addition, caution should be used in giving this to patients who have hearing problems or are taking other ototoxic drugs.

Side effects

Ototoxicity

Damage to both the vestibular and cochlear branches of auditory nerves, leading to hearing loss, dizziness, vertigo

Nephrotoxicity

Neuromuscular blockade causing paralysis

Dysfunction of the optic nerve

Skin rashes

Numbness around mouth and face

Ataxia

Blood dyscrasias

Anaphylactic shock

Drug interactions Avoid using streptomycin with other aminoglycosides cephalosporins, cisplatin, or vancomycin because of added nephrotoxicity. Do not use with lasix, mannitol, ethacrynic acid, because of added ototoxicity.

Dosage IM injection: 15 mg/kg/ day in a single dose.

Patient over 60 or with impaired renal function: 10mg/kg/day.

If it is used for longer than two months, frequency of injection can be reduced to 2–3 times/week

PYRAZINAMIDE (PZA)

Activity Bactericidal specifically for intracellular Mtb (within macrophages). Not effective against other bacteria.

Absorption Good absorption from GI tract.

Distribution Diffuses easily into body tissues and fluids, including CSF.

Metabolism By the liver

Excretion Slowly excreted in the urine.

Peak time 2 hours after oral dose.

Half life 9–10 hours

Indications Only for treatment of active TB

Contraindications History of allergic reaction to pyrazinamide in the past; severe liver disease.

Precautions Use carefully in patients with liver disease, alcoholism, diabetes, kidney disease, gout.

Side effects Hepatitis
This is the most common and serious side effect. All patients taking PZA should have liver function tests checked before initiation of therapy and at frequent intervals throughout the period of treatment. (see appendix)

Thrombocytopenia
Nausea
Anorexia
Vomiting
Arthralgias
Dysuria
Fever
Gout (PZA inhibits renal secretion of uric acid)

Drug interactions None significant or known

Dosage Adults: 25–35 mg/kg/day. Maximum 3000 mg/day.
Children: 15–30 mg/kg/day. Maximum 2000 mg/day.

CAPREOMYCIN (CM)

Activity Bactericidal against Mtb and other mycobacteria.

Absorption Not absorbed from GI tract; must be given by intramuscular injection.

Indications Second line treatment for TB, used in combination with other drugs.

Contraindications History of allergic reaction to capreomycin; patient taking other nephrotoxic or ototoxic drugs; pregnancy.

Precautions See streptomycin

Side effects See streptomycin

Drug interactions See streptomycin

Dosage 15–30mg/kg. Maximum dose 1000mg/day.

ETHIONAMIDE (ETA)

Activity Chemically related to INH. Effective against Mtb and some atypical mycobacteria.

Absorption About 80% is absorbed after an oral dose.

Distribution Rapidly and widely distributed in most tissues and body fluids, including CSF.

Metabolism By the liver

Excretion 1–5% excreted in active form in urine, the rest are metabolites.

Peak time 3 hours after oral dose.

Half life Half life is about 2 hours.

Indications As second line treatment for Mtb

Contraindications Allergy to ethionamide or related drugs (INH); severe liver disease; pregnancy.

Precautions Taking ethionamide with other anti-TB drugs increases risk of hepatotoxirity.

Side effects Most common: anorexia, nausea, vomiting
Hypotension

Depression
Peripheral neuropathy
Dizziness
Drowsiness
Metallic taste
Menstrual disturbances
Acne
Alopecia
Gynecomastia
Stomatitis
Hepatitis (monitor liver function tests before and during treatment)

Dosage Adults: 500–1000mg/day in divided doses, twice a day.
Children: 15–20mg/kg/day in divided in two doses.
Maximum dose is 1000mg/day.

PARA-AMINOSALICYLIC ACID (PAS)

Activity Bacteriostatic against Mtb

Absorption Well and quickly absorbed from GI tract.

Distribution Well distributed to most body tissues and body fluids and reaches high concentrations in pleural fluid and caseous tissue. However, poor distribution to the CSF unless the meninges are inflamed

Metabolism By the liver

Excretion 80%excreted in urine. Excretion decreased in renal disease.

Peak time 1.5–2 hours after oral dose

Half life Approximately one hour

Indications Used as second line drug against Mtb.

Contraindications History of allergy to PAS, allergy to salicylate (aspirin), allergic to sulfonamides, and severe liver disease.

Precautions Safety of use in pregnancy has not been established. Use carefully in patients with history of liver disease, gastric ulcer, kidney disease, goiter

Side effects GI: Anorexia, nausea, epigastric pain, abdominal distress, diarrhea, exacerbation of ulcer
Hyperserisitivity
Fever
Malaise
Joint pains
Skin eruptions
Hepatitis
Hematologic: leukopenia, agranulocytosis, eosinophilia, lymphocytosis, thrombocytopenia, acute hemolytic anemia

Dosage Adults: 12–15g/day divided into 2 doses.
Children: 150–300 mg/kg/day divided into 3–4 doses.
Should be given after meals to decrease GI toxicity.

CIPROFLOXACIN

Other name Cipro

Activity Bactericidal against Mtb and atypical mycobacteria. Also commonly used to treat gram negative organisms.

Absorption It is well absorbed after oral administration. Food does not impair oral absorption.

Distribution It is widely distributed in body tissues. It is concentrated in urine, kidney, lung, prostate tissue, stool, and bile in higher levels compared to serum. However, cerbrospinal fluid and prostatic fluid levels are lower than serum levels.

Metabolism By the liver

Excretion Primary renally excreted

Peak time 1–3 hours

Half life 3–5 hours

Indications Used as part of a multi-drug regimen for the treatment of MDK TB. It can also be used to treat atypical mycobacterial infections, as well as urinary tract infections, prostatitis, some sexually transmitted diseases, enteric fever caused by *Salmonella typhi*, and *M. avium* complex in AIDS.

Contraindications Do not use cipro in a patient with history of allergy to this drug or in a patient with end stage renal failure. Should not be given to children or pregnant/lactating women.

Precautions Dose needs to be decreased in patients with renal insufficiency (creatinine clearance < 50). Use carefully in patients with preexisting CNS disorder or seizure disorder.

Side Effects Most common: nausea, abdominal discomfort, headache, dizziness
Mild liver enzyme elevation
Rare: hallucination, delirium, seizure
(These are more likely to occur in patients who are also receiving. theophylline nr nonsteroidal anti-inflammatory drugs.)
Skin rash including photosensitivity
Arthralgias in children
Anaphylaxis (rare)
Pseudomembranous colitis
Hematologic: leukopenia, eosinophilia
Theophylline toxicity

Drug interactions Cipro can increase serum levels of theophylline, caffeine, and warfarin. Probenacid increases the serum level of cipro. Cipro increases serum creatinine in patients also taking cyclosporine. Its absorption is reduced by aluminum or magnesium-containing antacids. Concomitant use of nonsteroidal anti-inflammatory drugs may increase the risk of CNS reaction.

Dosage Atlults: 500–700 mg oral or IV twice per day.

Appendix

Appendix

HEALTH HISTORY AND MEDICAL RECORDS

Talking with a patient and obtaining a health history are usually the first and often most important part of the health care process. Here you gather the information necessary to form a tentative diagnosis. You begin a relationship with the patient that fosters the patient's trust and ability to confide in you. Because TB is an infectious disease, often closely tied with poverty, poor living conditions, and social upheaval, it is important to understand how the disease is related to the patient's life situation. You share in the learning, where both the interviewer and the interviewee can be affected by the disease of TB. Finally, both you and the patient can start to define therapeutic goals.

The patient's medical record

The patient's medical record is a written document containing:

1. Medical history;
2. Findings from the physical examination;
3. Report of lab tests;
4. Findings and conclusions from special examinations for example: cultures, x-rays, or the consultant's opinions;
5. Diagnoses;
6. Notes on treatment, medication, surgical operations, X-rays, physical therapy;
7. Progress notes by health care providers.

The purpose of the medical record is to:

1. help medical personnel make a diagnosis;
2. help medical personnel in patient care and treatment;

3. have pertinent information such as patient allergies and other medical conditions that may impact care in a central confidential document;
4. serve as a record for teaching medicine and clinical research.

Conducting the interview

Physical setting:

1. The patient is seen in a room or office where the conversation cannot be overheard by others.
2. No time limit should be imposed.
3. The patient's spouse or relative is often helpful, but ask the patient whether a private interview is preferred.
4. The medical provider's manner should be unhurried, interested, and sympathetic.
5. Let the patient tell his/her own story in his/her own way.
6. Listen for a short time before starting the questions.
7. Gently but firmly concentrate upon patient's problem avoid discussing your own health or problems.

Writing strategies:

1. Write sparingly while patient talks.
2. After writing what is necessary, sit and listen before asking new questions.

Language usage:

1. Use language which is easy to understantl.
2. Remember, words may have different meanings for you and the patient.

3. Use simple words and avoid technical terms.

Patient motivation:

1. Encourage patients' cooperation by showing respect and respecting cultural diversity.
2. Help patients work out ways to gain control over their lives; your role is that of a helper and an advocate.

Beginning the interview

Before asking any questions, explain to the patient that you want him/her to reply as honestly as possible. A complete understanding will help in making an accurate diagnosis and in turn will help the patient receive more effective care. In addition, tell the patient that all information will be kept strictly confidential.

Basic information needed

1. Date of history
2. Identifying information (ID)
   a. Name
   b. Sex
   c. Age
   d. Race
   e. Place of birth
   f. Marital status
   g. Occupation
   h. Religion
3. Source of referral, if any.

Identifying the chief complaint (CC)

First ask "What is the problem?" or "Why have you come to see me?" Then, let the patient then describe his/her feelings. Note everything

the patient says, and when he/she has finished, ask what is most disturbing to the patient.

For example, the patient's general complaints are coughing, fever, tiredness, weakness, loss of weight, swelling of the lymph nodes, vaginal discharge, chest pain, etc. You might then ask, "Of all these problems, which one disturbs you the most'?" If the patient responds that the cough or the swollen lymph nodes are the most uncomfortable, then this should be noted as the chief complaint. When possible, the chief complaint should be put in the patient's own words.

History of the present illness (HPI)

In the present illness, the description of the patient's symptoms includes: a) location, b) quantity or severity, c) timing (onset, duration, frequency), d) associated symptoms, and e) associated manifestations (see old charts, lab reports, significant negative).

If the chief complaint is a cough, then you ask the following:

a. How long has it lasted? (i.e., 2 years, 2 months)
b. When is it worse'? (night, day, morning)
c. Coughing with sputum'?
d. If so, what color is the sputum'?
e. How long has it been that color'?
f. Do you cough up blood'? If so, is the blood bright red or dark?
g. When? How many times? How much'? When was the last time'?
h. Any vomiting?
i. Chest pain'? Where does it hurt the most'? When does it hurt the most?

If the patient complains about fever related to the cough, ask:

a. How many days have you been feverish'?
b. What is the fever's pattern (day, morning, afternoon, night)
c. Is there sweating'? What is the pattern of sweating (nighttime, daytime)?

If the patient complains about loss of appetite related to the cough:

a. How long have you had a poor appetite'?
b. Is there associated weight loss'? If so, how many kilos have been lost in how many months or years'?
c. Can you taste the food?
d. Does the thought of eating food make you sick (anorexia)'?
e. What was your original weight (pounds/kilograms)?

The interviewer can also ask about the patient's symptoms by system. First, ask the questions related to the organ system in which the patient is experiencing symptoms. For example, if the patient is short of breath (a respiratory complaint), ask whether the patient has any of the other symptoms listed in section h.

Then, after characterizing the primary complaints, ask about the remaining organ systems that were not already mentioned. This is referred to as the review of systems (KOS) and is used to identify symptoms related to the patient's primary complaints as well as to identify other areas of illness that may need to be addressed.

a. Skin: rash, lumps, itching, dryness, color change, change in hair and nails;
b. Head: head injury, headache, dizziness;
c. Eyes: vision, glasses or contact lenses, last eye examination, pain, redness, excessive tearing, double vision, glaucoma, cataracts;
d. Nose and sinuses: frequent cold, nasal congestion, seasonal allergies, bleeding, sinus trouble;
e. Mouth and throat: condition of teeth and gums, bleeding

gums, last dental examination, sore tongue, frequent sore throat, hoarseness;

f. Neck: lymph node swelling, discharge, goiter, pain in neck;

g. Breasts: lumps, pain, nipple discharge, self examination results;

h. Respiratory: cough, sputum (color, quantity), hemoptysis, wheezing, asthma, bronchitis, emphysema, pneumonia, tuberculosis, pleurisy, tuberculin test, last chest x-ray;

i. Cardiac: heart trouble, high blood pressure, rheumatic fever, heart murmurs, dyspnea, orthopnea, paroxysmal nocturnal dyspnea, edema, chest pain, palpitations, heart exam in the past;

j. Gastro-intestinal: trouble swallowing, heartburn, appetite, nausea, vomiting. vomiting with blood. indigestion. frequency of bowel movements, change in bowel habits, rectal bleeding or black tarry stool, constipation, diarrhea, abdominal pain, food intolerance, flatulence, hemorrhoids, jaundice, liver or gall bladder trouble, hepatitis;

k. Urinary: frequency of urination, polyuria, nocturia, dysuria, hematuria, urgency. hesitancy, incontinence, urinary tract infection, kidney stones;

l. Genito-reproductive:

   i. Male: discharge from penis, history of sexually-transmitted diseases (STDs) and their treatment, hernias, testicular pain or masses, frequency of intercourse, libido, sexual difficulty;

   ii. Female: age at menarche, regularity, frequency and duration of periods, amount of bleeding, bleeding between periods or after intercourse, last menstrual period (LMP), dysmenorrhea, age of menopause, menopausal symptoms, post-menopause bleeding, discharges, itching, STDs and their treatment, number of pregnancies, births, abortions, or complicated pregnancies, birth control methods, frequency of intercourse, libido, sexual difficulty;

m. Musculo-skeletal: joint pain or stiffness, arthritis, gout, back pain (any associated swelling, redness, pain, stiffness, weakness, limitation of motion or activity, muscle pain or cramps);

n. Peripheral vascular: intermittent claudication, cramps, varicose veins, thrombophlebitis;

o. Neurologic: syncope, seizures, paralysis, local weakness, numbness, tremors, memory loss;

p. Psychiatric: nervousness, tension, mood, depression;

q. Endocrine: thyroid trouble, heat or cold intolerance, diabetes (excessive thirst, hunger, or urination);

r. Hematologic: anemia, easy bruising or bleeding, past transfusions and possible reaction.

Past medical history (PMH)

In taking a past medical history, ask about any previous illnesses. Ask in different ways in order to get as clear a picture as possible. In some cultures, like the Cambodian culture, it is very hard for a patient to discuss openly any personal or physical problems. Even if the information is needed, let the patient choose how and when to disclose it.

1. First method of questioning: Ask about patient's health during different regimes or historical eras through which the patient may have lived. For example, in Cambodia one can ask whether the patient had any illnesses during King Sihanouk's time or during the Vietnamese occupation of Cambodia. If so, then

a. What disease and how long did it last?
b. What treatment was taken and for how long?
c. What drugs were prescribed and at what dosage?
d. Did the problem improve or worsen after treatment?
e. Did you experience any side effects or allergic symptoms? Describe.

2. Second method of questioning: Ask specific questions by chronological age. Some patients may remember their illnesses well in this way. Ask the same questions as in the first method of questioning. Was the patient ill:
   a. From birth to 10 years?
   b. From 11–20 years?
   c. From 21–30 or up to present age?
   d. From 31–40 or up to present age?
   e. From 41–50 or up to present age?
   f. From 51 to present age?

3. If the patient does not respond positively to any questions by the first and second methods, then he/she may remember more if asked specific questions:
   a. Any history of malaria?
   b. History of diabetes?
   c. History of chronic lung disease?
   d. History of heart disease?
   e. History of liver disease?
   f. History of kidney disease?
   g. History of epilepsy?
   h. History of leprosy?
   i. History of TB?
   j. Any operations'?
   k. Any hospitalization?

l. Any vaccinations for small pox, cholera, tetanus, BCG? If the patient is a baby or a child, check the vaccination card, which is used in many countries.

Prior TB therapy

If the patient has a history of prior TB treatment, find out what TB drugs the patient used in the past. The following are typical questions:

1. Have you ever taken TB drugs in the past? If so, what is the drug's name?
2. Have you ever had any injections? How many and for what period of time? Was a streptomycin injection used? Did you experience any side effects?
3. How was TB diagnosed? Sputum exam or chest X-ray?

Medications

Ask for a history of recently used drugs or medications and whether they were bought or prescribed by a health worker.

1. Name of the drug (if known)
2. How much/how many times per day/how long?
3. Did you buy the medication at a pharmacy, on the black market, or somewhere else?
4. Are you using any steroids (hydrocortisone, prednisone, prednisolone) at home?
5. Do you take traditional or herbal medication? If so, would you be willing to take prescribed TB medication along with traditional medicine?

Allergies

1. Are you allergic to any medicine? If so, what was the medicine and what was the reaction? Did anything relieve the symptoms?
2. Do you have any food or environmental allergies? If so, describe.

Family History

The family history is important to help find the source of TB infection. It is also important in finding other cases or sources of TB within the family. If more than one family member is identified and treated, the compliance rate will be higher.

1. Father's name, age. Is he dead, and if so, how did he die? If he is still alive, where does he live? Is he healthy or does he have any medical problems? If so, what diseases or illnesses and what kind of treatment?
2. Mother's name, age, alive or dead? (Repeat questions as above).
3. List the patient's siblings by age and ask about their general health.
4. Patient's immediate family, spouse and children (Repeat questions as above).

Social History

1. Where do you live currently? (Record address) How long have you been in this village or place of residence?
2. Are you married? Do you have any children'? How many people are in your householtl? lnclutle extended family and friends.

3. What is your present work or job, what work did you do in the past? This information is important to know for case finding and for the protection of others in the work place. It may also become important in helping the patient get leave, if necessary.

Alcohol History

1. Do you drink alcohol? At what age did the drinking begin? How often and how much each time?
2. Do you still drink now or have you stopped? Why did you stop? (money, health concerns, etc.) Did drinking make you feel worse, or better?

Drinking can affect not only the consistency of taking medication, but can also cause physical damage or disrupt the family support system.

Smoking History

1. Do you smoke? At what age did you begin? At what times do you smoke the most? How many cigarettes per day and for how many years?
2. Do you still srnoke or have you stopped? Why did you stop? How many years have you been smoke-free?

Physical Examination

1. General appearance: well-nourished, well-developed, emaciated, weak, etc. The initial observation of the patient's general physical and mental appearance will influence patient care, aiding in determining where he/she will enter the health care system. A patient who appears seriously ill may need immediate hospitalization.

2. Vital signs: Take the blood pressure, pulse, respiratory rate, and temperature.
3. Complete exam of skin, head, ears, eyes, nose, mouth, neck, chest, lung, heart, abdomen, back, extremities.
4. Neurological exam: Mental status, motor strength, walking and balance, cranial nerve response, coordination, reflex, and sensory response.

Laboratory Data

Results from sputum smears, chest x-rays, PPD tests. In addition, culture and sensitivity, biopsy, CBC, smears of CSF or other bodily fluids.

Assessment

Analyze all signs, symptoms, and lab results. Together these pieces of information will form the diagnoses. Prepare hypotheses with an openness and flexibility to new possibilities.

PRESENTATION OF TB IN 1,298 CASES

A chart review of all cases treated by the American Refugee Committee TB Program at Nong Samet and Site II refugee camps on the Thai-Cambodian border between 1981-1989 was conducted in January of 1990 and revealed the following clinical presentations.

• Pott's disease	64 cases
• Genital TB (female)	52 cases
• Genital TB (male)	4 cases
• Skin TB	4 cases[1]
• Abdominal TB and GI tract	95 cases
• Pericardial TB	4 cases
• Miliary TB	29 cases
• TB empyema	5 cases
• Pleurisy TB	32 cases
Pulmonary & scrofula TB	37 cases
• Pulmonary & urinary tract TB	17 cases
• Thyroid gland TB	1 case[1]
• Pharynx and gum TB	7 cases[1]
• TB of the ear	1 case
• TB meningitis	12 cases
• TB lymphadenitis	175 cases
• Open pulmonary TB	711 cases
• Smear negative pulmonary TB	39 cases
• Bone & joints	9 cases
• TB in children	136 cases[1]
	TOTAL : 1,298 CASES

[1] No age and sex distribution analysis was done for these due to the small number of cases.

Analyses of pediatric TB cases (children less than 10 years old) is integrated into that of each TB category above and is not counted separately in the total number of cases.

1. POTT'S DISEASE – OTHER BONE TB

	AGE AND SEX DISTRIBUTION														
	<1-10		11-20		21-30		31-40		41-50		51-60		61-100		TOTAL
LOCATION	M	F	M	F	M	F	M	F	M	F	M	F	M	F	
CERVICAL	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
THORACIC	3	4	8	0	5	7	4	5	1	3	0	5	1	1	47
LUMBAR	1	1	3	1	0	3	1	2	1	1	0	0	0	1	15
SACRUM	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1
COCYX	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TB OF THE BONE & JOINTS															
HIP	1	0	1	0	0	0	1	0	1	0	1	0	0	0	5
ANKLE	0	0	0	1	0	1	0	0	1	0	0	0	0	0	3
TIBULAR	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
TOTAL	6	5	12	2	5	11	7	7	4	4	1	6	1	2	73

All cases above were mainly diagnosed by a strong history of a TB-like illness or a history of contact with TB patients.

64 of the 73 patients had spine x-rays demonstrating vertebral wedging with triangular shadows (47 patients with thoracic involvement, 1 case cervical, 15 cases lumbar; 1 case sacrum and hip bone).

9 cases showed bone erosion (monoarticular vertebra or joint involved, 5 of them had positive AFB seen on direct pus smear from the joints).

All 73 cases of bone TB had strong positive PPD tests (mantoux test with 5 TU PPD, 18–20 mm in diameter). In these cases the PPD is usually positive in 8–24 hours.

Paralysis is most common in Pott's desase: 64 cases which were unable to walk on presentation were able to walk again after 5–7 months of treatment. There were only 2 cases in which there was permanent paralysis (a 13 year-old boy, and a 33 year-old man).

2. MALE AND FEMALE GENITAL TB

	AGE AND SEX DISTRIBUTION						
LOCATION	15-20	21-30	31-40	41-50	51-60	61-100	TOTAL
FEMALE							
OVARIES	0	3	2	1	0	0	6
FALLOPIAN TUBES	0	5	9	6	0	1	21
UTERUS	0	5	9	6	0	0	20
CERVIX	0	0	1	2	0	0	3
VAGINA	1	0	0	0	0	0	1
VULVAR	1	0	0	0	0	0	1
MALE							
TESTES	0	1	1	1	0	1	4
TOTAL	2	14	22	16	0	2	56

Notes on female pelvic TB in our case series:

All cases presented to the clinic with an unexplained illnesses. Fatigue and weakness were common. (Cambodian women are reluctant to report their genital symptoms.) Chronic vaginal discharge was reported in almost every case. Nothing remarkable on vaginal smear was noted in these patients (1 case presented with 3+ epithelial cells, 2 patients complained of pain on sexual activity).

Pelvic exam was done in all 52 cases. Chronic cervicitis was reported, caseous discharge from the cervix was noted in 40 cases. Biopsy of the endometrium was done in 20 cases (out of 52 cases) and all were compatible with TB with caseous material and granulomas visualized, but no AFB seen on direct tissue examination. The rest of the cases were diagnosed on history and physical exam; biopsy was not performed because of limited resources. All of these patients responded well to TB treatment. Menstrual periods, pregnancy, and/or noticeable weight gain (7-12 kg) usually occurred approximately 8 months after beginning TB treatment.

3. PULMONARY TB

SPUTUM RESULT	AGE AND SEX DISTRIBUTION														TOTAL
	<1-10		11-20		21-30		31-40		41-50		51-60		61-70		
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	
POSITIVE	4	4	25	14	113	53	110	75	99	69	100	45	0	0	711
NEGATIVE	13	18	1	0	1	0	1	0	1	1	2	0	1	0	39
TOTAL	17	22	26	14	114	53	111	75	100	70	102	45	1	0	750

711 patients had positive AFB after **3** sputum specimens were examined. 39 patients were negative or unable to produce sputum for examination. These mainly were children under the age of 10. In these cases, diagnoses were mainly based on x-rays of the chest and almost 100% showed a primary TB complex or ghon complex. In addition, we applied the Indian scoring technique and PPD tests ancl all responded well to treatment. Average weight gain after completion of the 6 month course of TB therapy was about 7–15 kg in adults ancl 1–4 kgs in children.

About 20–30% of our pulmonary TB patients developed "bad lungs" (chronic cough, bronchiectasis, shortness of breath) likely secondary to the late stage in their illness at which TB treatment was available to them.

.I. COMPLICATED PULMONARY TB

LOCATION	AGE AND SEX DISTRIBUTION												TOTAL
	<1-10		11-20		21-30		31-40		41-50		51-60		
	M	F	M	F	M	F	M	F	M	F	M	F	
PUL TB & LYMPHADENITIS	1	1	0	4	6	8	3	4	4	4	0	2	37
URINARY TRACT	0	0	1	1	4	0	1	2	1	2	2	3	17
EMPYEMA	0	1	0	0	1	2	0	0	1	0	0	0	5
PLEURAL EFFUSION	0	5	1	0	3	4	4	2	2	2	7	2	32
OTITIS MEDIA	0	0	0	0	1	0	0	0	0	0	0	0	1
PERICARDIAL EFFUSION	0	0	1	0	0	0	1	0	1	0	1	0	4
MILIARY	1	5	1	2	4	1	4	3	2	2	2	2	29
TOTAL	2	12	4	7	19	15	13	11	11	10	12	9	125

Notes:

It was noted that in our TB patients, females seemed to have a higher rate of complicated pulmonary TB than males in the same age groups.

The diagnosis of TB was made based on sputum results in the case of for example, associated pleural effusion, pericardial effusion. If the patient had sputum smear positive AFB with lymph node at the neck or pleural effusion, we would consider it an extrapulmonary case and the treatment would be 8 months.

5. ABDOMINAL TB CASES

LOCATION	SEX AND AGE DISTRIBUTION <1-10 M	<1-10 F	11-20 M	11-20 F	21-30 M	21-30 F	31-40 M	31-40 F	41-50 M	41-50 F	51-60 M	51-60 F	61-70 M	61-70 F	>70 M	>70 F	TOTAL
GI TRACT	0	0	2	0	2	0	1	1	0	0	0	0	1	0	6	1	14
ABDOMINAL MASS TB	0	0	0	2	0	2	2	3	3	3	0	3	0	4	5	14	41
PERITONITIS	1	0	0	0	2	3	2	3	1	2	1	2	0	0	7	10	34
ASCITIS	0	0	0	0	1	0	0	1	0	0	0	0	0	0	1	1	4
LIVER	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	2
TOTAL	1	0	2	2	5	5	5	8	5	5	1	5	1	4	20	26	95

Abdominal TB was commonly seen in our patient series. The most common symptoms reported were loss of body weight, chronic diarrhea (with over 1-3 years duration in 3 cases). An abdominal mass was appreciated in 22 cases; liver TB was rarely seen.

Diagnosis was mainly based on history, chest x-ray and laparotomy biopsy. PPD was not reliable in chronic diarrheal patients because of malnutrition, They all responded well to TB treatment. The improvement was noted in the first 2 months of treatment and weight gain was fast (7–10 kg in the first 2 months). They were all cured and no patient relapsed in the 2 years following completion of TB treatment.

6. TB MENINGITIS

AGE AND S		E		X		~		~						TOTAL	
<1-10		11-20		21-30		31-40		41-50		51-60		61-70		TOTAL	
M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	TOTAL
1	2	0	2	1	1	1	3	0	0	D		0	0	3	9	12

Notes:

Diagnosis was based on health history, chest or spine x-ray, PPD test. CSF examination was positive for high protein and low glucose (positive Pandy Test), and lymphocytes were increased (85–90%); PPD test was positive in all cases. Chest x-ray usually helped, and revealed an old TB scar or new activated lesion or infiltrates in the lung. None of our patients presented with open pulmonary TB. They all responded well to TR treatment and were cured with no neurological damage in our 12 cases.

7. TB LYMPHADENITIS

LOCATION	SEX AND AGE DISTRIBUTION <1-10 M	<1-10 F	11-20 M	11-20 F	21-30 M	21-30 F	31-40 M	31-40 F	41-50 M	41-50 F	51-60 M	51-60 F	61-70 M	61-70 F	TOTAL
AXILLARY	0	1	0	1	0	0	0	0	0	0	0	1	0	0	3
NECK	25	28	11	22	12	35	3	15	1	5	1	6	0	8	172
TOTAL	25	29	11	23	12	35	3	15	1	5	1	7	0	8	175

Notes:

TB of the lymph nodes was the second most common presentation of TB (after pulmonary TB) in our patient series.

Diagnosis of TB lymphadenitis was mainly based on a health history. A positive PPD test was important for us in diagnosing scrofula. Those patients who had TB of the lymph nodes were usually not very ill compared to other presentations of TB. On presentation, the lymph node is enlarged, but painless, and commonly there is drainage from this "cold abscess."

MANAGEMENT OF HEPATITIS INDUCED BY TB DRUGS: CASE REPORTS

The following three case histories are provided as examples of how TB therapy can be continued when there is an adverse reaction to TB drugs. Thirty-nine cases of drug induced hepatitis were managed in Nong Samet and Site 11 by the American Refugee Committee (ARC) TB Program. All thirty-nine successfully completed TB therapy using approaches similar to what was used in the three cases below. Drug induced hepatitis can result in the death of the patient. Therefore, this approach should not be attempted unless the health care provider has gone through in-depth training and works under the close supervision of an individual witlr extensive experience in managing such cases. Daily follow up of the patient, involvement and education of the patient regarding the situation and strong motivation on the part of the patient and the health worker is also required. We note that a history of drinking alcohol was common to all of the adult patients treated.

Case 1:

L.L., a 45 year old male first presented to the ARC TB Program in 1984 with pulmonary TB with AFB+ sputum. He successfully completed SCC (3SRHZ/3RH) with negative follow up sputums. One year later in 1985, he developed new pulmonary symptoms with AFB+ sputum. He was restarted on the same treatment regimen as before. After one month on the second course of treatment, his eyes and skin turned yellow. He reported occasional heavy drinking of alcohol during special occasions like wedding parties. We managed the case as described in table below:

Days	Patient's condition and actions taken	TB drug readjustment			
		INH in mg	Rifampin in mg	PZA in mg	SM in mg
1-30	Tolerated very well	250	450	1500	
31	Jaundice develops, stop all drugs	0	0	0	
31-45	Jaundice resolved	0	0	0	
*R1	Restart treatment with	50	50	250	500
*R2	Pt tolerating drugs, doll change regimen				
*R3					
*R4	Pt tolerating drugs, keep same doses	100	150	500	500
*R5	Pt is fine. Increase doses	200	200	750	500
*R6	Pt is fine, keep same doses	200	200	750	500
*R7	Pt is fine. Increase doses	250	300	1000	500
*R8	Pt is fine. Increase doses	250	450	1250	500
*R9	Pt is fine. Increase to full doses	250	450	1500	500
*R10	Pt feels fine till completion of regimen (3SRHZ/4RH) no further symptoms of TB until 1987, when he was) lost to follow-up	250	450	1500	500

**R1= restarted treatment day 1*

Case 2:

M.S., a 27 year old female, weighing 45 kg, presented to the ARC TB program in 1988 with pulmonary symptoms and AFB+ sputum. On physical exam it was noted that she also had enlarged cervical lymph nodes with drainage that was also AFB+. She reported no history of drinking alcohol, but admitted that she drank following giving birth approximately 1 liter of alcohol per day for about a month. She was begun on 2SRHZ/6RH to treat pulmonary and extrapulmonary TB. She developed hepatitis shortly after beginning TB chemotherapy.

Days	Patient's condition and actions taken	mg			
1-20	Tolerated regimen with some minor side effects (nausea)	300	600	2000	800
21	Jaundice, stop all drugs	"	"	"	"
	Sickness lasted within 10 days	0	"	"	"
*R1-R2	Restarted treatment.	50	100	250	800
*R3-R5	If tolerated drugs, increase doses	75	150	500	800
*R6	Pt developed jaundice again, stop all drugs	0	0	0	0
	Hepatitis lasted for 13 days this time	0	0	0	0
*R1	Restart treatment.	50	0	0	800
*R2	Pt tolerating drugs, increase dose of INH only	100	0	0	800
*R3	Pt is fine. Increase dose of INH higher.	150	0	0	800
*R4	Pt is fine. Increased doses of INH, Rif and SM	200	100	0	800
*R5	Pt is fine. Increase doses	250	150	0	800
*R6	Pt feels fine , increase doses	300	300	0	800
*R7	Pt feels fine, increase dose of Rif.	300	450	0	800
*R8	Pt feels fine, keep same doses	300	450	0	800
*R9	Pt feels fine, added lower dose of PZA	300	450	500	800
*R10	Pt developed jaundice again, stop all drugs. Jaundice lasted 7 days.	0	0	0	0
*R1	Pt recovered and all drugs restarted except PZA	300	450	0	800
*R11	Pt feels fine, keep the same doses	300	450	0	800
*R12	Pt feels fine, keep the same doses	300	450	0	800

In her case, we assumed that PZA was the likely drug that caused hepatitis and PZA was never reintroduced again. There were no new drugs substituted for PZA and the patient was treated with INH, Rifampin and Streptomycin for 12 months (instead of 9 months as she would have been had she been able to tolerate PZA). Streptomycin was reduced to 3 times per week during the 4th–6th month of therapy and then to 2 times per week between the 7th–12th month of therapy. Her sputum converted to AFB-negative at the third month of treatment, her lymph nodes shrank and she remained symptom free up until 1991 when she was lost to follow up.

Case 3:

N.N., a 50 year old male, weighing 47 kg, presented to the ARC TB program in 1990 with three AFB positive sputum smears and was diagnosed with pulmonary TB. The patient reported to heavy drinking of alcohol when he met with friends approximately 7–10 times yearly. He also reported a history of malaria 3 years earlier with an enlarged and painful liver. On physical examination his liver was enlarged 5 cm below the rib margin and was hard but not tender to palpation. The patient received treatment with 4 drugs, the United Nations protocol in 1989 (2SRHZ/4RH).

Days	Patient's condition and actions taken	TB drugs doses readjustment			
		INH mg	Rif. mg	PZA mg	SM mg
1-60	Tolerated medicine with some minor side effects (nausea)	250	500	1500	500
61-120	Completed intensive phase, stop PZA,SM	300	600	0	0
121	Some side effects (nausea), but same doses maintained	300	600	0	0
122-123	Drugs poorly tolerated (vomiting), decreased doses	200	450	0	0
124	Jaundice developed, stop drugs	0	0	0	0
On hold	Jaundice: [illegible] days to resolve		0		
*R1	Restart treatment with INH and Rif, but on same day ever and jaundice develop again	0	100	0	0
On hold	Janndice took7 days to resolve.	100	0	0	0
*R1	Reslart treatment with INH alone, mild nansea develops but no	50	0	0	0
[illegible]	Continue with same dose	50	0	0	0
[illegible]	Pt developed jaundice and fever again	[illegible]	[illegible]	[illegible]	[illegible]
On hold	Jaundice took 15 days tu recover this time	[illegible]	[illegible]	[illegible]	[illegible]
*R1	Stop INH, start with Rif. Alone, but the patient developed fever & jaundice again	0	100		

The patient had a severe allergic reaction to both INH and Rifampin. In this case, we decided to cut short the treatment at the 4th month of the 6 month treatment protocol. His sputum had converted to negative at the second month of treatment and was consistently negative at the third and fourth months. After recovering from hepatitis, the patient felt fine with no further symptoms of pulmonary TB. The patient remained well and was followetl on a monthly basis for another year until his family returned to Cambodia and he was lost to further follow-up.

References

References

I'revention and treatment of tuberculosis among patients infected with HlV: principles of therapy and revised recommendations. *MMWR* **47,** RR-20 (1998).

Adler, J. J. & Rose, D. N. in *Tuberculosis* (eds. Rom, W. N. & Garay, S. M.) 129-140 (Little, Brown and Company, Boston, 1996).

Ahmad, M. & Ahmed, A. Tuberculous peritonitis: fatality associated with delayed diagnosis. *South Med J* **92,** 406-408 (1999).

Alvarez, S. Z. Hepatobiliary tuberculosis. *J Gastroenterol Hepatol* **13,** 833-839 (1998).

Bai, K. J., Wu, l.H., Yu, M.C. *et al.* Tuberculous empyema. *Respirology* **3**, 261-266 (1998).

Baskaram, P., Hemalatha, P. & Rao, K. V. BCG vaccination in malnourished child population. *Indian Pediatr* **29,** 39-44 (1992).

Bergstermann, H. & Ruchardt, A. Ciprofloxacin once daily versus twice daily for the treatment of pulmonary tuberculosis. *Infection* **25**, 227-232 (1997).

Bloom, 13. R. (ed.) *Tuberculosis: pathogenesis, protection, and control* (ASM Press, Washington, D.C., 1994).

Brudney, K. & Dobkin, J. Resurgent tuberculosis in New York City. HIV, homelessness, and the decline of tuberculosis control programs. *Am Rev Respir Dis* **144,** 745-749 (1991).

Chakraborty, P., Roy, A., Bhattacharya, S., *et ul.* Tuberculous cervicitis: a clinicopathological and bacteriological stutly. *J Indian Med Assoc* **93**, 167-168 (1995).

Chaulk, C. P., Moore-Rice, K., Rizzo, R. & Chaisson, R. E. Eleven years of community-based directly observed therapy for tuberculosis. *JAMA* **274**, 945 951 (1995)

Cohn, D. L., Bustreo, F. & Raviglione. M. C. Drug-resistant tuberculosis: review of the worldwide situation and the WHO/IUATLD Global Surveillance Project. International Union Against Tuberculosis and Lung Disease. *Clin Infect Dis* **24.** S121-130 (1997).

Combs, D. L., O'Brien, R. J. & Geiter, L. J. USPHS tuberculosis short-course chemotherapy trial 21: effectiveness, toxicity, and acceptability. The report of final results. *Ann Intern Med* **112,** 397-406 (1990).

Coninx, R. WFP/UNBRO TB Guidelines (WPF/UNBRO, Aranyaprathet, Thailand, 1986).

Connolly, M. & Nunn, P. Women and tuberculosis. *World Health Stat Q* **49,** 115-119 (1996).

Demiroglu, H. & Dundar, S. Vitamin B6 responsive sideroblastic anemia in a patient with tuberculosis. *Br J Clin Pract* **51,** 51-52 (1997).

Donald, P. R. & Sellars, S. L. Streptomycin ototoxicity in the unborn child. *S Afr Med J* **60,** 316-318 (1981).

Durand, F., Jebrak, G., Pessayre. D., *et al.* Hepatotoxicity of antitubercular treatments. Rationale for monitoring liver status. *Drug Saf* **15,** 394-405 (1996).

Farina, M. C., Gegundez, M.I., Pique, E., *etal.* Cutaneous tuberculosis: a clincial, histopathologic, and bacteriologic study. *J Am Acad Dermatol* **33**, 433-440 (1995).

Farmer, P., Robin, S., Ramilus, S. L. & Kim, J. Y. Tuberculosis, povertv, and 'compliance': lessons from rural Haiti. *Semin Respir Infect* **6,** 254-260 (1991).

Ferrer, J. Pleural tuberculosis. *Eur Respir J* **10,** 942-947 (1997)

Fine, P. E. & Small, P. M. Exogenous reinfection in tuberculosis. N *Eng J Med* **341,** 1226-1227 (1999).

Fowler, N. O. Tuberculous pericarditis. *JAMA* **266,** 99-103 (1991)

Garay, S. M. in *Tuberculosis* (eds. Rom, W. N. & Garay, S. M.) 443 165 (Little, Brown and Company, Boston, 1996)

Goldfeld, A. E. Cambodia: A humanitarian agenda (Asia Pacific Sub-Committee of the House Foreign Affairs Committee, Washington, D.C., 1991).

Goldfeld, A. E. & Myers, H. Cambodia Can't Wait (The Congressional Record: Asia Pacific Subcommittee of the House Foreign Affairs Committee, Washington, D.C., 1993).

Goldfeld, A. E. Tuberculosis and poverty in Cambodia (Congressional Hunger Caucus, Washington, D.C., 1994).

Goldfeld, A. E., Delgado, J.C., Thim, S., *et al.* Association of an HLA-DQ allele with clinical tuberculosis. *JAMA* **279,** 226-228 (1998).

Gorse, G. J. & Belshe, R. B. Male genital tuberculosis: a review of the literature with instructive case reports. *Rev Infect Dis* **7,** 511-524 (1985).

Grange, J. & Zumla, A. Tuberculosis and the poverty-disease cycle. *J R Soc Med* **92**, 157-160 (1999).

Heifets, L. B. & C., G. R. in *Tuberculosis: pathogenesis, protection, and control* (ed. Bloom, B. R.) 85-110 (ASM Press, Washington, D.C., 1994).

Heifets, L. B. Antirrlycobacterial drugs. *Semin Respir Infect* **9,** *84-103* (1994).

Heinrich, A. E., Quale, J. M. & Burack, J. H. in *Tuberculosis* (eds. Rom, W. N. & Garay, S. M.) 531-540 (Little, Brown and Company, Boston, 1996).

Hilman, B. C. Pediatric tuberculosis: problems in diagnosis and issues in management. *J La State Med Soc* **150,** 601-610 (1998).

Holdiness, M. R. Clinical pharmacokinetics of the antituberculosis drugs. *Clin Pharmacokinet* **9**, 511-544 (1984).

Hong, R. & Sok, T. Retrospective study of empyema cases in National Pediatric Hospital, Cambodia. *Southeast Asian J Trop Med Public Health* 28, 801 802 (1997)

Hopewell, P. C. in *Tuberculosis: pathogenesis, protection, and control* (ed. Bloom, B. R.) 25 46 (ASM Press, Washington, D.C., 1994).

Hsu, C. J., Bai, K.l., Chiang, l.M., *et al.* Tuberculous pleurisy with effusion. *J Formos Med Assoc 98,* 678-682 (1999).

lseman, M. D. Extrapulmonary tuberculosis

Isenian, M. D. Treatment of multidrug-resistant tuberculosis. *N Eng* J *Med 329,* 784-791 (1993).

lshikawa, N. *Draft TB manual* (Volunteer Health Services Society, Bangladesh, 1982).

Johansson, E., Long, N. H., Diwan, V. K. & Winkvist, A. Attitudes to compliance with tuberculosis treatment among women and men in Vietnam. *Int J Tuberc Lung Dis 3,* 862-868 (1999).

Kirsch, C. M., Wehner, J. H., Jensen, W.A., *et al.* Tuberculosis otitis media. *South Med J 88,* 363-366 (1995).

Maat, R. History and physical: evaluating a patient suspected to have TB. (ARC handout, 1982).

Maranetra, K. N. Quinolones and multidrug-resistant tuberculosis. *Chemotherapy 45,* 12-18 (1999).

Marshall, J. B. Tuberculosis of the gastrointestinal tract and peritoneum. *Am J Gastroenterol* **88**, 989-999 (1993).

Martinez, E., Collazos, J. & Mayo, J. Hypersensitivity reactions to rifampin. Pathogenetic mechanisms, clinical manifestations, management strategies, and review of the anaphylactic-like reactions. *Medicine 78,* 361-369 (1999).

Matz, G. J. Aminoglycoside cochlear ototoxicity. *Otolaryngol Clin North Am 26,* 705-712 (1993).

McHutchison, J. G. Differential diagnosis of ascites. *Semin Liver Dis 17,* 191-202 (1997).

Menzies, R. & Vissandjee, B. Effect of bacille Calmette-Guerin vaccination on tuberculin reactivity. *Am Rev Respir Dis 145,* 621-625 (1992).

Menzies, D. Effect of treatment on contagiousness of patients with active pulmonary tuberculosis. *Infect Control Hosp Epidemiol* **18**, 582-586 (1997).

Miles, S. H. & Maat, R. B. A successful supervised outpatient short-course tuberculosis treatment program in an open refugee camp on the Thai-Cambodian border. *Am Rev Respir Dis 130,* 827-830 (1984).

Moore, M., Onorato, I.M., McCray, E. & Castro, K.G. Trends in drug-resistant tuberculosis in the United States, 1993-1996. *JAMA 278,* 833-837 (1997).

Mudido, P. M., Guwatudde, D., Nakakeeto, M.K., *et al.* The effect of bacille Calmette-Guerin vaccination at birth on tuberculin skin test reactivity in Ugandan children. *Int J Tuberc Lung Dis 3,* 891-895 (1999).

Murhekar, M. V., Kulkarni, H. R., Zodpey, S. P. & Dehankar, A. G. Effectiveness of mass neonatal BCG vaccination in the prevention of pulmonary tuberculosis: a case-control study in Nagpur, India. *Tuber Lung Dis 76,* 545-549 (1995).

Noble, R. C. Infectiousness of pulmonary tuberculosis after starting chemotherapy. *Am J Infect Control 9,* 6-10 (1981).

Peloquin, C. A. Pharmacology of the antiniycobacterial drugs. *Med Clin North Am 77.* 1253-1262 (1993).

Petrini, B. & Hoffner, S. Drug-resistant and multidrug-resistant tubercle bacilli. *Int J Antimicrob Agents 13,* 93-97 (1999).

National Tuberculosis Programme. TB control: concern for all (Cambodia National Tuberculosis Programme, Phnom Penh, 1998).

Rajeswari, R., Balasubramanian, R., Munigandi, M. *et al.* Socio-economic impact of tuberculosis on patients and family in India. *Int J Tuberc Lung Dis* **3**, 869-877 (1999).

Ramadan, H. H., Tarazi, A. E. & Baroudy, F. M. Laryngeal tuberculosis: presentation of 16 cases and review of the literature. *J Otolaryngol* 22, 39-41 (1993).

Rieder, H. L., Snider, D. E., Jr. & Cauthen, G. M. Extrapulmonary tuberculosis in the United States. *Am Rev Respir Dis* **141**, 347-351 (1990).

Riley, R. L. Airborne infection. *Am J Med* 57, 466-475 (1974).

Rom, W. N. & Garay, S. M. (eds.) *Tuberculosis* (Little, Brown and Company, Boston, 1996).

Rossouw, J. E. & Saunders, S. J. Hepatic complications of antituberculous therapy. Q *J Med* 44, 1-16 (1975).

Sahn, S. A. & Neff, T.A. Miliary tuberculosis. *Am J Med* 56, 494-505 (1974).

Sahn, S. A. & lseman, M. D. Tuberculous empyema. *Semin Respir Infect* 14, 82-87 (1999).

Samb, B., Henzel, D., Daley, C.L., *et al.* Methods for diagnosing tuberculosis among in-patients in eastern Africa whose sputum smears are negative. *Int J Tuberc Lung Dis* 1, 25-30 (1997).

Saracoglu, O. F., Mungan, T. & Tanzer, F. Pelvic tuberculosis. *Int J Gynuecol Obstet 37,* 115-120 (1992).

Sbarbaro, J. A. Compliance: inducements and enforcements. *Chest* 76, 750-756 (1979).

Sbarbaro, J. A. Skin testing in the diagnosis of tuberculosis. *Semin Respir Infect* 1, 234-238 (1986).

Sbarbaro, J. A. The patient-physician relationship: compliance revisited. *Ann Allergy* 64, 325-331 (1990).

Sehgal, V. N. Cutaneous tuberculosis. *Dermatol Clin* 12, 645-653 (1994).

Sepkowitz, K. A. How contagious is tuberculosis? *Clin Infect Dis* 23, 954-962 (1996).

Sivakumaran, P., Harrison, A. C., Marschner, J. & Martin, P. Ocular toxicity from ethambutol: a review of four cases ancl recommended precautions. N Z *Med J* **11**1,428-430 (1998).

Skolnik, P. R., Nadol, J. B., Jr. & Baker, A. S. Tuberculosis of the middle ear: review of the literature with an instructive case report *Rev Infect Dis* 8, 403-410 (1986).

Starke. J. R., Jacobs, R. I. & Jereb, J. Resurgence of tuberculosis in children. *J Pediatr* **120**, 839-855 (1992).

References

Starke, J. R. Tuberculosis: an old disease but a new threat to the mother, fetus, and neonate. *Clin Perinatol* 24, 107-127 (1997).

Steadman, W. *Understunding tuberculosis toduy* (1980).

Steele, M. A., Burk, R. F. & DesPrez, R. M. Toxic hepatitis with isoniazid and rifampin. A meta-analysis. *Chest* **99,** 465-471 (1991).

Sutherland, A. M. Gynaecological tuberculosis: analysis of a personal series of 710 cases. *Aust* N Z *J Obstet Gynuecol* 25, 203-207 (1985).

Temmerman, W., Dhondt, A. & Vandewoude, K. Acute isoniazid intoxication: seizures, acidosis and coma. *Actu Clin Belg* 54, 211-216 (1999).

Trebucq, A. Should ethambutol be recommendecl for routine treatment of tuberculosis in children'? A review of the literature. *Int J Tuberc Lung Dis* **1,** 12-15 (1997).

Tuberculosis Research Centre (ICMR) Fifteen vear follow up of trial of BCG vaccines in south India for tuberculosis prevention. *Indian J Med Res* 110, 56-69 (1999).

van Kie, A., Warren, R.M., Beyers, N., *et al.* Exogenous reinfection as a cause of recurrent tuberculosis after curative treatment. N *Eng J Med* 341, 1174-1179 (1999).

Viallard, J.F. & Blanco, P. lmages in clinical medicine. Tuberculous meningitis. N *Eng J Med* 341. 1197 (1999).

Weerakiet, S., Rojanasakul, A. & Rochanawutanon, M. Female genital tuberculosis: clinical features and trend. *J Med Assoc Thai* 82, 27-32 (1999).

Weiss, K. L & Addington, W. W. Tuberculosis: poverty's penalty. *Am I Respir Crit Care Med 157,* 1011 (1998).

Wilkinson, D., Squires, S.B., Garner, P. Effect of preventive treatment for tuberculosis in adults infected with HIV: systematic review of randomised placebo controlled trials. *BMJ* **317**, 625-629 (1998).

Yagi, M., Kawabata, I., Izaki, S. & Hosako, Y. Primary tuberculosis of the nasopharynx with erythema induratum of Bazin. *ORL J Otorhinolaryngol Relat Spec* **56**, 291-294 (1994).

Zodpey, S. P., Shrikhande, S. N., Maldhure, B. R., Vasudeo, N. D. & Kulkarni, S. W, Effectiveness of Bacillus Calmette Guerin (BCG) vaccination in the prevention of childhood pulmonary tuberculosis: a case control study in Nagpur, India. *Southeast Asian J Trop Med Public Health* **29**, *285-288* (1998).

Zuger, A. & Lowy, F. D. in *Tuberculosis* (eds. Rom, W. N. & Garay, S. M.) 541-556 (Little, Brown and Company, Boston, 1996).

The Authors

SOK THIM *is the executive director and a co-founder of the Cambodian Health Committee. He served as the director of the American Refugee Committee TB program from 1987 to 1989 and us TB coordinator for the United Nations Border Relief Organization from 1990 to 1991 on the Thai-Cambodian border.*

ANNE GOLDFELD *is an Assistant Professor of Medicine at Harvard Medical School and Investigator at The Center for Blood Research in Boston. She served as medical coordinator of the American Refugee Committee's program at Site II on the Thai-Cambodian border in 1989–90 and is a co-founder of the Cambodian Health Committee*

EUNICE TSAI, *a medical resident at Stanford University Hospital, has worked with the Cambodian Health Committee and participuted in studies of genetic susceptibility to tuberculosis in Cambodia.*

STEVE MILES *is Professor of Medicine at the University of Minnesota where he works on issues of bioethics and geriatrics. As medical coordinator for the American Refugee Program on the Thai-Cumbodian border, he initiated the TB treatment program at the Thai-Cambodian border in 1981.*

All drawings are by **SOKHA**. *The photos on pages 25 und 118 are by* **DEBBIE WEBBER**, *and the photo on page 113 is by* **CHRIS DASCHER.** *All other photos are by* **ANNE GOLDFELD**