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Community dermatology

Leprosy in the Philippines: a review

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Abstract

Leprosy is a skin disease that accounts for serious deformities and disabilities, leading to stigmatization and psychosocial suffering. It is included in "The Neglected Tropical Diseases". Not surprisingly, its management is increasingly reported as a function of Dermatology Departments, with a strong community-orientated bias. Prompt and accurate diagnosis of leprosy is crucial in the control of leprosy. Its management requires a multidisciplinary team of skilled physicians, laboratory staff, and nurses. All members of the health sectors should remain vigilant to combat this battle against leprosy.

Introduction

Leprosy has been depicted as a disease responsible for serious deformities and disabilities leading to stigmatization and psychosocial suffering. It has remained endemic in many countries, especially affecting the poorest sector of these nations. Three million people worldwide are estimated to be disabled by the consequences of this chronic, debilitating disease, with many co-morbidities and personal implications.[1]

History

Leprosy was recognized in the ancient civilizations of China, Egypt and India. The first known written mention of leprosy dates back to 600 BC. Throughout history, the afflicted have often been excluded from society.

In 1904, a leper colony was formed in the Philippines on the remote island of Culion (Island of Living Dead). Situated in the northernmost chain of Palawan islands, it housed 670 patients with leprosy. Those more active patients engaged in crude agriculture and fishing. Some started families in Culion, but most of them were separated from relatives, and lived in isolation and poverty.[2]

In 1921, the USA governor-general of the Philippines, Major General Leonard Wood visited the leprosarium on Culion Island, which had 7000 patients with leprosy. By 1928, The Leonard Wood Memorial (LWM) for the eradication of leprosy was established. A modern leprosy research laboratory was set up on Cebu Island while work continued at Culion. With modern medicine the number of active leprosy patients was reduced. The island welcomed settlers, primarily non-lepers who were families and friends of previous patients. The non-patient population began to grow, while the patient population slowly lessened in number (Fig. 1a,b).[3]

LWM remaines functional to this day with a unique multidisciplinary biomedical research facility, consisting of three branches: Clinical Research, Skin Clinic, and Epidemiology and Laboratory. These branches provide no-fee medical consultation, diagnostic and treatment services to patients with leprosy and other skin diseases, such as psoriasis. They also conduct good clinical practices-compliant clinical trials to evaluate new drugs, drug regimens and vaccines.

The Central Luzon Sanitarium (Tala Leprosarium) became operational in 1940, and is one of the eight institutes in the Philippines that once served patients with

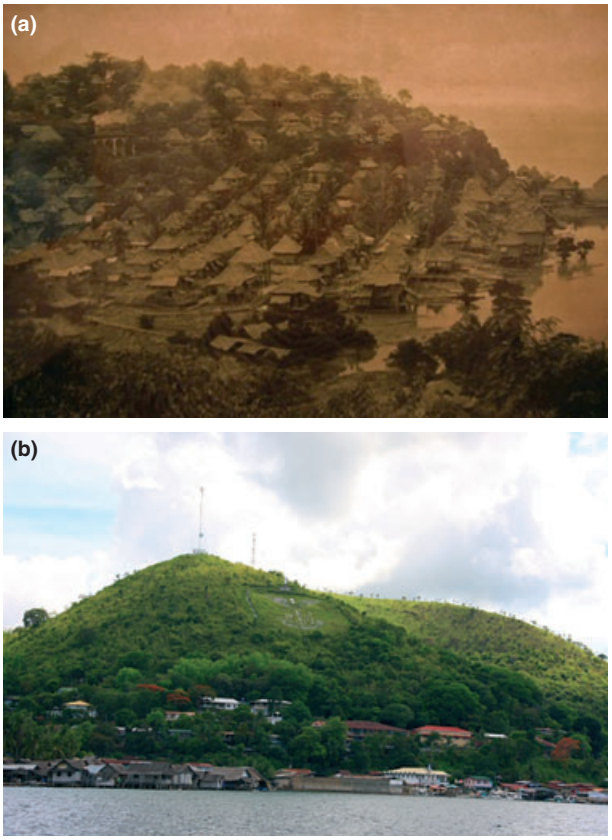

Figure 1 (a, b) Culion Island (then and now)

Figure 2 Doctor Jose N. Rodriguez Memorial Hospital (DJNRMH)

leprosy. It was renamed the Doctor Jose N. Rodriguez Memorial Medical Hospital (DJNRMH) in 1970. It is a 2000-bed special tertiary hospital for patients with Hansen's disease being utilized for custodial care (1800 beds) and general care (200 beds) of non-leprosy cases. The facility offers outpatient clinics, ward, custodial care,

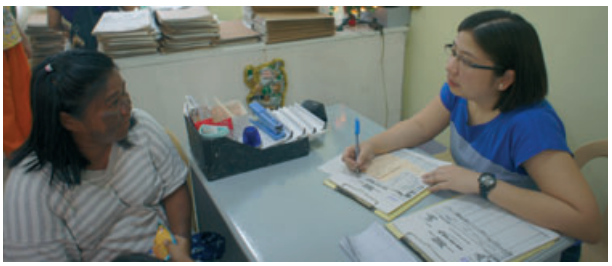

Figure 3 A patient with lepromatous leprosy consults at the out-patient clinic

Table 1 Eight actively operating sanitaria in the Philippines (National Leprosy Control program, Department of Health Philippines, 2010)

Name of sanitarium	Location
Dr. Jose N. Rodriguez Memorial Hospital	Tala, Caloocan City
Culion Sanitarium and General Hospital	Culion, Palawan
Bicol Sanitarium, Cabusao	Bicol Region
Western Visayas Sanitarium	Sta Barbara, Iloilo
Eversley Child Sanitarium	Mandaue City
Cotabato Sanitarium	Cotabato Province
Mindanao Central Sanitarium	Sta Maria, Zamboanga City
Sulu Sanitarium	Jolo, Sulu

wound care, foot and rehabilitation services (physical, occupational therapy and foot wear).[4] Currently, it houses 100 patients in the custodial unit and 100 registered patients at the outpatient clinic (Figs 2 and 3; Table 1).

Epidemiology and etiology

Transmission

Hansen's disease is a chronic infectious disease caused by *Mycobacterium leprae* and *Mycobacterium lepromatosis*.[5,6] *Mycobacterium leprae* was one of the first microorganisms directly linked with a specific disease. Conversely, considerable disparity still exists in our comprehension concerning its immunological, pathological and epidemiological aspects.

Individuals who suffer from the disease, particularly those with multibacillary (MB) leprosy, are sources for spread of the infection. The most important port of entry and exit of *M. leprae* is the respiratory system, mainly the nose; its dissemination through skin lesions seems to be less important.[7] Patients' household contacts, neighbors and social contacts have an increased risk of contracting the disease. However, is this largely a result of closer contacts to the index case, similar genetic and immunological backgrounds, environmental factors, or a combination of

Table 2 Trends in the detection of new cases of leprosy, by WHO region, 2003–2009[43]

	Number of new cases detected, 2003–2009						
WHO region	2003	2004	2005	2006	2007	2008	2009
Africa	47 006	46 918	45 179	34 480	34 468	29 814	28 935
America	52 435	52 662	41 952	47 612	42 135	41 891	40 474
South-East Asia	405 147	298 603	201 635	174 118	171 576	167 505	166 115
Eastern Mediterranean	3940	3392	3133	3261	4091	3938	4029
Western pacific- Pacifique occidental	6190	6216	7137	6190	5863	5859	5243
Total	514 718	407 791	299 036	265 661	258 133	249 007	244 796

No reports were received from the European region.

Table 3 Statistical trend on National Leprosy Control of the Philippines (National Leprosy Control Program, International Conference of Leprosy, Manila, Philippines: November 2010)

	No. of cases (rate %)		
	2006	**2007**	**2008**
Prevalent cases (per 10 000 pop.)	3787 (0.42)	2514 (0.26)	3338 (0.35)
New cases (per 100 000 pop.)	2517 (2.91)	2279 (2.89)	2373 (2.47)
MB among new cases	2278 (90%)	1541 (61%)	2142 (90%)
Disability grade 2 among new cases	74 (2%)	69 (2.7%)	45 (1.9%)
Children < 15 years old among new cases	199 (7%)	96 (4.37%)	110 (4.6%)
Women among new cases	482 (21%)	512 (20%)	285 (12%)
Cured cases (treatment completed)			
MB	3771 (90%)	2795 (88%)	3864 (85%)
PB	279 (93%)	254 (90%)	434 (90%)
No. of cases that need rehabilitation – Physical	70	65	45

MB, multibacillary; PB, paucibacillary.

all these; its still unknown.[7,8] A study in Korea and the Philippines suggested that a high prevalence of anti-PGL-I IgM antibodies among children may indicate an active transmission of *M. leprae*, resulting in higher incidence of leprosy in the population.[9]

Moreover, the immune status of the patient remains a significant factor. Bacillus Calmette-Guerin (BCG) vaccination provides protection against leprosy, although studies have shown the degree of protection varies from 20 to 80%.[10] It may also be responsible for a shift in immune response from MB to paucibacillary (PB) leprosy.[11] BCG vaccination is currently recommended for all newborns in the Philippines as part of the Standard Routine immunization of the Expanded Program on Immunization.[12]

Distribution and trends

The geographic distribution of leprosy varied in the past, but is presently endemic mainly in sub-tropical areas. In 1991, WHO's governing body, the World Health Assembly (WHA) passed a resolution to eliminate leprosy as a public health problem by 2000. Elimination of leprosy as a public health problem is defined as a prevalence rate of less than one case per 10 000 persons. Efforts currently focus on eliminating leprosy at a national level in the remaining endemic countries and at a sub-national level from the others. Leprosy has been eliminated from 119 countries out of 122 countries where the disease was considered as a public health problem in 1985.[13]

The number of new cases detected in 2008 was 240,007 globally, and has fallen by 9126 (4% decrease) compared with 2007. However, there was a slight increase at the end of 2009 to 244,796 (Table 2).

In 1986, there were 38,570 registered patients with leprosy in the Philippines, with a prevalence rate of 7.2 per 10,000 Filipinos. There was a dramatic decrease in prevalence by the end of 1998, to 0.90 per 10,000 population, and leprosy was no longer considered to be a public health problem of the country. In 2004, the prevalence was further reduced to 0.38 per 10,000 population, translating to a total decline of 3146 from 7005 in 1998. In the same year, 2120 new cases of leprosy were diagnosed and were all treated with multiple drug therapy (MDT).[14]

In 2006, the prevalence of leprosy in the Philippines was more than 3000 cases (0.42%), while the number of new cases detected was 2517. There was a decrease in the number of patients in 2007. However, an upward trend was observed in 2008 to 3338 (0.35%). The number of MB cases with or without grade 2 disabilities was also significantly higher than PB; 85–93% of cases were successfully treated (Tables 3 and 4).[15]

At the Research Institute for Tropical Medicine Department of Dermatology, where more than 20,000 dermatological cases are seen per annum, leprosy was one of the top three diseases seen, after acne vulgaris and psoriasis

Table 4 Top 10 diseases seen in RITM (2003–2010; RITM Registry of Patients)

	2003	2004	2005	2006	2007	2008	2009	2010
1	Acne[a]	Acne	Acne	Acne	Acne	AD[b]	Acne	Psoriasis
2	Psoriasis	Psoriasis	Leprosy	Psoriasis	Psoriasis	Acne	Psoriasis	Acne
3	AD	Leprosy	AD	Leprosy	Leprosy	Psoriasis	Leprosy	Leprosy
4	Leprosy	Verruca	ACD/ICD[c]	AD	AD	Leprosy	Verruca	ACD/ICD
5	ACD/ICD	AD	Psoriasis	ACD/ICD	ACD/ICD	ACD/ICD	AD	AD
6	Scabies	ACD/ICD	Verruca	Verruca	Verruca	Scabies	Scabies	Scabies
7	T. versicolor[d]	SD[e]	SD	Melasma	Scabies	Verruca	ACD/ICD	SD
8	SD	LSC[f]	Melasma	Scabies	LSC	T. versicolor	Urticaria	Melasma
9	Urticaria	Melasma	LSC	T. versicolor	SD	Urticaria	Melasma	Verruca
10	LSC	Urticaria	Urticaria	Urticaria	T. versicolor	SD	SD	Folliculitis

[a]Acne vulgaris.
[b]Atopic dermatitis (AD).
[c]Allergic contact dermatitis/Irritant contact dermatitis (ACD/ICD).
[d]Tinea versicolor.
[e]Seborrheic dermatitis (SD).
[f]Lichen simplex chronicus (LSC).

vulgaris, from January 2003 to December 2010, except in 2008 where it ranked fourth.

Diagnosis of leprosy

Leprosy is highly infective with low pathogenicity and virulence, and a long incubation period. The skin, superficial peripheral nerves, anterior chamber of the eyes and testes are the most frequently affected organs. Prompt and accurate diagnosis and therapy are most important for control of the disease, management of the patient and prevention of disabilities.[16,17]

A patient with leprosy was defined at the Seventh Meeting of the WHO Expert Committee on Leprosy in 1997 as an individual who has not completed a course of treatment and has one or more of the three cardinal signs:[18] hypopigmented or reddish skin lesions with loss of sensation; involvement of the peripheral nerves as demonstrated by their thickening and associated loss of sensation; skin smear positive for acid-fast bacilli. Any one of these signs has been regarded as sufficient for diagnosis of leprosy, so that the sensitivity is high. Each sign is also quite specific in itself, so the specificity is also high. The most important potential cause of error is the reliability on the examination by unskilled health workers.[19]

By using the macular anesthetic lesions as a single diagnostic criterion for MB disease, the diagnosis was missed in 30% of patients. On the other hand, maculoanesthetic lesions of PB disease are reportedly diagnostic in 90% of cases. Peripheral nerve enlargement usually appears later than skin lesions. The most commonly involved nerves are the ulnar and common peroneal. The presence of one or more enlarged nerves is seen more commonly in MB disease.[16,17]

Delay in diagnosis may result in avertable disabilities with the accompanying psychosocial sequelae. Overdiagnosis on the other hand will result in needless treatment and lead to detrimental psychosocial consequences of the diagnosis of leprosy.[20]

Classification of leprosy

The classification of leprosy was based on the five-group system of Ridley and Jopling. These criteria were based on the immunological response of the host to *M. leprae*: TT (polar tuberculoid); BT (borderline tuberculoid); BB (borderline); BL (borderline lepromatous); LL (polar lepromatous).[21,22]

In 1982, the WHO study group for chemotherapy for control programs recommended the classification of all patients be based on the Ridley–Jopling Classification and the estimated bacterial load in slit-skin smears. The TT and BT patients who had bacillary index (BI) < 2+ were classified as PB disease, and BB, BL and LL who had BI > 2+ were classified as MB disease (Fig. 4).[21,22]

In 1998, the Who Expert Committee on leprosy declared that slit-skin smears were not essential for MDT and the basis for classification would be the number of skin lesions. The new recommendation is as follows: patients who are not experiencing reactions and have less than five skin lesions are to be classified as PB, and those with greater than five lesions are to be categorized as MB.[23]

There are two distinct categories of reactions in leprosy: Type I reaction[24] (Lepra reaction) is an example of Type IV cell-mediated hypersensitivity reaction (Coombs and Gell); and Type II reaction[25] (erythema nodosum leprosum) is an example of Type III humoral hypersensitivity

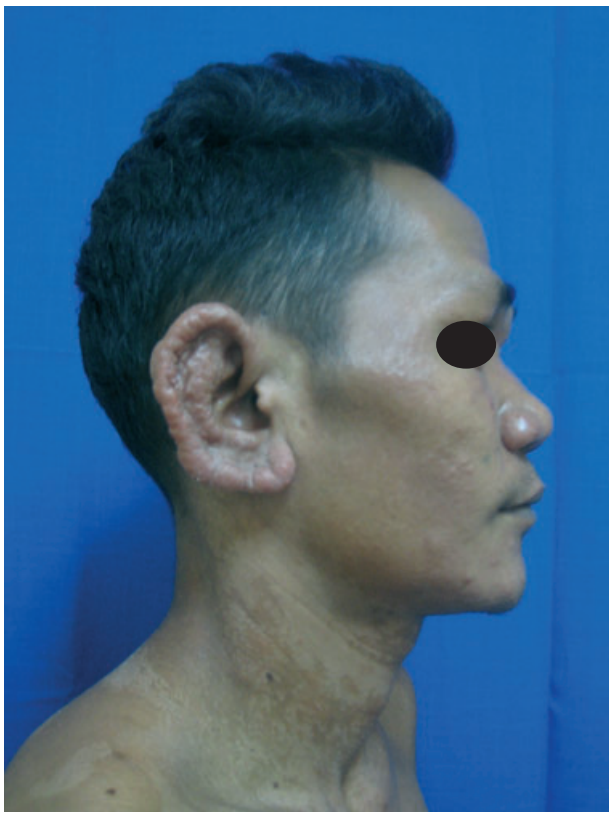

Figure 4 Hansen's disease, LL

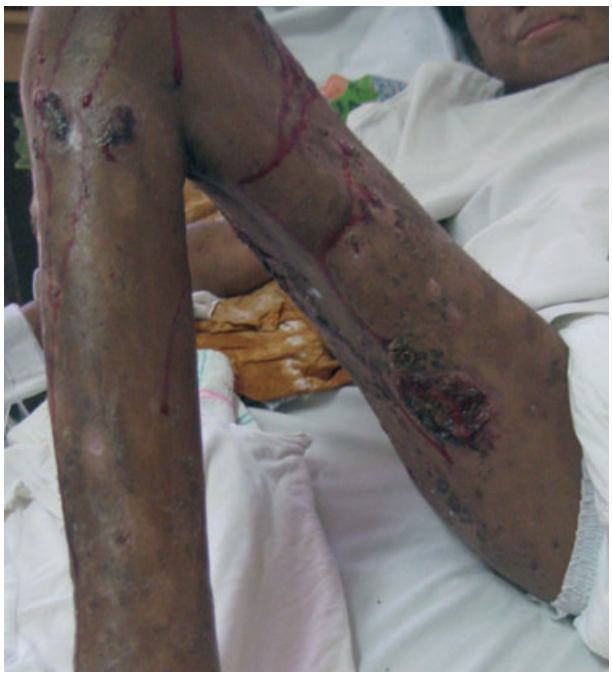

Figure 5 Thirty-eight-year-old pregnant patient with erythema nodosum leprosum

reaction (Coombs and Gell). Reactions are often initiated by stress, MDT, vaccines, pregnancy, surgical procedures, injuries, infections and antibiotics (Fig. 5).

Reactions in leprosy may present as edema of the hands, feet and face, and could be associated nerve pain and tenderness. The most frequent nerves affected are ulnar, facial, median, common peroneal and posterior tibial nerves, resulting in striking impairment such as facial paralysis or foot drop. Type I reaction more commonly occurs in BT, BB and TT.[24] Type II reaction takes place in LL and occasionally in BL.[25] Lucio's phenomenon, a rare third type is usually restricted to Central and South America and immigrants from those areas. It occurs in a subtype of lepromatous leprosy called primary diffuse lepromatous leprosy (la lepra bonita) characterized by diffuse infiltration of the skin by a granulomatous process heavily loaded with mycobacterium leprae.[24,25]

Diagnostic modalities

Leprosy is mainly a clinical diagnosis. Laboratory techniques may serve as adjuncts in the diagnosis. AFB microscopy is still being used in this country; however, it has been abandoned by some countries where leprosy is still endemic. Routine skin punch biopsy with hematoxylin-eosin stain and Fite-Faraco are also being requested in training institutions but not routinely done in leprosy control programs and rural health centers. In subclinical cases seen in clinics, a clinicopathological correlation may deem necessary. In a study performed in China, immunohistopathological studies staining biopsies of patients with PB with phenolic glycolipid-1 antigen proved to be more diagnostically specific than routine hematoxylin and eosin histopathological examination.[26]

Leprosy with co-morbidities

Changes in immune responses occur during pregnancy, which makes patients with leprosy more prone to develop Type I and Type II reactions. Type II reactions usually take place during the third trimester and lactation, while Type I reactions occur during puerperium. It has been recommended that rifampin be given only as a single monthly dose during pregnancy, but dapsone and clofazimine can be used or continued. Prednisone and clofazimine can be given for reactions, but thalidomide ought to be avoided. It is prudent to delay pregnancy in the interim of post-therapy period if there is evidence of reaction, relapse and neuritis.[27,28]

It has been reported that neuritis in leprosy with co-infection of HIV can have a more severe and more frequent reaction after therapy. However, the incidence of leprosy was not increased in areas endemic of HIV.[29,30]

Table 5 Antibacterial treatment of leprosy recommendations[35,44,45]

Recommending organization	Disease type	Rifampin (mg/month)	Dapsone (mg/day)	Clofazimine	Duration	Follow-up
World Health Organization (WHO)	PB	600	100	–	6 months	No mandated follow-up. To return prn
	MB	600	100	50 mg/day 300 mg/month	1 year	No mandated follow-up. To return prn
US Public Health Service	PB	600	100	–	1 year	At 6-month intervals for 5 years
	MB	600	100	50 mg/day	2 years	At 6-month intervals for 10 years

Other antimicrobial agents	Dose (mg/day)
Clarithromycin	500
Minocycline	100
Levofloxacin	500

MB, multibacillary; PB, paucibacillary.

Table 6 Medical management of reaction states[46]

	Thalidomide	Prednisone or prednisolone	Duration	Other agents of unproven value
Reversal reactions (Type I)	Of no value	0.5–1.0 mg/kg. Rifampin may increase their catabolism. Taper slowly. Alternate-day treatment may be well tolerated	Usually needed for 6 months–2 years. Maybe longer or shorter	Non-steroidal anti-inflammatory agents
Erythema nodosum leprosum (Type II)	The most efficacious drug if available and not contraindicated Initially one dose of 100–200 mg qd hs Maintainable dose range 50 mg every other day to 500 mg daily	If thalidomide not available, 0.5–1.0 mg/kg/day	Median duration of treatment is approximately 5 years. Can persist for 10 years	Pentoxifylline
Lucio phenomenon (usually ceases with the use of a microbicidal agent	Of no value	May be helpful	–	Plasmapheresis reported as helpful in unremitting patients

The Philippine healthcare system

The Philippines (i/fpinz/; Filipino: *Pilipinas* [ppines]), officially known as the Republic of the Philippines (Filipino: *Republika ng Pilipinas*), is a country in Southeast Asia in the western Pacific Ocean. An archipelago comprising 7107 islands, the Philippines is categorized broadly into three main geographical divisions: Luzon (where the capital city Manila is located), Visayas and Mindanao. With an estimated population of about 92 million people, the Philippines is the world's 12th most populous country.[31]

The current healthcare system in the Philippines consists of government and private initiatives. The National Leprosy Control Program (NLCP) of the Philippines was established in 1986 under the supervision of the National Center for Disease Prevention and Control (NCDPC) of the Department of Health (DOH).[14] Leprosy Control Program envisions to eliminate leprosy as a human disease by 2020. The program thrust is towards finding hidden cases of leprosy and putting them on MDT, emphasizing the completion of treatment within the WHO-prescribed duration.[32]

Control strategies

Strategic planning consists of case-finding, treatment, advocacy, rehabilitation, manpower development and evaluation. An effective case-finding activity of the DOH: "Kilatis Kutis Campaign" (Skin Screening Campaign) is a year-round skin-screening activity in all health facilities, with regular skin clinic consultations.

Figure 6 (a, b) Patient with leprosy with contractures on rehabilitation

The goal is for all referral centers to have efficient, effective and accessible human and facility resources, with principal goals of the campaigns to include training of health workers through regular workshops and training courses at all levels of the government health unit. The NLCP's Enhanced Strategy and Operational Guidelines for 2011–2015 included the following achievable goals: new policies, review guidelines, establish sentinel sites and referral centers in all regions of the country.[15]

Treatment

The first advancement in the management of leprosy occurred in the 1940s with the development of the drug dapsone, which arrested the disease. But due to prolonged duration of treatment, 5 years for PB, lifetime treatment for MB, and emerging drug resistance, rifampicin and clofazimine were added, which comprise the present MDT. MDT was officially recommended for use by the WHO Study Group in 1981.[33] This therapy has proven to be the most reliable and practical method of treating leprosy.

Through the concerted efforts of WHO and Nippon Foundation in 1995, free MDT was provided to patients until 2000, when Novartis and Novartis Foundation for Sustainable Development (NFSD) signed an agreement with WHO for the extension of their donation until at least the end of 2010 (Table 5).[34]

Rifampin 600 mg, ofloxacin 400 mg and minocycline 100 mg (ROM) are given for single PB lesion. Because of a lack of long-term follow-up, this recommendation should be considered experimental. Single-lesion leprosy, which is often indeterminate leprosy, heals spontaneously in 80% of patients. It is too early to determine if those of the 20% who develop classifiable leprosy will benefit from single ROM treatment, it may cure some patients but will only defer the onset of MB disease in others.[35,36] In a study by Balagon,[37] ofloxacin-containing regimen appeared generally efficacious compared with standard WHO-MDT in patients with PB and resulted only in a few relapses.

Consequently, relapse cases were detected in many patients who completed MDT. WHO has defined relapse as a patient who successfully completes an adequate course of MDT, but subsequently develops new signs and symptoms of the disease during the surveillance period or thereafter. In general, the number of leprosy relapses reported in control programs has been low (Table 6).[38,39]

Prevention of disabilities and rehabilitation

Hansen's disease can lead to disabilities and deformities of the eyes, hands and feet. These changes are secondary to nerve damage due to neuritis and leprosy reactions resulting in loss of muscle strength and loss of sensation.

Neuritis is defined as the presence of painful peripheral nerve with or without nerve enlargement or functional compromise. A study by Pimentel[40] reported that of 103 patients with MB leprosy, 4.9% had worsening of their disability status without pain or clinical signs of neuritis. This silent neuropathy can be detected by a routine neurological examination or electroneuromyography studies.[41]

Every new case of leprosy is assigned a WHO disability grade,[42] which shows the condition of the patient at the time of diagnosis (scale, 0–2). Each eye, hand and foot is given its own grade, and the highest grade becomes the overall disability grade for that patient. Grade 0 indicates no disability. Grade 1 is given for loss of sensation in the hand or foot (eyes are not given a grade of 1). Grade 2 for eyes is given for redness or inability to fully close; grade 2 for hands and feet is given for wounds, ulcers, deformity or loss of tissue.

The management of neuropathies and disabilities requires a multidisciplinary team of orthopedic surgeons, physiotherapists, nurses, neurologists and dermatologists. Shoes, prostheses and ortheses are custom handcrafted for patients with deformities, and are provided free of charge by the government. These services usually are available at tertiary centers, national referral centers or both (Fig. 6a,b).

Conclusion

Prompt and accurate diagnosis of leprosy is crucial in the control of leprosy. Therefore, by strengthening the capacity of healthcare providers in the early detection of leprosy, we can ultimately prevent its complications. The training of nurses, laboratory staff and physicians from all subspecialties is imperative for the timely recognition of leprosy. Considerable imminent issues in the Philippines include the provision of medical assistance to remote areas and the constant supply of medications. The DOH had provided good access to free medication and medical care for the entire population. Tertiary centers are available in which severe cases can be referred, and rehabilitation services are offered mostly free to patients with leprosy. The DOH has also provided public awareness programs for leprosy. The development of effective and operational strategies to manage chronic diseases should be broad and be able to cover primary prevention, compliance and access to medications. All members of the health sectors should remain vigilant to combat this battle against leprosy.

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