# Hansen's Disease

## in NWFP, Pakistan

## &

## Afghanistan

## for comedical workers

PMS (Peshawar-kai (Japan) Medical Services)

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Photographed by Shigeo Matsumoto

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# Contents

Mountainous area in northern Pakistan


Bazaar in Peshawar

# Preface

You may think that a guidebook like this is not needed since numerous books about leprosy (Hansen's disease) have been already published. However, most of the guidebooks available in Peshawar in the North West Frontier Province (NWFP) of Pakistan, or those used in Afghanistan, have the disadvantage of being either translated versions or based on cases in other countries, making them at times unsuitable for use in the actual situations found on the ground.

In contrast, this guidebook uses case photographs that have been carefully selected from a set of 4,000 shots taken in the Peshawar area from 1984 onwards by Mr. Shigeo Matsumoto (a laboratory technician who previously worked for the National Oku Komyoen Leprosarium, Japan). The guidebook also describes the situation in NWFP and north-eastern Afghanistan in an easily understandable way by making full use of the photographs as well as the textbooks used in the training of Peshawar-kai Medical Services (PMS) nurses and laboratory technicians. Translated texts on diseases, including Hansen's disease, describe cases, situations and treatments in other countries are not all applicable to NWFP and north-eastern Afghanistan. Available examination procedures and treatments, the patients' description of symptoms, and common symptom patterns, as well as complications in these areas, are different from those reported in cases found in other countries. In particular, it is the treatment approaches seen in Afghanistan and NWFP that are the most peculiar to the local situation. Hence the urgent need to publish this guidebook.

In Pakistan, the Marie Adelaide Leprosy Centre has since 1984 been very successful in carrying out leprosy control programmes as part of the provincial health care programme, with the co-operation of the NWFP government. However, interest in the disease has abruptly waned since the 1990s despite there still being no sign of a significant decline in new cases. In fact there are quite a lot of relapsed cases. Even MDT (Multiple Drug Therapy), which has been hailed as the new wonder drug regimen to treat the disease, cannot always solve all the problems of each individual patient.

Against such a background, this guidebook ought to be valuable to all medical professionals, especially those in the Northwest region of Pakistan and in Afghanistan. It focuses on practical measures chosen as being

appropriate to the actual conditions, avoiding unnecessary detail.

Our past twenty-year experience in treating leprosy in Pakistan and Afghanistan has enabled this book to come into being. In those two decades we have made it our policy never to draw attention to ourselves but instead to back up the existing institutions. We hope that we will continue to stay in these areas to support the local staff and that this guidebook can in some small way help relieve people's suffering.

Tetsu Nakamura
Executive Director,
Peshawar-kai Medical Services ( PMS ) Hospital

Photographed by Shigeo Matsumoto
Former laboratory technician,
National Oku Komyoen Leprosarium

October, 2004

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# I.
# Outline of Hansen's Disease (Leprosy)

Hansen's disease is a chronic infectious disease caused by Mycobacterium leprae, which is closely related to tubercle bacillus. The disease mainly affects the peripheral nerves and the skin. Its infectious capacity is low and it is not heritable. If treated at an early stage, it can be completely cured. However, if it is not treated promptly and allowed to develop, other symptoms such as limb paralysis and/or eye disorders appear. It then becomes difficult to treat and may require not only internal medicine but also reconstructive surgery, plastic surgery or ophthalmologic treatment.

Professional expertise is required to treat the disease, and of the three million patients receiving medical treatment in the world, the largest number is found in India. According to the World Health Organisation (WHO) in 2002, about 600,000 to 700,000 new cases are reported every year, and the number is increasing.

Pakistan has 50,000 cases including 7,000 cases in NWFP (in 2002). These figures, however, are only the registered cases. Although more than 200 new cases are detected every year in Peshawar alone, in reality, the exact number of cases or prevalence rate is unknown. The WHO warns that a prevalence rate of more than two out of every 10,000 people means the situation is critical. The rate varies from region to region and is particularly high in mountainous areas-the region from where a lot of patients arrive at our hospital.

In Afghanistan there are no reliable statistics. The Hazarajad region (including Bamiyan and other provinces) in the central part of the Hindu Khush Ranges, and the northeast mountainous areas (Kunar and Badakhshan Provinces), are known as hot spots with a high incidence of leprosy. The patients in Hazarajad tend to go to Kabul, to Quetta and then to Karachi, while patients in the northeast region (Kunar Province) come to Peshawar via Jalalabad. In NWFP, hot spots with a high incidence of the disease are found in Swat, Dir, Bajour and Kohistan. Cases are sometimes seen even in Chitral. In general, more cases are found in villages in cold mountainous areas than in urban and lowland areas.

Today Hansen's disease is curable, but deep-rooted prejudices still remain. Even some medical staff do not fully understand the disease. The number of cases of the disease is certainly less than that of other infectious diseases, but it has diverse complications, which will be discussed later. Occasionally, some advanced cases need to be cared for throughout their lives. For example, some patients may have to take medicine for long periods. This is not easy for those who live in remote areas. Female patients in particular find it hard to take medicine and be regularly examined because it is difficult for them to travel to medical institutions. Furthermore, the recent increase in drug resistant cases and relapses after treatment with MDT, coupled with the shortage of medical doctors and nurses engaged in this disease, have made the problems more difficult to address.

Long-term commitment is required for Hansen's disease control and there are no easy solutions. However, if medical staff regard Hansen's disease as a special disease, and treat patients differently from patients of other diseases, then such patients are increasingly discriminated against by ordinary members of society, resulting in them facing additional difficulties in living in the community. It is vital that all the local medical staff acquire the correct knowledge about the disease and that medical institutions treating complications of the disease keep functioning for a long time. Fortunately, the notorious segregation policy seen in the West has not been adopted in Pakistan or Afghanistan.

Since the name of the disease, "leprosy", may give rise to misunderstanding and prejudices, the disease has come to be called "Hansen's disease" worldwide. In PMS Hospital, we have also started to instruct staff to avoid treating the patients differently and to call the disease HD (Hansen's disease) rather than leprosy.

# II.
# Hansen's Disease and Mycobacterium Leprae

Although "leprosy" is the correct medical term, the name of "Hansen's disease" has recently become common to avoid the prejudice and discrimination that have been associated with the word leprosy in the past. When this disease is explained to the staff in PMS Hospital, it is summarised by using the following "3Cs".

- Chronic bacterial infection, affecting mainly skin and peripheral nerves
- Caused by Mycobacterium leprae
- Curable with proper treatment

Knowledge of the characteristics of leprosy bacilli or Mycobacterium leprae (M. leprae) helps in understanding the disease. M. leprae is a kind of mycobacterium and closely related to the tubercle bacillus. The Ziel-Nielsen staining method is used as in tuberculosis. It is difficult to differentiate the two bacilli with a microscope, but they do have slightly different characteristics. M. leprae has not yet been grown in cell culture.

M. leprae characteristics can be simplified as follows.
1. Multiply at low temperatures
2. Multiply significantly slowly ( very long generation time)
3. Symptoms depend on the strength of a patient's immunity
4. Infection limited to humans

Because of its low multiplication temperature (optimum temperature for breeding is 33℃), M. leprae damages body surface organs, e.g. skin, peripheral nerves, eyes and testicles, whereas tuberculosis does not. Hansen's disease has a long incubation period-because of its low multiplication speed-and develops gradually. The following comparison of cell division time (generation time) with other bacilli clearly demonstrates this characteristic.

- Shigella dysenteriae: 5 to 10 minutes
- Tubercle bacillus: 10 to 20 hours
- Leprosy bacillus: 10 to 14 days

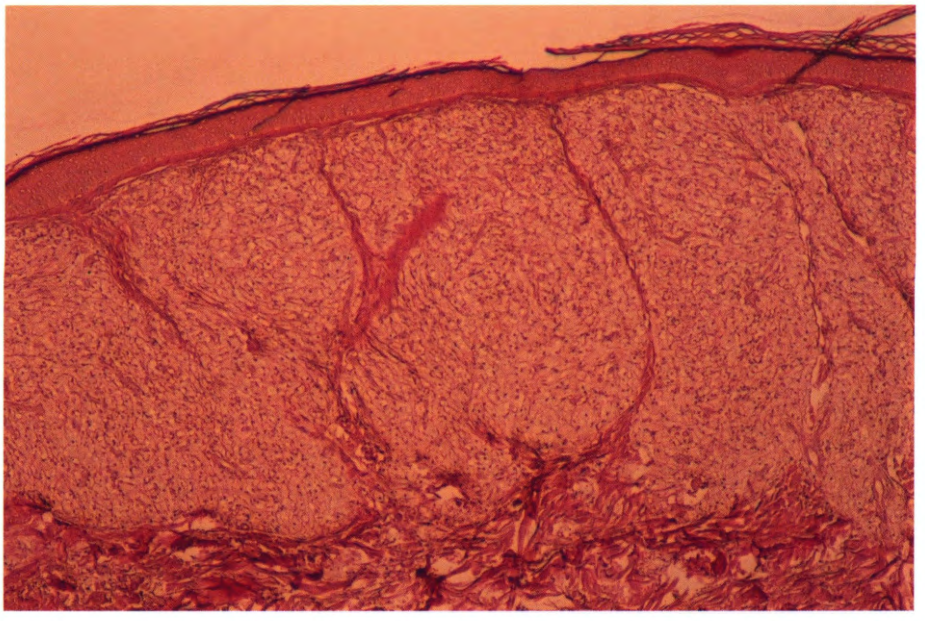
It only takes several hours for dysentery bacilli to reach number levels capable of developing symptoms. By contrast M. leprae requires several years to do so. This symptom-free time is called the incubation period. For this disease, symptoms usually develop 3 to 5 years after infection and a period of more than 20 years has been reported in some cases.

The development of symptoms depends on the strength of the infected person's immunity, as is the case with other bacterial infectious diseases. For instance, if tuberculosis infects people under the same external conditions, the symptoms vary from no symptoms or only minor symptoms — such as spontaneous curing with only hilus infiltration or pleural effusion — to severe cases like miliary tuberculosis or tuberculosis meningitis. The same can be said of Hansen's disease. Most people have sufficient immunity against the disease and do not develop symptoms of the disease even if infected. The severity of the symptoms of those people who do develop them largely depends on their immunity.

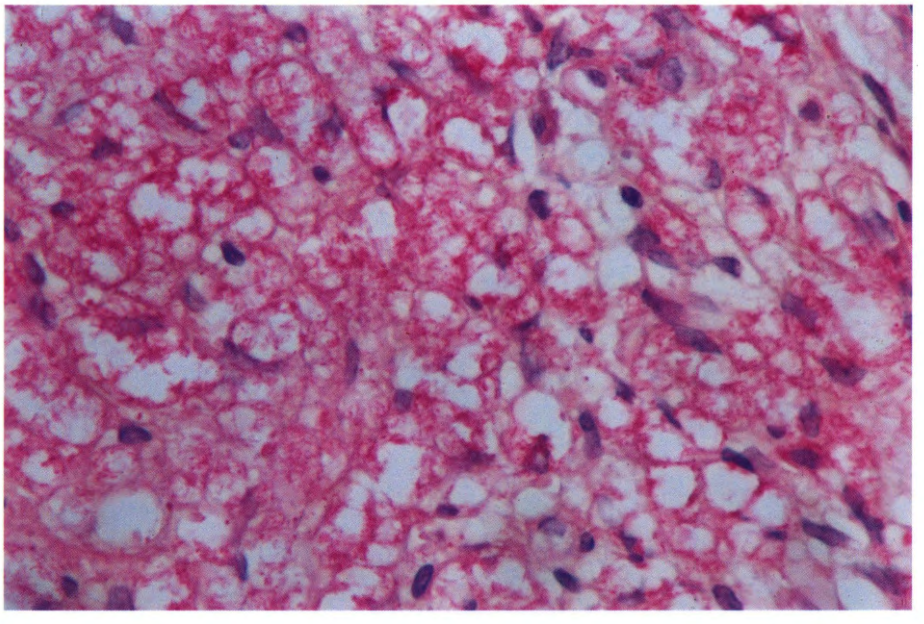
Development types are classified by the symptoms caused by cell-mediated immunity as follows:

- Sufficient cell immunity: No development (latent infection)
- Strong immunity: Symptoms appears on a single part of the skin and spontaneously cure (Tuberculoid type)
- Weak immunity: Symptoms appear on multiple parts of the skin and multiple symptoms appear on peripheral nerves (Borderline type)
- No immunity: Symptoms appear diffusely over the whole skin (Lepromatous type)

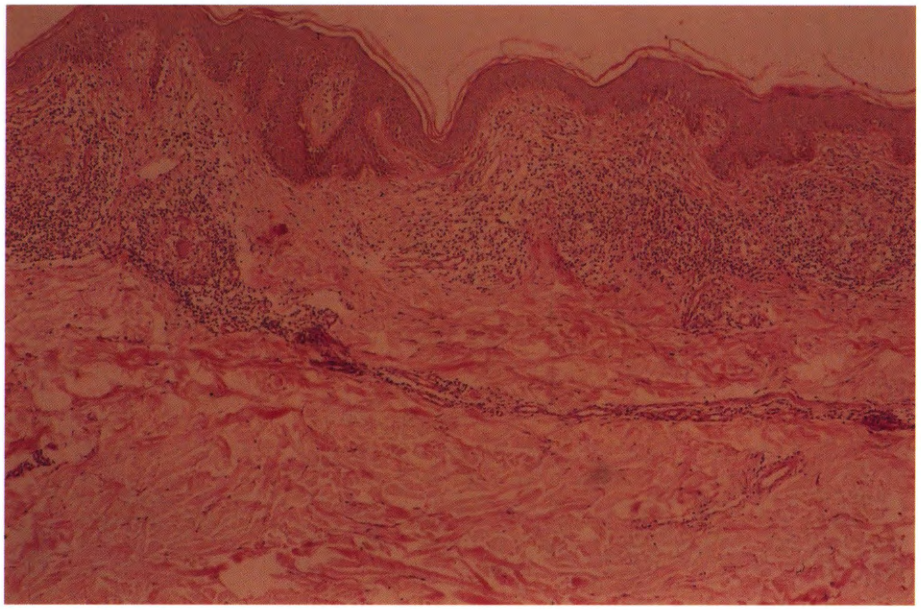
As regards other species, the infection of armadillos has been confirmed. Experiments have proved that chimpanzees and mice or rats, which don't have immunity, can also be infected by artificial inoculation of the bacillus. However, in general, humans are the only source of infection and the disease is transmitted between humans only. Thus early detection and treatment are important preventive measures.



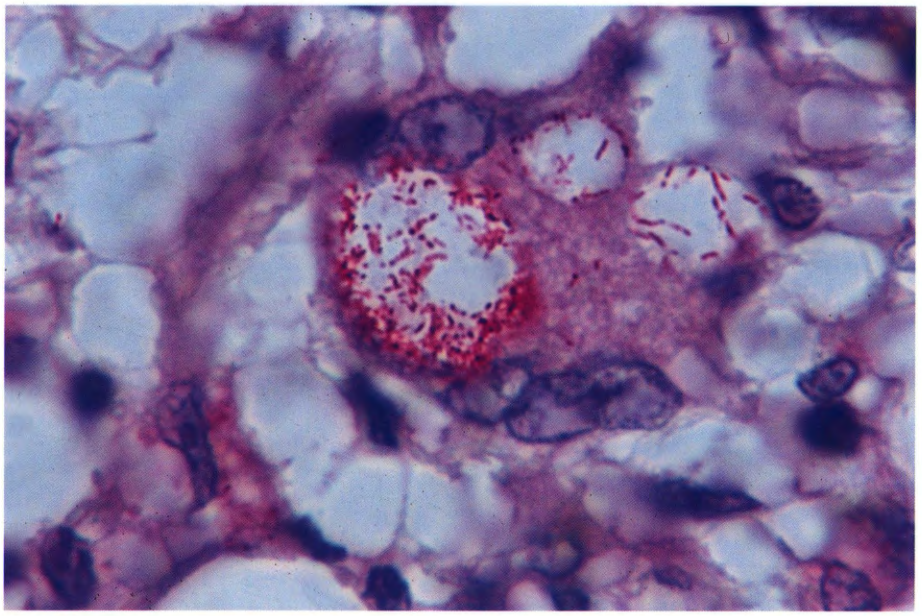
Picture 2-1 (HE stain)
A lesion of the Lepromatous type (skin biopsy). Cells that contain a huge quantity of Mycobacterium leprae are concentrated in the epitheloid cell layer.



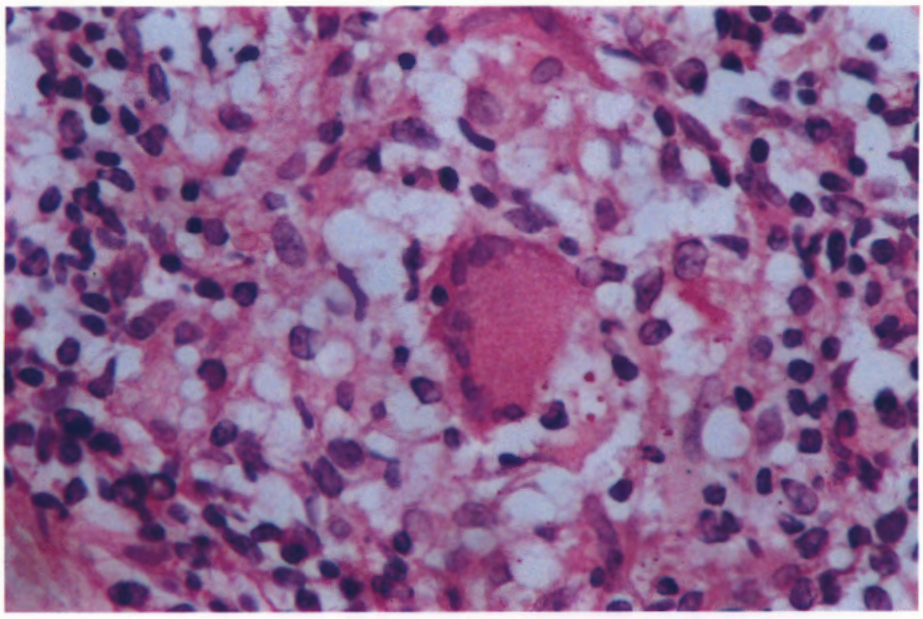
Picture 2-2 (HE stain)
A magnified image of the above picture. Many foam cells are observed. These cells are phagocytes and each cell is full of M.leprae. The foam appearance is due to the bacteria that become colourless after staining and is a characteristic of the multi-bacilli type.



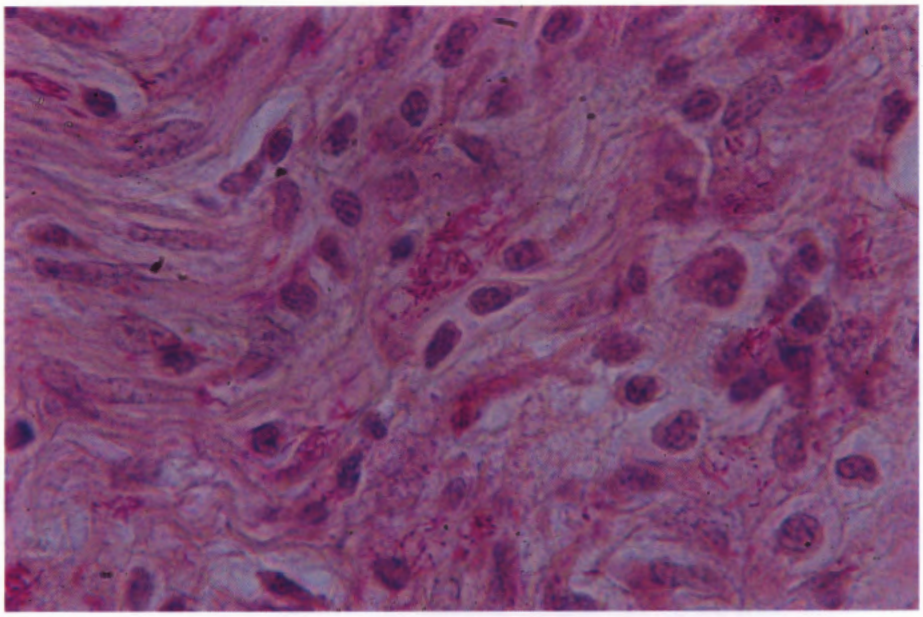
Picture 2-3 (HE stain)
Skin biopsy in a Borderline-type case. Granulomatous lesion with lymphocytic infiltration. Further infiltration in cells would be observed for the tuberculoid type. The borderline type is sometimes confused with the ENL reaction, which also shows a similar picture.



Picture 2-4 (Matsumoto's modified method)
Many acid-fast bacilli are observed in the cells, which look like foam.



Picture 2-5 (HE stain)
A magnified image of the above picture. Cells surrounded by many nuclei (Rosetta Cells) are commonly observed in the Borderline type. In case of the Tuberculoid type, the cells are larger (giant cells) and tend to show signs of caseous necrosis.



Picture 2-6 (HE stain)
Many Mycobacterium leprae are seen, which have been phagocitized by epitheloid cells, and show granulomatous changes.

## Importance of Bacteriological Examination (Skin-Smear Test)

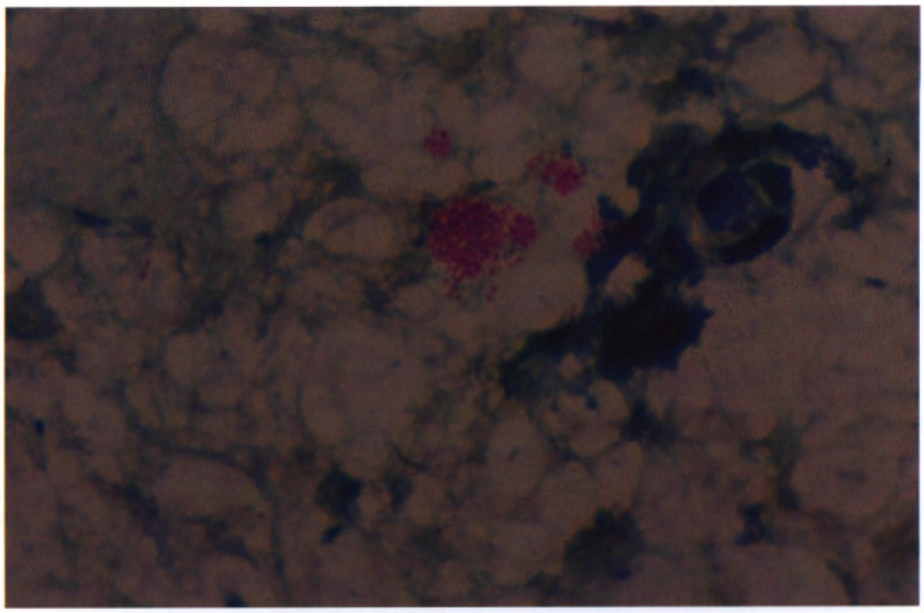
The most reliable method of detecting M. leprae is by a skin-smear examination. First, tissue fluid of the skin is removed with a blade and placed on a slide. Second, the smear is stained using an acid-fast bacilli (AFB) stain method. Lastly, the organisms are counted under a microscope. Ideally, the skin should have no blood in it. The skin should be lightly pinched to prevent blood staining the specimen. Then a shallow incision is made with the tip of a scalpel blade. Only tissue fluid or lymph should be removed and scraped. This is not easy to do without experience and training. Poor preparation of samples for examination often makes deciding on appropriate treatment difficult.

With appropriate staining, M. leprae can be detected easily with a microscope. The organism is stained in a beautiful vivid red colour against a background of methylene blue. The smear should have no contamination of mould and hair and so forth, for proper examination. Since Peshawar and Afghanistan are dusty, stains should be routinely filtered to avoid contamination with dust or crystals.

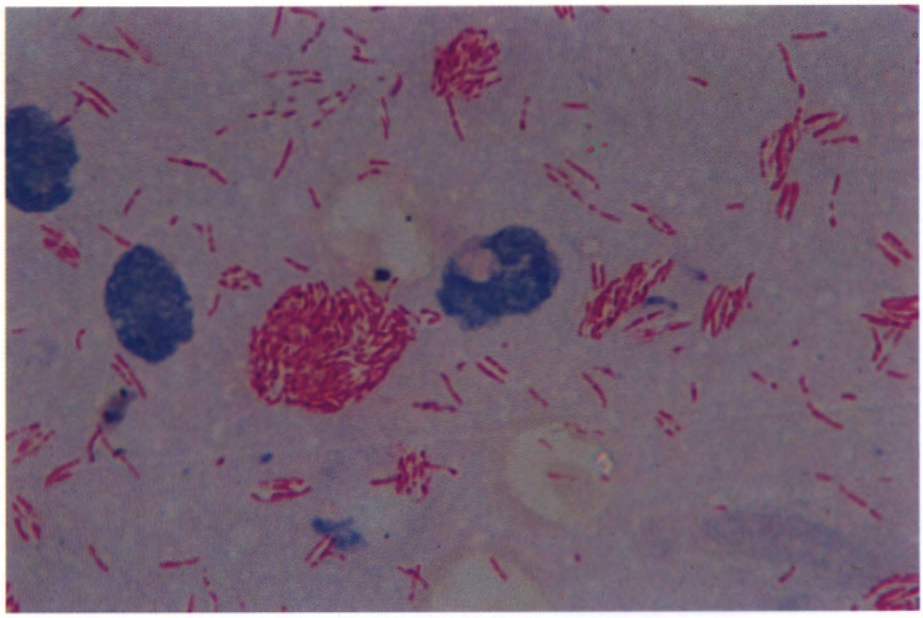
In PMS Hospital, the examination results are reported as Ridley's Bacteriological Index (BI). The results vary depending on the regions of the body sampled and the skills of the laboratory technicians. The WHO simply classifies Hansen's disease into two types namely, paucibacillary leprosy type (PB type) and multibacillary leprosy type (MB type) – a convenient classification for MDT. This simple classification is probably the most practical for NWFP and Afghanistan.

M. leprae do not disappear so soon even after starting chemotherapy. Dead bacilli remain in the body for a fairly long period. On average, it takes several years for them to become negative. Therefore positive cases are not always infectious.

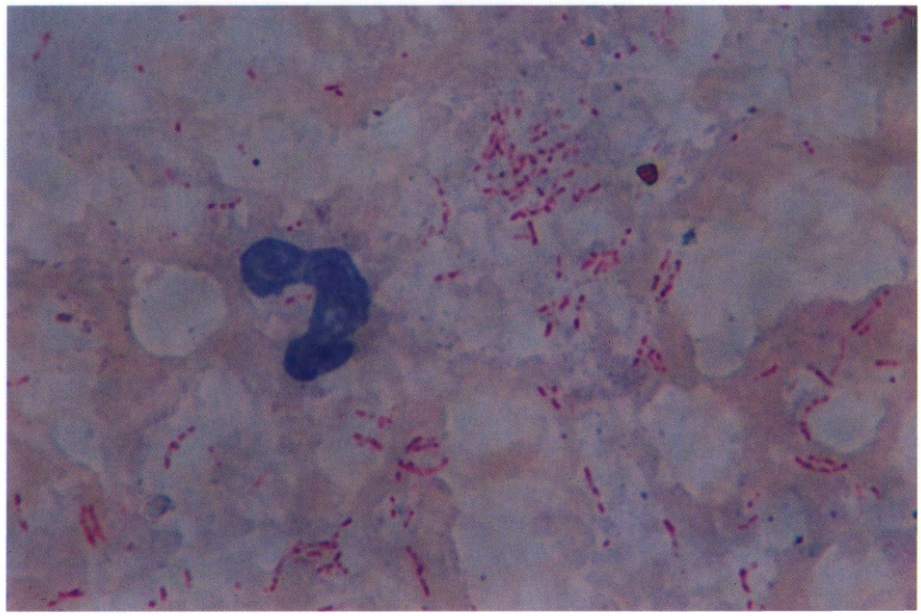
It is possible to estimate whether bacilli are active or dead from their shapes. Active, rod-shaped bacilli stain solid. On the other hand, dead bacilli begin to fragment within several weeks of starting treatment and are granulated with a gradually fading colour under staining. Morphological indices can be used in order to evaluate these changes, but it is not practical clinically. In our institution, just the comments of the laboratory technician are added to the results.



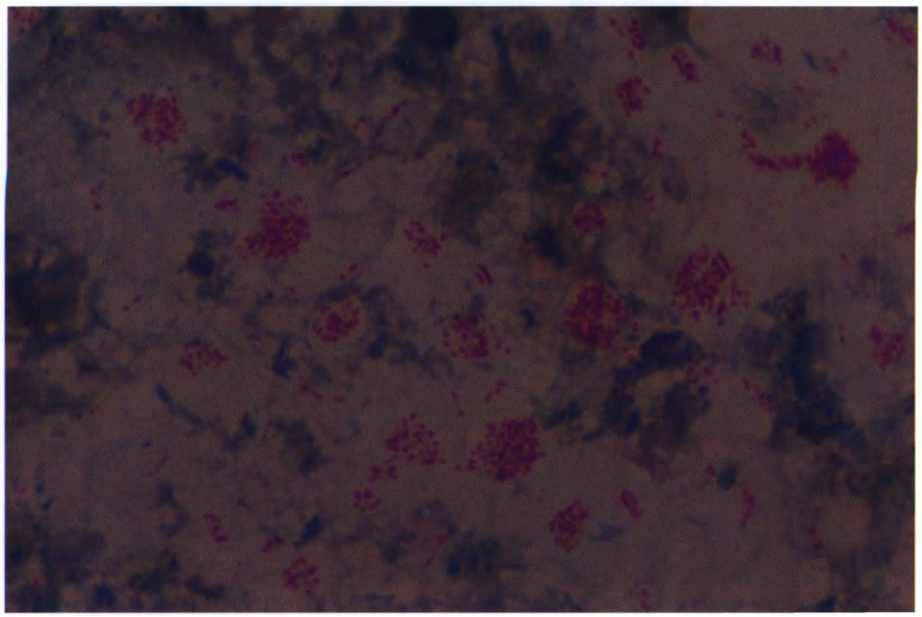
Picture 2-7 (Matsumoto method of acid-fast bacilli stain)
Solid bacilli in cells. A case of lepromatous type before treatment. The bacilli are homogeneously and deeply stained.



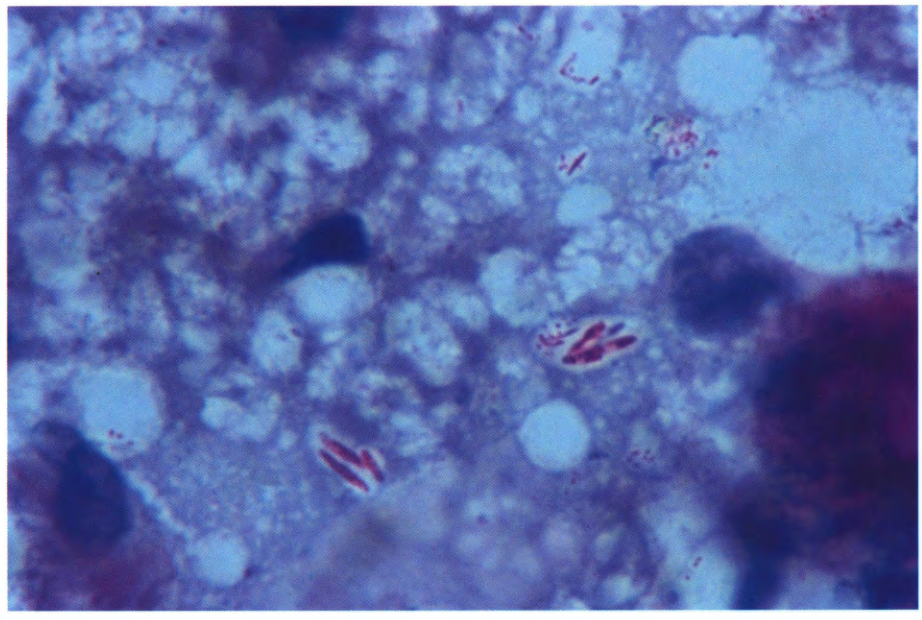
Picture 2-8 (Ziel-Nielsen stain)
Smear in a Lepromatous type. Spherical clusters, which are called globi, appear multiplied and swollen in the phagocytes. They are often observed in the multi-bacilli type. This picture was taken several months after treatment. Fragmentation has already begun.



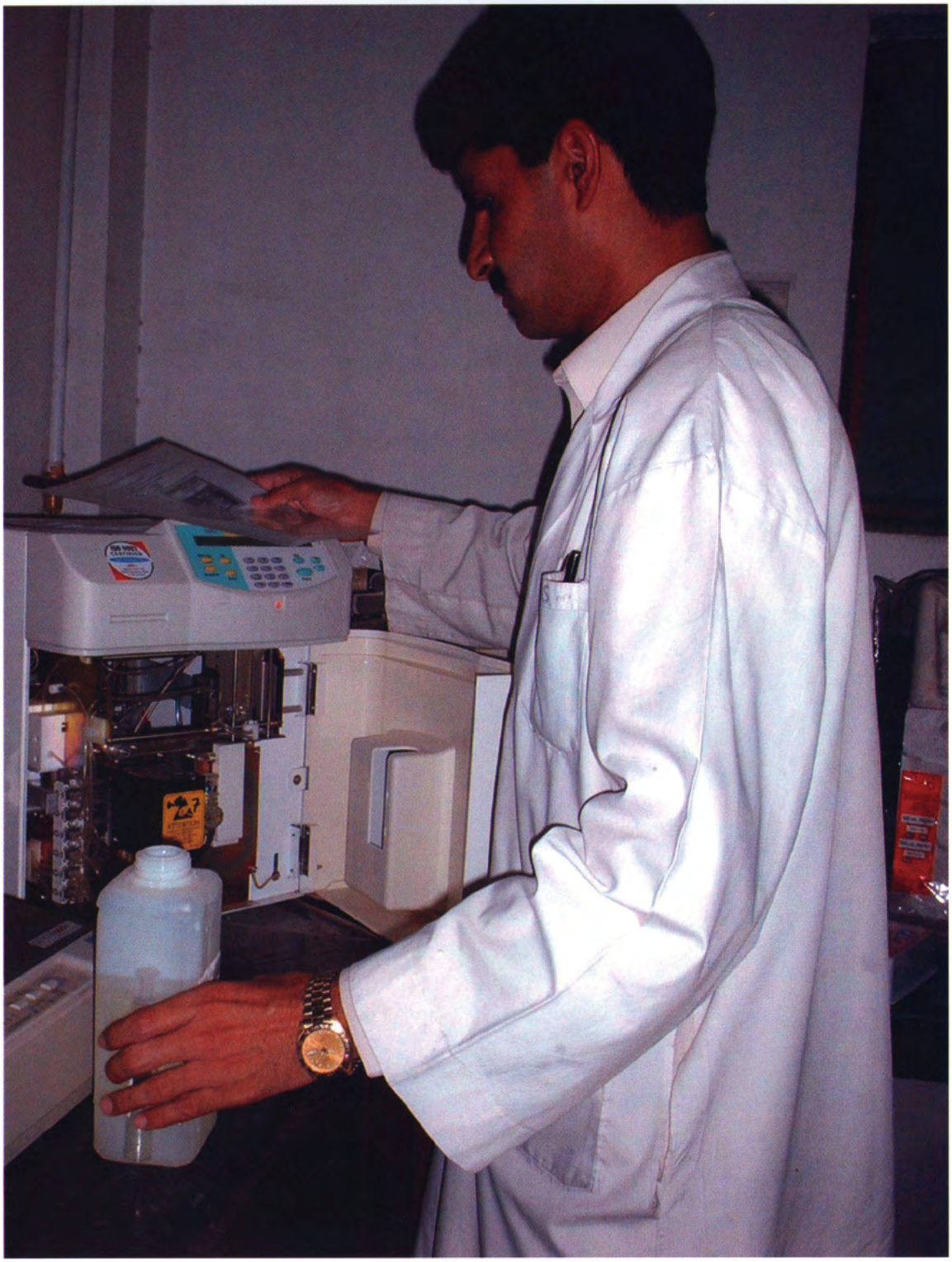
Picture 2-9 (Ziel-Nielsen stain)
Smear in a multi-bacilli type case. Bacilli are weakly stained and granulation has begun.



Picture 2-10 (Ziel-Nielsen stain)
Smear in multi-bacilli type case. Numerous globi are observed. This case had no symptoms other than pale red coloured erythema. As this picture was taken one year after starting treatment, the bacilli have granulated.



Picture 2-11 (Ziel-Nielsen stain)
Smear in multi-bacilli type case. Giant bacilli are sometimes seen in Peshawar. According to Mr. Matsumoto, they are on rare occasions observed in India, too. The reason is unknown.



# III.
# Infection and Development of the Disease, and Epidemiology

Infection and development of the disease have been discussed a little in the previous chapter. In summary, those who have enough cell-mediated immunity (CMI) do not develop the disease. The degree of immunity affects the severity of the symptoms. Most people do not develop symptoms even after being infected. Due to the long incubation period of more than 2 to 3 years, however, patients often do not realize they have become infected until symptoms are observed.

For a long time skin to skin contact was believed to be the main mode of transmission. However, this view has been doubted recently. Today the major route of infection is believed to be inhalation into the lungs like in tuberculosis. M. leprae are present in house-dust and in sleeping mats, and inhaled bacilli enter the body through the blood stream, reaching to surface organs like the skin (epidermis), peripheral nerves (Schwan Cells), testis and eyes, where they multiply easily. In fact, a high incidence is observed in certain families. For example, when conducting household surveys, new cases are often discovered in the same families.

The problems in NWFP and Afghanistan are that most cases are observed in poor villages in remote mountainous areas and that such patients do not visit medical institutions until their symptoms have severely progressed. In many cases it is difficult not only for the patients to visit medical institutions, but also for medical staff to visit and survey the families. Due to the long incubation period, regular surveys are required on a long-term basis. At present the number of registered cases is approaching 8,000, but the number of potential patients might be far larger.

The incidence of the disease is largely unaffected by either ethnicity or nationality. In NWFP, a high incidence is seen in Kohistan (Kohistani tribe), in Swat and Bajour agencies (Pashtun tribe), and in the northern Chitral district (Khowari tribe). In eastern Afghanistan, a significantly high incidence is observed in Kunar Province (Pashutun tribe), in Badakhshan Province (Tajik tribe), and in the Hazarajad region (Hazara tribe-located in the central part of the Hindu Khush Ranges) whereas lower incidence occurs

in the Nuristan tribe. The fact that all these areas are remote mountainous areas does not fully explain why they have such a high incidence of the disease. In urban areas, the incidence has dramatically dropped. It is clear that malnutrition and difficulty of access to medical institutions influence the incidence of the disease.

Male patients of Hansen's disease are observed more often than female ones. The ratio between male and female patients with the disease is 2:1 worldwide. In contrast, in Afghanistan and Peshawar, the ratio is 3:1, or 4:1 in some areas. This is largely because of the geographical condition, that makes it hard for patients to access proper medical institutes, and hard for staff to contact survey the patients' families. It is very difficult for people, especially women, to leave their homes to make a long trip.

The WHO has been committed to spreading MDT throughout the world since the early 1980s, contributing to the decrease in infectious cases everywhere. However, interest in Hansen's disease has rapidly waned since the 1990s and early detection efforts seem to have been stalled. This loss of interest, combined with both the appearance of medicine-resistant cases and an increase in relapsed cases, has made the disease as difficult to treat as tuberculoses.

# IV.
# Symptoms and Diagnosis

To diagnose Hansen's disease is not so difficult. With a simple examination, the disease can be not only diagnosed but also the disease type can be easily detected. We should always suspect the possibility of the disease and take precautions whenever we examine patients with skin conditions or suffering from paralysis. Early diagnosis and treatment of the disease are a great blessing to patients since they help prevent subsequent complications, which are difficult to treat.

## Major Criteria for Diagnosis

The following diagnostic criteria have been internationally adopted.
1) Presence of Mycobacterium leprae
2) Thickened peripheral nerves
3) Loss of sensation

If an individual shows more than two of these signs, s/he should be regarded as having Hansen's disease. However, according to our experiences, "long-lasting skin lesions without pain or itchiness" should be added as a fourth criterion. With some experience and training, medical staff can detect the disease type simply by the examining symptoms and the location of sensory disturbance on the skin.

A variety of skin lesions are seen, e.g. protruded lesions such as nodules and plaque, and macular lesions such as erythema or depigmented macula. From appearance alone it is hard to differentiate Hansen's desease cases from other skin diseases. For a more detailed explanation, please refer to other literature. The major indicators in diagnosing the disease are as follows: (See Table 1.)

(1) Long-lasting skin lesions without pain or itchiness should at first be suspected.
(2) Local skin lesions with loss of sensation can be diagnosed with certainty as the Tuberculoid type or a Borderline Tuberculoid type. Most skin

lesions of the Tuberculoid type occur at a single place.

(3) Diffuse skin lesions over the whole body with glove and stocking type anesthesia is a sign of a fairly advanced Lepromatous type. Loss of sensation is not seen in the early stages.

(4) Many patterns are seen in the Borderline-type lesions varing from those close to Tuberculoid type to those close to Lepromatous type. The central part of the lesion shows a tendency to heal. The characteristic features for this type are described in textbooks as “ring lesions”, “annular lesions” or “punched out lesions”, all of which indicate a tendency for “central healing”.

(5) In the skin smear many bacilli are observed for the Lepromatous type, whereas it is negative for the Tuberculoid type. For the Borderline type the skin smear varies depending on the degree of immunity.

Some experience is needed to diagnose thickened nerves. Extremely thickened nerves are diagnosed by inspection and palpation. Thickened nerves of the Borderline type are often irregularly distributed.

## Types of Hansen’s Disease

The following classification is widely used in the world. The types of Hansen’s disease can be regarded as a spectrum determined by the cell-mediated immunity of the individual.

- TT or Tuberculoid type: Strong cell immunity. Self-healing.
- BT or Borderline-Tuberculoid type: Borderline type close to the Tuberculoid type.
- BB or Pure Borderline type: Quite a high level of cell immunity remains.
- BL or Borderline-Lepromatous type: Borderline type close to the Lepromatous type.
- LL or Lepromatous type: Lack of cell immunity. Spread diffusely over the whole body.
- Ne or Pure Neuritic type: Only local nerves show symptoms without skin lesions.
- I or Indeterminate type: Small sized of skin lesions at an early stage of the disease. Self-healing.

There are further detailed classifications, but they are not very practical clinically. A test, given to specially trained staff showing various leprosy skin lesions, was answered correctly for the Tuberculoid and Lepromatous types.

Picture 4-1 Thickening of great auricular nerve. It is hard and elastic.

Picture 4-2
Thickening of great auricular nerve. It is sometimes hypertrophied as if they are nodes.

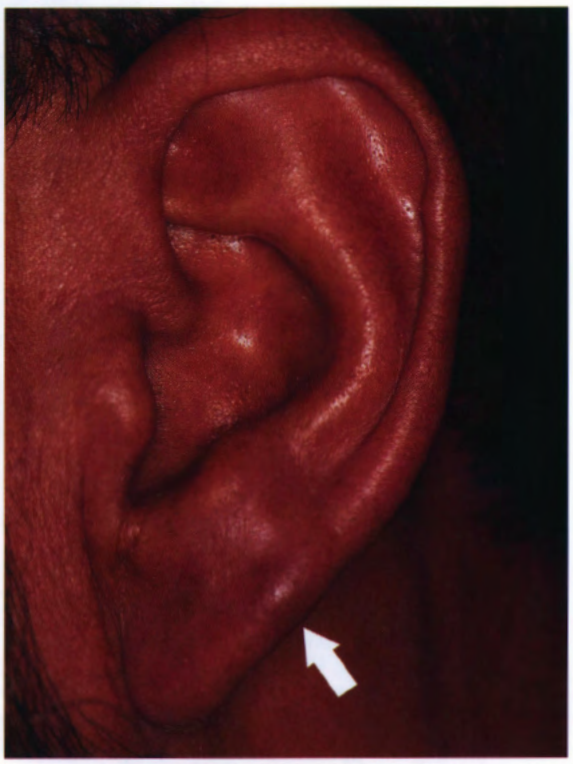
However, when shown the Borderline type, each staff member's answers were quite different from one to another's, according to their subjective opinions. Practically, if they can classify those cases as "the Borderline type close to the Tuberculoid case" or "the Borderline type close to the Lepromatous case", it's enough for clinical purposes. In practice the Ne type is difficult to diagnose or to differentiate from other neurological disorders. The I type is only occasionally found during family contact surveys and few patients with the condition come to the medical centres.

The Borderline type is quite common in NWFP and Afghanistan. Typical BB is rarely found because the immune condition of BB is unstable and BB easily shifts to BT or BL. The WHO uses two categories, PB (pauci-bacillary) and MB (multi-bacillary) types, as a convenient classification for MDT as shown in the following table.

| | tuberculoid type | borderline type | lepromatous type |
|---|---|---|---|
| Ridley | TT | BT BB BL | LL |
| WHO | PB | | MB |
| skin lesion | single, localized | multiple, asymmetrical tendency of central healing | diffusely on whole body |
| bacilli ( skin smear ) | (—) | (—) or (+) | (++) |
| sensory loss | localized on the skin lesion | often mononeuritis multiplex | gloves and stocking type at advanced stage |

**Table 1: Classifications by Lidley & WHO**

Picture 4-3
A 15-year-old male patient. Infiltrative lesion in a Lepromatous type. Loss of eyebrow (madarosis) is observed and the whole face looks swollen. Some cases in children were misdiagnosed as nephrotic syndrome. The result of a smear test is highly positive.

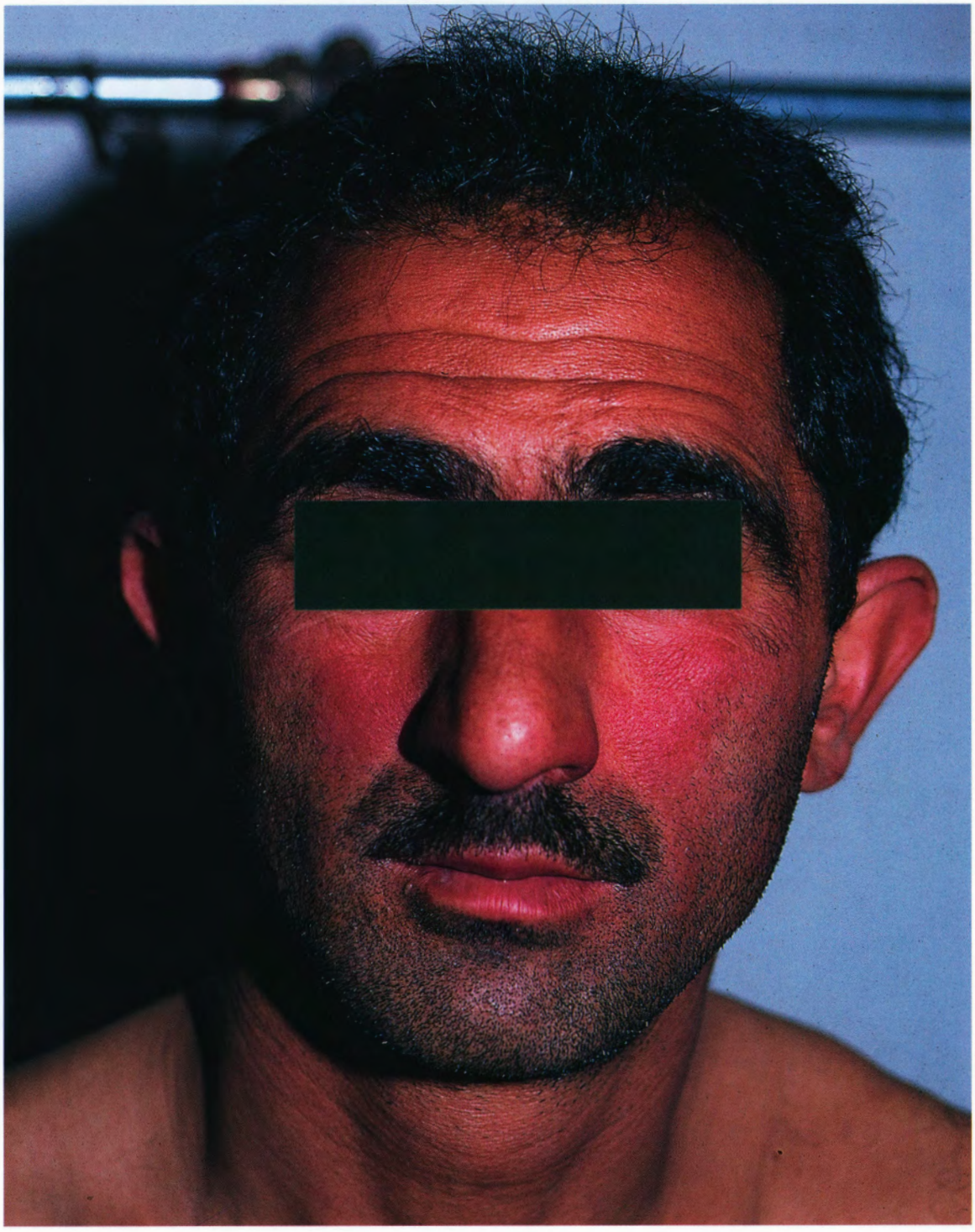


Picture 4-4
Small nodules are observed (indicated by the arrow). Because it is easy to detect bacilli in ear lobes, they are included as regions to investigate in a routine smear test.

Picture 4-5
A macular lepromatous lesion in a 55-year-old male patient. Diffuse macular lesions may be observed in a Lepromatous type. The patient was diagnosed as having "chronic allergic dermatitis" and had received long-term medication with steroids. He has suffered no loss of sensation. The result of a smear test gave a strong positive. Cases like this often tend to be misdiagnosed.

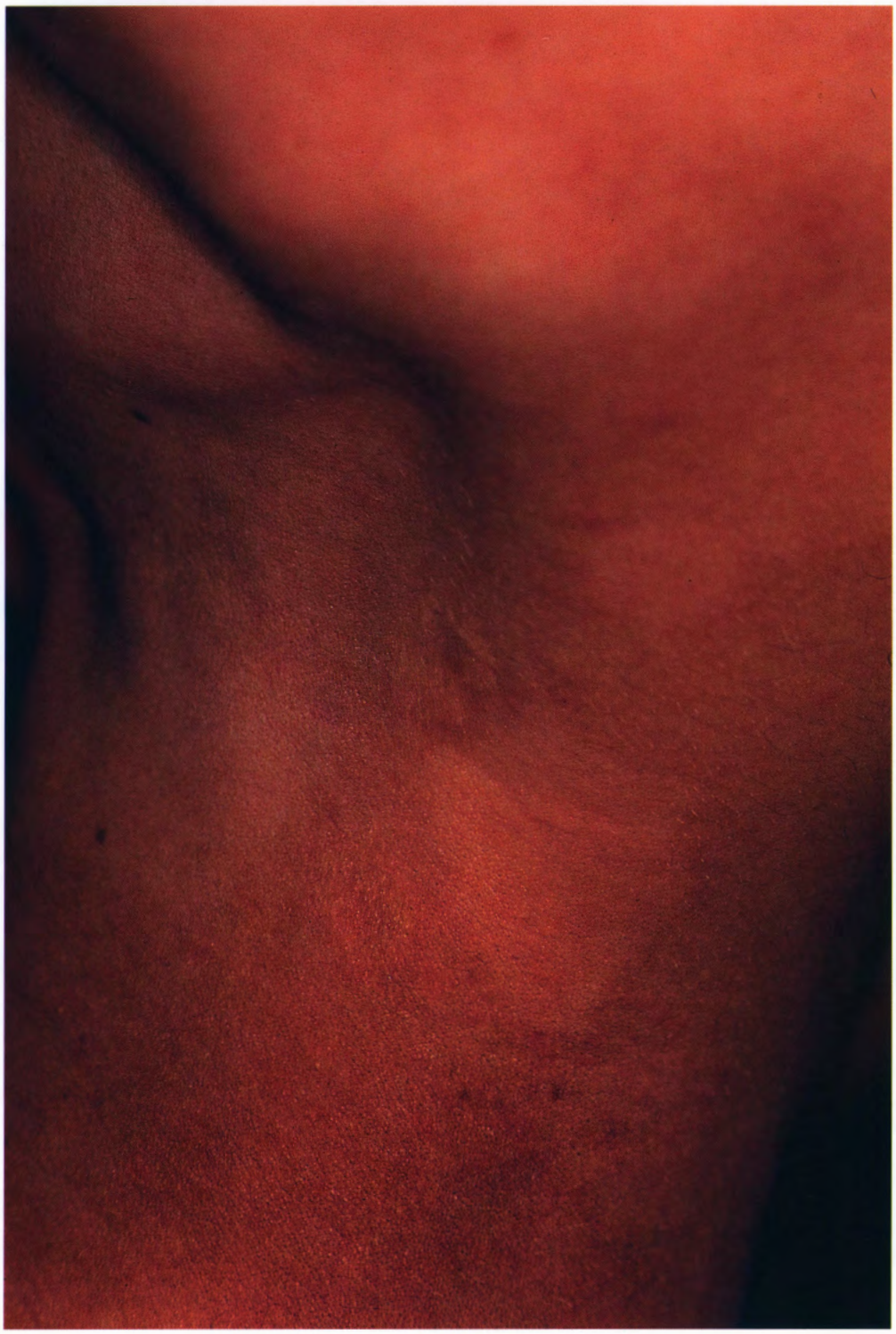
Picture 4-6
Plaque in a BL case. The whole lesion lifts up evenly and looks greasy. In most cases numerous bacilli are detected. When a case cannot be distinguished from the Lepromatous type or the Borderline type, it should be treated as a multiple-bacilli case.

Picture 4-7
Nodular lesion in Lepromatous type. A 60-year-old male patient. He visited our hospital to be examined after he had had treatment for "chronic dermatitis" for two years. The result of a smear test gave a strong positive. Small nodular lesions are scattered over the whole body and gynecomastia is observed. Fortunately, there were no other symptoms and he was completely cured four years later.

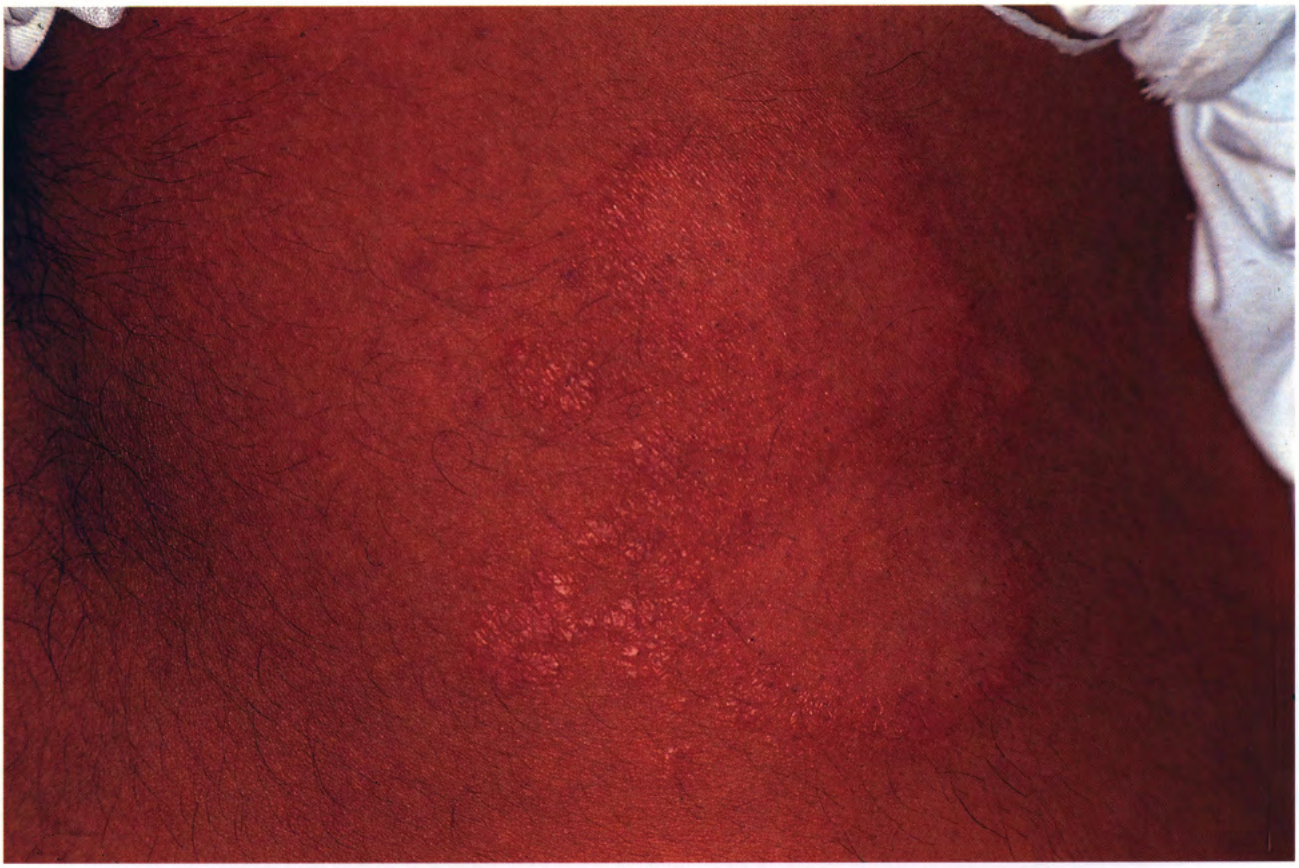


Picture 4-8
Erythema and infiltrative lesion on the face. A 35-year-old male patient. BL case. When the patient saw a doctor in the department of neurology for minor palsy on his right-hand fingers, he was diagnosed as having carpal tunnel syndrome and had an operation. He later consulted a physician because palsy developed even after the operation. He was suspected of having SLE (systemic lupus erythematosus) and had taken steroid medication. This is similar to butterfly erythema, but numerous Mycobacterium leprae were detected in the skin on the earlobes and cheeks.

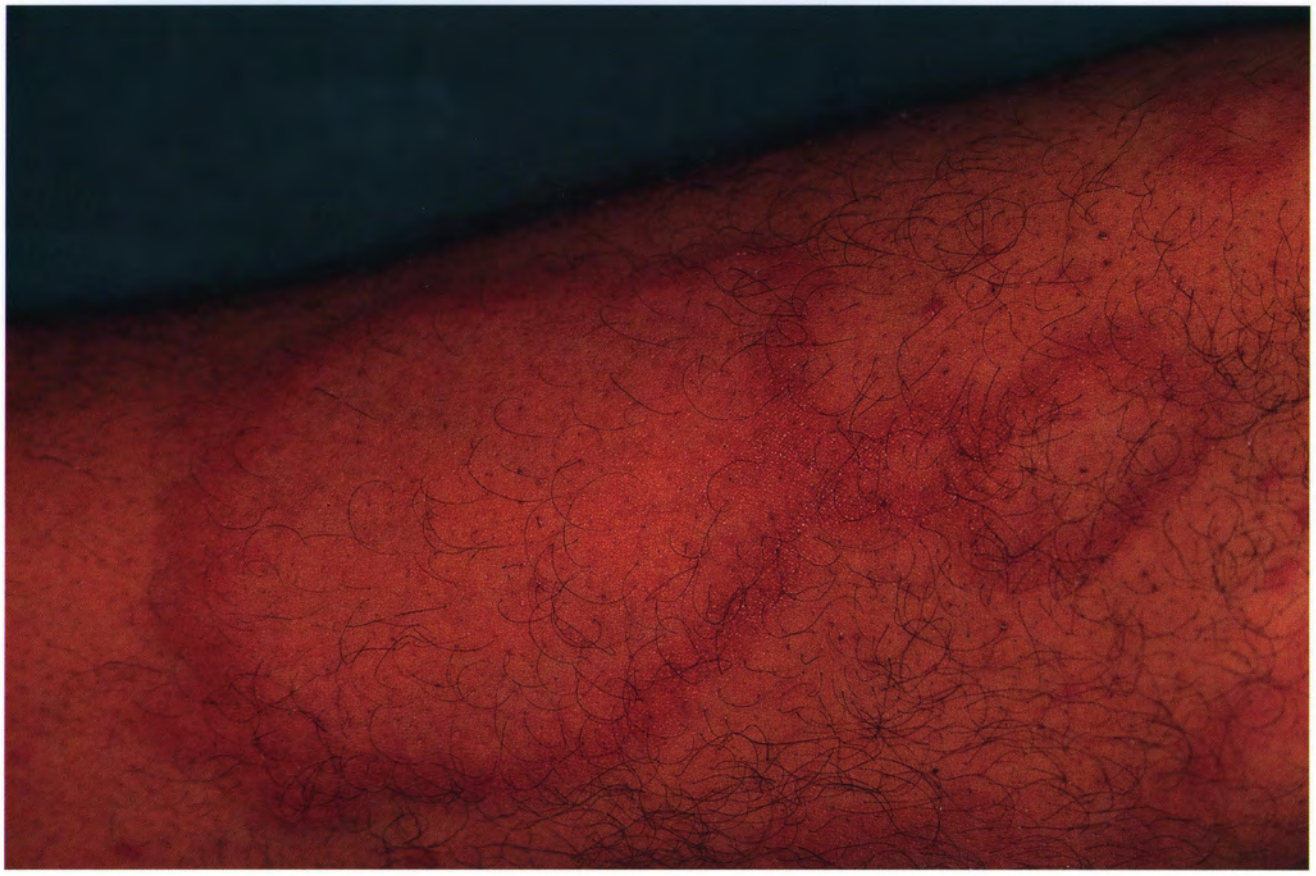
Picture 4-9
A fresh tuberculoid lesion. It is dry and there is no sweating. Hairs are lost. There is strong loss of sensation on the skin lesion. A smear test is negative. This case cures spontaneously, but the family members of the patient should be examined because of the possibility of contagious cases. In most cases, this lesion turns into hypopigmented macules, but loss of sensation remains.



Picture 4-10
A 35-year-old male patient. Hypopigmented macules on infra-axillary in a BT case. Hypesthesia is observed just on macules. Minor loss of sensation can easily be detected with a sheet of paper. No complex test is needed to diagnose the tuberculoid type or BT case.



Picture 4-11
An erythema in a BT case. This looks like a tuberculoid type, but the two lesions have coalesced and a satellite lesion is observed at their margin. Loss of sensation on the eruption is clearly seen, but it is not stronger than that of the tuberculoid type. The result of a smear test is negative.



Picture 4-12
A ring lesion observed in a BB type. Slight sensory disturbance may be observed on the same skin lesions. The central part has a tendency to heal, which is a characteristic of the Borderline type. The result of a smear test is a negative or a weak positive.

Picture 4-13
A larger skin lesion in the BB case. The central area shows signs of healing as in the Picture 4-12.

Picture 4-14
BL type. Many lesions are scattered irregularly throughout the whole body. Loss of sensation is hardly noticeable. The central parts of the individual lesions show signs of healing. The result of a smear test is positive.

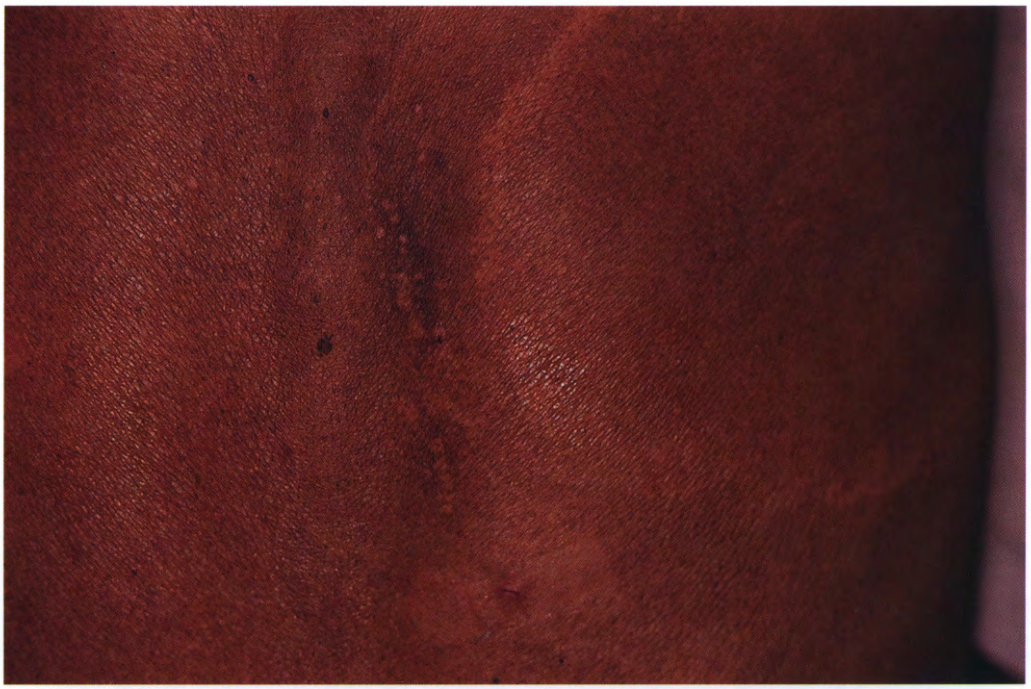

Picture 4-15
A 40-year-old male patient. A case of BL type. Lesions, which are smaller than in the Picture 4-14, are scattered throughout the whole body. A minor loss of sensation is observed symmetrically on the hands and feet, which does not coincide with skin lesions. The result of a smear test is a strong positive. Loss of sensation disappeared after treatment.

## Differential Diagnosis (Diseases may be Misdiagnosed as being Hansen's Disease in NWFP and Afghanistan)

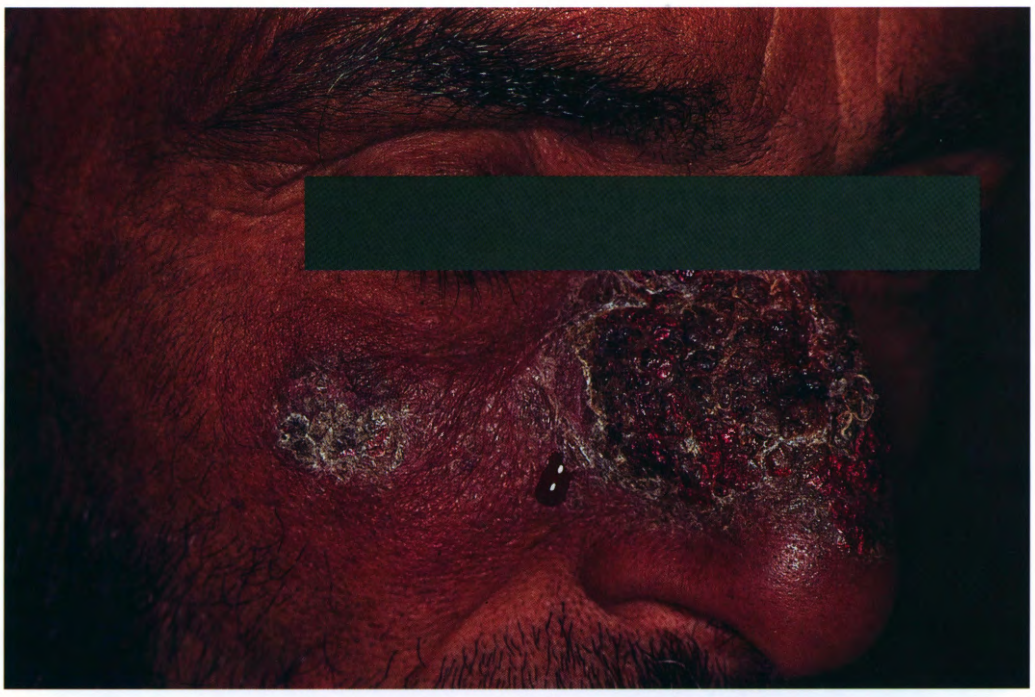
Some cases have been misdiagnosed as Hansen's disease and mistreated. Conversely, other cases have been misdiagnosed as not being Hansen's disease and have not been treated appropriately for a long time. Diseases that show chronic skin lesions or similar neurological disorders tend to be misdiagnosed as Hansen's disease. The following diseases are of misdiagnosed cases excluded from the 1,200 registered at the leprosy unit of Mission Hospital, Peshawar from 1985 to 1990.

Chronic dermatitis
Cutaneous leishmaniasis
Skin tuberculosis
Skin neuromatosis (von Reckling-Hausen disease)
PKDL (post-Kala-Azar dermal leishumaniasis)
Psoriasis
SLE (Systematic Lupus Erythematosus)
Hereditary sensory neuropathy
Charcot-Marie-Tooth disease
Traumatic nerve damage
Diabetic neuropathy
Dupuytran contracture
Carpal Tunnel Syndrome
Motor neuron disease

All these cases were misdiagnosed because of chronic skin lesions, limb deformities similar to Hansen's disease and plantar ulcers caused by loss of sensation. If the medical staff have knowledge of Hansen's disease, such cases can be avoided. Many hereditary degenerative diseases are not uncommon in NWFP and Afghanistan. They present a similar picture to advanced Hansen's disease. In PMS Hospital, we provide medical care for these cases, too.

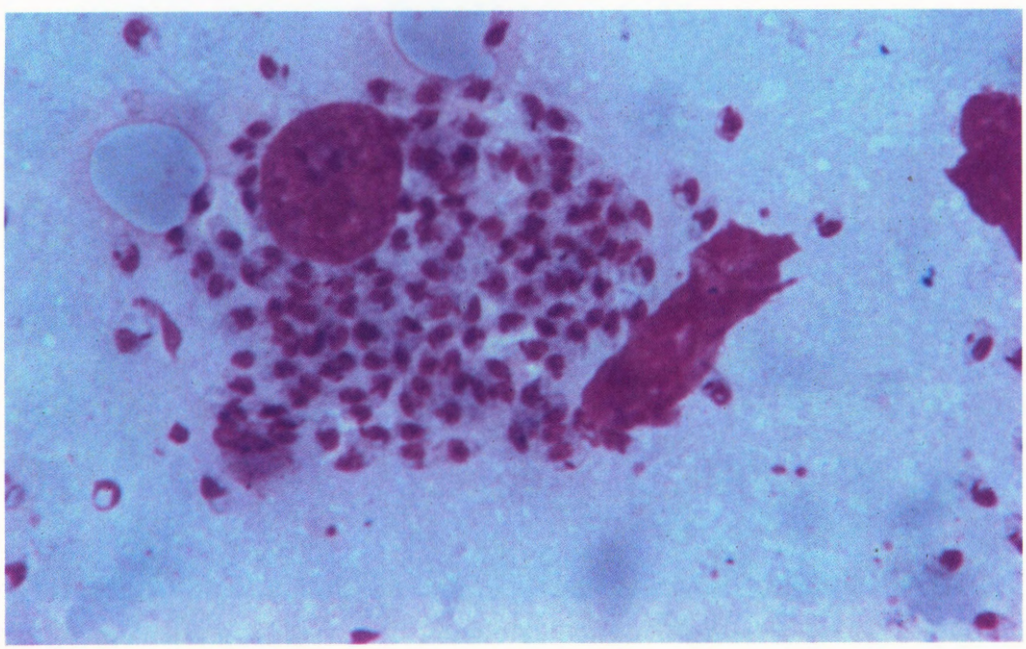


Picture 4-16
A case of cutaneous tuberculosis. Such cases are rare in Afghanistan. A giant eruption occurs at a single region. Tubercle bacillus (acid-fast bacillus) is usually not detected. There is no loss of sensation. It heals spontaneously. A biopsy is necessary for exact diagnosis.



Picture 4-17
A case of cutaneous leishmaniasis. This is known as "Sal-dana" (One-year tumor) in Afghanistan, and usually heals spontaneously in one or two years. Women in endemic areas fear this disease because the symptoms mainly appear on the exposed parts of the body like the face, hands and legs. It is obvious that the disease has dramatically increased to epidemic levels since the late 1990s. The disease is caused by protozoa of leishmania. Rodents are the hosts and sand flies transmit the disease to humans.

Picture 4-18
A case of cutaneous leishmaniasis. This Infiltration type, also called the Urban type, mainly occurs on the hands and legs. A large-scale outbreak of this type has occurred in Kabul since around 1994 and it has been gradually spreading to rural areas. The outbreak may be affected by the increase of insect vectors and rodents due to climate change and the increasing number of derelict buildings in the city. Local administration of Antimony drug is better than systemic administration.



Picture 4-19
Smear of Leishmaniasis. To confirm diagnosis, take a smear sample from the central part of the lesion and examine it with Leishman's stain in the same way as for malaria. If it is an active lesion, amastigote is detected.

Picture 4-20
A case of psoriasis. The psoriasis symptoms sometimes progress throughout the whole body in patients who are often referred to us under suspicion of lepromatous leprosy. With its unique shape and severe itching, it is easy to identify. Steroid is temporarily effective, but long-term administration of the drug is not recommended.

Picture 4-21
Scabiasis. This is caused by infection of the scabie mite. This disease often occurs in refugee camps and so on. where many people are malnourished. Young children with low immunity sometimes develop the disease over the whole body.

# V.
# Complications and Treatment

## 1. Leprosy Reactions

Leprosy reactions are closely related with the immune system. They can be clinically divided into the Erythema Nodosum Leprosum (ENL) reaction and the Borderline reaction. The ENL reaction is an antigen-antibody reaction, in which "B-Type" lymphocytes generate antibodies against the dead leprosy bacilli, causing an inflammatory reaction. On the other hand, the Borderline type reaction is found in its namesake, Borderline Leprosy, and is caused by a change in the cell-mediated immunity (CMI). When CMI increases rapidly in T-lymphocytes, they attack the bacilli and cause an inflammatory reaction (up-grading reaction). Conversely, when CMI decreases, bacilli are prone to multiply more easily (down-grading reaction). The up-grading reaction is clinically problematic and called "the Borderline reaction".

As a matter of course, an ENL reaction frequently occurs in multi-bacillary cases. Naturally this occurs in both the Lepromatous type (LL) and the Borderline-lepromatous type (BL). Borderline reaction occurs only in Borderline leprosy, where the immune condition is unstable. Knowledge of the disease type is useful in estimating the possible reactions to the treatment.

In general patients are extremely concerned about their symptoms, so medical staff should convince them that such reactions will certainly be controlled over a number of years, despite occasional relapses. Often patients visit again and complain that another nodule has appeared. Many such cases, however, are just nodules that have shrunk after healing. The more a doctor pays attention to it, the more anxious patients become. If these hard nodules are not painful, the doctor should disregard them and tell the patient not to worry about them.

# A. ENL Reaction

This reaction often occurs several weeks to months after starting chemotherapy. An ENL reaction sometimes occurs under natural conditions and the multi-bacillary type of Hansen's disease may be detected by this reaction.

The whole body is affected with fever and severe pain in typical cases. These symptoms are especially remarkable at skin lesions such as nodules, where many M.leprae concentrate. ENL (Erythema Nodosum Leprosum) was named by a Japanese researcher of Hansen's disease and the name derives from such "fever nodes". The symptoms continue for several weeks to months, and repeatedly occur, causing patients to suffer until a smear test shows a negative result. Small nodes on the whole body may become pustules (ulcerative reaction) and scars remain on the skin.

Among the complications of the ENL reaction, precautions should, in particular, be taken against 1) acute iritis and 2) acute orchitis. Dyspnea caused by edema of the pharingo-larynx is also most dangerous and requires tracheotomy. Deaths from dyspnea were occasionally seen in the past, but recently have been dramatically reduced due to the availability of steroids.

## Acute Iritis

Repeating iritis causes adhesion of the iris and the glaucoma, which may also result in blindness. Intraocular pressure should be regularly measured to detect glaucoma. Adhesion of the iris can be detected by observing the patient's pupils. A light-reaction should always be examined. When anisoconia or irregularity at pupillary margins is observed, atropine eye drops should be applied to prevent adhesion of the iris.

## Acute Orchitis

Since a patient may hesitate out of embarrassment to complain about these symptoms, medical staff should ask him indirectly. If not treated, a patient will not only have pain but also be infertile due to azoospermia. Because in Afghan society it is a serious matter if the family line dies out, the patients are deeply concerned about it. Deficiency of androgen secreted by the testes may cause gynecomastia.

## Treatment with Anti-inflammatory Agents

General analgesics like aspirin are not very effective. Steroid is quite effective, but prolonged administration causes side effects. Steroid should be properly managed.

Picture 5-1a
Swollen and reddish leproma in ENL reaction. This tortures the patient with severe pain, often accompanied by general body symptoms like fever. Patients suffer repeatedly but can be assured the symptoms will disappear as the bacilli become negative.

Inappropriate administration may prolong the symptoms by lowering immunity causing some patients to die from the perforation of a gastroduodenal ulcer. Frequently, patients purchase the medicine by themselves to use it continuously.

Thalidomide is dramatically effective against the ENL reaction. It is, however, absolutely contra-indicated to pregnant women because of its teratogenenic effect. It also should not be given to outpatients. The WHO (the World Health Organisation) has issued a strict warning that the use of thalidomide should be limited to patients with the ENL reaction. The effectiveness of thalidomide against multiple myeloma and Behcet's Syndrome has recently become evident, resulting in the medicine being used more widely. However, the use of the medicine is officially limited to the ENL reaction against which it has been proved to be effective.

In PMS Hospital, we handle the ENL reaction in the following ways.
(1) A daily dosage 200-300mg of thalidomide is given in two or three parts according to the symptoms. The dose is decreased gradually every one or two weeks, and eventually should be stopped within several months. (2) At the same time, the dose of Clofazimine (B663), an anti-leprosy drug, is increased to 300mg and continued for at least several months. (3) Steroids can be used at the same time only when the symptoms are difficult to differentiate from those of the Borderline reaction accompanied with acute neuritis. The dose should be gradually decreased and stopped after some weeks.

When thalidomide is unavailable and there is no alternative, steroid is the only choice. However, careful monitoring is required and the patients should be warned of the dangers.

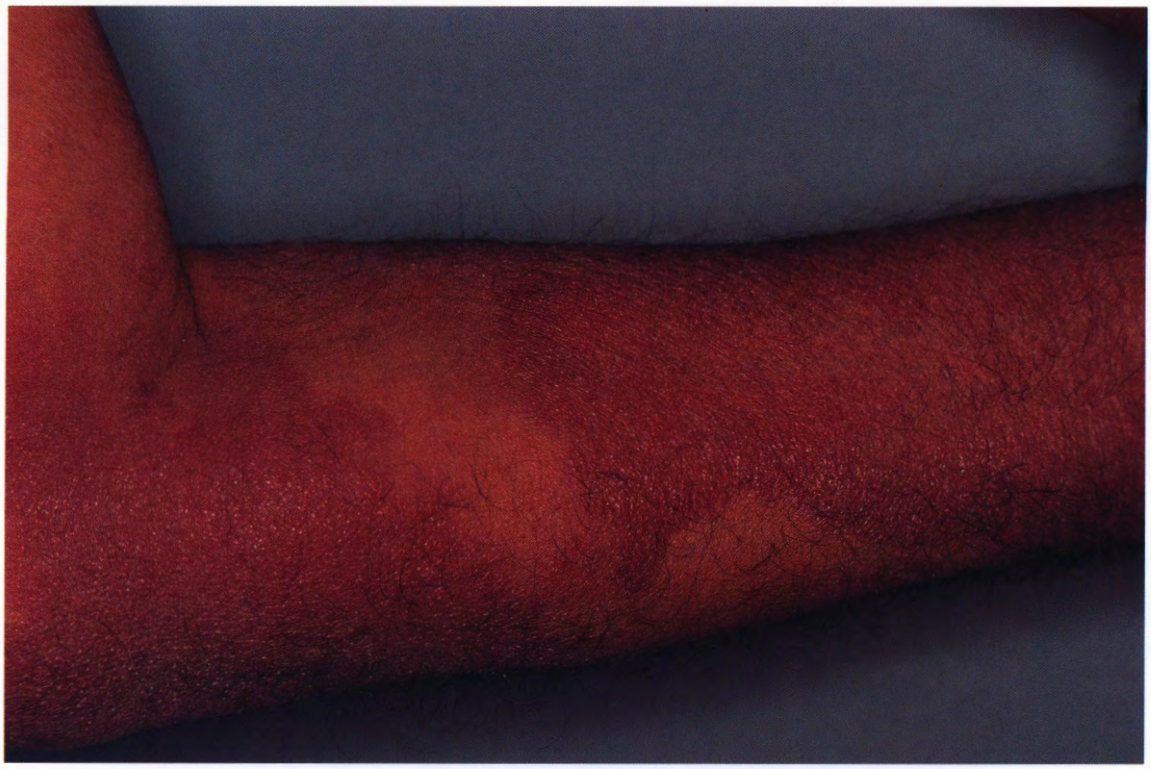
## B. Borderline Reaction

As described before, this reaction occurs only in Borderline leprosy. Skin lesions rise up and become reddish, but there is no pain like in the ENL reaction.

Precautions should be taken to avoid **acute neuritis**. Major disorders are foot drop caused by peroneal nerve paralysis and drop hand caused by radial nerve paralysis. In acute cases, paralysis may appear within a few hours.

If steroid is given immediately after the reaction, paralysis can be prevented. Since the Borderline reaction subsides spontaneously within several months, it should be controlled with steroids during this period.

Picture 5-1b
Enlarged Leproma in ENL reaction. If a patient continues to be given B663 (Clofazimine), pigmentation occurs at the bacilli concentrated parts. Some patients do not like to use Clofazimine for cosmetic reasons, but they should be advised that pigmentation disappears after stopping the administration of the drug.



Picture 5-2
Skin lesion in Borderline reaction. The whole part of the eruption lifts up evenly with a red colouration without pain or itching. It disappears within several months. Change of skin lesion is a good rule of thumb to evaluate the course of a Borderline reaction. Take precautions against acute neuritis.

# 2. Foot Complications

Most foot complications are caused by chronic sensory nerve paralysis. The next most common cause is acute neuritis in the Borderline reaction. Foot complications affect patients' daily life more seriously than hand complications. Attentive care is required.

## Plantar Ulcer due to Anesthesia

Plantar ulcers occur not only in Hansen's disease but also in any diseases that causes a sensory disturbance of the feet. When walking long distances with unfit shoes, or shoes containing a foreign body, normal people feel pain caused by blisters or a minor injury on their sole, and quickly go for treatment. Patients, however, if they feel no pain, do not know about the wound, and get skin ulcers by repeatedly injuring the same region. This is known as a "plantar ulcer".

In general, plantar ulcers are most frequently seen on the metatarsal head, which at times supports whole body weight when walking. If not treated, the skin ulcer expands, foot bones are exposed and acute purulent arthritis, osteomyelitis, and so forth occur. Long-term ulcers may often cause squamous carcinoma. Prevention and treatment should be carried out before an amputation of the lower thigh becoming necessary. Since many villagers in mountainous areas walk long distances and wear coarse shoes, even just improving shoes can help prevent ulcers. When a protrusion of transformed foot bones causes an ulcer, the protruded part can be scraped away to avoid any relapse.

Ankle ulcers: As people in NWFP and Afghanistan have a custom of sitting cross-legged like in Japan, ankle ulcers are often seen. The use of a small cut-out cushion ring made from torn sheets is a considerable help in the healing of pressure sores.

## Foot Drop

Acute neuritis on the peroneal nerve in the Borderline reaction causes foot drop due to paralysis of the foot extensor muscles. At the acute stage it is advisable to wait for self-healing by taking preventive measures only against contracture. If it does not cure spontaneously after more than one year, surgical treatment should be considered. Reconstructive surgery (tendon transfer) brings good results. Transfer from tendon to tendon should be conducted as transfer from tendon to bone may often cause a neuropathic joint later.

Picture 5-3
Plantar ulcer. Many cases are also observed on the heels. Examine the transformation of the bone by X-ray. If a sharp tip of bone is detected subcutaneously, it should be removed.

## Neuropathic Joint

If the foot loses not only superficial but also deep sensation, the patient feels no pain even if the bone is fractured or dislocated. In cases where the ankle region is affected, patients are not aware of unnatural twisting or how much body weight they are bearing, which destroys the structure of the ankle joint. (Early signs are foot swelling, localized reddening and dull pain.) Most cases can be resolved by fixation for more than several weeks. Walking distance should be gradually increased after the plaster is removed. If a patient starts walking soon, a relapse may happen. If not treated, serious ankle deformity (Charcot joint) occurs. This may happen after the removal of a plaster cast for the treatment of a plantar ulcer etc.

## Claw Toe Deformity

This is common in advanced Lepromatous type. It is caused by posterior tibial nerve paralysis and is often combined with sensory disturbance of the toes.
Claw toe without contracture is an indication of surgical treatment. This deformity increases the pressure on the metatarsal head on the sole and is likely to cause plantar ulcers.

## Others

Dry skin due to a sweating disorder: This is caused by peripheral automic nerve damage. Damage of the sweat glands and vasomotion makes the skin of the feet dry with an appearance of fish-like scales (ichtiosis). Ichtiosis also occurs as a side effect of B663, an anti-leprosy drug. This side effect disappears after stopping the drug, so is not of great concern. Cracks on the soles easily become a source of suppurative infection. The marginal edges of the cracks should be scraped off and softened by applying edible oil.

Picture 5-4
Claw toe deformity. This is caused by paralysis of the posterior tibial nerve. It is mostly observed in the multi-bacilli type. It is desirable to conduct surgical correction before contracture occurs, in fact; however, few patients see a doctor in the early stages.

Picture 5-5
Plantar ulcer. This is mainly observed on the metatarsal head, which bears the weight of the body when walking.

Picture 5-6
A foot drop corrected by a tendon transfer operation. This is caused by acute neuritis along with a Borderline reaction. Many cases develop sub-acutely within several hours to weeks, but others progress chronically for some months.

Picture 5-7
Ichthyosis on the lower limbs. Peripheral autonomic nerve disturbance causes disorders of sweating and blood circulation resulting in scaly dry skin. The administration of Clofazimine also often causes these signs, though they disappear after the administration is stopped.

# 3. Complications on hands

## Claw-finger Deformity

This is commonly seen in the advanced multibacillary type. It is caused by paralysis of the ulnar nerve and progresses chronically. If not treated contracture occurs. Repeated injury to the contracted joint results in loss of fingers (absorption). Contracture can be prevented at an early stage. Patients should be fully trained in preventive measures during admission so that they can do it themselves at home. They should learn how to massage their hands and stretch the finger joints using edible oil to soften dry skin. Because Vaseline or glycerol is rarely available in rural areas, the patients should be convinced that all edible oils are suitable. Just a few minutes soaking the fingers in water is also effective.

## Drop Hand

Most drop hand cases are due to radial nerve paralysis caused by acute neuritis in the Borderline reaction. The hand cannot be raised at the wrist. It can be treated by reconstructive surgery. If appropriately treated at an early stage, this can be prevented.

## Nerve abscess

If caseous necrosis occurs at thickened nerves, abscess swelling occurs accompanied by severe pain. This is often seen on the ulnar nerve at the elbow. With a small incision carefully made under local anaesthesia, fixing with a plaster splint and immobilising for a while, the patient can soon be released from pain and paralysis can be prevented.

A

Picture 5-8, 9and 10 (A, B and C in sequence)
Claw finger deformity. This is caused by ulnar nerve paralysis. This symptom is most often observed in contracture deformity of the Lepromatous type.

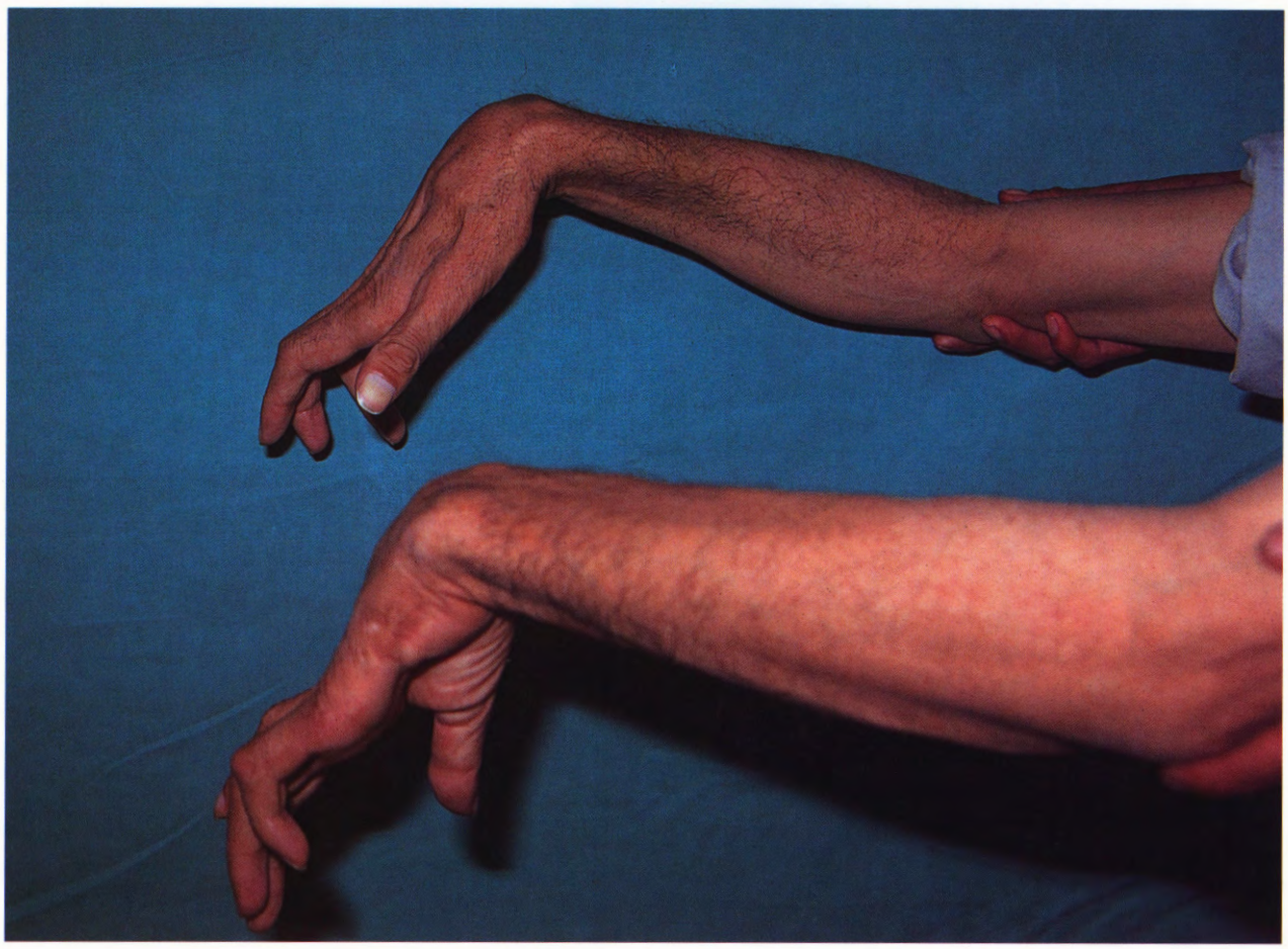
A- The normal stretching motion of the hands and fingers, and pinching an object with the fingers are affected at an early stage, but deformity is preventable at this stage.

B

B- If it is untreated, contracture of the bones occurs with hyperextension at the MP joint and flexion at the PIP joint. Correction is difficult at this stage.

C

C- Fingers are easily injured due to loss of sensation. With repeated dislocation, minor bone fracture and suppurative inflammation, the fingers are gradually lost (absorption).



Picture 5-11
Drop hand. Radial nerve paralysis is caused by acute neuritis in a Borderline reaction. Ulnar nerve paralysis also may develop in this case. Drop hand occurs less frequently than foot drop, though it may easily progress to contracture. Monitor the condition to prevent contracture. If there is no recovery a tendon-transfer operation should be performed. Preventive measures during a Borderline reaction period are crucial.

Picture 5-12
Rehabilitation of hands to prevent contracture. Exercises to prevent contracture should be carried out in a group during admission so that each patient will make a habit of it at their own homes. If patients can learn to conduct the exercise on their laps whenever they can, this will prevent contracture. Flexing the hyper-extended MP joint is a key feature of the exercise.

# 4. Complications in eyes

Complications in the eyes are very often seen in Hansen's disease. Blindness is not uncommon. The complications are, however, preventable at an early stage. Major complications in the eyes are as follows:

## Lagopthalmos

This is caused by facial nerve palsy. When a patient tries to close their eyes, the eyelids cannot be shut and the white of the eye (sclera) remains visible. If not treated, the surface of the cornea, becomes dry and vulnerable to inflammation (exposure keratitis). A linear cornea lesion is seen in the middle of the eyeball at an early stage. As the condition advances with repeating pyogenic infection, an ulcer occurs on the cornea which sometimes results in blindness.

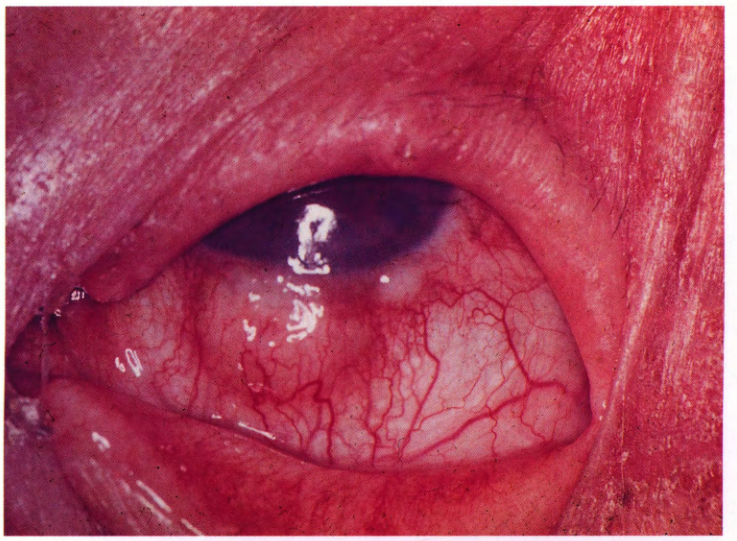
Tarsoraphy is often carried out because of its simple procedure, but it is only effective for mild cases. For moderate and more serious cases, TMT (temporal muscle transfer) should be performed. Ophthalmic ointment and/or an eye mask can be used during sleeping to protect the eyes temporarily.

## Uveitis and Iritis

Refer to the items of ENL reaction. Steroid eye-drops should be applied for cases caused by the ENL reaction. Chronically advancing cases should be carefully handled. The examination should be carried out whenever the patient consults a doctor. In particular, treatment for synechia of the iris should not be neglected. Mycobacterium leprae may directly infiltrate into the cornea, sclera and iris.

## Madarosis

This is a kind of skin damage rather than eye damage. The presence of madarosis helps to diagnose the Lepromatous type. If a patient does not mind the condition, it is advisable just to observe it without attempting to transplant hair, which has low success rate.



Picture 5-13
Leproma on cornea and ENL reaction. Small leproma sometimes occur in the sclera or the cornea. Take precautions against visual disorders caused by an ENL reaction. Curled eye lashes touching the corneal surface have to be removed because a loss of sensation on the corneal surface often occurs and the cornea can be damaged by trichiasis or ingrowing eyelashes.

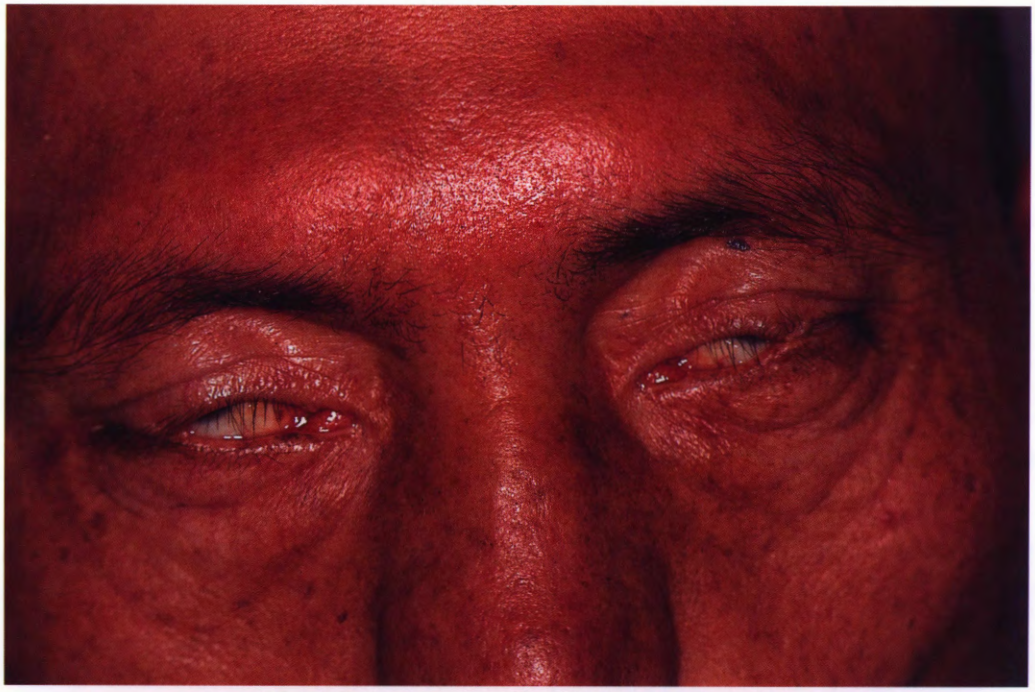
Picture 5-14
Dry type keratitis caused by lagopthalmos. Inflammatory change occurs on the equatorial part of the eyeball.

Picture 5-15
Too late! Trichiasis and turbidity of lens. Secondary infection leads to blindness.

## Others

Leproma is sometimes detected in the cornea. Sensory disturbance of the cornea surface combined with lagopthalmos is more prone to cause cornea damage due to lack of pain. At an advanced stage, the normal positions of the eyelashes are lost due to atrophy of their supporting tissue. The lashes turn in toward the eye (trichiasis), which injures the corneal surface, causing an ulcer on it like a foreign body. Opacity of the cornea or crystallization of the lens can occur causing a visual disorder.

If some inflammation causes glaucoma, a severe eyeball pain occurs due to an increase of intraocular pressure. In this case, the intraocular pressure should be urgently decreased. With the application of atropine eye drops and treatment for reduction of intra ocular pressure, the condition can be temporarily improved. But the patient should be urgently transferred to an ophthalmologist.



Picture 5-16
Lagopthalmos of both eyes. Facial nerve palsy causes incomplete eye closing. Constant exposure of the cornea leads to dry keratitis.

Picture 5-17
After a temporal muscle transfer operation of his right eye. The patient became able to close the eye completely using a chewing motion and now is able to close the eye normally.

# VI.
# Current Situation and Outlook of Chemotherapy

At present, the "short-term and multi-drug therapy" recommended by the WHO since the 1980s is the standard regimen in NWFP and Afghanistan.

**Table 2: Drug Regimen in MDT (WHO)**

| | | Adult | Child (10-14 age) |
|---|---|---|---|
| MB: | | | |
| Once a month supervised | | | |
| | Rifampicin | 600mg | 450mg |
| | Clofazimine | 300mg | 150mg |
| | Dapsone (DDS) | 100mg | 50mg |
| Unsupervised | | | |
| | Clofazimine | 50mg (everyday) | 50mg (alternate-days) |
| | Dapsone | 100mg (everyday) | 50mg (alternate-days) |
| The above 24-month doses should be given for 24 months, or at longest 36 months. | | | |
| PB: | | | |
| Once a month supervised | | | |
| | Rifampicin | 600mg | 450mg |
| | Dapsone (DDS) | 100mg | 50mg |
| Unsupervised | | | |
| | Dapsone (DDS) | 100mg (everyday) | 50mg (everyday) |
| The above 6-month doses should be given for 6 months, or at longest 9 months. | | | |

**Table 3: Classification for MDT (WHO)**

| Symptom: | PB | MB |
|---|---|---|
| Skin lesion: | Nos.: 1-5 | Nos.: 6 or more |
| (macule, papule, nodule) | | |
| | Macules are hypopigmented or erythematous. | |
| | Asymmetrical distribution | Symmetrical distribution |
| | Anaesthesia well-defined | Anaesthesia ill-defined or not present |
| Nerve damage: | | |
| | Single nerve damaged | Multiple nerve damaged |

Note: A positive skin smear (bacilli test) should be treated as MB. Uncertain cases should be treated as MB. MB cases should not be treated as PB.

In general, 99% of Mycobacterium leprae die within 48 hours of administering Rifampicin. The case then becomes non-infectious.

MDT (multi-drug therapy regimen) has remarkably shortened the medication period compared with previously used Dapsone mono-therapy, and has brought epoch-making changes. Relapse has dramatically decreased. For individual patients, however, it does not solve all the problems.

Treatment of deformed cases should be continued. The cases resistant to DDS are becoming common and recently cases resistant to Rifampicin have been seen. These facts indicate that the chemotherapy for Hansen's disease will, in the long run, become less effective as happened with tuberculosis.

Difficulties in NWFP and Afghanistan are as follows:

(1) Due to the poor reliability of skin smears, it is hard to determine whether healing has occurred or not.
(2) Once the superficial symptoms have disappeared, patients tend not to cooperate in long-term regular medication.
(3) We cannot afford financially to give expensive new drugs.

These may be the very reasons why MDT has been developed. MDT has contributed so much in solving problems from the viewpoint of public health, but it may be risky to determine the treatment period based only on the simple classification of the disease into its two types; multibacillary and paucibacillary. Furthermore, the carrying out of skin smears tends to be neglected because of MDT's high effectiveness. As a matter of fact, the incident rate has not been reduced much in spite of a reduction in the prevalence rate.

The challenge facing us now is how closely we can care for individual patients. Relapse is not common, but it is slowly on the rise. It occurs especially in "clinical relapse" cases. These are cases which, despite showing a negative smear, result in paralysis, or which look like a minor ENL reaction.

The cases resistant to Rifampicin have also been identified at PMS Hospital. New anti-leprosy drugs such as Minocycline, Ofloxacin and Levoflaxacin have been proved to be effective and a clinical trial has been started. In Japan, Ofloxacin and Minocycline have already been introduced as primary drugs. Yet their administration has not been established. Since they are sold at exorbitant prices for the people of Peshawar and Afghanistan, neither medical institutions nor patients can afford them.

In this regard, PMS Hospital, in close collaboration with Marie Adelaide Leprosy Centre in Karachi, follows the following principles.

(1) For "clinical relapse" cases, despite a negative smear, MDT should be restarted.
(2) If no improvement is seen in skin smears, and resistance is doubted, Minocycline or Ofloxacin is given with MDT for a certain period and the effectiveness is monitored.
(3) Even after stopping MDT, regular follow-up with skin smears should be conducted as often as possible.
(4) Type, whether PB (paucibacillary) or MB (multibacillary), should not be determined simply from the shapes or number of skin lesions. Continued surveillance with skin smears is necessary. If many bacilli are detected even in small lesions, the treatment period should be long term as for MB.
(5) For Borderline type cases, Clofazimine, which has an anti-inflammatory effect, should always be used with an MDT regimen for either PB or MB.
(6) Even if bacilli are granulated, MDT should be continued until a negative smear is obtained.

Actually a majority of leprologists feel, "Chemotherapy for Hansen's disease cannot end with just the application of MDT". Considering that the generation time of Mycobacterium leprae is dozens of times greater than that of TB bacilli, it may take a much longer time to determine the treatment effect. Furthermore, in a country like Afghanistan, which has been devastated by wars and drought, we will have to continue to address the disease in the long term.

Full view of PMS Hospital

Appendix: Medical institutions which treat Hansen's disease in NWFP and Afghanistan (PMS Hospital includes the department in the general department).

**Kabul City**

German Leprosy Clinic

**Bamiyan Province**

Clinics of the Marie Adelaide Leprosy Centre

**Nangarhar Province**

PMS Dara-e-Noor Clinic

**Kunar Province**

Dara-e-Pech Clinic (Okinawa Peace Clinic)

**Nuristan Province**

Dara-e-Wama Clinic

**Peshawar City**

Leprosy Ward (Dept. of Dermatology), Lady Reading Hospital

Special Unit of PMS (Peshawar-kai (Japan) Medical Services)

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