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Leprosy

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LEPROSY

by

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THESIS

PRESENTED TO THE COLLEGE OF MEDICINE,

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HISTORICAL CONSIDERATIONS

The nomenclature of the disease which we are about to discuss has been a source of confusion. Hippocrates and other ancient Greek writers employed the term lepra (in the plural) to designate patches on the skin covered with white, rough scales; these signs are those known to moderns as part of the dermatologic affection, psoriasis. True leprosy did not exist in Greece in the days of Hippocrates and Pericles.

By the time of Aretaeus (c. 100 A.D.) leprosy had appeared in south-eastern Europe. Leprosy was described under the name of leontiasis in those days.

In the works of Lucretius and Celsus we find the word elephantiasis serving as the medical appellation for leprosy.

Thus we find the terms lepra graecorum signifying psoriasis and leontiasis or elephantiasis graecorum standing for true leprosy.

But unfortunately the Latin translators of the works of Arabian authors chose to render Dal-Fil or elephant-leg by the designation elephantiasis. Elephant-leg, the same as Barbadoes leg, is a form of filariasis unheard of by the ancient Greeks. Hence, we find elephantiasis applied to two distinct diseases

which we are obliged to distinguish from each other by the names elephantiasis graecorum and elephantiasis arabum.

In addition, these same translators into Latin abused the term, lepra, making it serve as a name for true leprosy. The works of these men were resurrected in the fourteenth century and closely scrutinized. Since in these old works the same names were applied to utterly different diseases, great confusion arose.¹

Leprosy or lepra is the most ancient and exclusively human of diseases. It has followed man in all his migrations. Tradition ascribes an existence of more than two thousand years to leprosy in China. The earliest mention of leprosy is the Chinese Nei Ching of Huang Ti, dated 2697 B.C.²

The Old Testament offers abundant testimony that the ancient Jews knew of its existence. But even superficial study of the Bible reveals that the Jews either could not or would not distinguish leprosy from the numerous other skin affections prevalent in ancient times.²

The Ebers papyrus of 1550 B.C. refers unmistakably to leprosy. Here are mentioned for the first time such prominent aspects of this disease as alo-

pecia, epistaxis, and hyperesthesia.²

The first important invasion of Europe by this plague occurred when Pompey's legions returned from Asia Minor in the first century before Christ. By the sixth century A.D. lepra had affected the whole of western Europe to such an extent that most of the petty political entities of those days were obliged to pass laws of segregation and to erect asylums in which the victims could be confined.³ In passing we might remark that the very first asylum for lepers was erected at Caesarea by St. Basil in the fourth century.⁴

In 757 A.D. Pepin the Short decreed lepers' marriages illegal and the disease a cause for divorce in France. By the ninth century leprosy was a scourge to be reckoned with in the British Isles, and by the eleventh century it was a problem in the Scandinavian peninsula.³

We may say with confidence that leprosy was the first pestilence to be controlled in Europe. It was, and is, a disease easily managed by methods available in medieval times. The first principle of control, avoidance of contact with the sick, had been conceived by the ancient Jews and plainly set forth in the Bible.

Medieval history affords indisputable evidence

that systematic isolation of those afflicted eventually brings to an end this scourge. The eradication of leprosy was undertaken with the brutality which was an ever-present accompaniment to the deeds of men in medieval times. In France (1313) Philip the Handsome ordained that all lepers in his dominions should be burned. But this atrocious measure could not be carried out; so the monasteries of St. Lazarus were set aside for the residence of lepers alone. These institutions came to be known as lazarettos. Into them were crowded "Christ's poor", as the lepers certainly were. In western Europe alone, as a result of unhygienic living conditions that prevailed in medieval Europe and as a consequence of the return of hundreds of crusaders recently infected in Asia Minor, there came to be need for the 19,000 or so lazarettos in existence.

The unfortunate victims of this blight could truly be termed the living dead. When a leper was torn from his family and friends, the burial ritual was read over him. He was from that time forward legally deceased, and the lazar-house was his tomb. If he was allowed to leave his filthy abode at all, he had to wear some distinctive costume and to shake a bell or rattle to warn healthy individuals of the presence of one unspeakably polluted.⁵

The indignities with which lepers were visited were effective, however, in eradicating leprosy from Western civilization (with the aid of the bubonic plague which eradicated millions of people in all states and kinds of physical infirmity). Certainly leprosy was not an important disease in Europe by the end of the sixteenth century.

The history of leprosy in the New World begins in an age when that disease was declining in Europe. The credit for its initial introduction into the Western Hemisphere goes to the conquistadors, but spread to imposing proportions was the result of several centuries of African slave trade. Africa remains to-day an inexhaustible reservoir for many of man's worst afflictions.

The island-peoples inhabiting the vast reaches of the Pacific Ocean were unaffected until white men imported Chinese coolies to do the manual labor which the indolent natives could not be hired to do. The first Chinese lepers arrived in the Hawaiian Islands in 1859. So rapid was the spread of leprosy here that by 1871 one out of thirty of the native population had the disease.

To quote a more modern instance of the spread

of leprosy in a small, circumscribed area of land: In 1920 there were but four lepers on the Island of Nauru in the central Pacific Ocean, almost on the equator. Although only twelve miles in circumference this island supported a population of about 2,500. By 1921 there were sixty lepers in place of four, and in 1927 there were 337, or one in seventy of the population.⁵

More than 3,000,000 lepers are presumed to exist in the world to-day. The chief strongholds are India, China, central Africa, and Japan. India and China each have more than 1,000,000 cases. South America has suffered much from this disease, too. Colombia is the worst off with her leper population of more than 100,000. The West Indies have also suffered terribly from leprosy.⁵

In the Europe of to-day leprosy occurs in sporadic form alone. A few centers remain in Italy, Finland, Russia, Norway, and Sweden. The incidence of the disease is declining rapidly in these localities. In England the last leper who derived that affection locally died in 1798.⁶

In the United States leprosy spreads only in Florida, Louisiana, Texas, and California, although not many years ago it presented a vexatious problem in Minnesota. New York State public health officials

act on the theory that cases of leprosy introduced within that state's borders are no danger to others. In New York City dozens of lepers are present, but no one contracts the disease from these people.⁵

Remarks in Regard to the Modern Study of Leprosy:

The first thorough clinical description of the disease was accomplished by Danielssen and Boeck of Norway in 1847. Danielssen recognized that certain peculiar cells which were to be found in leprous tissue were characteristic of leprosy.⁷ These two men classified the disease into neural and cutaneous types.

In 1868 G. Armauer Hansen discovered brown, oval masses (globi), and small rods within and without such masses, in fresh preparations of leprous lesions, which he regarded as diagnostically significant. In 1874 he described these supposedly motile rods as the true etiological factor.³ The application of staining methods by Neisser and Hansen showed these rods to be bacilli.⁸

This objective demonstration of a minute etiological agent in a specific lesion was preceded only by the discoveries of the anthrax bacillus in splenic fever of cattle, the spirochete of relapsing fever, and the fungus causing favus.³

DEFINITION

Leprosy is a chronic, infective, granulomatous disease produced by a specific bacterium, and characterized by lesions of the skin, nerves, and viscera, eventuating in local anesthesia, ulceration, and a great variety of trophic lesions.⁶

EPIDEMIOLOGY and ENDEMIOLOGY

Age: Cases are known where leprosy has been shown to exist in individuals only nineteen months⁹ to two years old, but these are quite out of the ordinary. Leprosy is rare before the fifth or sixth year, but Rodriguez¹⁰ has shown that forty-four per cent. of children who have lived seven to ten years with their leper parents become infected. In the great majority of cases the disease makes its appearance between the tenth and thirtieth years. Rarely does it commence after the age of forty, although it has been known to begin after seventy.⁶

Climate: Climate can in no respect be regarded as a cause for leprosy, a disease found in any populous region of the earth. Climate seems to be related, however, to the type the disease assumes. It would appear that the nodular form is more common in cold, damp climates, while the nerve form is seen preponderantly in dry climates. The morbidity of leprosy is highest in hot, humid areas such the Belgian Congo, the Cameroons, and the Ivory Coast (all in Africa).⁶

Social and hygienic conditions: Leprosy has its greatest incidence among semi-civilized populations living in dirt and squalor.

Sex: The disease is everywhere more preval-

ent among males than among females. Usually the ratio is two to one. No reason for this interesting fact has ever been advanced.⁵

Race: No race has shown lack of susceptibility to leprosy once it was firmly implanted. The form the disease assumes differs markedly in various countries. Thus, in Japan scalp lesions, blindness, and extreme nodular lesions are quite pronounced. In India the neural type of disease predominates, while in South Africa relatively large numbers of tuberculoid lesions occur. Some of these differences may be explained by local customs, as for example, the Shinto head shaving of Japanese children. But others may be attributed either to true racial differences or to change in the invasive power of the particular strain of organism locally present.³

ETIOLOGY

It is almost universally conceded that Mycobacterium leprae is the specific cause of leprosy. (But on February 14, 1937, newspapers everywhere were printing a statement by Dr. E. B. McKinley of George Washington University that "We believe we have isolated the true germ of leprosy". There is, as yet, no published work by Dr. McKinley for others to criticize or to confirm.)

Conveyance of the lepra bacillus from man to man: Many attempts have been made to communicate leprosy to man by inoculation. All deliberate efforts have been failures. Yet success twice attended accidental inoculations; in each a genuine leprotic lesion appeared, after some months, on the site of the original skin abrasion where inoculation was known to have occurred.³

Conveyance of the lepra bacillus from insects to man: Ever since the role of the insect vectors in malaria and yellow fever was satisfactorily established the scientific world has been agitated by the possibility that some insect or other might be vitally concerned in the transmission of leprosy. But no investigator has ever found Mycobacterium leprae in the vital organs of any insect. It is believed that mosquitoes that

have fed on lepers remain non-infectious because each one inserts the proboscis directly into a blood-vessel and obtains bacilli-free blood, unmixed with lymph.¹¹

Acquisition of the disease: There have been two principal views about the acquisition of leprosy --heredity and contagion.

Because it runs in families frequently, leprosy was once held to be hereditary. If this were true, leprous immigrants to the United States from Norway should have had leprous offspring. One hundred and sixty such lepers were studied by Hansen, but he did not discover a single leprous child from infected parents.⁶

The best authorities are firmly attached to the theory of the contagious spread of leprosy, but the precise mechanism of transfer still escapes those who are most interested in the subject.³

The Specific Agent, Mycobacterium Leprae:³

Hansen examined scrapings from leprous lesions and found brownish, unstained globoid bodies (globi) and small, separated rods which, as early as 1868, he regarded as of diagnostic significance. He described them more fully in 1874, using osmic acid for their clearer demonstration. Neisser (1879) was able to show these single and collected organisms in sections

of leprotic tissue with far greater precision by the use of fuchsin and gentian violet stains.

Diagnosis of leprosy depends on this organism's presence in typical locations and with its acid-fast staining properties. In the cutaneous form of the disease this acid-fast bacillus is found in the mononuclear macrophage cells that form the leproma or chronic granulation tissue. These lepromata exist in main superficial lymph nodes and in mucous membranes of the nose, mouth, and pharynx. Less frequently they may be found in testicles, liver, spleen, and in peripheral nerves.

Mycobacterium leprae varies markedly in size, appearance, and degree of acid-fastness. Thus it is stated to vary from 1.5 to 6 micra in length and from 0.2 to 0.5 micra in width.

The bacillary rods are often bent and, according to Gay³, are frequently pointed. The end of the rod is invariably straight in the opinion of Manson-Bahr.⁶ The rods occur in "cigar-bundle" masses and in colonial clumps; they may be present in enormous numbers. Most typical of all is the presence of both intra- and extra-cellular gloeal masses or globi, which are clumps of bacteria enclosed in a capsular material. Granules and spore-like spaces may fre-

quently be seen even in unstained preparations. A capsule has been described as enveloping the bacillus.

The organism is non-motile, and no flagella have been found. No spores are produced.

The leprosy bacillus has certain distinguishing characteristics which make it a simple matter to avoid confusing it with *Mycobacterium tuberculosis*. It is typically more abundant within tissue cells, is plumper, less angular, and has larger and more clearly separated granules.

The possibility of cultivating the bacillus is still problematical. The organism is non-pathogenic for animals, which further distinguishes it from the tubercle bacillus.

Mycobacterium leprae stains more readily than *Mycobacterium tuberculosis*, the former being colored with even dilute (one to five) Ziehl-Neelsen's carbol fuchsin in from three to five minutes at room temperature. The organism is more likely to lose its fastness to acids than is the tuberculosis agent.³

Non-acid-fast forms: Under a variety of conditions, both in leprous tissue and in reputed cultures from it, Gram positive but non-acid-fast

bacilli have been described. The so-called Much granules of both the tubercle bacillus and *Myc. leprae* are perhaps alive, free, and active in the tissues. At all events similar granules, more certainly identified by their presence in a bacillary sheath, have been found by Rodriguez, Mabalay, and Tolentino¹² in early, "closed", and paroled cases of leprosy, where acid-fast forms have not yet been found or are no longer present. Most significant as a control is the fact that these forms may also be found when the acid-fast organism is present.

These differences in form of the leprosy bacillus are so great that the leprosy organism has been variously classed as a *Mycobacterium* (acid-fast bacillus), a *Coccothrix*, and, on the basis of supposed cultures, as an *Actinomyces* (*Streptothrix*).³

Cultivation of the Leprosy Bacillus:³ The culture of the leprosy bacillus, so prolific in human tissues, has remained a challenge to bacteriologists for more than sixty years. Many have been unable to obtain any growth at all from leprosy tissues on the media and by methods at their disposal. Those who have obtained growth on culture media have usually found it sparse and tardy in appearance, and in such contrast to the swarming bacteria seen in the

tissues as to give the impression that most of the bacteria seemingly cultured were actually dead. The difficulty, however, is in deciding who, if any, of those who have obtained positive cultures have grown the actual etiological agent of the disease.

The general opinion of such authorities as Rogers and Muir¹³, von Klingmüller¹⁴, and Jadassohn³ is that the organism of leprosy has never been grown to a certainty.

These authorities list in detail the articles that have been written on the subject, and Rogers and Muir attempt to classify the findings in accordance with the type of organism obtained by the claimants to success in such attempts.

Gay³ investigated the claims of no less than sixty-two investigators who have reported the cultivation of the organism producing leprosy between the years 1886 and 1933.

In general the types of organism obtained from leprosy lesions may be classified as follows:

1. No less than thirty-two strains of acid-fast bacilli have been described. Acid-fastness has at times been described as "variable" in these strains (Kanthack and Barclay¹⁵), a matter of no little significance in postulating a relationship to the

diphtheroid organism which we shall presently mention.

2. Diphtheroids: Gram positive rods have been described no less than eighteen times (Neisser, 1886;¹⁶ Reenstierna, 1912;¹⁷ Walker, 1922).¹⁸ To these should be added the eleven strains called "streptothrix". Some of these diphtheroids and streptothrices were variably acid-fast (Levy;¹⁹ Kedrowski²⁰). They have been described as "branching" (Babes;²¹ Kedrowski²⁰). The isolation of this category of organisms suggests skin contamination owing to the wide distribution of diphtheroids in this tissue. Indeed, in the experiments of Fraser and Fletcher,²² where care was taken to avoid contaminants by reflecting the skin, only acid-fast were found, and these refused to grow on media.

3. A few authors (Duval;²³ Williams)²⁴ describe acid-fast bacilli, now acid-fast diphtheroids, and an acid-fast streptothrix.

4. The few anaerobes that have been mentioned, may, in the eyes of some, be accorded respectful consideration.³

Many of the organisms described failed to grow after primary isolation, a possible though not the usual course in adapting pathogens to culture media. A number grew slowly, a fact which seems significant

in view of the leisurely process of the human infection.

Animal inoculation with cultures isolated from lepers has usually given negative results. Of those few instances where cultures yielded positive results, the lesions in guinea pigs described by Clegg (1909)²⁵ and in mice may be questioned. The lesions in monkeys studied by Reenstierna¹⁷ and by Soule and McKinley²⁶ are at least suggestive. The fact that they have not been obtained in series recalls to some extent the difficulties of human adult infection.

One may interpret the confusing results concerning the bacteria isolated from leprous lesions in one of two ways. One may accept the usual opinion that since there are wide differences in the organisms isolated, no one of them is the true agent of the disease. The fact that Koch's postulates have not been fulfilled, particularly as regards the disease in animals, makes this opinion cogent. On the other hand, in view of the remarkable pleomorphism and tinctorial variation of the bacteria seen in leprous lesions, and further in view of the current wave of belief or, indeed, of certainty in the existence of bacterial variation, the critic may be willing to admit that several, many, or, perhaps, the majority of bacteria

that have been described are merely different growth phases of the same organism, and that in reality all may represent the true etiological agent. There is no inherent impossibility that with varying conditions of environment in the tissues as contrasted with the culture media employed, one should at times isolate a diphtheroid, a streptothrix with or without acid-fast properties, or an acid-fast bacillus.³

The proof of the variability of organisms in the general category to which the leprosy bacillus belongs was demonstrated years ago by Edith Claypool,²⁷ who found that in her collections of "Streptothrices", studied over a period of years, individual pure strains changed from acid-fast bacilli first to non-acid-fast, Gram positive bacteria, and later to branching, non-acid-fast forms. Data accumulated from observations of *Myc. leprae* in situ and the diverse cultures obtained from such lesions would seem to fit this interpretation. Williams²⁴ specifically noted each and all these variants in his studies of cultures from leper lesions. It remains only to show that a given culture of the leprosy bacillus isolated in pure and apparently fixed form, whether diphtheroid or acid-fast, may be transformed under artificial

conditions which definitely exclude contamination, into the other variety.

This, indeed, Salle²⁸ would claim to have accomplished in his acid-fast growths in chick embryo cultures which refuse to grow in ordinary media on primary isolation. So long as they remained in a medium of living cells they were acid-fast rods, but on subsequent transfer to ordinary media they grew as non-acid-fast diphtheroids. Although similar results are less directly suggested in other communications, repeated confirmation of the assumption of two or more phases in the growth cycle of the lepra bacillus is required before it can be generally accepted.

PATHOLOGY

The Primary Lesion of Leprosy:

Observations of Gomez, Basa, and Nicolas,²⁹ together with those of Rodriguez,¹⁰ on the appearance of a first and often a single macule in the children born of lepers have done much to convince us of what may well be the usual primary lesion of the disease. To group these observations we may say that the macules may appear at an early age (one or two years), singly or in groups, and that they are usually visible as hazy areas of depigmented skin. A "goose-flesh" papular eruption may precede or take the place of such macules. There is frequently disturbance of sensation in these areas, as is evidenced when the child is old enough to answer questions. These macules in the early stages contain no demonstrable acid-fast bacilli, and whether or not bacteriologically positive, in some instances disappear.

The primary lesion of childhood would seem to represent the prodromal sign of clinical leprosy. This may be true even in adults in whom its evolution may be delayed for many years.

The Microscopic Aspects of Leprous Lesions:³⁰

The lesions are all based on the formation of a specific granulation tissue which is composed of a loose network of branching connective-tissue cells, rich in blood-vessels and especially in wide lymphatics. It is infiltrated with mononuclear wandering cells of many forms and sizes. Many of these attain the size of giant-cells and are provided with several nuclei. All of the wandering cells are loaded with globules of fat. Such tissue occurs in discrete lobules beneath the skin or in the internal organs, which, when stained with Sudan, appear as solid, red masses. Some of the cells become so swollen with fat as to lose all recognizable cell structures, and in these large fat globules, which are sometimes surrounded by several cells, there is a mass of bluish staining granules which become apparent after the fat has been dissolved out. It does not appear that bacilli accumulate in such globules. All the cells are thus vacuolated, as seen in preparations from which the fat has been dissolved out; much has been written on the foamy cell characteristic of leprosy. All of these cells are phagocytic and may contain bacilli, but it is chiefly in the swollen endothelial cells of the lymphatics and

blood-vessels that they are heaped up in red-staining masses. In some cases the bacilli are so numerous that almost every wandering cell contains them. Leucocytes play very little part in the infiltration, but necrosis of the tissue occurs frequently, and in these areas there are many fragmented nuclei and some leucocytes.

In the nodules on the body surface the overlying epithelium is stretched out in a smooth layer so that the papillae are obliterated. The tissue beneath is hyaline and almost devoid of nuclei for a short distance. After it breaks down, an ulcer persists for a long time, but it is usually filled up at length by a dense scar. The mucosal surfaces of the nose and nasal sinuses are affected in exactly the same way, and ulcerations on a basis of the same type of tissue are found throughout the pharynx, larynx, and trachea. Some authors have described lepromatous lesions of the lungs which were hardly distinguishable from tuberculosis.

In the liver and spleen there are scattered everywhere minute foci of tissue made up of the same network with vacuolated or fat-holding cells as seen elsewhere. These military lepromata, which contain bacilli, are quite conspicuous in a microscopical

section, although they are invisible to the naked eye.³⁰

The spots which were anesthetic during life are usually converted largely into fibrous connective tissue, and the glands and hair in them tend to disappear.

The sweat and sebaceous glands and hair follicles in the infected regions are usually atrophied.³¹

In the lymph nodes the leprous granulation tissue is found to occupy the margins of the lymph cords, leaving the sinuses free.

Lesions of the intestines have been described but are quite rare.³⁰

The ovaries and testes often show infiltration and fibrosis of the interstitial tissue, which destroys the secretory elements, thereby causing the sterility so common in lepers.³¹

Nephritis and leprous infiltration of the kidneys are usual.

The nerves most markedly affected are the ulnar, median, peroneal, and posterior tibial. They are usually much thickened. There is a fusiform, reddish-gray swelling which is due to leprous tissue situated among the fibers. Bacilli are scattered in this tissue, and are also to be found in the medullary sheaths of the individual fibers.³¹ The fibers degen-

erate and sensation is lost long before any motor disturbances occur. Sometimes bacilli may be found in the ganglion cells of the root ganglia, the spinal cord, and brain.³⁰ The cord often shows posterior sclerosis and meningitis.³¹

Very striking are the atrophies of bones of the extremities which result from this interruption of the nerve supply. The phalanges shrink, and the bones fuse into thin, pointed remnants attached to the metacarpals or metatarsals. These, in their turn, may become disarranged after atrophy, so that finally the hand or foot, further cramped by contractures, assumes a distorted, claw-like aspect.³⁰ Harbitz,³² in discussing these, has pointed out the fact that this is a process of mutilation not necessarily associated with ulceration and inflammation. In fact, some of the most disfiguring mutilations arise from the insensibility of the hands and feet, which makes it possible for the patients to suffer burns or other injuries without drawing away or protecting themselves. Nevertheless, it seems that most of these deformities are the direct result of loss of nerve impulses.

In addition to the bony changes lepers often suffer from perforating ulcers of the plantar region,

as well as atrophy of the interosseous muscles, the thenar and hypothenar eminences.³¹

Leprosy frequently effects changes in the blood that are reflected in complement-fixation tests. Jose Puente³³ studied changes in the blood of 296 patients over a period of five years. He found the Wasserman reaction to be positive in over twenty per cent. of his cases. He feels that as the disease grows worse, reactions become more frequently positive.

Of course, a large per centage of lepers have syphilis as well. If a leper in an early stage has a positive Wasserman, chances are that he has syphilis. Antisyphilitic therapy should soon affect the Wasserman reaction if such is the case. The same therapy will not affect a case of pure leprosy.

In advanced leprosy the diagnosis of syphilis may be difficult because of the coincident pathologic processes of the two diseases.

A Modern International Type Classification of Leprosy

Germond³⁴ gives the new international classification of types of leprosy. First, as regards the definition of the most important terms: 1. It is suggested that the term leprotic be applied to changes

that present clinical or microscopic evidence of inflammatory processes, typically of granulomatous nature, which are apparently caused by *Mycobacterium leprae* situated therein. In such lesions the organism can usually be demonstrated by the ordinary methods. 2. Infiltration is a term commonly applied to a diffuse thickening of leprotic nature involving the skin or mucosa which is not of definite nodular, papular, or macular form. The term may also be applied to diffuse leprotic conditions in other organs. 3. A nodule is a definitely thickened, rounded, circumscribed mass of leprotic nature commonly occurring in the skin, subcutaneous tissue or mucosa. 4. A papule is a small, solid elevation of the skin, of leprotic nature, not more than five millimeters in diameter. 5. A macule is a circumscribed area of skin showing changes in color, sometimes with slight elevation or depression.

Secondly, Germond gives the proposed classification:

All neural (N) cases are those that show evidence of actual or previous nerve involvement, alterations of sensation with or without changes in pigmentation and circulation, trophic disturbances or paralyzes and their consequences: atrophies, con-

tractures, and ulcerations. These are not accompanied by leprotic changes in the skin.

All cutaneous (C) cases are those that show leprotic lesions in the skin. Such cases may or may not show, at any given time, clinical manifestations of neural involvement.

Subtypes are classed N I, N II, N III on one hand, and C I, etc. on the other, according to the degree of severity. In all cutaneous types there may be varying degrees of neural involvement; such cases should be recorded to indicate the degree of involvement; as, for example, C₂N₁. Secondary neural cases are those which were formerly cutaneous but from which active leprotic lesions have disappeared.

SYMPTOMS and SIGNS

Although the *Mycobacterium leprae* is generally conceded to be the specific etiologic agent in leprosy, the clinical manifestations of its presence are far from being identical in every case; indeed, they are almost as protean as those of syphilis.

In its earlier stages leprosy is anything but a striking disease. In rare cases it is a fulminating, rapidly fatal disease. In the vast majority of instances the early lesions are trifling and quite likely to be overlooked. Years elapse before serious mutilation or deformity occur.

To facilitate discussion we will divide the evolution of leprosy into stages⁶, premising, however, that the division proposed is entirely artificial.

I. Primary infection: There must have been a time in the history of every leper when the infectious agent entered the body, but there is no local lesion to mark the spot except in the most rare instances. We theorize that the inoculation occurs at the site of an accidental breach of surface.

The bacillus is found in the nasal mucus in the majority of early cases of leprosy. It is therefore considered by some (Heiser, 1916)³⁵ that the ini-

tial lesion of the disease is a specific ulceration of the cartilaginous septum of the nose, which in turn gives rise to epistaxis.

II. Period of incubation³: An estimate of the usual incubation period presents an infinitely more difficult problem than does a similar determination following exposure to a rapidly contagious disease such as chickenpox. The difference lies both in estimating what constitutes reasonable exposure and in determining the time that must elapse before clinical symptoms appear.

Assuming that the actual introduction of the organisms in the body is followed by a period of "latent infection", the primary lesion, which terminates this phase, is followed by a second period of true infection incubation which lasts until distinctive clinical symptoms are evident. These true symptoms such as pigment changes and disturbances in sensation are noted at a variable and often considerable period of time before the patient presents himself to the physician. The sum total of these long and ill-noted periods makes it difficult for the patient, particularly if of low mental caliber, to estimate the true lapse of time between actual infection and clinical lepra. In a series of cases collected by von Kling-

müller¹⁴ and comprising accidental inoculations, beginning exposure of healthy attendants, experimental inoculations, and methods of infection, the estimated incubation period to the beginning of clinical symptoms ranged from a few to thirty-two years. Certainly the incubation period is a long one; Rogers and Muir¹³ would put down as an average two to four years. Symptoms may be precipitated by an intercurrent disease such as malaria. In other words a primary lesion may be present in child or adult which is never perceived, and which either disappears or gives rise to frank leprous manifestations at a period remote from the original infection.

III. Prodromata⁶: Fever of greater or lesser intensity, occurring at varying intervals is an almost constant feature of the prodromal stage of leprosy. Febrile seizures with weakness and drowsiness may recur on and off during one or two years--and the patient be considered a victim of malaria. Dyspeptic troubles, associated with diarrhea in some patients, with constipation in others, are also frequent. Epistaxis and dryness of the nostrils have been noted. Headache; vertigo; perversions of sensation--such as pruritus, hyperesthesia, general aching, rheumatic-like pains in loins, back, and elsewhere--any or all

of these may prelude obvious leprosy.

Frequently excessive sweating without provocation occurs in early lepra. This hyperhidrosis may be general, or it may be confined to particular parts, most often the thorax, the limbs being unaffected or even being the subject of anhidrosis.

IV. The primary exanthem:⁶ After a longer or shorter period of indifferent health, sometimes preceded by an outburst of fever more severe than usual and by other prodromal phenomena, an eruption appears on the skin. The spots may be no larger than a millet-seed, or they may be inches in diameter; they may be numerous or sparse; they may be pigmented from the start, or they may be mere vitiliginous patches; then again, all three forms of macule may occur in the same individual--erythematous, pigmented, and vitiliginous. In some lepers, what in the first instance was an erythematous patch may in time become pigmented, or it may become pale; in the latter case we have a certain degree of atrophy of the cutis. In certain instances the eruption of the various forms of macule may be preceded by local paresthesias, such as a sense of burning, tingling, pricking, and the like.

A striking feature of this and of all leprous eruptions is the loss of hair in the affected areas.

Another interesting circumstance is the fact that the most hairy part of the body, the scalp, is never or varelly rarely affected either with leprous eruptions or with leprous alopecia. As the face, particularly the superciliary region, is prone to all forms of leprous eruption, depilation of the eyebrows is an early and characteristic sign. The beard, too, may be patchy.

The most frequent seats of the primary macular eruption are the face, especially the superciliary region, the nose, cheeks, and ears; the extensor surfaces of the limbs; the backs of the hands; the back, buttocks, abdomen, and chest. The palms of the hands and soles of the feet are rarely attacked. The mucous membranes are not affected at this stage of the disease.

V. Period of specific deposit:⁶ Eventually in this disease there is tissue growth of a specific nature. This growth takes places in the skin or in the peripheral nerve trunks, or in both sites. In the first situation tubercular or cutaneous leprosy is the result; in the second, we have neural or anesthetic leprosy; if in both of these situations we have "mixed" leprosy.

A. Cutaneous leprosy:³⁶

The lesions we see may appear slightly elevated or infiltrated, or smooth and shiny, and somewhat hyperesthetic. Eventually these patches become permanent and infiltrated with nodules which are pea-sized, yellowish- or reddish-brown in hue, and enlarge more or less rapidly, some of them becoming as large as a walnut or larger. Their surface presents a shining appearance, as if oiled, and the skin may be soft and natural or present slight desquamation. They may be grouped, forming areas of roundish or irregular contour, or may be isolated. By fusion broad infiltrations are formed; from the surfaces of these new nodules spring. These latter may be either cutaneous or subcutaneous in situation and are soft or firm to the touch. The development of these lesions is not limited to the site of the previous macules, for some appear on apparently normal skin, and their efflorescence is preceded by febrile symptoms. Their development is not one of gradual progress, but rather of successive crops, each new efflorescence being preceded by fever and epistaxis. The lesions are often anesthetic in various degrees.

The site of predilection of leprous nodules is the face; their massing in great numbers on this area produces the characteristic deformity of countenance

which has given the disease one of its names, leontiasis or lion-faced. In such faces the nodules are arranged in parallel series above the brows, down the nose, over the cheeks, the lips, and the chin. In consequence of the infiltration and development of the lesions, the brows deeply overhang the ocular globes, the eyelids become partially ptotic, the lips pout, and the ears are so studded with nodular masses that they may project from the side of the head. The lesions are also frequently found on the forearms, thighs, and other portions of the extremities. To a lesser degree they are found on the trunk and palms, rarely, as we have said before, on the scalp.

Hopkins, et al.,³⁷ in an investigation of this aspect of the subject, found certain areas completely immune to lesions of cutaneous leprosy. These areas are; 1. Posterior inferior auricular area. 2. Concha of the ear. 3. Lateral palpebral area. 4. Orbital side of the nose. 5. Axilla. 6. Inframammary fold in women. 7. Interdigital surfaces. 8. Perineum. These authors note that lesions do not occur in areas protected from external irritants.

Occasionally, with extensive development of nodules upon the face and ears, there may be not more than from five to fifty upon the rest of the body,

and these may be either widely dispersed and isolated, or agglomerated in a single, hard, flat, elevated plaque of infiltration upon elbow or thigh. When a confluence of nodules occurs, large plaques of infiltration may form lepromes en nappe, which are elevated and brownish or blackish in shade. These patches are inert, lasting unchanged for years. They may be the seat of itching, or the normal sensations may become less acute. The hair falls in the involved regions, which may finally ulcerate.³⁶

The nodules may degenerate into irregularly outlined, sharply cut, glazed ulcers, with a hemorrhagic or sloughing floor; some of these, under appropriate treatment, heal soon; others extend deeply, often become gangrenous, and destroy much tissue. Other nodules undergo resorption and disappear, leaving pigmented, atrophic depressions; or they may lose their shape in consequence of partial resorption. A large plaque not infrequently is absorbed centrally, leaving an annular disk.

Lymph nodes are affected in the nodular type of leprosy. They become more or less swollen early in the disease and may at times become quite large. This adenopathy is seen oftenest in neck and groin. Glands in the groin not infrequently undergo suppur-

ation followed by discharging fistulae.

Appendages of the skin show some involvement. The eyebrows and eyelashes fall, but as we have mentioned previously, the scalp is rarely attacked. Occasionally, the nutrition of the nails is interfered with and thinning occurs, as well as other deformities. The secretions of the sebaceous and coil glands are augmented early in the disease, but later become diminished or entirely lost in the affected area. Comparatively early in leprosy small, flattish nodules form on the conjunctiva and cornea, extending to and involving the iris, and gradually filling the anterior chamber.³⁶

The epiglottis, vocal cords, and other laryngeal structures become studded with nodules, as does the nasal septum; when ulceration occurs the cartilage and bony framework of the nose necrose, producing terrible deformity.³⁶

As a rule, the course of cutaneous lepra is exceedingly slow, and years may elapse before the changes above described are accomplished. The maldy often appears to be quiescent for months at a time, after which, with the occurrence of fever, acute or subacute manifestations appear, which may

be accompanied by relatively rapid ulcerative processes, followed by gangrene, in which case the disease may progress rapidly toward a fatal conclusion.³⁶

B. Neural leprosy:

This form of the disease is more common in tropical than in cold countries. In this variety the bacilli are located chiefly in the neuroglia of the peripheral nerves, and consequently the symptoms exhibited in the part supplied by the affected nerves are those which would naturally follow their irritation, compression, or degeneration.

Usually, however, the ulterior and more distinctive lesions are preceded by a long, well-marked macular stage, during which large areas of skin are occupied by erythematous, by pigmented, or by vitiliginous patches. The ringed form of elevated and, perhaps, slightly hyperesthetic border enclosing a larger or smaller area of pale, anesthetic, non-sweating integument--the whole resembling somewhat one of those extensive body ring-worms so common in natives of hot, damp climates, and for which these rings are sometimes mistaken.

A frequent and distinctive symptom of this type of leprosy is the sudden appearance of bullae

(pemphigus leprosus) of various sizes--one or more of them--on the hands, feet, knees, backs of thighs, or elsewhere. After a few days they rupture, exposing a reddish surface which presently crusts over, exfoliates, and finally becomes a pale, perhaps anesthetic spot with a sharply defined, pigmented border. More rarely the site of the bulla ulcerates.

The time finally and unavoidable comes when evidence of profound implication of the nervous system, in the shape of severe neuralgic pains, formication, hyperesthesia, or anesthesia, becomes evident. The lymph nodes enlarge, and there is often considerable fever with general distress. But, whether the skin lesions increase or regress, evidences of pathology of the peripheral nervous system are now distinct; neuralgic pains become greater, and hyperesthesia, anesthesia, and paresthesias, together with trophic changes in skin, muscle, and bone, the results of nerve destruction, become the dominating elements in the disease.

When the nerve trunks are the seat of severe neuritis, they become thickened and can readily be felt by the finger of the examiner. The fusiform enlargement of the ulnar nerve behind the olecranon process at the elbow is characteristic. Other nerves,

such as the anterior tibial, the peroneal, more rarely the median, radial, brachial, great auricular, and cervical nerves, especially where they pass over a bone and lie close under the skin, can be felt to be similarly swollen. Occasionally even the smaller nerves, where superficial, can also be detected hard and cord-like. At first these nerves are tender on pressure, and the parts they supply may be the seats of hyperesthesia and acute neuralgia. Gradually the thickening of the nerve trunks subsides somewhat, the hyperesthesia and neuralgia diminish, and anesthesia, paresis, muscular atrophy, and other trophic changes take place. Another and sometimes striking fact in nerve leprosy is the symmetry observed in the distribution of some of the anesthetic areas. It has been pointed out that the temperature of anesthetic digits is from two to three degrees lower than normal. Abscess formation on the ulnar nerve has been noted.

Step by step with the progress of anesthesia, atrophy of the subjacent muscles supplied by the thickened nerve proceeds. Along the atrophy there is a corresponding distortion and a loss of power. Thus the forearm wastes, the grasp is weakened, the thenar and hypothenar eminences and the interossei disappear, and a claw-hand is the result.

But, in the affected nerve areas, all muscles are not simultaneously or equally attacked, so that, especially in the face, curious distortions may ensue. Owing to muscular atrophy, the eyes finally cannot be closed; the upper lid droops, the lower lid becomes everted, and the eye itself may become fixed. At first, because of exposure of the organ, there is lachrymation; but eventually the secretion of tears ceases, the congested conjunctivae become cornified, the cornea ulcerates or becomes leucomatous, and ultimately sight is destroyed.

Trophic disturbances through nerve involvement are illustrated in the perforating ulcer of the foot and in the deep and destructive processes occurring in the fingers and toes.⁶

The ulcers are irregular, oval, round, or linear in outline; they are covered with thin, blackish, flattened, tenacious crusts and are anesthetic. The phalanges may become necrotic and drop off.³⁶

From the foregoing description of the clinical course of the disease it would seem that cases of cutaneous leprosy on one hand and neural leprosy on the other are quite different. The difference, however, is due to the selection of the skin in the one case

for the growth of the organism and selection of the nerves in the other. The cutaneous variety very frequently terminates in the maculo-anesthetic or neural form; only occasionally is the reverse true. In practically all cases of cutaneous leprosy there is some anesthesia. The type described as the mixed form merely indicates the development of nodules in a case once presenting symptoms of the maculo-anesthetic type; or formerly exhibiting anesthesia and other trophic disturbances following in the course of a nodular case.

We must not forget that in leprosy there is but one morbid principle. To distinguish varieties is merely to facilitate diagnosis.

Lazarine leprosy:³⁸ This is an unusual type of the disease, characterized by erythematous patches, nodules, or pachydermic edema on which one or more bullae may develop; these lesions are succeeded by deep, sloughing ulcers and mutilation. Lesions appear in the extremities as a general rule.

Invariably Hansen's bacillus can be found in the fluid from bullae or ulcers. Lazarine leprosy is an early manifestation and is not accompanied by other symptoms of leprosy.

A Summary of the Symptoms and Signs of Leprosy as a
Whole²

Symptoms

1. Repeated attacks of coryza and epistaxis before medical attention is sought. Rheumatic pains in the smaller joints may be complained of.

2. Paresthesias: These are results of early nerve involvement. There are "pins and needles" sensations, formication, gnawing pains. Patient, feeling these in nose, picks it, causing epistaxis. Paresthesias can be elicited by pressure on the skin.

3. Hyperesthesia; Pain is an early manifestation. There are areas tender to touch. This symptom may last for a long time; it may be associated with fever for a few days. Pain may be associated with numbness.

4. Anesthesia; This is an early and constant symptom. It is the oldest recorded. It never disappears if the disease is progressing. Anesthesia over distribution of ulnar and peroneal nerves is commonest. Next are the areas supplied by the facial and great auricular--with paralyses as well.

5. Loss of thermal sensation: Patients often cannot distinguish between hot and cold, although

pressure sense is present. This is an early symptom that may escape notice until numbness comes.

6. Pyrexia: This may be an early sign.

Signs

1. Papillary ridge atrophy: Leprosy causes atrophy but not absence.

2. Macules: These occur on face and arms. They are accompanied by a sensation of heat due to fever.

3. Pigmentation: This is an early sign. It occurs at points of hyperesthesia and anesthesia.

4. Tubercles: These may occur on sites of former macules. They are late signs.

5. Vesicles: These form an early manifestation. They are round or oval in shape. At first they are red-brown, then yellow or sepia.

6. Ulcers: These come late. They form on the sites of burns and infected vesicles.

7. Fissures: These may occur at any time; they are to be found on the feet usually.

8. Other lesions:

a. Parakeratosis.

b. Anhydrosis

c. Dry rhinitis.

- d. Trophic blisters.
- e. Thickening of the superficial nerve trunks of the ulnar, peroneal, facial, great auricular, radial, and external saphenous.

DIAGNOSIS

In the opinion of Manson-Bahr⁶ the most significant and never failing diagnostic finding in any case of leprosy is the presence of anesthesia in some area of the skin. In no other skin disease is definite anesthesia a symptom.

Victor Heiser, whose experience with lepers is as extensive or more so than any other American, recounts his diagnostic procedures in brief as follows:⁵

"For the clinical examination of the anesthetic form the suspect was blindfolded. Then his skin was touched with a cotton swab, a feather, a camel's hair brush, or a paper spill, and he was asked to indicate where he had been touched. The head and the point of a pin was pressed alternately against suspected spots, and the patient was asked which caused the more pain. Test tubes, one filled with hot water and the other with cold, were held against his skin, and he was asked to tell which was warm and which was cold. Finally, a scraping was taken from the septum of the nose with a blunt, narrow-bladed scalpel, and put under the microscope."

Lepra bacilli had been demonstrated in septal scrapings in every individual confined at Culion dur-

ing Heiser's tenure of office as Director of Health. None was ever confined without this absolute proof of leprosy.

Others seem to differ as to the relative importance of the detection of lepra bacilli from scrapings taken from the nasal septum. The following are the conclusions of Brinckerhoff and Moore:³⁹

1. Routine examinations of the nasal septum and the nasal secretions of individuals of a race with a high incidence of leprous infection (Hawaiians) did not reveal as many cases of leprosy as would be expected from statistical data had the method been an efficient one for establishing a diagnosis of the disease in the incipient stage.
2. Examination of the nasal septum and the nasal secretions is not of dominant value in confirming a diagnosis of leprosy in the early stages of the disease.
3. The conditions found in noses of nonleprous children do not differ in important respects from those found in the descendants of nonlepers.
4. When it is not practicable to make a complete physical examination of all individuals of a class suspected of leprosy, examination of the nasal septum and the bacterial examination of nasal secretions

will prove to be of value by permitting the recognition of the most dangerous type of the disease, it is therefore worthwhile even if it does not reveal all cases of the disease in those who come under observation.³⁹

It is usually in the diagnosis of incipient cases that difficulty is liable to arise. Early deposits are frequently felt or seen on the forehead, and there is often a tell-tale thickening situated in or around the naso-labial fold. Furthermore, in the majority of male lepers hypertrophy of the nipple takes place.⁶

The occurrence of an acid-fast bacillus in the sputum of a patient coming from a country in which leprosy is common should be regarded with suspicion, and its true nature tested by injection of the sputum into the guinea-pig, as tuberculous infection is also frequently seen in lepers.

When confirmation of a clinical diagnosis is required, a portion of tissue may be excised for microscopic section, or the bacilli may be demonstrated in the nasal mucus or in serous fluid expressed from a nodule. By raising a blister on a nodule, or on an anesthetic patch, by means of carbon-dioxide snow, a quantity of serum may be obtained in which the myco-

bacterium leprae can be demonstrated after centrifuging.

From Basombrio⁴⁰ we are presented with an interesting concept of the importance of lymphadenopathy in diagnosis. He believes that persons living in a leprous environment should have their lymph nodes investigated either to eliminate leprosy or to make early diagnosis. Lymph nodes become enlarged early after inoculation. Enlarged nodes undergo characteristic changes that permit one to differentiate this form from other forms of adenopathy. The condition is a specific, early symptom.

Puncture of lymph nodes is a simple, practical method for early diagnosis. Presence of bacillary lymphadenopathy unassociated with other symptoms constitutes the lymph node type of latent leprosy which in some cases undergoes spontaneous cure.

One of the greatest needs in combatting leprosy to-day is a reliable serological test that can be depended on to detect the disease in its earliest stages. Unfortunately such a test does not yet exist.

The detection of incipient leprosy now depends on the finding of areas of anesthesia, the recognition of thickened nerves and superficial lymph nodes, the tak-

ing of a careful history, and the examination of external lesions as to appearance, location, and other characteristics previously mentioned in the section on symptoms and signs.

Accuracy of diagnosis depends on experience of the physician in charge of the case. Therefore, the introduction of any clinical test that will tend to minimize the influence of the personal equation will prove valuable.

When a dilute solution of histamine is pricked into the normal skin, a reaction occurs in about twenty seconds, resulting in a circular, sharply defined local reddening of three to four millimeters diameter. This is followed in another fifteen to thirty seconds by a flush or "flare" that appears on the surrounding skin. This flare must be distinguished from the local red reaction. The flare is a darker red or scarlet than the other. It has diffuse borders.

A wheal at the site of the prick forms after the flare. In three to five minutes, at its maximum development, it measures one to two millimeters in elevation and three to four in diameter.

The full reaction of the normal skin to histamine consists of a "triple response": 1) local redness; 2) a flare; and 3) a wheal. It is characteris-

tically that of the reaction of normal skin to any injury. Local redness and edema are due to direct action of injury on capillaries, while the flare is produced by the dilatation of arterioles and is reflex in nature, being dependent on integrity of the cutaneous nerves. This arteriolar dilatation is a local nervous reflex and does not depend on a spinal reflex arc.

The loss of the flare following the proper application of histamine is a sign of degeneration of the sensory nerves supplying the skin tested; possibly there is also direct involvement of the nerve endings as in local anesthesia.

Results of the histamine test in leprosy:⁴¹

In the pale macule: The flush is always absent in the pale macule of leprosy. When the histamine prick is made just outside its borders, a flare develops on normal skin but stop at the border of the macule. When the prick is on the inside of the border, the flare is prevented from appearing at all.

When the flare is abolished, one must remember that the local redness is all the more prominent.

A flare will be present when the test is done on the macules of tinea flava and other pale pityriases, leucoderma, old scars, and fading psoriasis.

In the reddish macule: When the lesion is quite red, only the wheal may be elicited.

When hyperesthesia is present and the lesion is contaminated with bacteria, the flare is not constant. If there is accompanying infiltration or edema, the wheal may be absent or slight.

In the nonleprotic lesion: The flare appears on the adjacent skin outside the borders; this is not the case in leprosy.

The test itself consists of the use of a one to one-thousand dilution of histamine phosphate. A drop of the solution is put on normal skin and a drop on a lesion. One then pricks through each drop into the skin--but not so deep as to cause bleeding. Then one wipes the histamine off immediately and observes the pricks with the aid of sunlight.⁴¹

Another interesting but uncommon diagnostic finding in leprosy is the alteration and even complete destruction of the fingerprints in the absence of visible lesions on the hands. The first observation of a case of leprosy discovered by means of dactyloscopy is that of Ribeiro in La Presse Medicale of April 22, 1936.⁴²

Diseases which simulate leprosy:

Syphilis³⁶: From syphilis, which is also a disorder the lesions of which are polymorphic in character, lepra can be distinguished by its much greater chronicity; its larger and brownish-yellow glazed, nodules; its frequent paresthetic and anesthetic symptoms; its bullous lesions, rare in acquired syphilis; the far more extended areas of its erythematous macules; its blackish crusts, lacking the rupioid aspect of those in syphilis; its leathery, mica-tinted cicatrices; and the characteristic leonine facies of its cutaneous forms. The Wasserman reaction, as we have previously mentioned, is of no use in differential diagnosis.

Morphea and vitiligō³⁶: These affections are unattended by constitutional symptoms and exhibit no hyperesthetic or anesthetic symptoms in the patches present.

Multiple sarcomata³⁶: Lesions of this disease, especially when on the face, are followed by much more rapid degeneration and fatal result.

Erythema multiforme³⁶: This affection has no areas of hyperesthesia or anesthesia.

Syringomyelia³⁶: This disease is to be differentiated by its display of lesions only in regions where there is muscular atrophy; by the greater ex-

tent and lack of definition of areas of perturbed sensation; by diminution of tendon reflexes, which are exaggerated in lepra if affected at all; and by a marked predominance of symptoms in the upper as distinguished from the lower extremities.

TREATMENT

A Few Word in Regard to General Measures of Control
in Leprosy:

It is easier to prevent a dozen cases of leprosy than to effect a cure in one. There is no one outstanding direct way to prevent leprosy, because there is no one outstanding source of infection.

The danger of infection becomes greater as contact with a leper becomes more intimate and of more protracted duration. Spread of leprosy is greatest where hygienic conditions are worst.⁴³ Any campaign against leprosy in backward races must have in the forefront the amelioration of poor social and economic conditions. The problem is a child problem because children are more susceptible by far to the disease than are adults. Further, children develop an active form of the disease which is more certain to spread infection.⁴⁴

We are forced to admit that we have no specific remedy, although "We have a form of treatment which, under favourable circumstances, will heal the less virulent cases". Compulsory isolation would never control the leprosy problem among vast, uneducated populations, because it drives the disease underground.⁴⁴

Ernest Muir believes that the chief difficulty against the control of leprosy in foreign colonies and dependencies of European powers is the ignorance and indifference of the people at home.⁴⁴ Money is necessary to establish leprosariums and to broadcast propaganda, in order that the lepers may be convinced that they will be happier and better cared for in institutions than they are at present in a hostile environment of citizenry who exhibit extremes of fear and horror when they encounter a leper in ordinary walks of life.⁵

General Care of Lepers

Experience has shown that if any leper is committed to an asylum where excellent hygienic conditions prevail, where food is both good and certain to be given, where work is within his physical powers, and where loneliness and worry are banished, a considerable clinical improvement will follow without the use of any medication at all.

Lowe⁴⁵ believes that ideally there should be three types of institution in every district in which leprosy is a problem. He suggests:

1. Hospitals: Here patients in more remediable stages are isolated and treatment is given according to the patient's needs after careful clinical evalu-

ation of cases.

2. Asylums: These are for those with less remediable forms of leprosy--in cases in which crippling has taken place.
3. Colonies: These are for the more able-bodied patients in whom the disease is no longer active. These patients, although eligible for parole, frequently do not wish to return to their old haunts. With the stigma of leprosy still attached to them their reception back home would not be cordial.

Specific Measures in Leprosy

Thirty years ago the future of a leper was most discouraging. Hundreds of remedies had been tried in centuries past, but failure was uniform with all drugs employed. It was difficult to appraise the true efficacy of a drug used in leprosy because of the fact that a leper applies for treatment usually when he is suffering a periodical exacerbation of his affliction. In the natural course of events, and without treatment of any description, acute manifestations of leprosy tend to become quiescent. There was always danger, therefore, of ascribing to a drug an improvement which would have

occurred without any medication at all.⁶

There were in use thirty years ago many age-old devices for the amelioration of symptoms. These were employed by the natives of the Orient without any knowledge of the reasons for the effects which resulted. For instance, the Japanese have used thermal springs for centuries under the impression that something in the water achieved beneficial results. Actually it was the heat alone that had a stimulating effect on the body's resistance.

Again, it has long been known to natives of India that to chew the leaves and twigs of the chaulmoogra tree has a salutary effect on leprosy. There is a pre-Buddhist legend, centuries old, that a leprous king of Burma had cured himself by eating the raw seeds. Eventually the Indians deduced that it was the oil of the chaulmoogra tree. The oil has since been found most abundantly in the nut, which contains the ameliorative substance.⁵

Heiser⁵ gives a resumé of the modern treatment of leprosy: "In 1907 Dr. Isadore Dyer, Professor of Dermatology at Tulane University, brought the properties of chaulmoogra oil arrestingly to the attention of the scientific world by reporting its successful use at the Louisiana colony for lep-

rosy in Iberville parish. I visited there the following year and gained a most favorable impression of the treatment.

"As soon as I had returned to the Islands (Philippines) Dr. Dyer's treatment was given a thorough trial. The drug had to be taken by mouth, and most patients became so nauseated that only one out of three hundred could retain the oil over a period long enough to be effective.....

"Then began an extended series of experiments to develop some method of administering the remedy without the resulting nausea. Chaulmoogra capsules were coated with salol or other substances so that they would pass through the stomach without digesting. Enemas were tried. Most of all we wanted to inject chaulmoogra hypodermically, but the oil would not absorb.

"At this point a letter was written to Merck and Company in Germany, in which we asked whether they could suggest any substance to add to the chaulmoogra oil which might cause it to absorb when injected hypodermically. They replied that they had no practical knowledge, but theoretically it was possible that the addition of camphor or ether might give the desired result. The testing of this possibility

was done by Elidoro Mercado, the house physician at San Lazaro. He added camphor to Unna's old prescription of resorcin and chaulmoogra oil. To our great joy we found that this combination was readily absorbed.....

"The camphor-resorcin solution proved a great advance. After the first year we were able to announce to the world that a number of cases had become negative. We promised that if any patient remained so for two years we would release him. When this actually happened, for the first time in history hope was aroused that a permanent cure might be found for this most hopeless disease.

"Few can imagine with what a thrill we watched the first case to which chaulmoogra was administered in hypodermic form, how we watched for the first faint suspicion of eyebrows beginning to grow in again and sensation returning to paralyzed areas. We took photographs at frequent and regular intervals to compare progress and to check on our observations, fearing our imagination might be playing tricks upon us, because in hundreds of years no remedy had been found which had more than slight influence on this disease."

Dr. Heiser then traveled over the world, en-

listing the aid of as many leprologists as possible. When he passed through Hawaii, he informed the Molokai officials of the work done in India. He told them how Sir Leonard Rogers' use of ethyl esters of chaulmoogra oil halved the time of treatment, because the dosage of the drug could be increased.

Other developments occurred in the treatment of leprosy. All chaulmoogra oil, previous to the year 1912, had been extracted from the seeds of *Taraktogenos kurzii*, a tree belonging to the family, Flacourtiaceae. But the collection of these seeds devolved upon natives in the remote regions of Burma. These people, as Heiser⁵ says, "allowed at least fifty percent of the crop to be eaten by wild pigs and other animals, when they were not themselves frightened away by tigers and elephants. The dealers in the oil had never seen the tree in its native state."

But in 1912 the crop of *Taraktogenos* failed. Under the pressure of necessity scientists discovered that the oil of a closely related species, *Hydnocarpus wightiana* or *anthelmintica* was just as good. The use of *Hydnocarpus wightiana*, a tree common in southern India and in Siam, both easily accessible regions, has now freed leprologists the world over of the worry that treatment of lepers everywhere might come to a sudden halt as a result of a crop failure in one of

the most inaccessible regions of Asia.

Oils of the *Hydnocarpus* group are now most commonly used in the form of ethyl esters, which cause less local irritation than other chaulmoogra oils. However, the choice of which to use is determined by such considerations as ease of procuring, cost of delivery, purity and freshness, and keeping qualities.

At Cullion, according to Heiser⁵, chaulmoogra oil treatment results in the recovery of ten per cent. of patients, while fifty per cent. attain a cosmetic cure, that is, the outward lesions disappear, and the disease does not progress. The disease is arrested in thirty per cent. more of cases, and there remains ten per cent. of patients who get steadily worse in spite of treatment. The earlier a leper's condition is detected and treatment is instituted, the greater is the likelihood of recovery.

The governors of every important leper colony in the world parole their inmates if a certain amount of satisfactory progress has been made under treatment. The criteria for an inmate's parole varies in different leprosariums, however. As an

example of a complete and rigorous system we will state the procedure followed in the leper colony not far from Rio de Janeiro.⁴⁶

1. The patient is examined clinically, dermatologically, and bacteriologically on his entrance.
2. He receives six months' treatment and is then re-examined.
3. If examination is negative, he goes "under observation". During the next six months he gets a monthly bacterial checkup after reactivation of the disease has been attempted with potassium iodide.
4. If still negative, the patient goes to a pavilion for "closed forms" of leprosy for six more months of treatment and six monthly examinations. This permits twelve negative examinations after reactivation and after being interned for eighteen months. Clinically the leper's active lesions must have disappeared.
5. The leper is then examined by a commission of specialists and may be discharged conditionally.
6. During the next three years he has to submit himself every three months to a clinical and bacteriological examination, after which he is permanently discharged.
7. A positive examination or appearance of any active lesion annuls all prerogatives acquired, and the patient is right back where he started on en-

trance.

Some Discussion of Drugs and Their Dosages Now Used
Against Leprosy

1. We shall list first Mercado's modification⁴⁷ of Unna's formula, previously discussed.

℞	Olei chaulmoograe	60.00 cc.
	Olei camphorae	60.00 cc.
	Resorcinolis	4.00 Gm.

Sig.: Sterilize. 1.00 cc. intramuscularly
once a week, gradually increasing to 5.00 cc.

2. Ethyl ester prescription, the one enjoying widest use to-day.

℞	Ethyl ester hydnocarpate	
	Olive oil (free from fatty acids)	aa 60.00 cc.
	Thymol	90.00 Gm.

Sig.: 1 to 10 cc. given according to di-
rections of Rogers and Muir in their
book, Leprosy.

3. Alepol: This is a recent Burroughs-Wellcome preparation. It is a sodium salt of a selected fraction of the less irritating lower melting-point fatty acid of hydnocarpus oil. A three per cent. solution can

usually be given subcutaneously or intramuscularly without causing pain, and one per cent. intravenously. Alepol is much cheaper than the ethyl esters; two doses weekly for a year will cost fifty cents. This drug has the disadvantage of obliterating veins, according to Bousfield.⁴⁸ He uses the drug intramuscularly after a patient's veins can no longer be penetrated.

4. As an adjunct to alepol this potassium iodide prescription is useful:

R	Potassii iodidi	30.00 cc.
	Aquae	q.s. ad 60.00 cc.

Sig.: One drop in water once daily, gradually increasing to 30 or 40 drops per day.

5. The most recent and encouraging innovation in treatment is that of Reenstierna.⁴⁹ This investigator used a strain of *Myc. leprae* from the blood of a patient with acute nodular leprosy for the production of an antileprosy serum by injecting the strain repeatedly into sheep under different conditions as partly acid-fast, partly non-acid-fast rods, filaments or coccoid types. The serum has been used to treat four lepers at Jarvso Leprosarium in Sweden; thirty-one at Betsaida Hospital, Addis Ababa, Ethiopia; thirty-three at Haile Selassie Leprosarium

near Addis Ababa; and one at Ethiopian Army Hospital. Physicians at these places believe the treatment is efficacious. Results consist of rapid healing of ulcers, resorption of nodules, complete healing of periosteal processes, return of lost sensibility in more than sixty-five per cent. of cases, renewal of mobility of paralyzed fingers and disappearance of foot swellings. This serum has worked at Betsaida when chaulmoogra absolutely failed.

If findings are corroborated by other workers, this new immunotherapy will prove a great advance.

6. Trypan blue, fluorescein, and other dyes: Intravenous injection of coal-tar dyes has been practiced in Malaya by Ryrie⁵⁰. He had previously noted that these dyes kill bacteria when they stain the organisms. It was a logical step to introduce these dyes into human tissues. (But all human tissues are not alike. Drugs seemingly working wonderful cures on Indian lepers would fail completely in the case of Chinese lepers. Racial differences complicate the treatment of leprosy.)

Trypan blue is given in 25 cc. doses of a 4 per cent. solution; brilliant green in 20 cc. of a 1 per cent. solution; fluorescein in 10 cc. of a 2 per cent. solution; eosin in 25 cc. of a 2 per cent. solution.⁶

These dyes are concentrated in the leprotic lesions after intravenous injections; a definite diminution of the external manifestations of leprosy has been observed. But the effect of these dyes is not permanent. Much work needs to be done with these materials first.

7. Protein-shock therapy: Philip Manson-Bahr⁶ has been using typhoid-paratyphoid vaccine in graduated doses as his choice among the numerous ways of stimulating a leper's resistance. Treatment is started with fifty million typhoid-paratyphoid organisms, and the dose is gradually increased to 300 million.

8. In the Philippines the "plancha" method is being used for the treatment of individual and localized granulomatous and macular lesions.^{5'} It consists of extensive and complete intradermal infiltration with refined chaulmoogra preparations. The method is truly heroic. Fortunately many of a leper's lesions are anesthetic; if they are not, he is in for a bad time. This treatment is contraindicated when there are numerous and important lesions on the face, as infiltrated areas become pigmented, and the patient's face would betray former leprosy as long as that pigment should last.

9. Treatment of leprous rhinitis: According to Wayson and Reinecke,⁵² the systematic use of a spray composed of acetozone 1 percent. and chloretone 0.5 percent. in liquid petrolatum serves to relieve the distressing nasal obstruction seen in leprosy and allows the patient to sleep. There is a cessation of epistaxis also.

Surgical Measures

When leprous nodules spread on to the cornea and threaten to interfere with the line of vision, extension of the leproma may be arrested by division of the cornea on the pupillary side of the lesion; it has been found that the bacilli do not traverse the cicatrix.

Tarsorrhaphy for extropion of the lower lid, iridectomy for iritis or synechiae, tracheotomy for laryngeal stenosis, and necrotomy for bone disease may have to be performed.

Amputation is the solution for perforating ulcers on the legs, as the general health is undermined by the presence of these sources of sepsis. The existence of leprosy does not interfere the success of surgery.

PROGNOSIS⁶

Complete recovery is such a rare event in leprosy that it may only be hoped for, never expected. In neural leprosy recovery from the disease itself may be expected, but the effects of the leprous process itself are permanent. Trophic lesions resulting from nerve destruction are irremediable. Such cases may live for decades, however, and die of some other disease.

Cutaneous leprosy is a much more acute disease than neural leprosy. It saps the patient's strength and general health more quickly and more effectively. It rarely runs its course, because the patient is so likely to die of some intercurrent disease. Tuberculosis, nephritis, pneumonia, and laryngeal stenosis are the more frequent causes of a fatal issue.

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