Volume 72, Number 4
*Printed in the U.S.A.*
(ISSN 0148-916X)

INTERNATIONAL JOURNAL OF LEPROSY
and Other Mycobacterial Diseases

VOLUME 72, NUMBER 4 DECEMBER 2004

# Analysis of 6000 Skin Biopsies of the National Leprosy Control Program in Mexico[1]

Francisco Vargas-Ocampo[2]

## ABSTRACT

Six thousand skin biopsy specimens taken from April 1978 to January 2002 under conditions as specified by the National Leprosy Control Program (NLCP), were analyzed to obtain information about the work of the program and contribute to the knowledge of this illness in the Mexico. Six-thousand request forms for histologic exam of the NLCP were reviewed. Sixty-two percent of the requests had all the required information and in 38% one or more data items were omitted. The age range was 2 to 98 yrs with a median of 50 yrs; a small number of cases was observed in the age group of 0 to 14 yrs, and the peak was in the age group of 41 to 50 yrs. Of the 6000 biopsies, 3693 were classified. Polar lepromatous (LL) was the most common form of the disease, in 60.3% of cases. Twice as many cases were multibacillary leprosy (MB) as paucibacillary (PB). MB predominated in males, and PB predominated in females. The Cohen's kappa index ($\kappa$) of clinical-histological agreement was 0.202 (95% CI 0.184–0.219) and showed a poor grade of agreement between clinical and histologic diagnosis, with a level of significance of 0.05 ($p < 0.001$).The results may indicate the end of leprosy in Mexico, a country in which the national goal of elimination was reached in 1994, with a prevalence since the year 2000 of 0.17/10 000.

## RÉSUMÉ

Six mille biopsies cutanées prélevées d'Avril 1978 à Janvier 2002, selon les spécifications du Programme National de Contrôle de la Lèpre (PNCL) furent analysées et traitées afin d'obtenir plus d'informations sur le travail de ce programme et à sa contribution à la connaissance de cette maladie au Mexique. Six mille demandes d'analyse histologique du PNCL furent revues. Soixante deux pour cent des requêtes présentaient tous les renseignements tandis que 38% de celles-ci avaient une ou plusieurs données manquantes. L'intervalle d'âge était de 2 à 98 ans avec un médian de 50 ans; un faible nombre de cas fut observé dans la classe d'âge de 0 à 14 ans, et le pic de demandes était parmi les 41–50 ans. De ces 6000 biopsies, 3693 furent classées. La lèpre lépromateuse polaire fut la forme la plus fréquente de la maladie avec 60,3% des cas. Il y avait deux fois plus de cas de lèpre multibacillaire (MB) que de lèpre paucibacillaire (PB). La lèpre MB dominait chez les patients de sexe masculins, tandis que la lèpre PB était plus fréquente chez les patientes. L'index kappa ($\kappa$) de Cohen de concordance clinico-pathologique était de 0.202 (IdC à 95% de 0,184 à

[1] Received for publication on 12 March 2003. Accepted for publication on 29 June 2004.

[2] F. Vargas-Ocampo, M.D., M.Sc., Laboratorio de Dermatopatologia, Instituto de Diagnóstico y Referencia Epidemiológicos, Secretaria de Salud de Mexico.

Reprint Requests to: Dr. Francisco Vargas-Ocampo, Laboratorio de Dermatopatologia, (InDRE), Carpio 470, Col. Santo Tomás, C.P. 11340, Mexico, D.F., MEXICO. E-mail: vargasocampo@correo.unam.mx

0,219) et montra un pouvoir faible d'association, avec un degré de signification de 0,05 (p <0,001). Ces résultats pourraient indiquer la fin de la lèpre au Mexique, un pays où l'objectif national d'éradication a été atteint en 1994, avec une prévalence depuis l'année 2000 de 0,17 cas/10 000.

## RESUMEN

Se analizaron seis mil biopsias de piel tomadas deAbril de 1987 a Enero de 2002 bajo las condiciones especificadas por el Programa Nacional de Control de la Lepra (PNCL) para obtener información sobre el trabajo del Programa y para contribuir al conocimiento de esta enfermedad en México. Se revisaron 6,000 solicitudes del PNCL para realizar el examen histológico de las biopsias. Sesenta y dos porciento de las solicitudes contenían toda la información requerida, mientras que en el 38% restante se habían omitido uno o más datos. El rango de edad fue de 2 a 98 años, con una media de 50 años; en el grupo de 0 a 14 años se observó un bajo número de casos, y el pico estuvo en el grupo de 41 a 50 años. De las 6000 biopsias, 3693 pudieron ser clasificadas. La lepra lepromatosa polar fue la más común de las enfermedades, con 60.3% de los casos. Los casos multibacilares (MB) fueron el doble de los paucibacilares (PB). Los casos MB predominaron en los hombres mientras que los PB predominaron en las mujeres. El índice kappa de Cohen (κ) de congruencia clínico-histológica fue 0.202 (95% CI 0.184–0.219) y mostró una fuerza de asociación pobre, con un nivel de significancia de 0.05 (p <0.001). Los resultados podrían indicar el final de la lepra en México, un país en el cual la meta nacional de eliminación de la lepra se alcanzó en 1994, con una prevalencia de 0.17/10,000 desde el año 2000.

This report describes the analyses of 6000 biopsies obtained from cutaneous lesions of subjects suspected to have clinical leprosy when the medical staf f of the National Leprosy Control Program (NLCP) examined them. In April 1978, the Laboratory of Dermatopathology of the Instituto de Diagnóstico y Referencia Epidemiológicos (InDRE), formerly Instituto de Salubridad y Enfermedades Tropicales, started the diagnosis and histopathologic classification of skin biopsies of the NLCP, and from that date to January 2002, 6000 skin specimens were received for microscopic diagnosis and histologic classification.

This study was designed to provide information about the work of the program and contribute to the knowledge of this illness in Mexico. With this purpose, the following secondary objectives were established: to determine the duration of the disease before subjects sought medical care at NLCP; to identify the errors that influenced the result of the biopsy; to correlate the topography and type of the lesions with the histologic classification; to specify the frequency of leprosy by age and gender in the country; to define the histologic spectrum of leprosy in Mexico and to determine the agreement between clinical and histologic diagnosis in skin biopsies of the NLCP.

## MATERIALS AND METHODS

Six thousand skin biopsy specimens and 6000 request forms, submitted from April 1978 to January 2002 for diagnosis and histologic classification of the NLCP, were reviewed and analyzed to determine: (i) duration of the disease; (ii) gender and age of the subjects suspected to have leprosy; (iii) clinical diagnosis; (iv) biopsy result; (v) confirmation of the clinical diagnosis for biopsy; (vi) characteristics of the type and site of lesion selected for biopsy; (vii) Errors that hindered the histologic examination.

All biopsy specimens were obtained from subjects suspected to have clinical leprosy, and dispatched in glass or plastic vials containing 10% formalin solution from different provinces of the country to the InDRE in Mexico City where all histologic processing was carried out. Specimens were embedded in paraffin and sections of 8 μm were obtained. They were stained with hematoxilin-eosin and with the Fite-Faraco modification of the Ziehl-Neelsen stain for acid-fast bacilli. Ten to 20 sections were cut from each block and the search for bacilli was done in various sections. All microscopic studies were made by one dermatohistopathologist. The histologic criteria for

diagnosis and classification of leprosy for tuberculoid, borderline tuberculoid, borderline, borderline lepromatous, and lepromatous, were those described by Ridley and Jopling ([11, 12]):

*Tuberculoid lepr osy* (TT). Epithelioid cell granulomas with Langhans giant cells surrounded by dense lymphocytic infiltrate, erosion of epidermis and infiltration of the nerves; acid-fact bacilli (AFB) zero.

*Borderline tuberculoid* (BT). Epithelioid cell granulomas with peripheral lymphocytes and Langhans giant cell, with a clear subepidermal zone and infiltration of the nerves; AFB 0 to 2+.

*Borderline* (BB). Epithelioid cells granulomas with dif fusely spread lymphocytes, presence of a subepidermal clear zone and nerve bundles recognizable; AFB 3 to 4+.

*Borderline lepromatous* (BL). Granuloma composed of histiocytic cells that show a tendency to epithelioid cells and sometimes to foamy change, with areas of dense lymphocyte infiltration as perineural cuffs or occupying a whole segment of the granuloma. Large globi absent. AFB 4 to 5+.

*Lepromatous leprosy* (LL). Granulomas composed of histiocytes and foamy cells and, eventually , globi. L ymphocytes are scanty: if present they are dif fusely spread. Nerves are without cellular infiltration or cuffing. There is a clear Grenz zone; AFB 5 to 6+.

*Intermediate* (I): Lymphocytes and histiocytes localized around skin structures. Acid-fast bacilli are very scanty in all cases.

*Diffuse leprosy* (DLL). An unusual variety of the lepromatous type of the disease, this was first described by Lucio and Alvarado in 1851 in Mexico ( [7]). Clinically, this is characterized by a diffuse infiltration of the skin over the entire body . The skin may appear normal on clinical inspection but *Mycobacterium leprae* are usually obtained by scraping from any region of the skin. Histologically there is an infiltrate with foam cells that surrounds the blood vessels. From the surface downward the density of the cellular infiltrate increases; it is slight to moderate around the blood vessels of the superficial plexus and denser with tendency to form small nodules around the blood vessels of the deep plexus. The most conspicuous feature is the presence of innumerable lepra bacilli within the endothelial cells of small vessels of the papillary and subpapillary dermis, and within the endothelial cells and muscular layer of the larger vessels of the deeper dermis and subcutaneous fat; AFB 6+. (These histologic criteria were based on personal observations not previously published).

*Histoid leprosy* (HLL). Nodules characteristically present over apparently normal skin. Histologically the lesions show circumscribed histoid lepromas characterized by the predominance of spindle-shaped histiocytes containing acid-fast bacilli; AFB 6+ ([15]).

The clinical diagnosis was made according to Madrid classification ([9]), which considers two polar types: lepromatous (L) and tuberculoid (T); and two groups: indeterminate (I) and dimorphous (D). And it includes the term variety as a subdivision of type or of group. Type includes the cases, defined as stable and invariable. Group includes the unstable cases, mutable, and of uncertain evolution. Clinically lepromatous is characterized by nodules, plaques, and macules. Tuberculoid is characterized by plaques, macules, and annular lesions. Dimorphous is a charecterized by a great variety of lesions with characteristics of L and T. Indeterminate is characterized by hypopigmented macules with dysesthesia, anidrosis, and alopecia (DAA).

Statistical significance was determined using the test for dif ferences between proportions; the numbers of males and females at each interval were compared by Kolmogorov-Smirnov test, and the Cohen's Index kappa was used to determine the correlation coef ficient between clinical and histologic diagnosis ([2]).

## RESULTS

Of the 6000 biopsy specimens of the skin from subjects suspected to have leprosy , 3693 (61.6%) were classified, 2010 (33.5%) did not show histological evidence of leprosy, and 297 (4.9%) were not included in this study, 86 because they were inadequate specimens, and 21 1 because they were specimens taken from treated subjects. Of the 2010 unclassified cases, 1463 showed nonspecific features, 358 had the histologic appearance of normal skin and 189 exhibited findings of other dermatosis dif ferent from leprosy (Fig. 1).

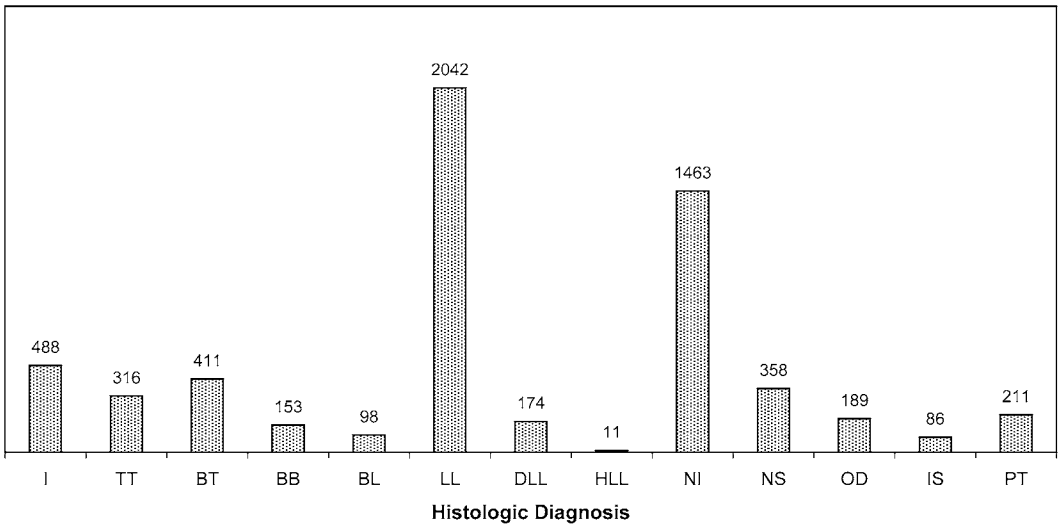


FIG. 1. Results of the total of the 6000 biopsies of the National Leprosy Control Program (NLCP) in Mexico. The graph includes 3693 classified cases, 2010 not classified, 86 inadequate specimens, and 21 1 patients previously treated.

**Duration of the disease before medical staff of the National Leprosy Control Program examined subjects.** Duration of the disease before medical staf f of the control program clinically examined the subjects ranged from one month to 60 yrs, with a median of 18 months Of the 3693 classified biopsies, in 7% of the requests the date of onset was omitted, 13% of the patients were examined from one to 12 months after onset, 30% after one to three years, 22% after 3 to 5 yrs, 13% after 5 to 10 yrs, 9% after from 10 to 20 ys, 3% after 20 to 40 yrs, one after 55 yrs and one patient 60 yrs after onset.

The relationship between the form of the leprosy and the duration of the disease was: for indeterminate, from one month to 25 yrs with a median of one year; for tuberculoid, from two months to 30 yrs with a median of 2 yrs; for borderline, from 45 days to 20 yrs with a median of 9 months; and for lepromatous, from two months to 60 yrs with a median of 3 yrs.

**Common err ors that r endered the biopsy specimen histologically unr eadable.** Most of the biopsy specimens of the skin were fusiform obtained with a scalpel, and contained subcutaneous fat tissue, but in 86 (1.4%) of the 6000 biopsy specimens, there were errors that rendered the pieces of tissue histologically unreadable. Of these, 51 were superficial and insufficient, consisting only of epidermis, without bacilli or inflammation, 24 were not well fixed (some of them were placed in distilled water), 7 specimens were received dry (six inside of an empty broken glass vial and one without vial), and 4 vials were received without a specimen (Fig. 2).

**The anatomic site fr om which the biopsy specimens wer e obtained and classified.** Forty percent (1461/3693) of the skin specimens were taken from the upper extremity and 33% (1203/3693) from the lower extremity . These specimens were mostly taken from the forearm (732/1461) and arm (562/1461); and from the leg (596/1203) and thigh (395/l203). However, the only site that provided the most precise information and with the best percentage of histological agreement were the specimens

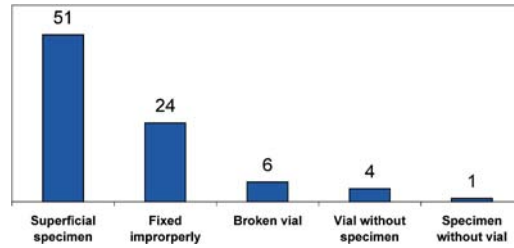


FIG. 2. Eighty-six inadequate specimens. The graph shows the causes that made the 86 biopsy specimens inadequate for their study.

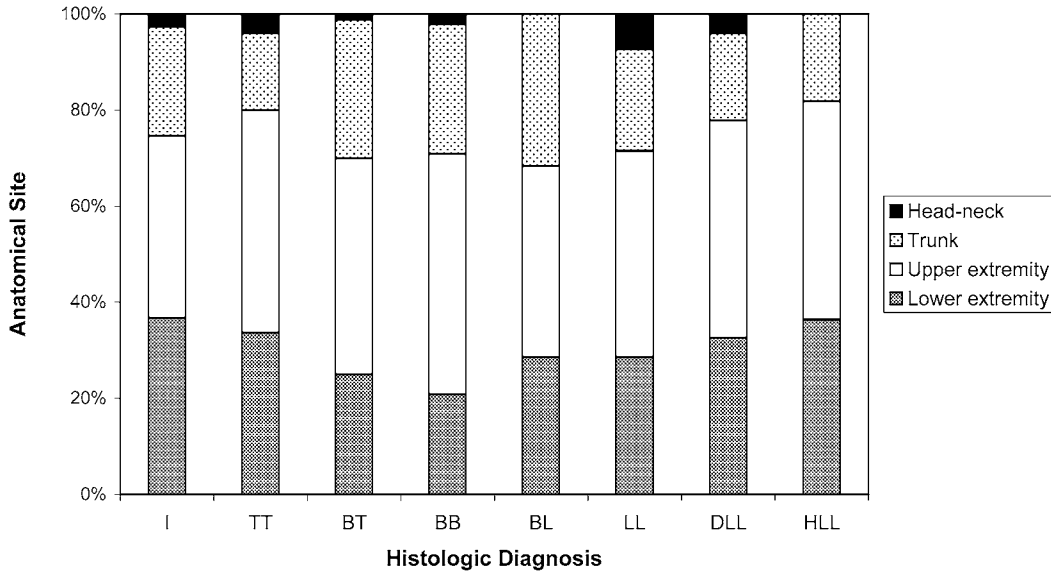


Fig. 3. Correlation between the site where the biopsy was taken and its histologic diagnosis.

taken from the ear; in 59% of them the diagnosis of LL was confirmed (Fig. 3).

**Correlation between the type of the clinical skin lesion and classification.** Macules, nodules, and plaques were the skin lesions most frequently biopsed (Fig. 3). In 38% (1392/3693) of the classified cases, a macule was the skin lesion selected for biopsy and the histologic features most frequently seen in this lesion were those of I, TT, and BT . Nodules accounted for 21% (779/3693) of the lesions biopsied. This was the only skin lesion that had high agreement with the biopsy result, 82% of the nodules showing histologic evidence of LL. Plaques were selected in 16% (578/3693) of the classified cases and the histologic signs of TT and BT were more commonly present in these biopsies.

The correlation between the skin lesion and histologic diagnosis showed the following results. In the indeterminate type, macules and skin with DAA were the most common skin lesions biopsed. In TT and dimorphous groups, macules and plaques were the most selected. In LL, nodules, macules, and plaques were observed, and in DLL, skin with DAA and macules were most common. Finally , in HLL, a nodule was most commonly biopsed.

**Distribution of 3693 classified cases, by age and gender.** Table 1 shows the age and gender distribution of all 3693 classified cases; 61.3% were male and 38.7% female, with a male-to-female ratio (M:F) of 1.6:1. The age range was 2 to 98 yrs, with a median of 50 yrs; 4.7% were children in the age group of 2 to14 yrs and the greatest percentage (19.2%) was seen in the age group of 41 to 50 yrs. When the frequency of ages of males and females was compared, by decade, there were no significant dif ferences in their distribution ($p < 0.3$) (Fig. 5).

The results of 3693 classified cases by histological examination are shown in Table 1. Four hundred eighty-eight (13.2%) cases revealed features of I, 316 (8.6%) of TT, 411 (11.1%) of BT, 153 (4.1%) of BB, 98 (2.7%) of BL, 2042 (55.3%) of LL, 174 (4.7%) of DLL and 1 1 (0.3%) of HLL. (Table 1).

LL was much more frequent in males (68.0%) than in females (32.0%), with M:F ratio of 2.1:1 ($p < 0.0001$). TT was the only form of leprosy more frequent in females (63.6%) than in males (36.4%), with F:M ratio of 1.7:1 ($p < 0.0001$); both differences are statistically highly significant. Multibacillary leprosy (MB) with 67.9% of the total, was twice as frequent as paucibacillary leprosy (PB), with 32.1% of the cases, and involved more males than females 2.1:1. PB was more common in girls (25/43) than in boys (18/43) in the age group 2 to 10 yrs old, and in women (400/669) than in men (269/669) in the age

TABLE 1. *Age and gender distribution of 3693 biopsies classified.*

| Age (years) | Number of cases | I (N = 488) | | TT (N = 316) | | BT (N = 411) | | BB (N = 153) | | BL (N = 98) | | LL (N = 2042) | | DLL (N = 174) | | HLL (N = 11) | | Total (N = 3693) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | M | F | M | F | M | F | M | F | M | F | M | F | M | F | M | F | M | F |
| 2–14 | 174 | 24 | 21 | 13 | 17 | 12 | 8 | 3 | 2 | 4 | 2 | 39 | 24 | 2 | 2 | 1 | | 98 | 76 |
| 15–44 | 1722 | 125 | 132 | 55 | 97 | 58 | 87 | 39 | 18 | 18 | 7 | 652 | 326 | 68 | 34 | 4 | 2 | 1019 | 703 |
| 45–64 | 1260 | 78 | 65 | 33 | 63 | 92 | 71 | 38 | 19 | 24 | 21 | 490 | 211 | 40 | 12 | 3 | | 798 | 462 |
| 65–98 | 498 | 27 | 16 | 20 | 16 | 46 | 36 | 24 | 9 | 14 | 7 | 187 | 79 | 11 | 5 | 1 | | 330 | 168 |
| No data* | 39 | | | | 2 | | 1 | | 1 | 1 | | 19 | 15 | | | | | 20 | 19 |
| Total | 3693 | 254 | 234 | 121 | 195 | 208 | 203 | 104 | 49 | 61 | 37 | 1387 | 655 | 121 | 53 | 9 | 2 | 2265 | 1428 |

I = Indeterminate, TT = tuberculoid, BT = Borderline tuberculoid, BB = Borderline, BL = Borderline lepromatous, LL = Lepromatous, DLL = Diffuse lepromatous, HLL = Histoid leprosy.
N = Number.
M = Male, F = Female.
* Ages unknown in 39 cases.




FIG. 4. Correlation between the type of the biopsed skin lesion and its histologic diagnosis.

group 16 to 50 yrs. In 174 children aged 2 to 14 yrs, a histologic diagnosis of lepromatous leprosy (including LL, DLL, and HLL) was made in 39.1% (63) of the cases, I in 25.9% (45), TT in 17.2% (30), BT in 11.5% (20), BL in 3.5% (6), and BB in 2.9% (5) (Table 1).

**Agreement between clinical and histologic diagnosis.** In 5199 biopsy specimens were examined histologically and the findings were correlated with their clinical diagnosis (Table 2). There was complete agreement between the clinical and histologic diagnosis in 42.9% of the cases (Fig. 5). We employing the Cohen's Kappa index ($\kappa$) and the 95% confidence intervals (CI) around kappa to evaluate the statistical significance of agreement between clinical and histologic diagnosis, $\kappa = 0.202$ with a 95% CI of 0.184 to 0.219 with a level of significance of 0.05 $p < 0.01$. The kappa index of agreement of the clinical diagnosis and the histopathologic diagnosis for the dif ferent forms of leprosy, and the 95% confidence interval for $\kappa$ are seen in Table 2 and Figure 6.

In the correlation of the clinical and histologic diagnosis, the agreement in the dimorphous group was not analyzed in its different varieties because the physicians of the control program, in accordance with the Madrid classification, only made a clinical diagnosis of dimorphous, and the histologic diagnosis was according Ridley and Jopling criteria.

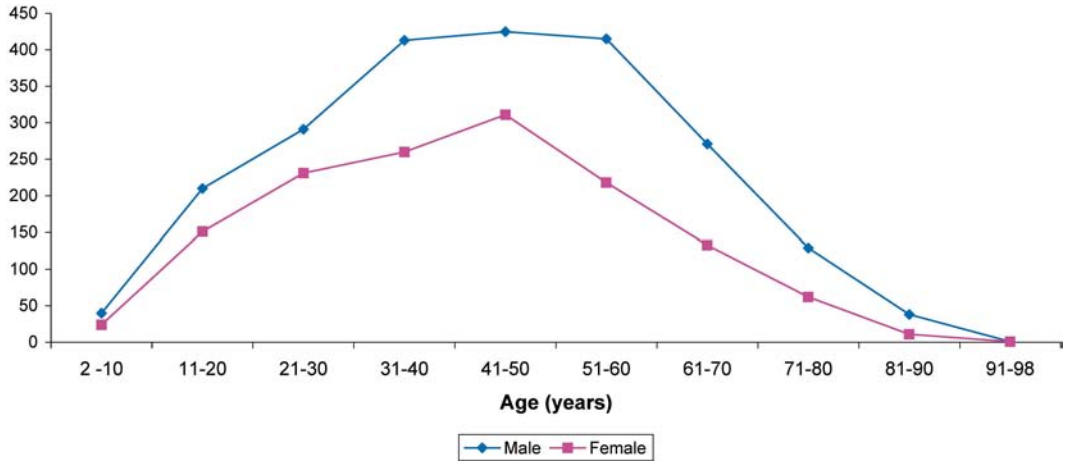


FIG. 5. The graph shows the 3693 cases of classified leprosy distributed in age groups in intervals of ten in ten. The range of ages was included between 2 to 98 yrs, with a median of 50 yrs.The graph shows that the highest incidence in both genders was in the age group of 41 to 50 years old. On the other hand, the frequency of ages of males and females did not have significant differences in their distribution. The numbers of males and females at each interval were compared by Kolmogorov-Smirnov test: $p < 0.3$.

## DISCUSSION

This a retrospective study of biopsies that have been routinely collected over a period of nearly 24 yrs from all cases suspected to have leprosy in a national control program. The main aims of this retrospective analysis were to try to obtain information on the work of the program, and to contribute to the knowledge of leprosy in the country.

This study was implemented under routine program conditions and with numerous limitations. Nonetheless, the data can be regarded as representative of the population of leprosy patients in general, and there is sufficient information to draw some conclusions.

The time of duration of disease before medical staff of the program diagnosed leprosy clinically, varied from one month to 60 yrs with a median of 18 months.The 44% of the cases were from one month to three years, 22% was from three to five years, and 30% was from five to 40 yrs. In various countries the majority of new cases detected have a delay of one to three years, and WHO collaborative studies indicate that the majority of new cases are detected late; i.e., that about 75% of new cases are

TABLE 2. *Concordance correlation coefficient (Cohen's kappa index) between clinical and histologic diagnosis.*

| Clinical diagnosis | Histologic diagnosis | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | I | TT | BT | BB | BL | LL | DLL | HLL | NCI | NS | NO | Total | κ Index | 95% CI* |
| Indeterminate | 307 | 80 | 63 | 11 | 4 | 204 | 7 | | 665 | 158 | 47 | 1546 | 0.205 | 0.187–0.223 |
| Tuberculoid | 51 | 168 | 85 | 9 | 4 | 61 | 1 | | 185 | 46 | 12 | 622 | 0.323 | 0.306–0.341 |
| Dimorphous** | 14 | 15 | 159 | 60 | 29 | 80 | 4 | | 84 | 16 | 12 | 473 | 0.409 | 0.391–0.427 |
| Lepromatous | 71 | 22 | 75 | 54 | 25 | 1432 | 86 | 11 | 292 | 92 | 81 | 2241 | 0.478 | 0.458–0.498 |
| Diffuse lepra | | 8 | 3 | 4 | 1 | 155 | 74 | | 59 | 12 | 1 | 317 | 0.271 | 0.254–0.289 |
| Total | 443 | 293 | 385 | 138 | 63 | 1932 | 172 | 11 | 1285 | 324 | 153 | 5199 | 0.202 | 0.184–0.219 |

I = Indeterminate, T = Tuberculoid, BT = Borderline tuberculoid, BB = Borderline, BL = Borderline lepromatous, LL = Lepromatous, DLL = Diffuse leprosy, HLL = Histoid leprosy, NCI = Nonspecific chronic inflammation, NS = Skin apparently normal, NO = Other diagnostic different from leprosy.

* CI = Confidence interval.

** Dimorphous = Includes BT, BB, BL.

This table does not include 801 cases (504 without clinic diagnosis, 21 1 from subjects treated and 86 inadequate specimens).

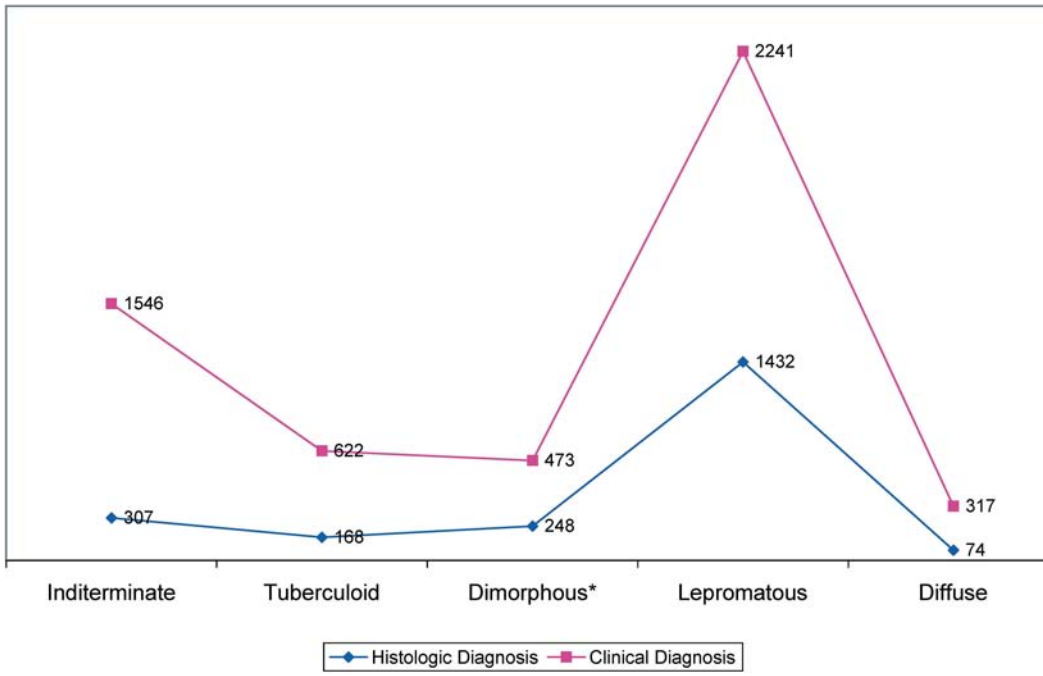


FIG. 6. Correlation between clinical and histological classification of 3693 biopsies.

detected 3 to 5 yrs after onset and about 15% are detected 5 to 10 yrs after the onset of the disease ([8]).

Of the skin biopsy specimens received, 86 (1.4%) could not be studied due to faults in the sampling, obtaining, fixation, or dispatch. Thus, it is necessary that clinicians be acquainted with the importance of proper selection of the site and type of lesion for histologic examination, as well as the correct methods for fixing the piece of tissue and packing and mailing it to the laboratory.

The preferred anatomic sites of the skin biopsy specimens were the forearm (20%) and the leg (16%), but the anatomical site with best percentage of positive clinicohistologic correlation was the ear , where 56% of the specimens confirmed the diagnosis of LL. Macules were the lesions most frequently biopsed, and in these skin lesions the histologic features of I, TT, and BT were more frequently found. The nodule was the most significant lesion for LL.

MB (67%) occurred twice as frequently as PB (33%) and affected more males than females (2:1), but TT was more common in females than in males. This agrees with most studies throughout the world that indicate that males are approximately twice as likely to contract lepromatous disease as are females.

According to these results, LL was by far the most common form of leprosy encountered in Mexico, with 60.3% (2227/3693) of cases. In Mexico the diffuse lepromatosis is more frequent. This is the most severe of all forms of leprosy and its striking histologic feature is the presence of innumerable lepra bacilli within the endothelial cells of the capillary vessels of the papillary and subpapillary dermis. These results indicate that a high percentage of the population of this country has a very low degree of resistance to this infection.

It is interesting to note that most previous authors have recorded a higher frequency rate in children (<14 yrs old), and that LLis infrequently seen in this group ([3, 6, 14]). However, in this study the frequency in children was low (4.7%), and the most common form of the disease in this age group was LL; it is also of note that in infants and children under 6 yrs old, TT was most common in girls and LL in boys.

The number of patients was greater in the 21 to 30 yrs age group, and the peak was reached in the 41 to 50 yrs age group, and declines in females aged 51 to 60 yrs, and

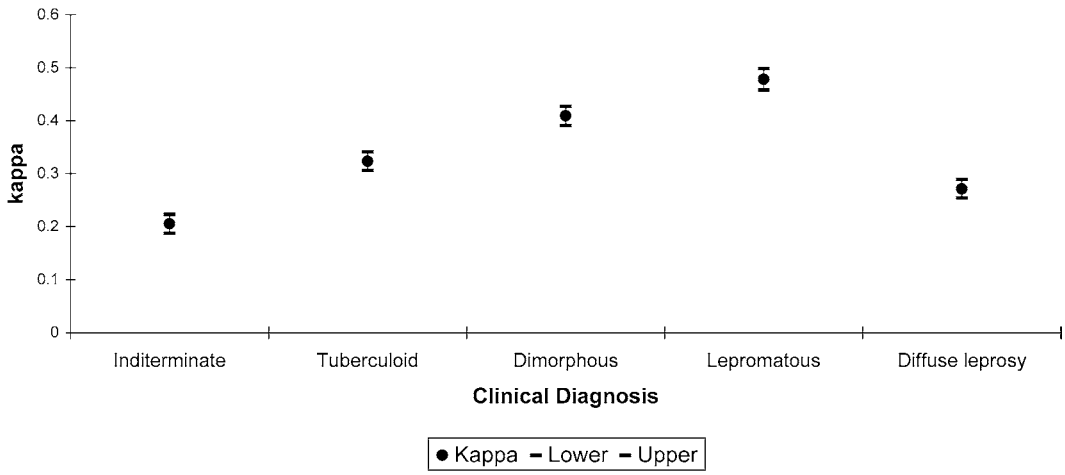


FIG. 7. The graph shows the agreement between clinical and histologic diagnosis in accordance with the kappa index of Cohen and their 95% confidence interval for each clinical form of leprosy.

in males aged 61 to 70 yrs. These data could indicate that we are facing the end of leprosy in Mexico, a country in which the national goal of elimination was reached in 1994, with a prevalence since the year 2000 of 0.17/10,000. However , areas persist in which the elimination has not been achieved and they require us to persevere with continuous efforts to achieve elimination in the whole country, to cut the transmission of the disease and in the future to achieve its eradication.

There was complete agreement between the clinical and histologic diagnosis in 42.9% of the cases in this study. Other authors have reported percentages of complete agreement between clinical and histological diagnosis in 33% to 89% of the cases ([3, 4, 5, 9, 10, 13]). The highest percent of agreement for individual types in this analysis was for LL (in 63% of the cases), and the lowest in I (20% of the cases). Agreement in the dimorphous group was not analyzed because the physicians of the control program, in accordance to classification from Madrid, only made a clinical diagnosis of dimorphous.

The concordance correlation coefficient between clinical and histologic diagnosis was determined using the index kappa of Cohen and was found $\kappa = 0.20$, which is a poor grade of agreement. This grade of agreement and the low percentage obtained, indicate the importance of measuring the accuracy of the clinical diagnosis, an important part of medical training that may allow reduction of failures in this field, since the clinical diagnosis still remains the mainstay for the detection of leprosy.

One hundred and eighty-nine studies requested with the clinical diagnosis of leprosy showed histologic findings of other dermatosis different from leprosy. Of these, the majority were interpreted as being neurofibromatosis, atopic dermatitis, pityriasis alba and lipomas.

Finally, the biopsy in leprosy is essential for the proper diagnosis, classification and prognosis of the disease and assessment of progression or regression of the disease in patients under treatment ([1]). But the biopsy has its limitations, with relative frequency it cannot enable a definitive diagnostis, but can only be suggestive in tuberculoid and indeterminate forms. The pathologist can give to the clinician enough information if the specimen is obtained, handled, fixed, and mailed correctly , and if the clinician provides detailed information of the patient and the disease when submitting a specimen to the laboratory for diagnosis. In order to use this knowledge most efficiently, close communication between pathologist and clinician is essential for their own understanding of the disease process, and for the benefit of the patients.

**Acknowledgment.** Thanks are due to Sergio Pastén, Biologist, from Department of Parasitology , for his help in statistical analysis.

## REFERENCES


1. Fite, G. L., and Mansfield, R. E. The role of histology in the study of leprosy . Arch. Dermatol. **100** (1969) 478–483.
2. Fleiss, J. L. *Statistical Methods for Rates and Proportions.* 2nd Edn. New York: Wiley, 2000. pp. 212–225.
3. Jayalakshmi, P., Tong, M., Sing, S., and Ganesapillai, T. Leprosy in children. Int. J. Lepr . Other Mycobact. Dis. **65** (1997) 95–97.
4. Jerath, V. P, and Desai, S. R. Diversities in clinical and histopathological classification of leprosy. Lepr. India **54** (1982) 130–134.
5. Kalla, G., S alodkar, A., and Kachhawad, D. Clinical and histopathological correlation in leprosy. Int. J. Lepr. Other Mycobact. Dis. **68** (2000) 184–185.
6. Kumar, B., and K aur, I. Childhood leprosy in Chandigarth; clinico-histopathological correlation. Int. J. Lepr . Other Mycobact. Dis. **68** (2000) 330–331.
7. Lucio, R., and Alvarado. In: *Opúsculo sobre el Mal de San Lázaro o Elefanciacis de los griegos. In González Ureña, J. La lepra en México.* Buenos Aires: El Ateneo, 1941. pp. 199–231.
8. Meinema, A., Gupte, M. D., Van Oortmarssen, G. J., and Habbema, J. D. F. Trends in leprosy case detection rates. Int. J. Lepr. Other Mycobact. Dis. **65** (1997) 305–319.
9. Memoria del VI Congreso Internacional de Leprología. Madrid: Gráficas González, 1954. pp. 75–80.
10. Meyers, W. M., Heggie, C. D., Kay, T. L., Staple, E. M., and Kvernes, S. The Ridley-Jopling five group classification of leprosy-correlation of parameters of the Classification in 1,429 leprosy patients. Int. J. Lepr . Other Mycobact. Dis. **47** (1979) 683–684.
11. Ridley, D. S. Review of the five-group system for the classification of leprosy according to inmmunity. (Table) Int. J. Lepr. Other Mycobact. Dis. **40** (1972) 102–103.
12. Ridley, D. S., and Jopling, W. H. Classification of leprosy according to immunity: a five-group system. Int. J. Lepr . Other Mycobact. Dis. **34** (1966) 255–273.
13. Sehgal, V. N., Rege,V. L., and Reys, M. Correlation between clinical and histopathologic classification in leprosy . Int. J. Lepr . Other Mycobact. Dis. **45** (1977) 278–280.
14. Sehgal, V. N., and S rivastava, G. Leprosy in children. Int. J. Dermatol. **26** (1987) 557–566.
15. Wade, H. W. The histoid variety of lepromatous leprosy. Int. J. Lepr . Other Mycobact. Dis. **31** (1963) 129–142.