EXTENDED REPORT

Incidence of ocular morbidity among multibacillary leprosy patients during a 2 year course of multidrug therapy

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Aim: To evaluate the incidence of and risk factors for ocular complications in multibacillary (MB) leprosy patients during their 2 year, fixed duration, multidrug therapy (MDT).

Methods: Periodic eye examinations were conducted prospectively on a cohort of 301 consecutive newly diagnosed MB patients every 6 months during their 2 year course of MDT. Incidence of ocular pathology was calculated as the number of events per person year of event free follow up of patients who did not have the specific finding at baseline.

Results: 292 (97%) patients had one or more follow up visits. The incidence of lagophthalmos was 1.2%/patient year (95% CI 0.5% to 2.8%); corneal opacity was 7.4%/patient year (95% CI 5.1% to 10.6%); uveal involvement was 5.1%/patient year (95% CI 3.3% to 7.8%), and cataract that reduced vision to 6/18 or less was seen in 4.3%/patient year (95% CI 2.7% to 6.9%) of patients. Overall, 23 individuals (5.8%/patient year, 95% CI 3.9 to 8.8) developed leprosy related potentially blinding pathology during the 2 years of MDT.

Conclusions: Approximately 20% of patients with MB leprosy can be expected to develop ocular complications of leprosy during a 2 year course of MDT, many (11%) of which are potentially vision threatening. Ophthalmological monitoring to detect and treat ocular complications at defined intervals during MDT is indicated.

Leprosy is a chronic infection that can be classified clinically into paucibacillary leprosy (PB), in which patients have a relatively intact cellular immune function against *Mycobacterium leprae* and consequently low bacillary loads, and multibacillary leprosy (MB), in which patients have markedly impaired cellular immunity and high bacillary loads.

Antileprosy multidrug therapy (MDT), given until recently as a standard regimen of 2 years' duration, has revolutionised the management of leprosy worldwide. While there are indications that the incidence of leprosy may be declining, the number of people taking MDT worldwide remains large (407 791 in 2004).[1] Accompanying the reduction in prevalence there has been a gradual shift in the proportion of the type of leprosy from the PB to the MB form, as well as a shift to an older age at diagnosis of disease.[2] The expansion of MDT programmes at a global level has given rise to hopes that disability and the other complications of leprosy need not occur as long as a person completes the required duration of therapy. However, monitoring of disability rates following diagnosis and treatment has been problematic because of the changes in definitions, particularly for ocular disabilities in leprosy patients. In particular, the extent to which complications of leprosy continue to occur during MDT has been unclear.[3 4]

Our previous work demonstrated that at the time of leprosy diagnosis, about 11% of MB leprosy patients have one or more significant leprosy related eye complications.[5] These complications were more common with increasing age, a short duration between onset and diagnosis, and when a previous reaction involving the face had been diagnosed. Individuals with ocular pathology at baseline also were three times as likely to have other disabilities (hands and feet) as individuals without ocular pathology.

While prevalence studies have documented ocular morbidity in leprosy patients on MDT, it has been impossible to differentiate pathology that was present at the time of initiation of MDT from incident ocular pathology during MDT.[6] While it is hoped that MDT would prevent the occurrence of further complications, pre-existing nerve damage, compounded by continuing reactions, may make it difficult to prevent the evolution of additional complications in these individuals. Knowledge of the magnitude and nature of incident morbidity in leprosy patients on treatment is critical from the programmatic point of view, in order to prevent and manage such complications expeditiously and effectively in worldwide programmes. Such information also could identify potential risk factors that may be amenable to intervention. We conducted a prospective study in India to determine the incidence of ocular complications in MB leprosy patients and associated risk factors and report our findings here.

MATERIAL AND METHODS

Details of the methods of the study have been published previously.[5] Briefly, all new, clinically diagnosed MB patients as defined by the World Health Organization starting on a 2 year multidrug therapy and living within the leprosy control area of the Schieffelin Leprosy Research and Training Center in southern India were invited to participate. Recruitment of patients was started in 1991 and completed in 1997. Consenting patients received a baseline ocular examination followed by prospective biannual examinations during MDT. Fifteen patients (13 men and two women) opted not to participate in the study. Based on sample size calculations taking into account possible losses to follow up resulting from migration and mortality, 301 MB leprosy patients were enrolled over a period of 6 years. Patients not returning for examination were contacted by public health

Abbreviations: BL, borderline lepromatous leprosy; LL, lepromatous leprosy; LROP, leprosy related ocular pathology; MB, multibacillary; MDT, multidrug therapy; PB, paucibacillary; PBLROP, potentially blinding leprosy related ocular pathology

Table 1 incidence of ocular morbidity during 2 year fixed MDT by patient*

Ocular conditions	No of patients†	Patient years	Events	Incidence rate per person year	95% CI
Lid conditions					
Orbicularis oculi weakness	276	432.13	10	0.023	0.013 to 0.043
Lagophthalmos	277	436.55	5	0.012	0.005 to 0.028
Ectropion	287	450.67	5	0.011	0.005 to 0.027
Trichiasis	286	451.68	5	0.011	0.005 to 0.027
Conjunctival conditions					
Nasolacrimal duct block	284	448.33	4	0.009	0.003 to 0.024
Pterygium	252	392.31	15	0.038	0.023 to 0.063
B663 crystals	288	452.64	4	0.009	0.003 to 0.024
Corneal conditions					
Corneal opacity	258	394.20	29	0.074	0.051 to 0.106
Corneal nerve beading	283	440.94	12	0.027	0.016 to 0.048
Punctate keratitis‡	284	447.18	6	0.013	0.006 to 0.030
Uveal conditions					
Flare and cell	287	452.59	2	0.004	0.001 to 0.018
Keratic precipitates	273	424.53	13	0.031	0.018 to 0.053
Irregular pupil	285	447.95	5	0.011	0.005 to 0.027
Iris atrophy	283	441.53	9	0.020	0.011 to 0.039
Any uveal involvement¶	268	410.87	21	0.051	0.033 to 0.078
Cataract					
Cataract	221	328.49	34	0.104	0.074 to 0.145
Cataract with vision of 6/18 or less	257	394.88	17	0.043	0.027 to 0.069
Grouped					
LROP	247	373.14	37	0.099	0.072 to 0.137
PBLROP	258	394.65	23	0.058	0.039 to 0.088

*MDT, multidrug therapy; B663, clofazamine crystals in cornea or conjunctiva. †The number of patients at risk for each event is based on the number of patients who were event free at the initiation of MDT and who had at least one follow up examination visit. ‡Neurotrophic or exposure related . ¶Any uveal involvement includes flare and cell, keratic precipitates and iris atrophy. LROP, leprosy related ocular pathology includes muscle weakness, lagophthalmos, ectropion, entropion, trichiasis, episcleritis, scleritis, corneal nerve beading, punctate keratitis, and uveal involvement. PBLROP, potentially blinding leprosy related ocular pathology includes lagophthalmos and/or uveal involvement.

workers in their own community to encourage follow up. Research methods and protocols were approved by the institutional review board of the Schieffelin Leprosy Research and Training Center, and were conducted in accordance with the principles of the Declaration of Helsinki. All patients were examined and treated free of charge.

At enrolment, the following leprosy characteristics were recorded; the type of MB leprosy based on the clinical classification of Ridley and Jopling[7]; WHO deformity grading of hands and legs[8]; the bacterial index calculated from the results of the acid fast staining of smears from specific skin sites[9]; type 1 (reversal reaction) or type 2 (erythema nodosum leprosum) reactions; history of hypopigmented or erythematous patches on the face.

At each visit, the following ophthalmic characteristics were recorded; visual acuity (with and without correction); presence of orbicularis oculi weakness, lagophthalmos (with both gentle and forced closure), ectropion, entropion, trichiasis, corneal opacity, corneal ulcer, episcleritis, scleritis, clofazamine crystals on the cornea or conjunctiva, flare and cells, posterior synechia, small pupil, sluggish pupillary reaction to light, iris atrophy, and cataract. When synechia or cataract were suspected, mydriatic drops were instilled and the patient was re-examined to confirm the diagnosis. For purposes of the analyses reported here, cataract was defined as the presence of lens opacity observed during slit lamp examination or distant direct ophthalmoscopy consistent with a corrected visual acuity of 6/18 or worse. Patients free of cataract at enrolment who underwent cataract surgery during follow up also were considered to have developed cataract.

Best corrected visual acuity was measured with Snellen's chart by a trained examiner. After examination of the adnexae, slit lamp biomicroscopy was done on all patients. Applanation tension was recorded in the upright position. Direct ophthalmoscopy without dilatation was performed in all cases during each visit; patients with decreased vision or with intraocular complications had dilatation and indirect ophthalmoscopy.

Incidence of ocular pathology was calculated as the number of each kind of event observed per person year of event free follow up while taking MDT among patients who did not have the specific finding at baseline. Information on patients following their last visit during treatment with MDT was not included in this report. Statistical analysis was conducted with the unit of observation being the individual rather than the eye. In addition, we created a number of grouped characteristics to describe the incidence of complications. Leprosy related ocular pathology (LROP) was defined as presence of any of the following: lagophthalmos, corneal nerve beading, corneal opacity, punctate keratitis, and observations indicative of uveal involvement (flare and cells, keratic precipitates, and/or iris atrophy). LROP was created to define all leprosy related ocular conditions, regardless of their contribution to disability or vision loss. Potentially blinding leprosy related ocular pathology (PBLROP) was defined as presence of any of the following—lagophthalmos and/or uveal involvement—constituting those leprosy related conditions known to be associated with disability or vision loss. Corneal opacity was not included under PBLROP as it could not be attributed to leprosy or associated with a drop in visual acuity.

Cox proportional hazards regression was used to analyse the occurrence of specific findings according to demographic and clinical characteristics associated ($p<0.05$) with pathology by univariate analysis. p Values, hazard ratios (HR), and 95% confidence intervals (CI) were generated.

Table 2 Risk factors for lagopthalmos*

	Hazard ratio	SE	p Value	95% CI
Patient characteristics:				
Age (per 10 years)	1.108	0.343	0.740	0.604 to 2.033
Female *v* male	0.603	0.674	0.651	0.067 to 5.393
Leprosy characteristics:				
Duration of disease				
Duration of leprosy ⩾1 year *v* <1 year	1.224	1.117	0.825	0.204 to 7.327
Reaction				
Type I reaction at enrolment	2.697	2.463	0.277	0.450 to 16.149
History of reactions	3.935	3.593	0.133	0.657 to 23.554
History of face patch *v* no face patch	2.061	1.881	0.428	0.344 to 12.333
Smear				
Bacterial index at enrolment	0.559	0.297	0.273	0.197 to 1.582
Smear positive *v* smear negative	0.934	1.044	0.951	0.104 to 8.355
Deformity				
Grade 2 deformity *v* no grade 2 deformity in all limbs	9.677	10.866	0.043	1.071 to 87.409

*SE, standard error; 95% CI, 95% confidence interval.

RESULTS

A total of 301 MB patients were enrolled. During the 2 year MDT treatment period 28 did not complete follow up (9.3%), comprising 14 deaths, six refusals, and eight migrations. Nine of these patients did not have any follow up visits after enrolment; thus, the analysis is based on 292 patients (97%) followed either until completion of MDT or until death or migration, whichever occurred earlier. The dropouts did not differ significantly in baseline characteristics from those who completed their 2 years of MDT.

Over the 2 year follow up, 16 patients (4.2%/patient year, 95% CI 2.5% to 6.8%) had their presenting vision of more than 6/18 reduced to 6/18 or worse and, among these, six patients became severely visually impaired (less than 6/60 vision in one or both eyes). In three severely visually impaired patients, the visual impairment was the result of cataract alone, one patient had cataract as well as a corneal opacity, another had cataract and pterygium and the other had cataract and lagophthalmos. One individual had bilateral cataract surgery during MDT, resulting in visual improvement from 3/60 to 6/24 (right eye) and 6/36 to 6/24 (left eye). The cumulative incidence of specific ocular morbidity during the 2 year fixed MDT by person years (patient year) is given in table 1.

The incidence of lagophthalmos was 1.2%/patient year (95% CI 0.48% to 2.76%), with five patients affected. Over an average of 1.576 years under observation, three patients developed lagophthalmos at the beginning of the seventh month after starting MDT, one at the end of the first year and one at the beginning of the last quarter of the second year after therapy (1.75 years). Although infrequent, incident lagophthalmos was found to be significantly associated with grade 2 deformity in all of the limbs (HR 9.68, 95% CI 1.07 to 87.41) (table 2).

All of the incident lagophthalmos cases occurred in borderline lepromatous (BL) patients, with none in the lepromatous leprosy (LL) patients. Patients with history of face patches or those presenting with type 1 or type 2 reactions at enrolment did not have a significantly higher incidence of lagophthalmos. None of the patients with or without lagophthalmos developed entropion or corneal ulcers.

Twenty nine individuals (7.4%/patient year 95% CI 5.1% to 10.6%) developed corneal opacities during follow up. Smear positivity at enrolment was associated with reduced risk of

Table 3 Risk factors for corneal opacity*

	Hazard ratio	SE	p Value	95% CI
Patient characteristics:				
Age (per 10 years)	1.092	0.143	0.502	0.845 to 1.410
Female *v* male	0.413	0.223	0.102	0.143 to 1.192
Leprosy characteristics:				
Duration of disease				
Duration ⩾1 year *v* < 1 year	1.469	0.563	0.316	0.693 to 3.115
Reaction at enrolment				
Type I reaction	0.636	0.344	0.403	0.221 to 1.836
Type II reaction	0.590	0.717	0.664	0.055 to 6.378
History of face patch *v* no face patch	0.987	0.370	0.971	0.473 to 2.057
Smear at enrolment				
Bacterial index	0.866	0.125	0.317	0.652 to 1.149
Smear positive *v* smear negative	0.382	0.147	0.012	0.180 to 0.813
Deformity at enrolment				
Hand deformity				
Grade 1 deformity *v* no deformity	1.055	0.552	0.919	0.378 to 2.942
Grade 2 deformity *v* no deformity	0.877	0.673	0.865	0.195 to 3.949
Leg deformity				
Grade 1 deformity *v* no deformity	2.129	0.947	0.089	0.891 to 5.090
Grade 2 deformity *v* no deformity	2.961	2.348	0.171	0.626 to 14.009
Grade 2 deformity *v* no deformity in all limbs	1.410	1.439	0.736	0.191 to 10.415

*SE, standard error; 95% CI, 95% confidence interval.

Table 4 Risk factors for uveal involvement*

	Hazard ratio	SE	p Value	95% CI
Patient characteristics:				
Age (per 10 years)	1.328	0.201	0.061	0.987 to 1.786
Female *v* male	0.277	0.207	0.085	0.064 to 1.195
Leprosy characteristics:				
Classification				
BL *v* LL	3.289	3.384	0.247	0.438 to 24.707
Duration of disease				
Duration ⩾1 year *v* <1 year	1.082	0.478	0.859	0.455 to 2.570
Reaction				
Type I reaction at enrolment	0.939	0.526	0.910	0.313 to 2.812
Type II reaction at enrolment	1.056	1.447	0.968	0.072 to 15.482
History of face patch *v* no face patch	1.088	0.261	0.726	0.680 to 1.7401
Smear				
Bacterial index at enrolment	0.728	0.145	0.111	0.493 to 1.076
Smear positive *v* smear negative	0.990	0.552	0.985	0.332 to 2.953
Deformity at enrolment				
Hand deformity				
Grade 1 deformity *v* no deformity	1.351	0.815	0.618	0.414 to 4.404
Grade 2 deformity *v* no deformity	2.844	1.746	0.089	0.854 to 9.474
Leg deformity				
Grade 1 deformity *v* no deformity	0.941	0.477	0.904	0.348 to 2.542
Grade 2 deformity *v* no deformity	3.696	2.900	0.096	0.794 to 17.199
Both hand and leg deformity				
Grade 2 deformity *v* no grade 2 deformity in all limbs	4.596	3.431	0.041	1.064 to 19.852

*SE, standard error; 95% CI, 95% confidence interval; BL, borderline lepromatous leprosy; LL, lepromatous leprosy; uveal involvement includes flare and cell, keratic precipitates, and iris atrophy.

incidence of corneal opacities during MDT (HR = 0.38, 95% CI 0.18 to 0.81). Other factors tested, including reduction of visual acuity to 6/18 or less, were not significantly associated with incidence of corneal opacities (table 3).

Characteristics indicating occurrence of uveitis during follow up (flare and cells and/or keratic precipitates and/or iris atrophy) were observed during MDT in 21 individuals (HR 5.1%; 95% CI 3.3% to 7.8%). Uveitis was significantly associated with grade 2 deformity in all the limbs (HR 4.6, 95% CI 1.06 to 19.85), but not with other characteristics (table 4). Survival analysis demonstrated that the incidence of uveal involvement and corneal opacities occurred evenly over the 2 years of MDT, with approximately a 25% chance of developing them during the first 6 months after starting MDT, 50% after 1 year and 75% after 1½ years.

Overall, there were 37 individuals (9.9%/patient year, 95% CI 7.2% to 13.7%) with LROP—one or more of the complications studied. Refining our definition of eye pathology to include only PBLROP reduced the number of people affected to 23 individuals (5.8%/patient year; 95% CI 3.9% to 8.8%). The most common PBLROP was uveal involvement. PBLROP was significantly associated (p = 0.036) with grade 2 deformity in all limbs (HR 4.74/patient year, 95% CI 1.11 to 20.31); no other variables were significantly associated with LROP or PBLROP (tables 5 and 6). Multiple regression analyses confirmed each of the significant risk factor associations reported above, with the exception that the association between uveitis and grade 2 deformity was reduced (p = 0.109) after adjusting for other variables (HR 3.4%/patient year 95% CI 0.76 to 15.14).

Table 5 Risk factors for leprosy related ocular pathology (LROP)*

	Hazard ratio	SE	p Value	95% CI
Patient characteristics:				
Age (per 10 years)	1.100	0.125	0.403	0.880 to 1.374
Female *v* male	0.584	0.246	0.202	0.256 to 1.334
Leprosy characteristics:				
Classification				
LL *v* BL	0.657	0.296	0.350	0.272 to 1.586
Duration of disease				
Duration ⩾1 year *v* <1 year	1.296	0.440	0.445	0.666 to 2.521
Reaction				
Type I reaction at enrolment	1.359	0.524	0.426	0.638 to 2.893
Type II reaction at enrolment	0.573	0.686	0.642	0.055 to 5.989
History of reactions	0.871	0.420	0.775	0.339 to 2.241
History of face patch *v* no face patch	0.879	0.295	0.701	0.455 to 1.698
Smear				
Bacterial index at enrolment	1.131	0.125	0.265	0.911 to 1.404
Smear positive *v* smear negative	1.370	0.613	0.482	0.570 to 3.291
Deformity				
Grade 2 deformity *v* no grade 2 deformity in all limbs	3.371	2.461	0.096	0.806 to 14.098

*SE, standard error; 95% CI, 95% confidence interval; LROP includes muscle weakness, lagophthalmos, ectropion, entropion, trichiasis, episcleritis, scleritis, corneal nerve beading, punctate keratitis and uveal conditions; LL = Lepromatous leprosy, BL = Borderline lepromatous leprosy.

Table 6 Risk factors for potentially blinding leprosy related ocular pathology (PBLROP)*

	Hazard ratio	SE	p Value	95% CI
Patient characteristics:				
Age (per 10 years)	1.271	0.183	0.095	0.959 to 1.685
Female *v* male	0.395	0.245	0.135	0.117 to 1.334
Leprosy characteristics:				
Classification (LL *v* BL)	3.756	3.852	0.197	0.503 to 28.036
Duration of disease				
Duration ⩾1 year *v* <1 year	0.859	0.359	0.716	0.379 to 1.948
Reaction				
Type I reaction at enrolment	1.206	0.614	0.713	0.444 to 3.273
Type II reaction at enrolment	1.002	1.353	0.999	0.071 to 14.132
History of any reactions	1.272	0.704	0.664	0.430 to 3.761
History of face patch *v* no face patch	1.050	0.444	0.909	0.458 to 2.405
Smear				
Bacterial index at enrolment	0.712	0.138	0.079	0.488 to 1.040
Smear positive *v* smear negative	1.155	0.637	0.794	0.392 to 3.404
Deformity				
Grade 2 deformity *v* no grade 2 deformity in all limbs	4.739	3.519	0.036	1.106 to 20.313

*SE, standard error; 95% CI, 95% confidence interval; PBLROP includes lagophthalmos and/or uveal conditions; LL, lepromatous leprosy, BL, borderline lepromatous leprosy.

DISCUSSION

Findings from this prospective study suggest that LROP will occur in approximately 10% of newly diagnosed MB patients between the time of their initiation of MDT treatment and completion of a standard 2 year regimen. Vision loss, mostly as a result of cataract had a potential for improvement with cataract surgery.[10–12]

Leprosy related uveal involvement accounts for a large proportion of the complications observed, which could reflect continued *M leprae* activity in the host tissues in the eye, or could reflect a para-infectious mechanism of autoimmune inflammation.[13–16] Further observation of the outcomes and clinical course of uveitis is needed to assess the contribution of leprosy related uveal involvement to long term damage of intraocular structures, to the development of cataract and, finally, to vision loss. Detection of uveitis requires slit lamp examination and specialised training, suggesting that certain ocular complications of leprosy during MDT cannot be managed effectively without the input of an ophthalmologist.

Incident lagophthalmos was relatively infrequent in this cohort and most of the cases occurred during the first 6 months of MDT. Monitoring of patients during the early period after institution of MDT may be particularly important. As well as previous work,[17 18] baseline findings from this cohort showed that, at leprosy diagnosis, the presence of lagophthalmos was associated with facial patch.[5] It was hypothesised at the outset of the study that incident lagophthalmos would be more frequent in patients with face patches and those with type 1 reactions; however, with the limited number of cases of lagophthalmos observed it was not possible to test this hypothesis with adequate statistical power.

Corneal opacities occurred in nearly 8% of patients per person year, but typically were small and peripheral in location, such that vision was not affected. The burden of visual morbidity caused by corneal opacification was less than anticipated. The appearance of opacities was not consistent with unrecalled trauma. They were more frequent among clinically diagnosed MB patients whose bacterial skin smears were negative for acid fast bacilli than those with positive smears. However, other locally occurring ocular complications including lagophthalmos, trichiasis, other lid deformities and inflammatory conditions were similarly distributed between smear negative and smear positive patients. One possible explanation of this observation, if clinically diagnosed MB leprosy is taken to cover a spectrum of immune competence against *M leprae*, is that patients whose smears were negative may have had relatively greater immunity against pathogens in peripheral corneal nerves, resulting in focal inflammation and opacification.

It must be recognised that some leprosy related ocular complications do not lead to vision loss; accordingly, we analysed the subset with PBLROP. Overall, 5.8%/patient year of our study population developed potentially blinding leprosy related ocular complications during MDT, which could result in vision loss over time if their condition(s) was not managed properly. If we include both the prevalence of PBLROP at the time of enrolment (9.6%) with the cumulative 2 year incidence of 5.8%/patient year we can estimate that approximately one fifth of MB leprosy patients will either have vision threatening LROP at diagnosis or will develop it during their treatment. We cannot extrapolate our data to estimate the incidence of ocular pathology in patients under recently recommended (6 month) short term MDT. However, based on these results, it seems likely that these patients are potentially at risk of vision threatening ocular complications during their treatment.[8]

Patients with severe and extensive deformities in the limbs were observed to be more likely to have additional ocular problems. Having extensive limb deformities increased the risk of having incident potentially blinding leprosy related ocular conditions during MDT fivefold. These patients may be further along the natural history trajectory of leprosy and may have the most to lose from ocular pathology and visual impairment.

Clinic based cohort studies have well characterised limitations, which should be considered in evaluating these results. Our cohort had a relatively high follow up rate, making it less likely that losses to follow up biased our results. Complications of eye diseases were ascertained systematically according to standardised protocol throughout the study by a consistent set of ophthalmologists, in an effort to minimise any ascertainment biases. However, this study is potentially limited in that patients were managed at a leading, specialised leprosy centre. Therefore, these results may represent a best case scenario, and the rate of ocular complications might be higher for patients in a less intensive MDT programme.

In summary, the risk of ocular complications of leprosy during MDT for MB patients appears to be approximately 10 %/person year, with approximately 5.6 % experiencing a treatable vision threatening complication. Based on these rates, approximately 11% can be expected to develop new sight threatening ocular complications during a standard

2 year course of MDT, indicating that ophthalmic evaluation during MDT is necessary to prevent needless morbidity in patients who already may have substantial somatosensory impairment. Our experience suggests that evaluation at the start of MDT (all patients), during MDT (targeted), and at completion of MDT (all patients), as recommended in recent guidelines, is necessary.[19] While incorporation of ophthalmology care into leprosy control and national treatment programmes may be logistically difficult, the high rate of vision threatening ocular complications observed during MDT makes ophthalmic monitoring an important component of any programme for which prevention of disability is a major goal.

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