Clinical aspects of nerve damage in leprosy
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Chapter 1

Introduction
1. NEPAL

1.1 HISTORY

The history of Nepal dates back to ancient time. Legend has it that Manjusri Bodhisattwa from China came on a Pilgrimage to worship Swayambhu. When he reached the top of Nagarkot he saw flames constantly emanating from Swayambhu in the midst of the lake “Nagarad.” Eager to reach the Divine Lotus he drained the lake by cutting the lowest part of the mountain thus creating the Kathmandu valley. The founder of Buddhism, Shakyamuni Gautama Buddha, was born in 560 BC in Rupandehi (Lumbini).

The period of 350 to 630 AD, known as the Lichavi period, is considered in many ways to be the Golden Age in the history of Nepal. Until the 12th century the majority of hill tribes of Tibeto-Burman origin lived in small autonomous chiefdoms. Trade with Tibet exposed them to Tibetan traditions of animism and later to Tibetan Buddhism. In the early 13th century the Islamic Mogul invaded North West India. The high caste Hindu Rajput nobility fled to the North and East into the contemporary Far West region of Nepal, bringing with them their fourfold Hindu caste system with the attendant Brahmans (the highest caste of the priests and teachers), the Kshatriyas (the second highest rulers and warrior’s caste of which the present caste name of Chetri is derived), the Vaisya (merchants and traders) and the Sudra (farmers, artisans and labourers). The fifth class of untouchables are the outcastes and the socially polluted like those who are diagnosed with leprosy. The Brahmans have the strictest rules with regard to purity and leprosy beggars will need to remove their leather protective footwear before being allowed to approach the house for receiving alms.

After the 14th century Nepal remained fragmented into a group of small prosperous kingdoms for centuries. The present kingdom was created about 200 years ago when the Gorkha King Prithvi Narayan Shah annexed the Eastern and Western hill states. This expansion gave him control over the major trade routes and the Terai with its sources of high revenue. The near-feudal rule of the Rana Prime Ministers dynasty isolated Nepal in the 19th century from the outside world and all their developments. The Ranas were actively opposed to popular education and engaged in a period of intensive Hinduisation. They laid the foundation for what till today is called: “Nepal; the only Hindu Kingdom in the world”, introducing Hindu religious laws which prohibit leprosy patients from entering a temple and exclude them from religious ceremonies, this in a country where religion is absorbed in every aspect of life.

At the time that the fight for Independence was gaining ground in India, discontent with the autocratic regime of the Ranas spread in Nepal. As long as British rule in India existed there was little hope for sympathy from that side, but after India’s Independence in 1947 all activities against the regime of the Ranas were carried out with backing from India. Under the
rule of the Rana Prime Ministers the Kings of the Shah Dynasty had become nominal figureheads and virtual prisoners, but King Tribhuvan still enjoyed the sympathy of his people.

In November 1950, on the pretext of going on a hunting party, the King fled with almost his whole family to the Indian Embassy in Kathmandu and took political asylum there. The Nepali Congress Party launched a country wide armed revolution and Birgunj and Biratnagar fell into their hands. Finally, the Rana Government had to sit at a table with the Nepali Congress in Delhi. With the Delhi agreement of November 1950, King Tribhuvan was restored to the throne and under his leadership a cabinet was formed consisting of five ministers from the Rana side and five ministers from the Nepali Congress. Dissatisfied with Parliamentary Democracy as it functioned in Nepal, his successor King Mahendra did away with it and replaced it by what he called Panchyat Democracy in 1962.

After considerable political turmoil in spring 1990 this Panchyat system\(^1\) of “indirect government”, also described as “partyless democracy\(^2\)”, was abandoned and Nepal shifted again towards democracy with King Birendra Bir Bikram Shah as constitutional monarch. On April 16th the King appointed members of the previously illegal Democratic Movement to form a new interim government. General elections were held in May 1991 in which the Nepali Congress gained the majority. Shortly after they formed a new Government with a significant number of Communists in the opposition. In the 1999 elections of the three major parties the Nepalese Congress Party (social-democratic) got 36.3 %, the Communist Party of Nepal-Unified Marxist-Leninists (communist) got 23%, and the Rastriya Prahantra Party (national democratic party, conservative) got 10.2 % of the votes. Since 1994 the dissatisfied Maoist faction of the communist party went underground and since then their guerrillas have launched numerous attacks against military barracks and police stations throughout the country.

On June 1\(^{st}\) 2001 the Crown Prince Dipendra assassinated almost all members of the Royal family and the brother of the King, Prince Gyendra was crowned as the new King. Since then the Maoist guerrillas have greatly stepped up their attacks in an attempt to end the monarchy. This has brought tourism, the major source of national income, almost to a complete standstill.

The future will show whether Nepal will succeed in maintaining a stable democratic system while trying to uplift its fragile economy. Nepal, in spite of its Shangri-La image, is poorer than Bangladesh with an average income of $214 per year, a population of about 22.6 million inhabitants, and a population growth of 2.6 %.

References:
Nepal is a landlocked country. It borders Tibet (China) in the North where the Himalayas form a natural barrier. The other three sides are bordered by India. It is located on a longitude 80°-88°.5’ east and latitude 26°.30'-30° north. The total land area is 147,181 sq.km stretching over 800 km from east to west and between 150 and 250 km from north to south. About 71% of Nepal is hilly and mountainous. The highest mountain peaks in the world are located in the northern area.

With these geographical conditions it is no surprise that many leprosy patients find it difficult to remain ulcer free once they have lost the sensation and the muscle balance in their feet. Because three mountain ranges (from north to south: the Himalayan range, the Mahabarath Lekh and the Churia range) run in the direction of the longitudinal axis of the country, there are three typical regions in Nepal:

1. The Terai; a strip of the Indo-Gangetic plain with an elevation of 150-300 meters containing the most fertile land in the country with rich deposits of alluvial soil and a belt of forest. It represents roughly 20% of the country.
2. The Trans-Himalayas or the “Hills.” This is the most heavily populated part of the country and accounts for 43% of the country’s land, this includes the valleys of Kathmandu, Pokhara and Surkhet.
3. The Inner-Himalayas or the Himalayan Highlands, range from 3000 to over 8000 meters, lying on the northern border. There are three major river systems having their origin here: the Karnali River, the Narayani River and the Saptakoshi, draining respectively the western, the central and the eastern part of the country. Each of these has a catchment area of about 12,500 square miles. With almost equal intermediate distances of about 180 miles the three rivers continue their courses through the Terai plain to the northern part of India.

1.3 CLIMATE.

The climate is determined by its topography and by the monsoons. The Terai is subtropical, the hill region temperate and the inner-Himalayas have an alpine climate. Rainfall is abundant. In general, in amount it decreases from east to west. The short monsoon (2 1/2 to 3 months) falls during the summer (June to September) and combined with melting snow causes excessive river levels. The dry season (September to June) coincides with the winter season when there is almost no glacier water. The result is great changes in river levels over the year. This is further influenced by the ongoing deforestation. As an example the Saptakoshi River has a top level of 450,000 cusec and a minimum level of only 9000 cusec, a decrease of 98%.

About one-third of all leprosy patients live in the hills and mountains where the roads and passes are frequently blocked by snowfall during winter. The remaining two-third live in the Terai where high water levels during the monsoon can block their way to the nearest antileprosy drug distribution centre. Apart from the present difficulties (mainly infrastructural and financial) that the leprosy control programme of His Majesty's Government is facing, the geographical and climatological situation of Nepal may be held responsible for the high defaulter plus irregularity rate (48%) and disability rate (30% of all new cases)\(^1\)\(^2\) of the leprosy patients in Nepal.

Nepal is endowed with an enormous hydroelectric potential of some 83.00 MW, in theory. Less than 200 MW has been tapped to date, and Nepal remains a country with inordinately low consumption of electricity. Anticipated rural electrification benefits have not yet materialised and electrification has yet to generate significant fuel-wood savings\(^3\).

References:
1.4 POPULATION.

In 2000 Nepal's total population was 22.6 million with an annual growth rate of 2.6% between 1995-2000. The average annual growth rate for the Terai is 4.1%, for the Terai urban areas 8-12% and for the Hills and Mountains 1.5%. The proportion of the overall urban population is rapidly increasing, amounting to 7.9% in 1998. In 1995 42% of the population was below 15 years.

The current national literacy rate is 40%. But woman, many caste, ethnic and regional groups and the poor have a much lower literacy rate. In 1995 two-thirds of the 6-10-year old children not enrolled in schools were girls.

Farm income is the major source of household earnings accounting for 61% of total household income in 1996. Only about 17% of the total land area of the country is comprised of agricultural land. The average size of landholding is only 0.24 ha, with, on average, more than four land parcels per holding. Forty-five percent of the population lives below the absolute poverty line.

Nepal has also provided shelter to migrants from both the north and south. Nowadays, the Nepalese population is broadly classified into three major ethnic groups in terms of their origin: Indo-Nepalese, Tibeto-Nepalese and indigenous Nepalis. Up to 60 different ethnic groups, self-defined by clan names, are identified in middle Nepal (Frank, 1974) while 25 languages are recorded in the 1981 Government census. Nepali, a language of Sanskrit origin, is actively promoted as the 'lingua franca' for the whole of Nepal and is the only language taught in schools. This policy meets resistance from a number of minority ethnic groups like the Newars who fear that their cultural heritage will be lost.

In the last two centuries Nepal has become increasingly a Hindu Kingdom with at the moment, according to official figures, about 90% of the population subscribing to this religion. This is at the cost of the Buddhists who now officially constitute only 5% of the population.

Nepal is, nevertheless, unique in the fact that religions have peacefully existed side by side over the past centuries and to a unique degree are amalgamated now. Nepal has been described as the contact zone of "Indian Hinduism" and "Tibetan Buddhism". There are small minorities of Muslims and Christians.

Natural immunological resistance to leprosy varies amongst the different races and in Nepal Indo-Aryan and Mongolian influences can be studied side by side, which is an almost unique situation. In the Hindu Caste system those affected by leprosy are regarded as "jutho", meaning unclean, which positions them at the very bottom of the social ladder.

References:
1.5 ECONOMIC SITUATION.

Few countries began developing as late and with such meagre resources as Nepal.\textsuperscript{1} The average per capita income in the year 2000 was $214, while the GDP growth rate was on an average of 5.2\% per year during 1991-1996, this with an annual rate of inflation of approximately 10\%. Approximately 45\% of the population live below the poverty line. The unemployment rate is high at 14\% (1997 figure).

The natural resource base has been undermined by human and livestock pressures resulting most critically in extensive degradation of the country's forest and pasture land. A major constraint to agricultural growth has been ineffective land irrigation, a problem already recognised in one of the first FAO reports on irrigation in Nepal, published in 1953.\textsuperscript{2} 82\% of Nepal's agricultural production consists of food grains (rice, maize, wheat and millet).

In 1997 63\% of the rural working day and 44.7\% of the urban working day were spent in underemployment. In view of the expanding labour force and the limitations for greater employment in agriculture, it is expected that this situation is likely to be aggravated in the future.

For over 90\% of the population, agriculture is the primary source of sustenance, income and employment. Two-thirds of the population are poor.\textsuperscript{3}

Leprosy patients who lose sensation of the extremities (about 33\%) are in general incapable of remaining free from ulcers if they continue to farm their land; this results in increased disability. Social isolation and disability may be the main reasons why leprosy patients contribute about 30\% of the cash and non-cash household income while for non-leprosy patients this is nearly 70\%.\textsuperscript{4}

There is considerable aid assistance from foreign programmes. Donors have financed about half of Nepal's development efforts in the past.

While enrolments to schools have risen more than fivefold between 1965 and 1986, two-thirds of Nepal's population still remains illiterate. This has major implications on the potential pace of development and on the success of health and population programmes.

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1.6 HEALTH SITUATION.

Approximately 5.3% of GDP is spent on health. Three-quarters of this expenditure, however, is made by households. The infant mortality rate in 1996 was 83.7/1000 for females and 101.9/1000 for male live births. The child mortality rate was 56.5/1000 for females and 45.5/1000 for males, while in the same year the life expectancy for males was 57 years and for females was 56 years. The maternal mortality ratio, 539/100,000, is one of the highest in the world. As only 61% of the population has access to safe drinking water, the incidence of waterborne diseases continues to remain at unacceptable levels. Diseases such as diarrhoea, dysentery, worm-infestations, typhoid and jaundice are the major causes of high mortality and morbidity, particularly among infants. The percentage of children underweight is 48%. Prevalence of anaemia in pre-school children is 78% (1998). The incidence of tuberculosis is approximately 3.5 per 100 persons. Nearly three out of five households report that they do not have adequate access to health facilities and services.

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2. LEPROSY IN NEPAL

2.1 HISTORY.

Leprosy could be the oldest disease known to man. In China\(^1\) the oldest reports of leprosy are found in the ancient medical text, the Nei Ching ("Canon of Internal Medicine"). Tradition ascribes its authorship to Huang Ti (2698-2598 BC), the legendary third emperor. Its actual authorship is dated in the transition period of the Eastern Chou (771-255) and early Chin (221-207) dynasties.

In India\(^2\) Sushruta is considered to be the father of Indian surgery. He is believed to have lived at least two centuries before the birth of Buddha (563 BC). In his writings leprosy is referred to as "Vat-Rathka" or "Vat-Shonita" and categorised among the diseases of the nervous system. It is also referred to as "Kushta" and as such is grouped under the diseases of the skin.

In Nepal leprosy is known as "Khustro". Its local written history starts in AD 1857 in which year King Surendra Bir Bikram Shah Deva issues an order that all leprosy patients are to be isolated at a leprosarium near Khokana, with the provision of shelter, food and clothes. Khokana is a small village at the side of the Bagmati River. It is likely that in this period people affected by leprosy who were ostracised by family, neighbours and society had already settled there. Khokana may have been chosen because the leprosy patients could beg for food from the worshippers of the Kathmandu valley on their way to visit Dakshin Kali, one of the most venerated deities in Nepal.

At the start of the year 2000 there were in Nepal 13,572 registered cases of leprosy with a prevalence of 5.7 per 10 000. In the year 1999, 18,693 new cases were detected with a detection rate of 78.7 per 100 000 inhabitants. On 1/7/1999 a total of 60,995 patients were mentioned as released from treatment after Multi Drug Therapy (Rifampicin, Clofazamine and Dapsone).

In the 1970s the Integrated Community Health Programme was initiated in several districts with the intention of moving towards full integration of the Leprosy Control Programme.

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2.2 THE SOCIAL CONSEQUENCES OF LEPROSY.

In societies where leprosy is found, or has been known, the disease promotes different degrees of fear and abhorrence\textsuperscript{1-9} which can have grave consequences for those recognised as having leprosy.

Differences in the behavioural patterns of patients and community members are determined by the differences in the social (thus cultural) perceptions of leprosy of each community.\textsuperscript{10} Identifying these differences is important in the selection of priorities, preventive strategies and the interpretation of epidemiological data.

Women face the greatest burden as the diagnosis is often a reason to cancel an arranged marriage. Leprosy has caused married women to be abandoned, often left with children to care for.

Furthermore a woman can only normally function in Nepali culture within the boundaries of family life. The very protection she requires, she often loses when diagnosed with leprosy. Marriage in Nepal is traditionally arranged by the parents; almost always in rural areas and still most common in the urban areas.

A survey in 1982 among leprosy patients\textsuperscript{11} showed that the overwhelming majority had taken a partner of their own choice. Generally this was either another leprosy patient or someone lower in caste hierarchy. This would indicate that their parents did not take the normal active part in the marriage process of their Leprosy children; either from lack of interest, social shame, or the inability to find suitable partners.

The traditional Hindu Wedding cannot be performed except in arranged marriages. The culminating point of the ceremony is the \textquoteleft{}Kanyadan\textquoteright{} or gift of a virgin, in which cleanliness in every sense is an important feature.

Female leprosy patients complained that suffering from leprosy made the local priest refuse to perform these rituals at their weddings.

We noticed at Anandaban Hospital that the majority of the referred young, female patients appeared to have lost contact with their social background. A number of them were discouraged by family members from returning to their paternal families, knowing that this would present difficulties for their parents when arranging a suitable marriage for the remaining brothers and sisters. These girls often married other more disabled leprosy patients whom they had met at Anandaban, regardless of differences in original caste hierarchy.

In the above-mentioned ethnographic survey\textsuperscript{10} among the population of non-leprosy people, it was revealed that 87\% of the boys and 40\% of the girls attended school. However of the children of leprosy patients only 42\% of the boys and 9\% of the girls attended school. Sixty two per cent of leprosy patients who had children of school age who were not actively or regularly attending school, admitted that the community had pressured them against sending their children to school. The remaining 38\% stated that for economic reasons they were unable to send their children to school.
In Bulu and Koluwa Districts the prime reason for not allowing the leprosy patients or their children to attend public schools was that the children of leprosy patients would undoubtedly (!) become unable to function normally with the advancing disease, and therefore the need to give them an education was denied.

This attitude reflected the assumption that once a person develops leprosy, he or she will become disabled and that children of leprosy patients would, of necessity, get leprosy. In Nepal the leprosy patient is regarded as "jutho," unclean, and will therefore be treated as an "untouchable", which automatically implies a severe degradation in caste position.

At the beginning of the New Millennium opinion seems to be improving. However, the above cited study suggests that leprosy is still widely assumed to be highly infectious, hereditary and incurable and that it is grossly deforming.

It is still believed that leprosy is a divine retribution for sins or misdemeanours committed in the past, or for offending the snake god which dwells at a corner of each field. It is also believed that the disease can be caused by a curse, a spell or inhaling the smoke of the funeral pyre of another leprosy patient.

As a result it is no surprise that very few Nepali health workers seek employment in the Leprosy Control Programme as an optimal way of making a career. Those who have made the step voluntarily, however, perform their work with exemplary care and dedication.

In Nepal rituals surrounding birth, life and death are all crucial to spiritual life. It is imperative that an individual be disposed of in the manner prescribed by the regulations of one's caste or ethnic group.

Leprosy patients, like those who died unnamed or who committed suicide, cannot be cremated but are buried or pushed over the cliff to provide carrion for other animals or birds. And, as mentioned, it is believed that you can get leprosy from inhaling the smoke from the pyre of someone who has concealed the disease.

The stigma attached to leprosy often discourages patients from taking care of their hands and feet in public. Those with loss of sensation or with muscle dysbalance are faithfully taught in every health education session that they should walk limited distances, inspect their feet regularly and do the exercises to prevent contracture of joints and muscles. Often health workers do not recognise that most patients try to conceal their affected limbs (unless the patient has made begging his/her profession), and that walking along the paths it is not possible to inspect the feet in private.

The same real life limitations apply to the advice of health educators to soak affected extremities, scrape callous skin with a stone, and oil the skin while it is still wet.

One mechanism for coping with the severe stigma associated with leprosy can be denial. This was found in more than half of the "non-compliant" patients examined for a study of compliance of leprosy patients in Pakistan. In this context it has to be remarked that the majority of the hospital inpatients, labelled as compliant, often owe their hospitalisation to the fact that they have been markedly non-compliant in the past.
In dealing with non-compliance in the early phase of disease and treatment, it has to be realised that this behaviour is often based on the fact that the patient is still making efforts to be part of a stigmatising society.

The success of a Leprosy Control Programme and especially its disability prevention and community based rehabilitation components may be largely dependent on its ability to reduce stigma, to recognise mechanisms leading to early non-compliance and to deal with these problems in the most constructive way.

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2.3 LEPROSY IN THE WORLD.

Leprosy continues to be a serious public health problem in developing countries, particularly because:

a. The populations at risk of contracting the disease are very large.
b. More than one third of all leprosy patients face the threat of permanent and progressive physical and social disability.
c. In most endemic areas the incidence rate is not coming down (yet).

In the year 2000, according to WHO figures, 1.5 billion people in South-East Asia and 0.8 billion people in the Americas live in areas where leprosy is a public health problem, i.e. where the prevalence is over 1 case per 10,000 persons, and therefore individuals are running a significant risk of contracting the disease. The prevalence rates in South-East Asia and the Americas are respectively 3.8 and 1.1 per 10,000.

Table 1. Global Leprosy situation by WHO Regions 2000.

<table>
<thead>
<tr>
<th>WHO REGION</th>
<th>Cases on treatment (rate per 10,000)</th>
<th>Number of new cases (rate per 1,000,000)</th>
<th>Cured with MDT.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>64.490 (1.0)</td>
<td>55.635 (8.6)</td>
<td>645.576</td>
</tr>
<tr>
<td>Americas</td>
<td>90.447 (1.1)</td>
<td>45.599 (5.7)</td>
<td>256.670</td>
</tr>
<tr>
<td>South East Asia</td>
<td>574.924 (3.8)</td>
<td>621.620 (41.3)</td>
<td>9.507.660</td>
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<tr>
<td>Western Pacific</td>
<td>13.771 (0.1)</td>
<td>9.501 (0.6)</td>
<td>273.161</td>
</tr>
<tr>
<td>Europe</td>
<td>846 (-)</td>
<td>172 (-)</td>
<td>3.683</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>753.263 (1.25)</strong></td>
<td><strong>738.284 (12.3)</strong></td>
<td><strong>10.759.213</strong></td>
</tr>
</tbody>
</table>

Last Available Update: 14 December 2000 http://www.who.int/lep/det.htm
Table 2. Leprosy trend in 32 endemic countries combined 1985-1999(1)

<table>
<thead>
<tr>
<th>End of year</th>
<th>Registered Cases</th>
<th>Prevalence per 10,000</th>
<th>Newly detected Cases during year</th>
<th>Detection rate per 100,000 pop.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1985</td>
<td>4003742</td>
<td>21.1</td>
<td>550224</td>
<td>29.0</td>
</tr>
<tr>
<td>1986</td>
<td>4047385</td>
<td>20.9</td>
<td>573790</td>
<td>29.7</td>
</tr>
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<td>1987</td>
<td>3968347</td>
<td>20.1</td>
<td>595145</td>
<td>30.2</td>
</tr>
<tr>
<td>1988</td>
<td>3729982</td>
<td>18.5</td>
<td>553597</td>
<td>27.5</td>
</tr>
<tr>
<td>1989</td>
<td>3500723</td>
<td>17.0</td>
<td>550743</td>
<td>26.8</td>
</tr>
<tr>
<td>1990</td>
<td>2916407</td>
<td>13.9</td>
<td>571792</td>
<td>27.3</td>
</tr>
<tr>
<td>1991</td>
<td>2361032</td>
<td>1.0</td>
<td>613016</td>
<td>28.7</td>
</tr>
<tr>
<td>1992</td>
<td>1820302</td>
<td>8.3</td>
<td>667133</td>
<td>30.6</td>
</tr>
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<td>1993</td>
<td>1485785</td>
<td>6.7</td>
<td>615830</td>
<td>27.7</td>
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<tr>
<td>1994</td>
<td>1171711</td>
<td>5.2</td>
<td>553768</td>
<td>24.4</td>
</tr>
<tr>
<td>1995</td>
<td>924064</td>
<td>4.0</td>
<td>552416</td>
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<td>1996</td>
<td>838718</td>
<td>3.5</td>
<td>614822</td>
<td>26.0</td>
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<td>1997</td>
<td>767893</td>
<td>3.0</td>
<td>676319</td>
<td>26.3</td>
</tr>
<tr>
<td>1998</td>
<td>787468</td>
<td>3.1</td>
<td>786312</td>
<td>30.7</td>
</tr>
<tr>
<td>1999(2)</td>
<td>720371</td>
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<td>716673</td>
<td>27.8</td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td></td>
<td></td>
<td>9,191,580</td>
</tr>
</tbody>
</table>

1) Bangladesh, Benin, Brazil, Burkina Faso, Cambodia, Chad, Colombia, Congo, Democratic Republic of Congo, Cote d'Ivoire, Egypt, Ethiopia, Guinea, India, Indonesia, Madagascar, Mali, Mexico, Mozambique, Myanmar, Nepal, Niger, Nigeria, Pakistan, Philippines, Senegal, Sudan, Thailand, Venezuela, Viet Nam, Yemen, Zambia.

2) Latest available information for Brazil, Colombia, Democratic Republic of Congo, Cote d'Ivoire, Ethiopia and Zambia

Last Available Update: 14 December 2000 http://www.who.int/lep/det.htm

At present, for WHO's operational purposes, only (!) those who need or are under chemotherapy are considered as cases of leprosy. The leprosy patient, who is faced with the threat of social isolation, nerve impairment and disability, may hold a completely different view. As much as a leprosy patient can be invalidated by an ulcer, the quality of a Leprosy Control Programme can be invalidated by officers who are mainly interested in MDT statistics and who neglect the primary concerns of those affected by leprosy. We, therefore, need more knowledge of the mechanisms causing physical, social, economic and spiritual disability in leprosy and more effective ways of preventing and controlling this.
CHAPTER 1

Insufficient figures are available on physical disability rates, while the present WHO disability grading system which combines grade 3 and 2 of the previous WHO system, only makes it much more difficult to assess accurately the development of nerve impairment and disability after starting chemotherapy.

The ILEP reports do not include data on the social, economic and spiritual consequences of the disease.

Even after having long killed the last *Mycobacterium leprae*, we will have to face "ex-leprosy (?) cases" who are disabled and dehabilitated, and who will need continuous care for decennia to come. Many highly specialised leprosy control programmes are already looking into possibilities of diversifying their activities, but one should be careful that this should never be at the cost of existing care for the disabled leprosy patients.

The present WHO disability-grading system as recommended in 1988:

**Hands and Feet:**
- Grade 0: No anaesthesia, no visible deformity or damage.
- Grade 1: Anaesthesia present but no visible deformity or damage.
- Grade 2: Visible deformity or damage present.

**Eyes:**
- Grade 0: No eye problems due to leprosy, no evidence of visual loss.
- Grade 1: Eye problems due to leprosy present but vision not severely affected as a result of these (vision 6/60 or better; can count fingers at six metres).
- Grade 2: Severe visual impairment (vision worse than 6/60; inability to count fingers at six metres).

References:

2.4 LEPROSY CONTROL PROGRAMME IN NEPAL.

The Leprosy Control Programme of His Majesty's Government of Nepal was launched in 1965 and the National Leprosy Control Project established in the whole country in 1972.

The multi-drug therapy was introduced in 1982 and complete MDT coverage of registered cases was reached in the year 1995/1996, in all 75 districts. Since the introduction of MDT there has been a gradual decrease in the prevalence of the disease. The child 'new case detection rate' and the disability rate among new cases have, however, largely remained the same.
A revised MDT treatment for MB (Multibacillary) cases (12 month instead of 24 month doses), and for single lesion PB (Paucibacillary) cases (single dose therapy) was started in January 1998. In July 1999, according to the WHO figures of Nepal, in a population of about 22 million inhabitants the prevalence was 19525, the new case detection 18569, the new case child rate 5.8%, the new case WHO grade 2 disability rate 8.7%, the new case MB proportion 56.1%. 60995 patients were recorded as cured with MDT.

In the Joint HMG/WHO/NGO’s Report of an Independent Evaluation of the National Leprosy Control Programme in Nepal in January 1996 one of the recommendations was that, in addition to the goal of elimination of leprosy through MDT, due attention should be given to the prevention of impairment and disability, including the early diagnosis and proper treatment of reactions and neuritis.

In the report the MDT completion rates for PB cases varied in the districts between 33 to 90%, while for MB cases the range was 44 to 68%. It was concluded that treatment default rates were very high. Recent figures of relapse rates are not available.

In the Eastern District Region and the Far West District Region (15 districts) the Leprosy Control Programme is implemented with assistance from the NLR (de Nederlandse Leprastichting or the Netherlands Leprosy Relief Association).

In Solukhumbu district the leprosy work is supported by the Himalayan Trust (Sir Edmund Hillary) hospitals at Kunde and Phaphlu. In Okhaldunga, Palpa and Gorkha districts the leprosy work is supported by the UMN (United Mission to Nepal) hospitals. Between 40-50% of all new cases seen at the regional clinic at Biratnagar come from India and most want to be treated in Nepal.

In the Central District Region, Anandaban Hospital, supported by TLMI (The Leprosy Mission International), services 19 districts. It functions as a 120 bedded leprosy referral hospital for the Central and Eastern Regions, and the Government of Nepal plans to appoint it as the National Leprosy Centre. It has a training centre and a M. leprae Research Centre. It also runs an outpatient clinic for non-leprosy patients and a community health programme for the district.

Assistance in Dhanusha and surrounding districts is given by the Nepal Leprosy Trust.

In the West and Midwestern District Regions, the INF (International Nepal Fellowship) assists the Leprosy Control Programme in 31 districts by providing referral facilities at Green Pastures Hospital, Pokhara. The INF also runs a training and rehabilitation programme. Patients are referred by INF referral centres at Jumla, Surkhet, Ghorahi, and Baglung as well as from two UMN hospitals at Tansen and Amp Pipal.

The National Leprosy Control Programme, The Leprosy Mission, The International Nepal Fellowship and the Dutch Leprosy Relief Association all co-operate excellently in the fields of training, technical assistance and research.
Nowadays most programmes put more emphasis on disability prevention, disability control and rehabilitation. These issues are traditionally regarded as being of secondary importance to the introduction of MDT.

In Nepal the average patient has little awareness of micro-organisms and therefore being put on MDT and the consequent killing of *M. leprae* in the body has little appeal if it does not solve the more practical problems like the fear of physical, social and economic disability.

In the future, with health education, disability prevention and rehabilitation, a large rehabilitation programme may be of secondary importance in a Leprosy Eradication Programme (LEP). These issues should be an integrated part of every LEP and should be addressed at the time of diagnosis. In the first six months of treatment a patient faces the greatest risk of developing reactions. There is also an increased risk of nerve damage at this time and consequently non-compliance and defaulting from treatment.

Disability prevention and control requires the involvement of all health workers.

References:
3. CLINICAL ASPECTS OF LEPROSY

3.1 INTRODUCTION

It is beyond the aim of this chapter to provide a complete up-date of all clinical aspects of leprosy. Basic information is presented in order to make the following chapters accessible for those with little experience in the treatment of leprosy, while relevant new data are added where necessary.

Leprosy is a chronic infectious disease of man caused by the bacterium *M. leprae*. It is essentially a disease of the skin and peripheral nerves but also affects other tissues. To a great extent it can also be considered to be an immunological disease as the susceptibility to the disease, most symptoms and important complications are due to immune reactions to the bacilli.

3.2 MICROBIOLOGY.

In *vivo* *M. leprae* is an obligate intracellular parasite residing and multiplying mainly in macrophages and Schwann cells. It seems likely that the latter are not antigen presenting cells, at least in the early stage of infection, and that bacilli lying within them are not recognized by the host lymphocytes. One can get Schwann cells to present antigen in vitro: what is not known is whether this happens in vivo.

*M. leprae* has an almost\(^1\) exclusive habitat in man, and is readily found inside cells in which other mycobacteria are rarely seen; it has very low virulence and it is non-toxic, so that damage done to the host results solely from the host's inflammatory response.\(^2\)

The frequency of subsequent development of clinical disease is dependent on various factors at present still largely unknown, but the majority of the infected cases develop a sub-clinical infection and will never develop any signs of the disease. When, though, a susceptible host is infected, the type of leprosy which will develop, will be determined by the way in which the immune cells respond to the infectious challenge. The first testing place is likely to be inside the peripheral nerves, for leprosy bacilli have a predilection for neural tissue and there the target is the Schwann cell, which they most likely reach via endoneurial blood vessels.\(^3\)

The incubation period can vary from a few weeks to 30 years but in general falls between two and five years.\(^4\)

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3.3 IMMUNOLOGY.

Lepromatous leprosy patients show evidence of a specific failure of the cell-mediated immune response to *M. leprae*. The cause of this is still unknown but in 1986 suppressor T-cells were recognised in the blood of leprosy patients that are triggered by a group of *M. leprae* antigens (group I antigens) and act specifically to suppress responses to these antigens.¹

The immunological responsiveness of circulating T lymphocytes to *M. leprae* as measured in vitro by the lymphocyte transformation test (LTT) shows a strong correlation between the mean test values and the position of the disease in the spectrum.² The response is the strongest in TT leprosy and declines towards the LL pole where it virtually becomes negative. A parallel responsiveness is found with the lymphocyte stimulation test (LST) in borderline patients where the strongest response is found in BT patients and the weakest in BL patients.³

The research into the immunological and serological aspects of leprosy are increasingly gaining importance as they may help to answer the following clinical questions:

1. Is it possible to identify parameters that correlate with an increased risk of developing reversal reactions and subsequent nerve damage?
   Leprosy would hardly be a clinical problem would it not be for the nerve damage that it causes as a part of a reaction or as a “silent” neuritis. Especially the reversal or Type-1 reactions are feared for the quick and sometimes dramatic onset of nerve involvement. The use of the anti-phenolic glycolipid-1 (PGL-1) as an independent prognostic marker of reaction remains a matter of controversy, but at the Mycobacterium Research Laboratory of Anandaban Hospital, Paul Roche was the first to demonstrate that of all the borderline patients with positivity to the IgM anti PGL-1 antibodies test and the lepromin test as well, 78% developed a reversal reaction at a later stage. Though this combined positivity is found in only a minority of the borderline patients, it is of the greatest clinical importance that a high-risk group has been identified and prophylactic measures to control nerve damage can be considered.⁴ It would therefore be of interest to see whether the same correlation can be found with nerve function loss over the time of treatment as there are indications that PGL-1 plays a role in the induction of tumour
necrosis factor during the natural infection. Perhaps the ML dipstick test, a simple field essay to detect IgM anti PGL-1 antibodies, can be used for assessing this under field conditions. Also patients with high levels of IL-1β appear to be more susceptible to the development of reactions after the initiation of treatment.

There is a great need to further develop these tools as corticosteroid treatment at the time of a diagnosed type 1 reaction/silent neuritis only results in an “improvement” in a minority of cases while considerable numbers of patients suffer from further nerve function loss while on prednisone. One can only guess at the percentage of patients in which this “improvement” also leads up to restoration of “protective sensation” and “functional muscle strength”.

2. Is it possible to modulate the deficient cellular immune response to M. leprae?
In the WHO Immunology of Leprosy (IMMLEP) programme several investigations are going on to assess the influence of either injected killed M. leprae alone or in combination with live BCG or of components of mycobacteria upon the immune system. Various mechanisms have been proposed to account for the specific cellular immune deficiency in leprosy.

One of these is based upon the lack of specific T cell cytokines. Though, in general, the hypo-responsiveness of most lepromatous leprosy patients to M. leprae appears to be mediated by an absence of antigen reactive cells, it appears that the addition of interleukin-2 to mononuclear cell preparations from lepromatous leprosy patients sometimes restores the ability to respond to M. leprae in lymphocyte stimulation tests.

Interleukin-2 is of paramount importance for the proliferation of T cells in vitro and vivo after specific antigen stimulation. Nogueira et al. found that peripheral blood lymphocytes of lepromatous patients failed to produce gamma-interferon upon exposure to M. leprae and detected that this deficiency was restored by the addition of purified human interleukin-2 to the lymphocyte cultures in vitro. Further studies show differences in the degree of proliferative responses and gamma-interferon production in lepromatous leprosy lymphocytes after addition of interleukin-2, suggesting heterogeneity in the (still poorly understood) causes of immune deficiency in this category of patients.

In 1989 in a collaborative study with the Ministry of Health of His Majesty’s Government of Nepal, the Rockefeller University (New York), the Dartmouth Medical School (New Hampshire) and the Gillis W. Long Hansen’s Disease Center (Louisiana), we injected at Anandaban human recombinant interleukin-2 intradermally in lepromatous leprosy patients.

The majority of the patients showed a significant upgrading of their disease according to clinical, histopathological and bacteriological parameters. Within two months, skin slit smears showed a 0.5 log or greater reduction in 12/14 patients with a mean of 0.65 log units. Historical controls in this Nepalese population...
showed a 0.5 log unit reduction following multidrug therapy in a period of 12 months. It can therefore be concluded that the administration of interleukin-2 upgrades the immune response to *M. leprae*

3. Is it possible to find tools sensitive enough for the early detection of leprosy?

Antibody molecules do not bind to the whole of an infectious agent. Because of their specificity in recognition, each antibody molecule tends to bind to only one of the many antigen molecules on the microorganism’s surface. Each antibody then again binds to a restricted part of the antigen molecule, called an epitope. Antibodies are specific for the epitopes rather than the whole antigen molecule and different antibodies to an antigen often bind to epitopes that overlap on the antigen surface. Antibodies against the capsular phenolic glycolipid (PG-1) are highly specific to the *M. leprae*. The serum levels of these antibodies to these *M. leprae* specific capsular epitopes correlate well with the type of the disease within the spectrum. As the levels of IgM anti-*M. leprae*-PG-1 antibodies correlate well with the bacterial load of *M. leprae*, it is no surprise that these levels are higher in untreated than in treated patients. In a majority of new MB patients, who were initially highly IgM anti-PG-1 seropositive, there is a 50% decrease of this antibody level in the first 12 months of MDT.16

Because of the low sero-positivity rate among paucibacillary patients, this antibody assay is not very specific in detecting PB leprosy though it could be helpful in assessing the indication for MB instead of PB-MDT for PB patients with an extensive form of the disease. In untreated paucibacillary leprosy patients in Nepal 20% have IgM anti-PGL-1 antibodies17 while this was 29% in untreated primary neuritic patients18 and 89% in multibacillary patients.19

It was noted that the seropositivity rate and the antibody level against a common mycobacterial carbohydrate antigen such as lipoarabinomannan (LAM), PG-1 and to the 35kD peptide specific to *M. leprae* tend to rise with increasing extent of the disease when measured by the number of skin patches, by the number of nerves involved and with a position closer to the lepromatous pole of the spectrum. On the other hand half of the TT/BT patients are seronegative so that seronegativity cannot exclude leprosy as a cause of peripheral neuropathy.

A more recent development is the use of the polymerase chain reaction (PCR) for the (often several million fold) multiplication and so the much easier demonstration of the presence of very small quantities of *M. leprae* specific DNA fragments in the body.20 The over-all detection rates of *M. leprae* in biopsy samples of leprosy patients are lower with standard PCR than when histopathology examination is used.21-23 A more specific technique is the reverse transcriptase polymerase chain reaction (RT-PCR) in which the starting template is not DNA but a specific RNA fragment, which with the use of reverse transcriptase is translated in copy DNA (cDNA), which, in turn and with the help of DNA polymerase, can be made ready for multiplication like in the standard PCR. When a RT-PCR assay is used, targeting the 16S rRNA fragment of *M. leprae*, 53 % of acid fast
bacillus negative biopsy specimens are RT-PCR positive.\textsuperscript{24}

Although it is encouraging to observe that some serology tests and the reverse transcription (RT)-PCR assay may demonstrate \textit{M. leprae} in a proportion of the paucibacillary patients, tools that are sensitive and specific enough to detect early leprosy are still lacking.

4. \textbf{Is it feasible and necessary to develop and to implement a vaccine against leprosy?}

In the year 2000 according to WHO figures 1.5 billion people in South-East Asia and 0.8 billion people in the Americas live in areas where leprosy is a public health problem, i.e. where the prevalence is over 1 case per 10,000 persons and therefore individuals are running a significant risk of contracting the disease. The prevalence rates in South-East Asia and the Americas are respectively 3.8 and 1.1 per 10,000.\textsuperscript{25}

The ratio for risk of contracting the disease for contacts of lepromatous cases against contacts of non-lepromatous cases and non-contacts have been described for the Philippines\textsuperscript{26} to be 8:2:1 and for South India\textsuperscript{27} to be 9.5:3.7:1.

Theoretically, vaccination of especially the contacts could greatly assist in eradicating the disease. But the slow multiplication time of \textit{M. leprae} will create the need of a long follow-up period of a large vaccinated population being at risk for assessing its protection rate against a similar non-vaccinated population.

Multiple vaccine trials are being conducted in several countries\textsuperscript{28-30} but at present, the priority of vaccine strategies for leprosy has diminished, since the costs of development and implementation far outweigh the costs of controlling ("eliminating") the disease with MDT.

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3.4 CLASSIFICATION.

The clinical picture of leprosy depends on the leprosy specific immunological response of the host. The differences in manifestation of the clinical, histological, immunological and bacteriological aspects form the basis of the classification. The immunopathological spectrum described for leprosy by Ridley and Jopling in 1966 arranged the immunological phenomena (skin tests and lymphocyte transformation tests), the clinical picture, the histological appearances and the bacillary density in a consistent manner so that patients could be placed along a continuous spectrum. On this basis they can then be compared, treatments decided upon, and complications predicted. The five-point classification based upon this spectrum is:

- **TT** = Tuberculoid leprosy.
- **BT** = Borderline Tuberculoid leprosy.
- **BB** = Borderline (Borderline) leprosy.
- **BL** = Borderline Lepromatous leprosy.
- **LL** = Lepromatous leprosy.

The more the disease has a position closer to the centre of the spectrum, the more unstable it will be. The most unstable position is BB leprosy where with treatment an upgrading of
the cellular immune response and therefore a shift in position towards the tuberculoid pole is common, while in the absence of treatment an opposite shift towards the lepromatous pole can often be observed.

Two additional classifications of leprosy are recognised outside the framework of the Ridley-Jopling spectrum. In Indeterminate (I) leprosy clinically and histologically the disease has not yet fully established itself. At this stage there is no doubt about the diagnosis of the skin lesion but its position in the spectrum is still unclassifiable. In the 1982 WHO \(^2\) system it is considered paucibacillary. Also Primary Neuritic or Pure Neural (PN) leprosy is an early form of leprosy but here it is totally confined to a manifestation in the nerve(s). Early PN leprosy without definite signs poses a great diagnostic challenge to the clinician.\(^3\)

On clinical grounds the number of nerves affected in pure neural cases is helpful. Only one nerve is usually affected in tuberculoid cases while in the borderline group several nerves are likely to be affected.

However, for the field worker the Ridley-Jopling classification with all its modifications is too complicated and therefore the 7\(^{th}\) WHO Expert Committee\(^4\) on Leprosy meeting of June 1997 proposed the following Clinical classification for Control Programmes:

**a. Paucibacillary single-lesion leprosy** (one skin lesion).

**b. Paucibacillary leprosy** (2-5 skin lesions).

**c. Multibacillary leprosy** (smear positive patients as well as patients with more than 5 skin lesions).

At Anandaban, in addition to counting the number of skin lesions, we also include the number of nerves involved (defined as enlarged, palpable, with function-loss) as serology seems to suggest that this is a better indicator of the extent of disease than the number of skin patches. We treat PN leprosy when more than 2 nerves are involved as MB leprosy. The reason is that the PGL-1 seropositivity in paucibacillary patients and in PN patients with only 1-2 nerves involved is about the same; 20% and 25% respectively, but is much higher when either more skin lesions and/or more nerves \(^5\)\(^6\) are involved.

**References:**
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3.5 DIAGNOSIS.

The diagnosis can in general be made by proper clinical examination and, if available, be supported by slit skin smears. For the diagnosis of leprosy four cardinal signs can be present:

a. **Anaesthesia.**
   This can be of individual skin lesions or in the area supplied by a large peripheral nerve.

b. **Thickened nerves.**
   This at the sites of predilection or as cutaneous branches supplying affected skin.

c. **Skin lesions.**
   These can show a change in colour, sensation, and can be infiltrated (inflamed), raised, and show diminished perspiration and hair growth.

d. **Acid fast bacilli** in slit skin smears.

Two out of the first three signs or the fourth sign should be present for the diagnosis to be made.
Sometimes only nerve involvement in the absence of skin lesions can be found. If in such a case the nerve is enlarged, a cytological aspiration of nerve fluid can assist in making the diagnosis. Slit skin smear taking, staining (the Slit and Scrape Method of Wade, 1935) and reading are often of insufficient quality in many field programmes.
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3.6 TREATMENT OF LEPROSY.

Dapsone (Diaminodiphenyl sulphone) for the treatment of leprosy was first used in 1941 by Guy Faget. This drug has appeared to be very effective, be it that it is only bacteriostatic. When either used in low dosages or in a patient who is not fully compliant, sulfone resistant *M. leprae* readily develops.

For this reason in 1977 the WHO's Fifth Expert Committee on Leprosy called for the replacement of monotherapy with combination drug therapy in the form of Dapsone combined with Rifampicin or Clofazamine. In this combination Rifampicin is a very potent bactericidal drug.

The present recommendations of the 7th WHO Expert Committee on Leprosy of June 1997 are:

For **Single Skin Lesion Paucibacillary Leprosy**: A single supervised dose of:
1. Rifampicin 600 mg.
2. Ofloxacin 400 mg.
3. Minocycline 100 mg.

For **Paucibacillary cases**: during 6 months:
1. Dapsone 100 mg daily, unsupervised.
2. Rifampicin 600 mg once monthly, supervised.

For **Multibacillary cases**: during 12 months:
1. Dapsone 100 mg daily, unsupervised.
2. Clofazamine 300 mg once monthly, supervised and 50 mg daily, unsupervised.
3. Rifampicin 600 mg once monthly, supervised.
MB patients who do not accept clofazimine can be treated with a monthly administration of a combination consisting of 600 mg rifampicin, 400 mg ofloxacin and 100 mg of minocycline for 24 months. For adult MB patients who cannot take rifampicin, the Committee recommended the daily administration of 50 mg of clofazimine, together with 400 mg of ofloxacin and 100 mg of minocycline for 6 months; followed by daily administration of 50 mg clofazimine, together with 100 mg of minocycline or 400 mg of ofloxacin for at least 18 months.

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   www.who.int/lep/exp/exp.htm

3.7 REACTIONS.

In leprosy the term reaction is used to describe acute inflammatory episodes superimposed on the usually relatively uneventful course of leprosy.

a. The type 1 or reversal reaction (RR)
   is caused by delayed cell-mediated hypersensitivity reactions with a shift of the patient’s position in the spectrum. They occur in patients with borderline leprosy.
   If there is an increase in immunity, the shift is towards the tuberculoid pole and is called upgrading or reversal reaction. Skin lesions become swollen and raised, macules become plaques or they develop raised edges. In lighter skinned individuals the lesions can become quite red. Usually the lesions become more erythematous, sometimes purple, or in white skin, coppery brown. Occasionally they are oedematous and pale. The edges become more distinct than before so that the lesions stand out sharply from the surrounding normal skin. The lesions are often tender or even painful. New lesions may appear. Usually they resemble the pre-existing ones, but sometimes they are very numerous and small and clinically confusing.
   When there is a reduction in immunity with a shift towards the lepromatous pole, one speaks of a downgrading reaction. Almost no downgrading reactions are seen in treated patients. The new lesions in an episode of downgrading may be more lepromatous in appearance than the previous ones, and if the reaction is severe the skin lesions may desquamate or even ulcerate. As the reaction starts to subside, the skin becomes dry and scaly and ultimately flattens, leaving a wrinkled hypo-pigmented surface. Untreated, type 1 reactions tend to last for months or years, and may relapse.
Neuritis with nerve function loss can be acute and dramatic in type 1 reactions and seems to be more common in men with BT leprosy, while women commonly get more extensive skin changes.

The neuritis presents classically with tender enlargement of nerves at the sites of predilection. Sometimes the nerves are grossly enlarged. Loss of function may be marked with sudden paralysis of the muscles of the hand or foot, wrist drop, foot drop or lagophthalmus or even hemi-facial paralysis.

Anaesthesia develops rapidly in the distribution of the affected nerve. Nerve pain may cause great suffering and may even mimic ischialgia when the lateral femoral cutaneous nerve is involved.

b. **Type 2 or erythema nodosum leprosum (ENL) reaction** are also known as lepromatous lepra reactions and erythema nodosum leprosum (ENL). They are associated with pockets of polymorphonuclear leucocytes and degenerate acid-fast bacilli in the skin (ENL), nerves (neuritis), lymph nodes, joints, eyes (iridocyclitis) and testis (orchitis) etc.

Type 2 reactions occur in patients with multi-bacillary leprosy. Often there is generalized illness, sometimes with a fatal outcome.

c. **Lucio phenomenon.**

occurs almost exclusively in patients of Mexican origin. It is characterised by marked small pink lesions, vasculitis and thrombosis of the superficial and deep vessels resulting in haemorrhage and necrosis of the skin, usually on one of the limbs.

A component causing tissue damage during type 1 reaction may be CD4+ *M. leprae* responsive T cells with a polarised Type 1-like phenotype. There is also evidence of a T helper-1 response with presence of interferon-gamma and absence of interleukin-4 (IL-4) mRNA in the peripheral blood mononuclear cells of 85% and 64% of type 1 and 2 reaction patients respectively, and in all reaction sites, whereas a T helper-0 was seen in some and a T-helper-2-like response was absent. IFN-gamma was detected in 84% of the patients with ENL and in 100% of the patients with a reversal reaction. Yet, the pathogenesis of reactions is still to be clearly elucidated. Recent immunologic studies have shown that heat-shock-protein 70 (HSP 70) is formed by *M. leprae* and also by Schwann cells under stressful conditions and that there is significant homology between the two HSP's. Therefore, T-cells of the host, primed against HSP-70 of *M. leprae* origin can cause an auto-immune reaction against Schwann cells. It is possible that this mechanism may be one of the important causes for extensive damage to peripheral nerves in borderline leprosy.

Skin changes, nerve function loss and nerve pain are often the first symptoms for which the patient seeks medical help.
INTRODUCTION

The detection of (early) nerve function loss is very dependent on the techniques used:

1. Electrophysiology.
Motor Nerve Conduction Velocity (Motor NCV) studies in leprosy patients as conducted by Naafs\(^8,9\) showed that tender nerves conduct more slowly than non-tender nerves, while the latter are slower again than the normal nerves of healthy individuals, and that affected tender and non-tender nerves both improved with steroid treatment.
In general, facilities to study Motor NCV are not available at the sites where most patients are seen.

2. Voluntary muscle testing (VMT) to test muscle strength\(^10\)
can be performed under field conditions but will only reveal pathology when already at least 30% of the nerve fibres are affected.

3. The Paper Grip test
for early detection of intrinsic muscle weakness in the foot.\(^11\)
Leprosy feet with a normal sensibility showed an abnormal paper grip test in 24.8% of the patients.

4. Sensory testing by using the Semmes-Weinstein monofilaments
for measuring light touch sensation can be extremely useful in assessing mild nerve involvement\(^12,13\) in a clinical setting.
At Anandaban we compared the bending forces of the same calibres of filaments coming from different sets of different age, but of the same manufacturer. We found a great variation in bending force and consequently a reduced reliability. Therefore, it deserves recommendation to use the same set of filaments for the follow-up of one and the same patient and to verify the calibration regularly.
The introduction of the monofilaments for sensory testing in order to identify damaged nerves at an earlier stage of disease almost doubled the number of patients put on corticosteroids at Anandaban Hospital.

In spite of the fact that we now have more sophisticated equipment available to measure also other modalities of sensation like temperature sensation and vibration, we are still looking for reliable and simple tools that can be used under field conditions.
In a study of 28 leprosy patients Jennekens & Jennekens\(^14\) found changes of position sense and decrease of some tendon reflexes in a minority of these cases. Though it is concluded that an extensive neurological examination is probably not required for the diagnosis, it provides more accurate information on the extent of damage to the peripheral nerve system.
References:

INTRODUCTION

3.8 TREATMENT OF REACTIONS AND PERIPHERAL NERVE FUNCTION LOSS.

Medical treatment:

NSAID’s
In mild reactions with only discomfort or mild pain NSAID’s in general suffice. In our experience, when acetylsalicylic acid (Aspirin) is taken in combination with a high dosage (200-300 mg daily) of Clofazamine, as sometimes required to control reaction, the risk of peptic irritation is strongly increased and additional precautions are advisable.

Corticosteroids
In severe nerve pain or when there is nerve function loss, corticosteroids like Prednisone and Prednisolone are the most commonly used preparations. Various regimens with, for example, 40 mg/day for the first 3 weeks, after which the dosage can be tapered off, are often used also in the field. Unfortunately the influence of Prednisone 40 mg/day on the recovery of nerve function seems rather limited.1
In this article an overall improvement was found in 37% of the patients only, while 40% remained the same and 23% even worsened during prednisone treatment.
Ongoing trials of high (“pulse therapy”) and low dose fixed duration prednisone treatment may produce better results.
While many encouraging publications on the outcome of prednisone therapy speak of “improvement” or “recovery rates” of nerves2, one has to interpret these data with caution as only results showing sufficient recovery of protective sensation and functional muscle activity may have clinical relevance.
Trials are going on to assess the effect of prophylactic corticosteroids on the incidence of reactions in newly diagnosed multibacillary leprosy patients.3 Preliminary results suggest that prophylactic corticosteroids decrease the number of reversal reactions during the first six months of MDT, but that, when compared with the effect of a placebo, there is no significant difference in loss of nerve function when assessed after one year of treatment.

Thalidomide
This drug is known to suppress ENL and often is the last option for treating a persistent and severe type 2 reaction.
Teratogenicity (“the Softenon effect”) is its most serious side effect and for this reason the use is still prohibited in many countries. Other serious side effects are thrombocytopenia, eosinophilia and peripheral neuropathies.

Clofazimine (Lamprene)
The drug is reported to be mildly bactericidal towards M. leprae, but it is also effective in the management of leprosy reactions, apparently because of its anti-inflammatory capacity.
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Physiotherapy:
Nerve function loss or severe nerve pain can further be treated with partial immobilisation and by padding joints. Controlled and supervised partial exercises of the joints are needed to preserve the gliding function of the nerve.

Surgery:
When corticosteroids fail to relieve severe nerve pain and to restore nerve function, nerve decompression with selective meshing of the epineurium to preserve the well-developed vascular plexus in the epineurium, is indicated.4

For an excellent discussion on the care of the neuropathic limbs I like to refer to the practical manual written by Grace Warren.5

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   Contribution of type 1 Reactions to Sensory and Motor Function Loss in Borderline Leprosy Patients and the efficacy of treatment with prednisone.
   A field trial of detection and treatment of nerve function impairment in leprosy-report from national POD pilot project.
3. Croft RP, Nicholls P et al.
   Effect of prophylactic corticosteroids on the incidence of reactions in newly diagnosed multibacillary leprosy patients.
4. Theuvenet WJ, Roche PW et al.
   Nerve decompression by selective meshing of the epineurium.
   submitted for publication. 2002.
5. Warren G and Nade S.
   The care of the neuropathic limbs, a practical manual.

3.9 PREVENTION OF IMPAIRMENT AND SUBSEQUENT DISABILITY (POID) AND REHABILITATION.

According to the WHO Expert Committee on Leprosy, Fifth Report of 1977: 1

“...In an efficiently conducted programme no new cases with irreversible disabilities should be detected, and further deterioration can and should always be prevented”.

It is clear from the chapter on "Leprosy in Nepal" that in 2002 this is neither the current situation in Nepal, where in the past ten years the percentage of patients with disabilities
amongst newly detected cases has lingered around 10, nor elsewhere in the world. At national level, hardly any leprosy control programme has a clear strategy for POID and rehabilitation yet.

1. The prevention of impairment and disability
Besides early case detection, POID research priorities include studies of methods
   a. to strengthen health education,
   b. to prevent social, economic and mental malfunctioning,
   c. to promote patient compliance,
   d. to improve the early detection of autonomic, sensory and motor neuropathy;
   e. studies of the use of various POID monitoring systems.

Concentration on medical care of people affected with leprosy (MDT, surgery, etc), though vastly beneficial, has for a long time led to a neglect of POID, this resulting in a poor quality of life of many affected by leprosy.

2. Rehabilitation
On the other hand it is encouraging to note that (finally) by the year 2000 POID and the Social and Economic Rehabilitation (SER) of people affected by leprosy has become a major priority and Leprosy Review devoted a special issue to this topic in December of the same year. More than 10 million persons affected by leprosy have been cured with MDT in the last decade but studies done by IDEA, DAHW and ALES suggest that up to 35% of leprosy-affected persons may need socio-economic rehabilitation and that barely 5% of the disabled persons have access to any rehabilitation services at this moment. In these studies there is no mention at all of the disabling influence of having leprosy on the mental status of those affected. Immediately after diagnosis grief appears to be the first and most general reaction experienced by leprosy patients, while mental stress can further increase when self, social and community acceptance become a problem and visible signs of leprosy set in. According to van Parisis one-third of leprosy patients suffer desertion by marriage partners, while more women than men suffer from isolation, rejection and decreased family support. It is no surprise that also in Nepal persons affected by leprosy try to hide their disease, out of fear for negative family and community behaviour.

As a result a need was felt to conduct a specialized study of the psychosocial effects of leprosy in Nepal. This study was titled "Psychiatric morbidity in people affected by leprosy in Nepal assessed with the WHO Self-Reporting Questionnaire (SRQ)". The results are presented in Chapter 9.
Rehabilitation is a unique task and the approach may not be duplicated between places or even from one person to another, and therefore in the report on the WHO AIFO Joint workshop emphasis was placed on the need to adopt a multi-sectorial, holistic approach to address the issues of physical, psychological and socio-economic rehabilitation for the affected individuals as well their communities.

At the ILA Conference in Beijing in 1998 it was stated that the approach to SER should be based on three principles:

a. Recognition of the broad impact of leprosy on the individual; in other words, its physical, psychological, social and economic effects.

b. Responsiveness to the concerns of the individuals affected by leprosy. This requires an approach that restores dignity and self-respect; in other words participation and empowerment.

c. Sensitivity to the concerns of the families and communities affected by leprosy as members of the family and the community have an important role to play in rehabilitation.

Just as with the prevention of impairment and deformity, the assessment of the needs and skills of patients affected by leprosy should be done at the earliest possible opportunity after diagnosis.

References:
1. World Health Organization.
   WHO Expert Committee on leprosy.
2. Smith WCS.
   Special Issue on Socio-Economic Rehabilitation,
3. Scott J.
   The psychosocial needs of leprosy patients.
4. Van Parijs LG.
   Health education in leprosy work. A manual for health workers,
5. Zodpey SP, Tiwari RR et al.
   Gender differentials in the social and family life of leprosy patients.
6. Floyd-Richard M and Gurung S.
   Stigma reduction through group counselling of persons affected by leprosy - a pilot study.
3.10 (RECONSTRUCTIVE) SURGERY IN LEPROSY.

The first responsibility of a reconstructive surgeon involved in leprosy is to prevent impairment and deformity. It is, therefore, that only at this stage of the introduction, a summary is given of some of the main procedures used in reconstructive surgery in leprosy.

These reconstructive procedures can be divided into:

A. Operations for the restoration of dynamic function:

1. In the face for the compensation of facial nerve paralysis:
   - lagophthalmus correction by e.g.: medial canthopexy
   - medial and/or lateral suspension plasty
   - facial sling procedure
   - temporalis muscle transfer
     (The tarsoraphy procedure is simple but gives a terrible cosmetic result).
   - facial paralysis
     - temporalis muscle many tail procedure
     - masseter sling procedure

2. In the hand for the compensation of ulnar/median/radial nerve paralysis:
   - claw hand correction by e.g.: palmaris longus transfer*
     - Zancolli-Lasso procedure
     - EF4T (= extensor to flexor many tail) procedure*
     - FDS-III (= sublimus) transfer*
   - opponens plasty by e.g.: FDS-IV transfer#
   - wrist drop correction by e.g.: extensor indicis proprius transfer#
     - pronator teres and flexor carpi radialis transfer
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Lagophthalmus right eye

pre-operative; eyes light closure

post-operative; eyes light closure after right temporalis muscle transfer

pre-operative; eyes open

post-operative; eyes open
Ulnar and Median Claw Hands

pre-operative; fingers in "intrinsic position"

pre-operative; fingers in extension

post-operative; sublimus IV transfer right hand, fingers in "intrinsic position"

post-operative; fingers in extension
Right footdrop

pre-operative; right footdrop

pre-operative; loss of dorsiflexion at time of heel-strike

peroperative; transfer tibialis posterior tendon

post-operative; corrected footdrop

post-operative; corrected dorsiflexion at time of heel-strike
* In claw-hand correction the proper selection of the site of insertion of the slips into the extensor apparatus of the digits gives a tool to further balance the fingers when there is a difference in the degree of clawing at PIP joint level. Insertion either distally (a) or proximally (b) at the conjoined tendon will influence the strength of the mechanical arm of the transferred tendon over the MCP joint and thus create a variable degree of MCP flexion. Insertion of the transferred slip either laterally (conjoined tendon) or dorsally (c, central slip) will cause a variable degree of PIP and DIP extension.

# In the absence of FPB function the transfer should cross the dorsum of the thumb distally from the MCP joint in order to add MCP flexion.

3. In the foot
   a. for the compensation of peroneal nerve paralysis:
      complete foot drop correction by e.g. TPT, circumferential or interosseous route.
      lateral foot drop correction by e.g. Peroneus Longus transfer.
   b. for the compensation of n.n. plantares paralysis:
      claw toe correction by e.g. FDP to extensor transfer.
      this merely corrects the position and not as much function at MTP and PIP joint level.

   At Anandaban Leprosy Hospital we developed a new technique named nerve decompression by selective meshing of the epineurium, described in chapter 5, page 88.

B. Operations for the restoration of joint position:
   In general these are the arthrodesis operations for finger, toe, wrist and ankle joint position.
C. **Operations for cosmetic correction:**

For instance reconstructions of the eyebrows, the collapsed nose and the atrophied first web-space of the hand, correction of ear lobe hypertrophy and the face-lift for facial wrinkling after reaction etc.

Although the septic surgery procedures are in a stricter sense more salvage operations and not as much reconstructive procedures, they form a major part of the routine surgical interventions and are therefore included here.

D. **Septic surgery:**

Foot ulcers are by far the most frequent indication for admission in a hospital.

In general it is not difficult to get an ulcer healed but the real challenge lies in the understanding of *why* it has occurred and how to *prevent* recurrence.

For this it is essential that one has a thorough knowledge of the normal functional anatomy and of the disturbances caused by specific nerve function loss as caused by the *Mycobacterium leprae*.

In the last 15 years these techniques have been the subject of team-training courses in POID and reconstructive surgery in Asia, Africa and South-America on behalf of The Leprosy Mission International and the Netherlands Leprosy Relief Association.

### 3.11 OCULAR PATHOLOGY IN LEPROSY

It is estimated\(^1\) that there are a total number of 350,000-400,000 blind leprosy patients, by WHO standards blindness is visual acuity (VA) of <3/60.

In control programmes, after implementation of MDT, potentially sight threatening lesions are reported in 15 to 20 percent; blindness in 1-3 percent. This is about double the level of blindness in the general population in developing countries. It is reported\(^2\) that blind leprosy patients have a 4.8-fold excess risk of dying compared to nonblind leprosy patients of the same age.

Eye complications are caused by the same mechanisms that cause complications in general in leprosy:

- **a.** Type 1 reactions: lagophthalmus and corneal anaesthesia.
- **b.** Type 2 reactions: acute iritis and scleritis
- **c.** Infiltration and secondary atrophy: a series of extra and intra-ocular lesions.

It speaks for itself that just as with leprosy neuritis in general, also eye complications need to be diagnosed and treated in an early stage. Age-related cataract is the most important cause of blindness in leprosy nowadays and it is rightfully stressed by Hogeweg\(^3\) that leprosy patients with loss of sensation in hands and feet should receive early cataract surgery as
severe visual impairment or blindness may hamper or preclude self-care and is, therefore, more disabling in leprosy patients than in the general population. Facial patches over the facial nerve almost seem to announce a lagophthalmus. And when conservative treatment fails and a 5-6 mm lid gap in mild closure remains, lid surgery is indicated by an experienced surgeon (see page 47).

In order to improve eye care in leprosy, routine assessment of VA should be included in the protocol for the screening of the early signs of nerve function loss, this especially during the time that a patient is prone to develop type 1 and 2 reactions but also during the "care after cure".

Leprosy programmes should establish cooperation with the local eye care services for referral of patients.

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   a retrospective study among 1226 paucibacillary leprosy patients.

4. SCOPE OF THIS THESIS.

Without nerve damage there would be neither physical impairment nor disability in those affected by leprosy and leprosy would not be very different to many of the other contagious diseases of the skin that can be successfully treated nowadays. It is for this reason that in leprosy we need to focus on the clinical aspects of nerve damage.

From Anandaban hospital between 1985 and 1990 an intense (house-to-house) survey of Lalitpur district was conducted in order to improve on early case finding and the early diagnosis of neuritis (Chapter 2). An unknown manifestation of neuritis in leprosy, the neuritis of the lateral femoral cutaneous nerve (meralgia paraesthetica), was detected (Chapter 3). In order to facilitate the diagnosis of pure neural leprosy, we developed the cytological needle aspiration of the nerve (Chapter 4).

Foot ulcers are the most frequent reason for admission in leprosy hospitals and in spite of protective footwear they tend to have too high a recurrence rate. In order to improve on the early detection of intrinsic muscle function loss in the foot, a simple test was developed that may
assist in taking timely preventive measures to protect the foot (Chapter 5). A nerve decompression study using a new technique of selective meshing of the epineurium was conducted to improve nerve function loss when steroids had failed (Chapter 6). Reversal (type-1) reactions are the main contributor to nerve damage and besides the need to identify risk factors for type-1 reactions (Chapter 7), there is a need to understand more of the immuno-pathological mechanisms involved and the efficacy of prednisone in leprosy neuritis (Chapter 8). All the previous chapters deal with issues seen from the medical perspective, but the people affected by leprosy have hardly any notion of germs, the struggle to implement MDT, reactions etc. Their main concerns lie at a totally different level where they fear isolation, rejection, disability and the social and economic consequences of these for themselves and their families. In order to bring the patient's perspective in line with the medical perspective, we assessed the mental stress factors that a patient affected by leprosy is facing in daily life (Chapter 9).