INTERNATIONAL JOURNAL OF LEPROSY Volume 41, Number 2
Printed in the U.S.A.

Notes from the History of Leprosy

Olaf K. Skinsnes[1]

I. Interpretive Chronology of Leprosy Concept and Practice

This chronological presentation of developments in concepts and practices relating to leprosy is not intended to be comprehensive, nor is it an attempt to assign priorities for these developments. It is an attempt, at this centennial point in time, to provide a simple, readily comprehendable overview of the flow of development and change related to this disease. As time passes those who become interested in the problems of leprosy face an ever-expanding problem of familiarizing themselves with that which has transpired in the past, especially as related to areas of endeavor other than their particular field of expertise. One recalls with some nostalgia the remark attributed to Armauer Hansen in 1901 to the effect that "there is already too much literature on leprosy."

When this chronology was first initiated, it seemed fairly simple but as its construction progressed it became evermore complex and time-consuming till finally publication deadline and the pressure of other *Festskrift* preparations necessitated an end to its expansion.

Some 18,000 references to work in leprosy were at hand, but the publications to which they relate are in many instances not readily available or obtainable only with great effort. Just when some notion was traced to its root it appeared that somewhere in the past another individual had a similar notion. This is exemplified by the chronicled 1893 dietary thesis of Hutchinson regarding the consumption of decayed fish as being generative of leprosy and the subsequent finding that Bernhard de Gordon (1285-1307) had a similar idea. Of course, each such earlier reference requires some evaluation of its basis and seriousness, for fish consumption, for example, has been held in the folklore of many societies for unknown lengths of time as being etiogenic of leprosy, as is noted in the etymology of the term "cucubay" for leprosy as used in Guyana.

Many references given to the pre-Christian period will be disputed by some as not being provable reference to leprosy *per se*, as is often stated to be the case with Biblical references to leprosy. This unsettled point will not be argued here. They are noted in this chronology as leprosy, the point not being settled, for those who may wish to consider the problem themselves and because it has not been proven that leprosy was not included in the society encompassed by the given designation.

With these, and other unnoted limitations, this chronology is nevertheless presented as a quick reference point for the flow of many concepts and experiences that have played a role in the development of the present vantage point. Where feasible, while still attempting to avoid cumbersomeness and pretensions to historical judgement of priority, the concepts are referenced. Where possible, the references used for older literature are to publication, reprint or abstracts in the INTERNATIONAL JOURNAL OF LEPROSY (IJL) that will give a quick lead to the original and other related references.

[1] Olaf K. Skinsnes, M.D., Ph.D., ALM Leprosy Atelier, Department of Pathology, School of Medicine, University of Hawaii, Honolulu, Hawaii.

Pre-Century of Progress

c. 1500 *Rgveda Samhita* (India) mentions *kushtha* (a term covering leprosy as well as some other skin afflictions).

c. 1400-1300 Leprosy presence in Canaan (Palestine) suggested by a clay jar molded with leontine-like facies. (Yeoli. J. Hist. Med. **10**) [1955] 331-333.)

c. 1300-1000 *Ebers Papyrus* and *Brugsch Papyrus* (Egypt) mention of leprosy under term *Uchedu.*

c. 1000 *Susrutas Ayurvedas* by Hanvalare of India, described leprosy.

c. 880 *Manava Dharma–Sastra* or *Manu Smriti* (Laws of Manu) prophylactic advice against leprosy including proscription against marriage with offspring of persons having leprosy.

756 Treaty forced on Arpad of Syria by Ashur-nirari of Assyria stipulated that the god *Sin* would clothe violators of the treaty with leprosy. (Olmstead, *History of Assyria,* 1923, p 172.)

782-732 King Azariah (Uzziah)[2] of Israel became a victim of leprosy (*tsaraath*). His duties thereafter being discharged by his son. The disease was contracted as punishment for sin of assuming priestly functions. (The Bible, II Kings **15**: 1-7; II Chron. **26**: 1-23).

c. 600 *Sushruta samhita* (India) clear description of leprosy. Under terms "Vat-Rakta" and "Vatasonita" there is characterized hyperesthesia, anesthesia, formication and deformities. Under designation *kushtha* there were two kinds of skin lesions. In one the prominent symptoms and signs were local anesthesia and deformities. In the other the features were ulceration, falling off of fingers and sinking of the nose. (Dharmendra, *Notes on Leprosy,* 1967; IJL **15** [1947] 424-430.) If the affliction affected the fat particularly there would be lameness of the hands, inability to walk, decay of limbs, spreading of wounds from one part of the body to another. In marrow and bones there would be collapse or decay of nose, redness of eyes, maggots forming in the wounds, voice choked. If present in the *sukradhātu* (semen) of the father and in the menstrual blood of the mother, the leprosy would be transferred to both the offspring. *Kustha* is the worst of all diseases and one who dies due to that is again attacked by it in the future birth. *Kushta* is also contagious like fever, consumption, ophthalmia and the epidemic diseases by constant contact, breathing together, eating together, lying or sitting together, clothes, garlands and ointments. The expansion of *kushta* from skin to the remaining elements of the body is compared with the gradual expansion of the roots of a tree in the earth. (Jolly, J. Indian Med. [1951] pp 142-144.)

6th century Disciple of Confucius presumed to have leprosy.

c. 500 *Nei Ching Su Wen*–Attributed to Huang Ti (Trad. B.C. 2698-2598)–regarding leprosy, notes loss of eyebrows, nodules, ulceration, "and because of the stagnant movement of the *wei-chi* (defensive force) numbness results." "The vital spirits degenerate and turn cloudy causing the bridge of the nose to change color and rot, and the skin to ulcerate." Used term *li-feng* (severe paralysis).

[2] This is included as a type reference for the many other Old Testament Biblical references.

5th century	Herodotus wrote of Persia: ". . . and whosoever of the men of the city has leprosy or whiteness of the skin, he does not come into a city nor mingle with the other Persians: . . . but a stranger who is taken by these diseases in many regions they drive out of the country altogether."
c. 480	Leprosy introduced to Greece, following conquest by Darius and by Xerxes.
345	Leprosy described by Aristotle.
c. 300	*Septaugint* (Greek) translation of Hebrew Bible, Old Testament, rendered *tsaraàth* as *lepra.*
c. 97-54	Lucretius in *De Natura Rerum* wrote: "High up the Nile midst Egypt's central plain Springs the dread leprosy, and there alone."
	B.C.———O———A.D.
c. 4 B.C. 29 A.D.	Jesus Christ, in practice and teaching, indicated that persons with leprosy are not outcasts before God but equally the recipients of His grace.
62	Leprosy possibly introduced to Europe by Roman soldiers of Pompey withdrawn from legions in the East.
c. 150	Hua T'o, preeminent Chinese surgeon: "The symptoms of leprosy may first appear on the skin but the poison is actually stored in the internal organs. The skin is first numb without sensation, gradually red spots appear on it, then it is swollen and ulcerated without any pus. And later the disease develops to such an extent that the eyebrows fall, the eyes may become blind, the lips deformed and the voice hoarse. The patient may also experience ringing in his ears and the soles of his feet develop rotted holes; his finger joints may become dislocated and the bridge of his nose flattened."
100-900	India, *Ayurveda Susruta* and *Bagvat* described a *tubarak* oil (believed to be a hydrocarpus oil) in treatment of leprosy.
c. 150	Aretaeus (Greek)—first comprehensive clinical description of leprosy in Europe; *Leonine facies* noted. "The disease is also called *Leo* on account of the resemblance of the eyebrows—and *Satyriasis* from the redness of the cheeks, and the irresistible and shameless impulse *ad coitum.*" Did not record anesthesia as characteristic. (Adams; Extant Works of Aretaeus, the Cappadocian, 1856, pp 368-372).
180	Galen wrote of leprosy in Germany.
281-341	Ko Hung (China): "The first symptom of *lai-ping* (leprosy) is numbness of the skin or a sensation of worms creeping."
5th-6th centuries	Leprosy brought to Spain by Roman troops.
610	*Chao's Pathology* (China) included a long account of the etiology and symptoms of leprosy in detail: loss of sensation, absence of sweating, loss of hair and eyebrows, perforating ulcers, distorted ears and fingers, disfigured face, bleared eyes, hoarse and raucous voice, nasal deformity, etc.
625 or 638	First leprosy hospital in England at Nottingham (Blyth Leper Hospital).
625-1798	Leprosy endemic in Great Britain.

640	Sun Szu-mo (China), devoted a chapter to leprosy in his "Thousand Golden Remedies," Vol. 23. Said he had treated over 600 cases, the cures being about one in ten. Insisted that treatment must be continued for a long time. Treatment included dietary measures and the use of dried, powdered turpentine prepared from pinewood.
720-759	Oldest known Swiss leprosarium at Convent in St. Gallen, and in 871 at Moutien.
757	Pepin (France), issued a decree making marriage of those with leprosy illegal and the disease a reason for divorce.
701-760	Empress Komyo (Japan), provides care for leprosy victims.
758	Empress Komyo founded, in Nara, the first leprosy hospital in Japan.
833	*Reino-Gige*, Japanese law commentary, regarded leprosy as contagious from man to man.
982	*Ishinhō*, oldest Japanese medical book in existence declared that "leprosy is a communicable disease transmitted directly from man to man."
1000-1400	Leprosy epidemic in Europe (peak), following dissemination during the Crusades.
1067	First leprosarium in Spain, at Palenca, established by the Cid.
12th-13th centuries	Leprosy first known in Iceland.
1235	St. Elizabeth (1207-31), patron saint of those with leprosy, canonized four years after her death at age 24. Daughter of King of Hungary, wed in political marriage at age 14 to Louis, Landgrove of Thuringia; sublimated herself in service to those with leprosy.
1246	Franciscan monk, Bartholomaeus Angelicus, recognized contagious nature of leprosy; believed that it was hereditary, and also that it was induced by eating hot food, pepper, garlic and the meat of diseased hogs. (Marti-Ibañez, *Epic of Medicine*, 1959, p 155.)
1285-1312	Philip IV ("Philip the Fair"), King of France. Suggested that all persons with leprosy be gathered together and burned, and that the practice continue until the disease was eradicated.
1383	All *cagots* (gafet, capots, caqueux, cacous—all terms derived from Spanish *gafo*, *gafedad* from *gaf* of Latin, meaning "hook, claw") defined as leprosy by Guy de Chauliac.
1396	All *cagots* (France) required to wear a "Sign d'infamie."
1400-1410	St. Jörgen's Hospital founded in Bergen, Norway.
1484-1492	Pope Innocent VIII, suppressed the Knights of St. Lazarus as an order. They had been devoted to the service of those with leprosy and many of their order had leprosy. At one time the Order of St. Lazarus required that only a person with leprosy could be elected as Grand Master.
1595	*Pen T'sao Kang Mu* ("The Great Herbal," China) by Li Shi-chan notes *lu-braco* (probably *H. anthelmentica*) as an effective leprosy treatment. Imported from Siam.
16th century	Leprosy spread from Portugal to Brazil.
16th-18th centuries	Leprosy spread from Spain to Colombia, Equador, Cuba, Mexico, and southern United States.
	Leprosy spread from Africa to Santo Domingo, Cartagena, Jamaica, parts of South America and southern United States.

1612	Louis XIII of France forbade the marriage of persons with leprosy to anyone.
1716	Chaulmoogra seeds used in treatment of leprosy in Japan (IJL **1**: 161).
1749	Chinese medical classic "Golden Mirror of Medicine" recognized contagious nature of leprosy, citing causes as infection by contact with those having leprosy, unclean privies, houses, bedding, etc.
1781	Japanese treatise on syphilis and leprosy published by Katakara Genshiu, Tokio, notes "that some cases are absolutely incurable; it is useless to attempt to cure a patient whose eyes have a yellow hue, whose fingernails have no white crescents at the bottom, whose hands are wholly anesthetic, whose palm or sole bleeds, whose eyeballs are ulcerated, whose penis is putrified, whose hands or feet are clawed, whose skin is spotted with black, whose fingers have melted off leaving frog-foot shaped ends, whose body hairs fall off, whose nose is gone, whose bones are poisoned and putrified . . . men who contact the disease after their fortieth year, people with very emaciated bodies." (Ashmead. JAMA **22** [1894] 605-608.)
18th century	Leprosy spread from Norway to Minnesota, U.S.A., and from France to Canada.
c. 1823	First reference to leprosy in Hawaii.
1840	Tertiary syphilis (Radesyge) and leprosy differentiated (Hjorts, Norsk Mag. Laegevidensk).
1847	*Atlas Colorié de Spedalskhed*, Danielssen and Boeck and *Om Spedalskhed* (Virchow called this the beginning of the biologic knowledge of leprosy). Danielssen, however, regarded leprosy as a "hereditary dyscrasia sanguinis."
1844, 1856, 1858	Danielssen made repeated efforts to transmit leprosy by inoculation of himself and nine volunteers with leprosy material without success.
1848	Danish government, influenced by the noncontagionist views of Danielssen and Boeck, closed the four extant leprosy hospitals in Iceland. Hospitals rebuilt in 1897.
1852	Diffuse leprosy of Lucio and Latapi described by Lucio. (Franken, *Diffuse Leprosy of Lucio and Latapi*, 1963).
1854	Chaulmoogra oil introduced to Western medicine for the treatment of leprosy (Mouat).
1855	Successful use of chaulmoogra oil in China (Hobson).
1857	Successful use of chaulmoogra oil in Bengal (Monat).
1858	"Syphilisation" of leprosy reported as failing to alter or modify general features of leprosy (Danielssen, *Syphilisationen*, Bergen).
1859	Rudolf Virchow visited Bergen and Danielssen demonstrated the "brown bodies" he regarded as characteristic of leprosy and which are now regarded as conglomerations of leprosy bacilli, "globi." Virchow discounted the notion of some casual relationship, regarding the nodules as clumps of degenerated fat, much to Danielssen's later regret. (IJL **28** [1960] 328-329.)
1863	Jonathan Hutchinson postulated that leprosy was "Fisheater's gout" dependent on consumption of badly preserved or decomposed fish. He was echoing the concept of Bernhard de Gordon, a teacher at Montpellier (1285-1307), who said: *"Comedere lac et pisces eadem mensa inducit Lepram."*

1864 Virchow described the "lepra cell," holding the vacuoles to be due to hydropic degeneration. (IJL **21:** 372-272; **22:** 71-79 and 205-217.)

1865 First leprosy in New Hebrides.

1868-1873 Obermeier observed the spiral *Borrelia recurrentis* in the blood of a patient with relapsing fever, and reproduced the disease in man by the injection of infected blood. (IJL **33** [1965] 905-907.)

1868-1875 Profita, G. and Cagnina, inoculated themselves and eight volunteers with leprosy material without causing leprosy.

Century of Progress in Understanding

1873 Gerhard Armauer Hansen discovered *M. leprae* ("Bacillus leprae"); published findings in 1874. (IJL **23:** 307-309.)

"The discovery of the specific bacillus of leprosy by Hansen ruined many a (cherished) hypothesis, and reduced to the status of secondary causes many etiological factors to which previously a preponderant role had been attributed."

"Nevertheless, a number of leprologists did not at first appreciate the significance of this decisive discovery. The authority of Danielssen and Boeck, who attributed leprosy to multiple and disparate origins, remained great, and Hansen had much to overcome to obtain recognition of the specific agent. Neisser in Germany (1869), Brocq (1885), Leloir (1886) and Ernest Besnier (1887) in France, contributed to the triumph of the idea of contagion." (Jeanslme, *La Lepre,* 1934, p 213.)

Father Damien de Veuster took up residence with leprosy patients on Molokai, Hawaii.

1874 The Mission to Lepers (London) founded. Name changed to "The Leprosy Mission" in 1966.

1875 Death of C. W. Boeck.

1878 First leprosy in New Caledonia.

1879 Neisser, applying staining methods of Weigert and Koch to leprosy material, found bacilli most beautifully with fuchsin and gentian violet to be abundantly present in skin, liver, spleen, testes, lymph nodes and cornea. (IJL **23** [1955] 418-428.) Regarded the vacuoles of lepra cells as due to fatty degeneration.

1881 Demonstration of leprosy bacilli in large numbers in affected nerves. (Babes, *Les Bacteries et leur Rôle dans l'Anatomie et l'Histologie des Maladies Infectieves.* Paris: F. Alcan, 1885.)

1884 Arning (Hawaii), inoculated convicted murdered Kenau (with his permission) with a freshly excised leproma. Leproma sutured to belly of supinator radii longus muscle of right forearm. Twenty-five months later, October 1886, Kenau showed nodular leprosy all over body.

1886 Culicidian theory of leprosy transmission advocated by Beboeuf. Strongly supported by Adolpho Lutz, 1915.

1887 Dorsal root ganglia invasion by acid-fast bacilli noted. (Sudakewitch. Beitr. Path. Anat. **2**: 129.)

1889 Death of Father Damien.

1892 Ziferino Falcão (Portugal), at International Congress of Dermatology, held that in most cases "the first symptom of leprosy is rhinitis. . . . Not seldom, the perforations of the septum may con-

stitute for a very long time, the sole symptom." Found Hansen's bacillus in rubbings from septal mucosa. As a consequence the concept of leprosy transmission through the nasal mucosa became widespread.

1894 Death of D. C. Danielssen.

First leprosy autopsy series, 125 cases. (Hansen, G. A. and Looft, C., *Die Lepra vom klinischen und pathologisch Standpunkt.*) Later extended by Mitsuda and Ogawa, 1937; Black, 1938; Kean and Childress, 1942; Powell and Schwan, 1955; Junnarkar, 1957; Bernard, 1936; Desikan and Job, 1968; Bernard, 1973.

1897 First International Leprosy Congress, Berlin. Recognized skin and nasal discharge of bacilli, contageousness of leprosy; and recommended control by segregation of patients having leprosy.

First leprosy in Fiji.

Postulate, based on histopathologic studies, that leprosy infections spreads from skin by way of sensory nerves to large nerves of extremities, whereas previously Arning and Unna had postulated skin lesion formation as being secondary to primary affection of the nervous system. (Gerlack and Dehio; Translated in Leprosy in India **24** [1952] 78-83.)

1898 "Tuberculoid" type lesion and term definitively introduced. (Jadassohn, Verhandl. VI Deutsch Dermat. Kongr. Strassburg, p 508; IJL **28** [1960] 444-452).

1900 Publication of LEPRA initiated (ceased 1915). (Edward L. Ehlers, ed.)

1903 Murine leprosy described (Stefansky. Centralbl. f. Bakteriol. **33**: 481-487.)

1906 American Committee of the Leprosy Mission (London) established. Name changed to American Leprosy Mission, 1917, and independently incorporated.

Culion Leprosy Colony inaugurated by Victor G. Heiser.

1907 Japan enacted legislation for the erection of interprefectural leprosy colonies in several locations.

1908 First leprosy in Australia.

1909 Second International Leprosy Congress, Bergen. Reaffirmed recommendation for control by isolation and segregation; recommended removal of children from leprous parents as soon as possible; recognized probable hematogenous dissemination of leprosy.

Successful cultivation of *M. leprae* in symbiosis with other bacteria and amoeba reported. (Clegg, M. T., Philippine J. Sci. **4**: 77-141). Several other attempts at cultivation reported as successful in this period (e.g., Bayon, H., Brit. Med. J. [1912] 424, 458, 1191; Kedrowski. Verslg-Dtsch. Naturforsch., Königsburg).

1912 Death of Gerhard Armauer Hansen (February 12).

Bacillemia demonstrated in leprosy (Rivas); confirmed 1915, Hoveij; 1919, Iyengar; 1933, Lowe; 1953, Rhodes-Jones; 1972, Drutz.

1912-1929 Acute leprosy epidemic in epidemiologically virgin population of Nauru, a Pacific island west of the Gilbert Islands. Within 17 years of the first case 35% of the population had leprosy. (IJL **2** [1934] 319-323; **20** [1952] 1-29.)

1916 Mouritz reported having made inoculation attempts in 15 *kokuas* (assistants or helpers at leprosarium) with leprosy material without producing leprosy. Reported also having made over 100 at-

tempts to create, without success, fresh leprosy lesions in mild nodular (lepromatous) leprosy cases by inoculation of leprosy material. Vigorously espoused probability of contagion by alimentary tract through contaminated food and drink and reported experimental infection of one rat and one cat by this route. Advocated bacillary "instinct of location" for skin and neural localization. Concluded that mosquitoes could not be leprosy vector on basis that all races in Hawaii were not equally attacked by leprosy. (*Path of the Destroyer.*)

1917 Incorporation of American Mission to Lepers. Name changed to American Leprosy Mission.

1918 Lipid nature of lepra cell vacuoles demonstrated. (Cedercreutz, Finska Läk. sällsk Hld **60**: 1; Mitsuda IJL **4** [1936] 491-508.)

Lepromin reaction described by Hayashi (IJL **21** [1953] 370; and by Mitsuda in 1919 (IJL **21** [1953] 347).

1923 Lepra cell origin from histocytes and like cells of the system described by Aschoff as "reticulo-endothelial" demonstrated (G. Herxheimer).

Third International Leprosy Congress, Strasbourg.

Founding of British Empire Leprosy Relief Association (B.E.L.R.A.). Name changed to LEPRA (1963). One aim was to modify compulsary segregation so as to prevent its causing wholesale hiding of the early cases of leprosy. (IJL **10** [1942] 87-95.)

1925 Fordyce and Wise discarded theory of leprosy spread by acarus, the fly, the louse, the mosquito or other sucking insect; essentially similar reasons to those of Mouritz in 1916.

1925-1931 Vaccine treatment of leprosy attempted with preparations from *M. leprae* (Gohar. J. Trop. Med. Hyg. **34** [1931] 166-168); *M. leprae* and *B. pyocyaneus* (Hasson. Trans. Roy. Soc. Trop. Med. **19** [1925] 349); and *M. tuberculosis* (Row. Trans. Roy. Soc. Trop. Med. **20** [1926] 40).

1926 *Lepra bubalorum* (water buffalo), first described (Kok and Roseli); studied by Lobel (1934). (IJL **4** [1936] 79-96).

Chinese Mission to Lepers founded.

1927 Slit-skin bacterial smear evaluation method (Wade and Rodriguez, *A Description of Leprosy*; Wade, Leprosy Rev. **6** [1935] 54-60). Modified by Cochrane, 1947, and standardized to a logarithmic scale by Ridley in 1959. (Cochrane, Ed. *Leprosy in Theory and Practice,* 1959, p 371.)

1928 Leonard Wood Memorial Foundation incorporated.

1929 LEPROSY IN INDIA, publication begun.

1930 LEPROSY REVIEW, publication by British Empire Leprosy Relief Association begun.

LA LEPRO, publication begun by the Leprosy Prevention Society (Japan). Japan leprosy legislation extended to provide segregation throughout the country.

1931 International Leprosy Association established (IJL **1** [1933] 94-108).

Establishment of the Leprosy Prevention Society in Japan.

Histamine test proposed as differential test between leprotic lesions and nonleprotic macules (Rodriguez and Plantilla. IJL **1** [1933] 49-52b.)

Monkey infection by *M. leprae* reported (Soule and McKinley. **Amer. J. Trop. Med. 12**: 1-36, 441-452; IJL **32**: 201-206; **33**: 104-105,,361-362). This claim will typify the many which have been offered, none of which are generally accepted and none of which methods are in general laboratory use.

1932-1939 Widely noted chemical fractionation studies on presumed *M. leprae* from a great number of *in vitro* bacillary cultures which evidently were not the leprosy bacillus. (Anderson, R. J. *et al,* referenced in: Anderson, C. G. *Bacteriological Chemistry,* 1946, pp 374-384; Long, E. R. *The Chemistry and Chemotherapy of Tuberculosis,* 1958, pp 418-443.)

1933 INTERNATIONAL JOURNAL OF LEPROSY, publication begun by International Leprosy Association.

Hypothesis advanced that "granularity" of *M. leprae* results from degeneration and disintegration of bacilli. (Hoffman. IJL **1** [1933] 149-158.)

1934 Recognition and delineation of tuberculoid immunologic pole of leprosy on histopathologic basis. (Wade, IJL **2** 7-38; 279-292; 293-300.)

1936 Father Damien's remains moved from Hawaii to his native Belgium IJL **4**: 527).

Minimal leprosy incubation period said to be three months. (Tisseul. IJL **4**: 256.)

Absence of significant central nervous system involvement in leprosy established. (Ermakova. IJL **4**: 325.)

Concept proposed that lepra reaction is beneficial because it impedes the progress of the disease and improved the skin lesions. (Schujman, S. Rev. brasileira Leprol. 4 [1936] 129.) General disagreement with the hypothesis expressed in a "Correspondence Symposium" (IJL **25** [1957] 403-408; **26** [1958] 160-162).

1937 Syrian hamster reported susceptible to *M. leprae.* (Alder. Lancet **2**: 714; IJL **33** [1965] 297.)

1938 Fourth International Leprosy Congress, Cairo, Egypt. Classification accepted as L_{1-3}; N_{1-3} and LN, or "mixed"; with various subclassifications.

Colocasia antiquorum claimed to be etiologic factor in leprosy through saprotoxin destruction of adrenal cortex resulting in reduced resistance to inoculum (Oberdoeffer, Trans. Far East Assoc. Med.).

Possible value of BCG for prevention of leprosy suggested by Fernandez (Rev. Argent. Dermato. **23**: 425).

1940 Early lepromin reaction defined. (Fernandez. IJL **8**: 1-14.)

Diptheria antitoxin or toxoid tried in leprosy treatment (Collier & McKean).

1942 Chemical analysis of *M. leprae* and preparation of a standardized refined lepromin. (Dharmendra. Indian J. Med. Res. **30** [1942] 1-15.)

THE STAR begins publication. Produced by patients at U.S.P.H.S. Hospital, Carville, Louisiana.

1943 Promin introduced as specific treatment for leprosy (Faget, *et al.* Bull. U.S.P.H.S. **58**: 1729).

1947 Diaminodiphenyl sulfone (DDS) introduced as treatment for leprosy (Cochrane).

Disparate cell reaction to *M. leprae* (tissue culture) in tuberculoid and lepromatous leprosy noted. (Hanks. IJL **15**: 31-64.)

High leprosy prevalence in cast villages compared to low or absent prevalence in nearby, related outcast villages (India).Cited as evidence against insect transmission and in favor of human contact transmission in leprosy. (Cochrane. *Practical Textbook of Leprosy*, pp 15-16.)

1948 Fifth International Leprosy Congress, Havana, Cuba. Leprosy classification accepted as polar "Tuberculoid" and "Lepromatous" types with "Intermediate" lying between and "Indeterminate" for early unclassified types. Use of the term "leper" proscribed.

BCG vaccination for leprosy advocated (Chaussinand. IJL **16**: 431-438).

1949 Light microscopy observed granularity of *M. leprae* under sulfone therapy suggested as evidence of their degeneration and death. (Lowe & Smith. IJL **17**: 185; Cochrane. Leprosy Rev. **20**: 59.)

1950 Bacillary Index (BI) introduced. (Muir. Lep. India **22**: 43-45.)

1951 Sister Marie Suzanne, *et al*, reported isolation and cultivation of *M. leprae* with the development of a therapeutic antiserum. (Ann. Inst. Pasteur **81**: 288-241; IJL **20** [1952] 297.) Subsequent reports of therapy effectiveness. (Blanc, *et al.* IJL **23** [1957] 23-31; Babalawis, *et al.* Leprosy Rev. **37** [1966] 51-55.)

1952 Korean War. British troops accused of participation in germ warfare by "planting lepers" behind enemy lines (Hong Kong, *South China Morning Post*, July 5, 1952).

Steroids introduced for reactions in leprosy. (Lowe. Brit. Med. J. **2** [1952] 746-749.)

Reconstructive surgery of leprosy deformed hand introduced. Specific pattern of muscle paralysis in over 1000 cases presented. (Brand, P. W. Leprosy Rev. **24** [1953] 104-116.)

1953 Sixth International Leprosy Congress kept Havana classification with some additional subclassifications but changed "Intermediate" to a third "polar", definitely defined "Dimorphous" type. "Dimorphous" soon came to be synonymous with "Intermediate" and "Borderline."

International Leprosy Conference, the Leprosy Mission and American Leprosy Missions, Lucknow, India (November 7-16).

Hypothesis advanced that leprosy is the result of trace element deficiency and therefore is a symptom and not a disease. (Gay, L. P. The Star **13**: 7-10.)

Damien-Dutton Award established. Stanley Stein first recipient.

Granularity and degenerative changes in *M. leprae* under sulfone therapy noted and suggested as evidence of loss of bacterial vitality. (Malfatti & Jonquieres. IJL **21**: 323-329.)

M. leprae resistance to sulfone therapy reported. (Wolcott and Ross. IJL **21**:437-440;confirmed Pettit & Rees, IJL **34** [1966] 375-390.)

1954 Lepra-like infection reported in frogs. (Machicao & La Plica. Lab. Invest. **3**: 219-227.)

1955 Total stripping of epineural sheath recommended for thickened, painful nerves (Gramberg. IJL **23**: 115-123). Later opposed and modified (*Leprosy in Theory and Practice.* Cochrane & Davey, Eds. 1964, pp 473-474).

Immunologic dichotomy of leprosy (effective immunologic response but absence of humoral antibody response in tuberculoid; absence of effective immunologic response but presence of humoral antibody response in lepromatous leprosy) noted. (Lowe. Leprosy Rev. **26**: 15-24.)

1956 Postulated predilection of *M. leprae* for sites of low temperature. (Binford. Publ. Hlth. Rep., Wash. **21**: 995.)

Documentation that ¾ of children developing leprosy in a leprosarium healed spontaneously. (Lara & Nolasco. IJL **24**: 245-263.)

Diphenylthiourea (Ciba 1906) therapy introduced (Davey).

Harking back to earlier suggested relationship between fish-eating and leprosy, hypothesis proposed that leprosy results from autoxidation of lipids, ingestion of excessive quantity of unsaturated fatty acids accompanied by a deficiency of tocopherol (Vitamin E) providing a favorable milieu for growth of *M. leprae*. (Bergel, M. Semana Medica **109**: 251, 321; IJL **26** [1958] 64-66; Leprosy Rev. **30** [1959] 153-158, **37** [1966] 163-166.)

Significance of early, often asymptomatic, leprosy lesions called to attention. (Lara and Nolasco. IJL **24**: 245-263; Khanolkar. Indian Council Med. Res., Spec. Report No. 19, 1951; Correspondence IJL **23** [1955] 198-200; Taylor *et al.* IJL **33** [1965] 716-731.) Intraneural injection of hyalase and procaine advanced for treatment of neural pain. (Garrett. Leprosy Rev. **27**: 61.)

1958 Seventh International Leprosy Congress, Tokyo, Japan.

Postulate that *M. leprae* and *M. lepraemurium* granularity represents loss of viability. (MacFadzian and Valentine. Trans. VII Int. Congress, 89-90.)

Increasing proportion of degenerate bacillary forms correlated with effective chemotherapy. (Davey. Trans. VII Int. Congress, 252-259; confirmed Waters and Rees. IJL **30** [1962] 266-277.)

Reported heavy infection of young hybrid black mice with *M. leprae* (Chatterjee, K. R. Trans. VII Int. Congress, 67-73). Has not been confirmed.

1959 Reported infection of total body irradiated rats with *M. leprae* with bacillary proliferation and proliferative extension to viscera. (Carpenter & Naylor-Foote. *Leprosy in Theory and Practice*, R. Cochrane, ed. 1st ed., pp 15-18.)

1960 Mouse foot pad infection with *M. leprae* established. Opened possibilities of study of *M. leprae* and drug screening. (Shepard. J. Exper. Med. **112**: 445-454.)

Immuno-epidemiological differences between virgin and leprosy endemic societies noted. (Leiker. Leprosy Rev. **31**: 241-259.)

Electron microscopic differences in macrophage ultrastructure in tuberculoid and lepromatous leprosy delineated with description of "opaque bodies" later (see 1963) related to "dense bodies" of Brieger and Allen and lysosomes of DeDuve. (Nishiura. IJL **28**: 357-379.)

Controlled BCG trial for leprosy prophylaxis begun in Uganda.

Treatment of acute neuritis with injection of hyalase and cortisone advocated. (Thangaraj and Thangaraj. Leprosy Rev. **31**: 295.)

1960's Value of chemoprophylaxis in leprosy demonstrated (Dharmendra, Noordeen, Wardekar).

1961 Presence and significance of *M. leprae* capsule noted. (Hanks. IJL **29**: 74-83, 84-87, 175-178, 179-182.)

Retrospective study of 907 Caucasian missionaries living in leprosy endemic areas of Africa revealed 12 instances of contracting leprosy, giving a prevalence rate of 13.2 per 1000 persons. (Gray and Driesbach. IJL **29**: 279-290.)

Symposium on Research in Leprosy, Leonard Wood Memorial and Johns Hopkins University (May 8-10).

Good correlation of histopathology and clinical leprosy types. (Cochrane. Ciba Symposium **9**: 238-247.)

Radiologic studies demonstrated vascular alterations in extremities associated with nerve paralysis and produced classification of multiple factors in development of bone deformity. (Paterson. IJL **29**: 393-442; Lechat. **30** [1962] 125-137; Job. **31** [1963] 26-33.)

1962 Hypothesis advanced that leprosy bacillus enters body through stomach or lungs and is carried to the sensory nerves by the blood. (Weddell and Palmer. Leprosy Rev. **34** [1963] 57-61, 54-56; The Star **22** [1963] No. 3. p 12; IJL **31** [1963] 375.)

Proposed use of solid staining versus granular bacillary forms as an index of therapeutic effectiveness to be known as the "Morphologic Index." (Waters and Rees. IJL **30**: 266-277.) See also 1953, 1958.

Controlled BCG trial for leprosy prophylaxis begun in E. New Guinea.

Standardization and codification of leprosy classification. (Ridley and Jopling. Leprosy Rev. **33**:119-128; IJL **34** [1966] 255-273.)

1963 Eighth International Leprosy Congress, Rio de Janeiro, Brazil.

Rifamycins introduced in leprosy treatment. (Opromolla. IJL **31**: 552.)

"Dense bodies" ("cytosomes") in Virchow cell cytoplasm related to lysosomes of DeDuve and possible role in digestion of *M. leprae* suggested. (Brieger and Allen. Ciba Foundation, *The Pathogenesis of Leprosy.*)

1964 Hypothesis advanced that tuberculoid reaction is essentially that of delayed hypersensitivity while *erythema nodosum leprosum* is essentially a humoral antigen-antibody reaction. (Skinsnes. *In:* Leprosy in Theory and Practice. Cochrane and Davey, Eds. 1964, pp 156-182.)

Controlled BCG trial for leprosy prophylaxis begun in Burma (WHO).

Pathologic basis for leprosy opprobrium postulated. (Skinsnes. Leprosy Rev. **35**: 175-181.)

1965 Thalidomide introduced for the treatment of lepra reaction. (Sheskin. Clin. Pharmacol. Ther. **6**: 303.)

Variant macrophage response to *M. leprae* and *M. lepraemurium* in guinea pigs (epithelioid cell transformation) and rats (foam cell transformation) reported to be similar to variant response respectively in tuberculoid and lepromatous leprosy and to be associated with feeble lipase, alkaline and acid phosphatase activity, sluggish lysing of bacilli and lipid storage in the foam cell type of reaction. (Hadler. Leprosy Rev. **36** [1965] 171-181.)

U.S.-Japan Cooperative Medical Science Program including a Leprosy Panel, inaugurated.

Conference on Research Problems in Leprosy, Leonard Wood Memorial and Armed Forces Institute of Pathology (IJL **33**, No. 3, part 2).

Clofazimine (B663) anti-inflammatory reaction reported (Browne, Leprosy Rev. **36**: 9).

University of Bombay (India) Symposium of Leprosy.

1966 Formation of ELEP (contraction of "Europe Leprosy"), the European Coordination Committee of the Anti-Leprosy Association, of which the members are:

a) Aide Aux Lepreux, Emmaüs-Suisse (Switzerland)
b) Amici dei Lebbrosi (Italy)
c) Les Amis du Père Damien (Belgium)
d) Comité Exécutif International pour l'Assistance aux Lépreux (Ordre de Malte)
e) Cüzzam Savas ve Arastirma Dernegi (Turkey)
f) Deutsches Aussätzigen-Hilfswerk (Federal Republic of Germany)
g) Evangelische Aussazhilfe (Federal Republic of Germany)
h) Association des Fondations Follereau (France)
i) Fondation Raoul Follereau (Luxembourg)
j) Foundation Père Damien (Belgium)
k) Hartdegen Stifting (Federal Republic of Germany)
l) The Leprosy Mission (United Kingdom)
m) The Order of Charity (United Kingdom)
n) I Thia Haris (Greece)

Enhanced susceptibility of thymectomized and irradiated mice to infection with *Mycobacterium leprae*. (Rees, R. J. W. Nature **221**: 657-658.)

1967 Growth of *M. lepraemurium* in mouse peritonial macrophage culture. (Chang. *et al.* J. Bact. **93**: 1119-1131.)

1968 Ninth International Leprosy Congress, London, England.

"Chemical isolation" of contagious leprosy shown to be effective. (Worth. IJL **36**: 296-302.)

Progressive loss of infectiousness for mouse foot pads of *M. leprae* from DDS treated patients, with total loss of infectiousness demonstrated after 90-100 days. (Shepard, *et al.* Amer. J. Trop. Med. **17**: 769-775.)

Immunologic spectrum of leprosy formulated in analogy to immunologic pattern of certain mycotic and protozoal diseases as well as tuberculosis. Noted that "Yersin" type tuberculosis and systemic fungal and protozoal infection may represent "lepromatoid" disease, analogous immunologically to lepromatous leprosy. Leprosy is therefore noted as a broader based immunopathologic disease model than other infectious granulomata. (Skinsnes. Ann. N.Y. Acad. Sci. **154**, Art. **1**: 19-31.)

Experimental evidence of defective cell-mediated immunity in leprosy. Reduced lymphocyte blast cell transformation in response to phytohemagglutinin, leprolin and tuberculin in lepromatous leprosy. (Paradisi, *et al.* Lancet **1**: 308-309; Dierks and Shepard. Proc. Soc. Exp. Biol. Med. **127** 391-395; Wong, *et al.* IJL **39** [1971] 7-13; Han, *et al.* IJL **39** [1971] 789-795.)

Generalized depression of delayed allergic inflammatory response in leprosy in response to picryl chloride and protein antigens. (Bullock, New Eng. J. Med. **278**: 298-304.)

1969 After 22 years of legally supported substitution of term "Hansen's Disease" for leprosy, Hawaii deemed the change harmful rather

than helpful and officially returned to use of the designation "leprosy." (Gould. IJL **37**: 194-196.)

1970 Borstel International Leprosy Colloquium, August 26-27 (IJL **39**, No. 2, part 2).

1971 Chemotherapy effectiveness of DADDS (Acedapsone) long-acting sulfone demonstrated. (Sloan, *et al.* IJL **40**: 40-52.)

M. leprae infection established in thymectomized, irradiated, bone marrow shielded mice. (Binford, *et al.* IJL **40**: [1972] 99-100.)

M. leprae growth in Lewis rats enhanced by thymectomy and antithymocytic serum administration. (Fieldsteel and McIntosh. IJL **40** [1972] 98-99.)

Nine-banded armadillo reported to sustain widespread lepromatoid infection with *M. leprae*. (Kirchheimer and Storrs. IJL **39**: 693-702.)

M. lepraemurium reported to grow in cell-free environment by use of cell-impermeable diffusion chambers placed in mouse peritoneum. (Rightsel and Wiygul. Infec. and Immunity, **3**: 127-132.)

M. leprae shown to vary genetically into "fast" growing strains (less than 25 days replication time) and "slow" growing strains (more than 30 days replication time) with continuous spectrum between. No significant differences related to geographical source of bacilli. (Shepard and McRae. Infec. and Immunity **3**: 121-126; Abstract. IJL **40** [1972] 337.)

Lymphocytes of leprosy patients, particularly lepromatous, defective with respect to capacity to induce lymphocyte transfer reaction in lepromatous recipients. (Han *et al.* IJL **39**: 715-717.)

Leprous lymphocytes limited in capacity to produce lymphotoxin in response to specific antigen, leprolin, and nonspecific agent, phytohemagglutinin. (Han *et al.* IJL **39**: 719-725.)

Prolonged survival of skin allografts in leprosy patients, particularly lepromatous leprosy. (IJL **39**: 1-6.)

In vitro macrophage activation of blood macrophages exposed to *M. leprae* in tuberculoid leprosy but absence of activation in macrophages derived from lepromatous patients. (Godal, *et al.* Clin. Exp. Immunol. **8**: 625-637.)

Lepromatous lymph node paracortical areas infiltrated with undifferentiated macrophages, failing to eliminate *M. leprae*. In tuberculoid paracortical areas infiltrated with epithelioid macrophages and well populated with lymphocytes and immunoblasts. (Turk and 'Vaters, Clin. Exp. Immunol. **8**: 363-379.)

1972 Significance recognized of circulatory change attendant on nerve injury in pathogenesis of leprous bone resorption. (Skinsnes, *et al.* IJL **40**: pp 375-388.)

Cure proclaimed in three months, of lepromatous leprosy patients harboring drug resistant *M. leprae* by weekly i.v. transfusions of healthy donor peripheral blood leucocytes. (Good R. and Lim. S. D. *Time Magazine*, March 19, 1973; Clin. Immunol. Immunopath. **1**: 122-139.)

Morphologic evidence of probable extracellular existence and perhaps growth of *M. leprae* in armadillo. (Kirchheimer, *et al.* IJL **40**: 232.)

1973 Bone marrow (B) lymphocytes reported increased and thymic lymphocytes (T) decreased in lepromatous leprosy. (Gajl-Peczalska *et al.* New Eng. J. Med. **288**: 1033; Dwyer *et al. Ibid.* **288**: 1036.)

Tenth International Leprosy Congress, Bergen, Norway, Aug. 13-18.