RAT LEPROSY

A CRITICAL REVIEW OF THE LITERATURE

By John Lowe, M.B., Ch.B.

(Conclusion)

FILTRABILITY

Markianos (73, 74, 76, 77) was the first to report investigations on the filtrability of the rat leprosy bacillus, following reports made by many workers of the transmission of tuberculosis by filtrates of bacillary emulsions.

An emulsion of rat leproma was filtered through Chamberland L2 filters, under a pressure of 25 to 30 centimeters of mercury. In rats the filtrate caused inflammation in the local lymphatic glands and, later, lesions in the viscera. The filtrable virus first developed into acid-fast granules, later into granular bacilli, and finally into true bacillary forms. The last were found in twenty days in young rats and in two or three months in adults. The granular forms, commonly seen in rat leprosy, were regarded as a stage between the filtrable virus and the true bacilli. Marchoux was quoted as supporting this opinion.

Lowe in an attempt to confirm these findings, injected 53 rats with material passed through Chamberland L2 and L3 filters; four of them showed a few acid-fast bacilli at postmortem, and one showed a generalized rat leprosy infection. He considered that the positive findings could probably be explained by experimental errors or faulty candles, and concluded that his experiments gave strong evidence against the existence of a filtrable form of the organism.

Walker and Sweeney (129) showed by direct microscopic examination of centrifugal precipitates of filtrates that a few acid-fast bacilli occasionally pass through the pores of bacterial filters that hold back *B. prodigiosus*, which is commonly used as a control of the efficacy of the filters; and they also found that filters are equally permeable to the leprosy bacilli. Later (130, 131) they reported that after filtration of human and rat leprosy material through Seitz, Berkefeld M, Berkfeld W, Chamberland L2 and L3 filters, they had obtained growths from the filtrate.

Many of the cultures remained sterile indefinitely, but some acquired a slight finely granular sediment at the bottom of the flask composed of small coccoid organisms, single, in pairs or in short chains. In every case the

primary culture contained only acid-sensitive organisms, but on transplantation to Musgrave-Clegg medium they sooner or later became acid-fast. In appropriate media they exhibited the extreme pleomorphism and facultative acid-fastness characteristic of the organism cultivable from unfiltered murine and human leprosy.

Walker and Sweeney did not regard these results as proving the existence of a true filter-passing form of the bacillus, though they believed that these supported their claims of successful cultivation of the bacilli of human and rat leprosy.

CULTIVATION

REPORTS OF CULTURE WORK

Though many workers have attempted to cultivate the bacillus of rat leprosy, only a few have claimed success. A good review of the earlier attempts was published in 1914 by Wolbach and Honeij (140).

On two occasions Dean grew from rat leprosy material a nonacid-fast diptheroid which could not be made acid-fast even by animal inoculation and was not markedly pathogenic to rats. Chapin (20) obtained a growth of acid-fast bacilli on a special trypsin egg medium. Marchoux and Sorel reported marked multiplication of bacilli with filamentous and branching forms in pieces of leprous tissue embedded in culture media. They failed to produce any subcultures except that some growth occurred on the spleen of a rat sterilized by heating to 110° C. and partially digested by trypsin. This growth appeared within a few days and then ceased suddenly, and at the end of six weeks the bacilli were granular and dead. Wellman and Hand (135) stated that acid-fast organisms grew from leprous tissues of either human or rat origin on Wellman's placental agar "so readily that microscopic growth can be discerned in five to seven days," but gave no details.

Hollmann (42) obtained a culture by Clegg's method, inoculating the heart's blood of a diseased rat onto the Musgrave-Clegg medium on which amebae and cholera vibrios were growing. For six days the bacilli increased in size and sometimes showed branching forms; later they appeared small and coccoid. After the ninth generation the vibrios and amebae were killed by heat and on subculture a pure bacterial growth was obtained, visible in twenty-one days. The culture injected into rats produced local lesions with acid-fast bacilli, which were also found in the lungs and spleen, though after 116 days there were no gross lesions. Later Currie and Hollmann reported failure by the same and other methods; they did not secure a single culture of an organism which they considered to be that of rat leprosy. In one attempt they grew an acid-fast streptothrix from an ulcerated lesion, but they considered it a contamination, as is very likely in such a lesion.

Bayon (10), using fish-juice agar, obtained in fourteen days from spleen material a white moist creamy growth of a pleomorphic acid-fast rod indistinguishable from a culture obtained from a leper. On injection into rats this culture produced visceral lesions described as identical with those of

experimental rat leprosy. These findings have not been confirmed by other workers.

Walker and Sweeney (127) obtained cultures of a pleomorphic organism "like those of human leprosy" from 24 of 37 rats in which acid-fast bacilli were found but no gross lesions; they used the Musgrave and Clegg medium, incubating at 22° to 25° C. Similar organisms were cultivated from soil. They hold that the two organisms are identical, that human and rat leprosy are the same disease, and that both are due to a soil actinomyces. No report was made of animal inoculations with the culture. These findings have not been verified.

Cilento and North reported that in one of many attempts, one primary culture was obtained on Dorset's egg medium. The isolated bacilli were said to have produced typical lesions in young rats. Lowe has failed to produce rat leprosy with this culture.

Marchoux, Markianos and Chorine (70) applied to this problem the methods by which Shiga and Wherry claimed to have obtained cultures of the human leprosy bacillus. An emulsion of rat leproma was centrifuged at a high speed and two drops of the supernatant fluid, free from pieces of tissue and large masses of bacilli, were spread on the medium. In twenty-four hours the bacilli tended to gather together and later were grouped in masses, particularly at the bottom of the tube. These masses looked like colonies of bacilli. In subcultures large numbers of these bacilli were transferred to the fresh medium and this was repeated in diminishing degree for several transfers. The bacilli ceased to be pathogenic to rats after about two months, but they remained morphologically unchanged for a much longer period. The authors concluded that the appearance of successful culture and subculture was an artefact.

Uchida (120) isolated from rats five strains of acid-fast organisms which Ota and Asami (95) considered to be true cultures of the rat leprosy organism. Ota and Asami, and Asami (5, 6) reported that cultures made from 17 rats by the modified Loewenstein-Sumiyoshi method used by Ota and Sato in cultivating *M. leprae hominis* gave 12 strains of acid-fast bacilli, growth appearing after periods varying from 5 to 110 days. The cultures were of two main varieties, grayish and orange. Subcultures grew on various media. The cultures were injected into rats and from 23 to 41 percent of them became infected. The most marked lesions were in the lymph glands; sometimes there were lesions in the skin, seldom in the spleen. The difference between the lesions produced and those seen in animals infected in nature was one of degree and not of kind. The infection thus produced could be transmitted to rats in series. Guinea pigs and rabbits were also infected.

Gerbinis (38) and Lowe have reported failure to obtain cultures by the method of Ota and Asami. Wayson applied the methods of Soule and McKinley and of McKinley and Verder without success.

Zinsser and Carey (141) observed multiplication of the bacillus in two of a number of tissue cultures obtained by explantation of fragments of young rats' spleen in rat plasma. Friedheim cultured rats' spleen in a mixture of rat plasma and rat embryo extract and infected these cultures with bacilli from rats but got no multiplication.

Salle (104) and Salle and Moser (105, 106) cultivated chick tissue in guinea pig plasms and chick embryo extract and inoculated these cultures.

In four out of thirteen multiplication was observed. The acid-fast bacilli gradually disappeared and nonacid-fast diptheroids predominated. On subculture some of the bacilli first became acid-fast and again nonacid-fast later, this cycle being repeated in each subculture. After five generations in tissue cultures, bacilli were transferred to chick embryo medium, in which the cycle was again repeated. Salle concluded that the acid-fast rod and the nonacid-fast diptheroid are both forms of a pleomorphic organism which is the cause of both rat and human leprosy. No attempt to produce rat leprosy by injection of the isolated organism was reported.

Lowe reviewed the reports of successful cultivation of this organism by ordinary bacteriological methods (62) and by tissue culture methods (65). He pointed out that the only way of proving that any organism isolated from rat leprosy tissue is really *M. leprae muris* is to subculture it for a number of generations to exclude mechanical transference and then to produce experimental rat leprosy transmissible indefinitely in series; practically none of the claimants of successful culture had attempted this. He had failed completely with the methods of Clegg, Bayon, Walker and Sweeney, Uchida, Ota and Asami, Cilento and North, Loewenstein, Soule and McKinley and McKinley and Verder. He (unpublished) has cultivated rat tissue in vitro and inoculated them, but has failed to detect any definite increase in the number of bacilli within two weeks, which is the longest time the tissues have been kept alive. Injection experiments with the organism isolated by Cilento and North, and with three of Uchida's five cultures did not produce rat leprosy. He pointed out that nonpathogenic acid-fast organisms are sometimes found in rats, and that such organisms may be cultivated; also that with the enormous numbers of bacilli present in rat leprosy material used for seeding culture media, and with their extraordinary powers of persistence (up to a year or more), an appearance of multiplication in the primary culture and of successful subculture for a few generations can be produced when in reality only mechanical transference of bacilli from the tissues has occurred.

DISCUSSION OF CULTURE WORK

The chief characteristics of the leprosy organisms in the lesions are (*a*) a constant morphology, with only minor variations in size, shape and appearance, (*b*) acid-fastness, and (*c*) slow multiplication. It is reasonable to expect that in cultures the bacilli will show the same characteristics. Nevertheless, many of the claims of successful cultivation have been based on the occasional isolation of organisms that did not show these characteristics. Such claims must be accepted with caution.

Pleomorphism.—In order to explain the great variety of the organ-

isms which have been isolated from leprosy material (chiefly of human leprosy, but also of rat leprosy) various workers have postulated that the organisms are pleomorphic. For examples, Bayon wrote of coccoid forms, rod forms of varying sizes and shapes, diphtheroid and branching forms, and acid-sensitive, and acid-fast forms of the leprosy bacillus. Such pleomorphism is perhaps not impossible, but it is not in keeping with our knowledge of other acid-fast organisms. In the tissues we find that the leprosy organism is always an acid-fast rod, varying somewhat in morphology but only within certain limits. Also, these minor variations are often more apparent than real. By various modifications of the Ziehl-Neelsen staining technique one may produce marked differences of appearance of leprosy bacilli, one method giving granular forms and another uniformly stained rods. Interesting granular appearances are brought out by staining by Much's method, by a combination of it and the Ziehl-Neelsen method, and by dark-ground illumination.

Variability of acid-fastness.—All attempts that I have made to detect a nonacid-fast form of the organism in the tissues have been fruitless. It is possible that in culture it might be nonacid-fast, but strong supporting evidence must be obtained before this idea can be considered as anything more than a hypothesis, and rather an improbable one; such evidence has not yet been produced. There is no absolute criterion of acid-fastness. Some workers have called an isolated organism "acid-fast" when one percent acid does not decolorize it in a few seconds, but judged on this basis a great many organisms are acid-fast. The powers of really acid-fast organisms to resist decolorization by acids and alcohol vary very much according to the nature of the material examined. As Lowe (64) has pointed out, leprosy bacilli are much more easily decolorized in paraffin-embedded tissue sections than in smears taken direct from tissues. Also certain bacilli which are nonacid-fast or partly acid-fast in cultures on ordinary media may acquire or increase that character on media containing glycerin egg albumen, and particularly when injected into animals. These facts have been used to support the claims of some workers who have cultivated acid-sensitive bacilli from leprous lesions.

Fallacies in cultivation work.—The chief difficulties encountered in interpreting results of attempts at culture are: (*a*) Persistence and transference of bacilli may produce appearances suggesting multiplication. The persistence of the enormous numbers of bacilli usually introduced, and the ease with which mechanical transference of these bacilli can be interpreted as successful subcultivation, have already

been referred to. This difficulty should be overcome by subculturing an organism for several generations before using it for injection experiments. (*b*) Contamination of the inoculum or the culture medium may occur. Saprophytic acid-fast bacilli are found widely in nature, and even in stored distilled water. They have frequently been demonstrated in the skin and its secretions, mucous membranes, glands and blood of healthy persons and animals. This matter is fully discussed by Wilson (139) in his critical study of tuberculous bacillemia, particularly with reference to Loewenstein's work; he concluded that many of the reported positive results of blood cultures were due to failure to pay adequate attention to the numerous fallacies attending the demonstration of the tubercle bacillus. This point is equally applicable to the problem of cultivating *M. leprae*. The media used are usually very favorable to the growth of acid-fast organisms of all kinds. They also usually contain glycerin and egg albumen, which favor the development of acid-fastness in organisms which normally are acid-sensitive. The original leprous tissue may be contaminated, or contamination may occur during the preparation of the medium or the inoculum. The media when seeded are usually incubated for a long period, which favors the development of contamination.

(*c*) Saprophytic organisms on injection into animals may produce lesions resembling leprosy. The local lesions which may be produced in the rat by the injection of large numbers of almost any acid-fast organism, living or dead, have frequently been interpreted as proving the pathogenicity of the particular organism used. This matter is discussed more fully later, under "the susceptibility of rats and mice to acid-fast bacilli."

Proof of a genuine culture.—The genuineness of a culture of the rat leprosy bacillus should be easy to prove or disprove, since it should be possible to infect rats with it and to maintain the infection in series for an indefinite period. Apparently the only workers who claim to have done this are Ota and Asami, and their results are far from conclusive. In from 23 to 41 percent of rats inoculated with their organism they produced lesions with acid-fast bacilli, almost entirely confined to the glands. This is very different from the massive generalized infection produced in 100 percent of rats with material from a leprous rat.

Before any method of cultivating *M. leprae* can be given recognition it should give a constantly high proportion of positive results in the hands of the original worker and of other workers using the same technique. As yet no method of cultivation has given a high

percentage of positive results even at the hands of the original worker, and practically no claim of successful culture has been verified by any other worker. The whole situation regarding the cultivation of leprosy organisms is confused, but most workers appear to be of the opinion that it is extremely doubtful if anyone has succeeded in cultivating the organism of either human or rat leprosy.

IMMUNITY

All rats appear to be susceptible to rat leprosy, experimental transmission from rat to rat usually being successful in all cases. A few workers have tried to demonstrate the presence of immune bodies in rats infected with rat leprosy, and attempts have been made to make rats immune to the infection.

Dean reported that the diphtheroid bacilli of doubtful nature cultivated by him from rat leprosy material was agglutinated by serum from leprous rats but not by that from healthy ones. Wherry found that injection of killed rat leprosy bacilli caused marked retardation of the development of the disease after subsequent inoculation. Markianos (79) gave rats preliminary injections with defatted bacilli, with similar results. On the other hand Lowe (unpublished) saw no evidence of the production of immunity in rats injected with heat-killed bacilli. Muir and Henderson injected rats with B.C.G. culture and subsequently inoculated them; there was no evidence that immunity had been produced. With a view to lowering general resistance, rather than in connection with specific immunity, the same workers kept experimentally infected rats on diets deficient in vitamins A or B and consisting of decomposed protein, to see whether the rapidity of development of the disease would be increased, but that result was not obtained.

TREATMENT

Vaccines.—Wherry treated experimentally infected rats by injecting suspensions of killed bacilli, with no apparent effect upon the course of the disease. Markianos (78) used defatted bacilli and Valtis and Markianos (123) used B.C.G. vaccine, in both cases reporting the healing of ulcers and retardation in the generalization of the disease. Tisseuil (115, 116) injected emulsions of bacilli prepared by extracting rat lepromas with acetone and with methyl alcohol; the second preparation appeared to accelerate the development of the disease, while the first retarded it to some extent. Gillier and Tisseuil (39) found that tubercle bacilli extracted similarly caused retardation of the disease.

Chaulmoogra preparations.—Koch (50), noting that several workers had obtained apparent cures of rat leprosy following the breaking down of nodules under treatment with chaulmoogra prepa-

rations, tried hydnocarpus esters subcutaneously. Nodules broke down but cessation of treatment was followed by generalization of the disease. Tisseuil reported that chaulmoogra ethyl esters had proved beneficial, and that creosoted hydnocarpus esters and a chaulmoograte of gold guaiacol retarded the disease somewhat.

Other preparations.—Markianos (80) experimented with subcutaneous injection of a series of nine preparations: (1) "fleolate" of sodium; (2) tribromometaxylenol; (3) methoxyphenylhydnocarpate; (4) 541 of Fourneau and Baranger—phenyl ethyl ester of hydnocarpus oil; (5 and 6) 580 and 581 of Fourneau and Sivadjan—sodium salts of an acid of turtle oil; (7, 8 and 9) 579 A, B, and C of Fourneau and Sivadjan—esters of turtle oil. The first six preparations were well tolerated but produced no effect upon the disease. The last three preparations caused considerable local reaction, and two of them, 579 A and B, appeared to exert a beneficial influence on the course of the disease, delaying its development.

Tisseuil used injections of potassium iodide, lipiodol, and ammonium molybdate. In animals treated with potassium iodide the lesions appeared more slowly but developed more quickly than in control animals. Lipiodol appeared to be beneficial, but the effect of ammonium molybdate was slight. Berny (12) found that leprous rats were susceptible to potassium iodide, the minimum lethal dose in them being much lower than in healthy rats. Gillier and Tisseuil injected sulphate of cobalt and ammonium, oxalate of titanium and potassium, chloride of cadmium, castor oil with guaiacol and alcohol, ammonium molybdate with eosin, and turtle oil. The most promising results were obtained with the chlorides of nickel and cadmium. Koch used "solganol B"; as with chaulmoogra esters the nodules broke down, but on cessation of treatment the disease progressed.

X-rays.—Prudhomme (99) found that local irradiation of the lesions did not cure the disease but retarded its progress, that the infected cells were more easily killed than normal cells, and that bacilli liberated by cell destruction remained viable for ten days.

RELATION OF THE INFECTION TO HUMAN LEPROSY

Stefansky, Dean, Rabinowitsch and most later workers have been in agreement that *M. leprae muris* is closely allied to but not identical with *M. leprae hominis.* Marchoux and Sorel considered that the relationship of the two organisms is similar to that of *M. tuberculosis hominis* and *M. tuberculosis avis.*

Bayon considered the organisms of human and rat leprosy very

closely related, if not identical, while Walker and Sweeney, and Salle and Moser held the view that they are identical. These opinions were based on the claims of these authors to have succeeded in cultivating both organisms and transmitting the infection to animals.

Attempts have been made to study the relation of the two organisms by immunological methods. Mezinescu found that complement was deviated in the presence of Stefansky's bacillus and serum of human lepers, though Wherry (138) reported that the serum of human lepers does not agglutinate the bacillus. Muir (87) compared in lepers and healthy controls the reactions to leprolin made from human and rat lepromata. In healthy controls and in neural leprosy both substances caused positive reactions, but in cutaneous leprosy only the Stefansky leprolin gave positive results, which is evidence against the identity of the two organisms. Ohtawari and Ichihara (93) reported similar findings.

North (91), Cilento and North, and Cook (24) have considered the epidemiology of rat and human leprosy in Australia from the point of view of the identity of the causative organisms. Cilento and North found no convincing evidence of any connection between a human leprosy case and rat leprosy. Cook concluded that the available evidence did not support the hypothesis that the disease might be transmitted from rats to men by the flea *Xenopsylla cheopis*. Soule (109) found no rat leprosy in the rats in the Culion Leper Colony.

Walker and Sweeney considered that, in nature, both diseases are contracted by infection of wounds by soil containing the organism, leprosy being really a soil infection. However, Rabinowitsch, whose knowledge of acid-fast organisms was unique, had pointed out that the known acid-fast bacilli of dung and the soil are easily cultivated and are not pathogenic to rats, whereas *M. leprae muris* is grown either with great difficulty or not at all and is pathogenic. There is no very strong reason to believe that rat leprosy is a soil infection.

Lampe and de Moor believe that originally there may have been a single common saprophytic acid-fast organism, various strains of which have only secondarily adapted themselves to the various members of the animal kingdom, having become pathogenic to man, rats and other animals. They suggest that human leprosy is only one of a group of similar diseases in animals, and that a comparative study of the whole group and of their causative organisms and their adaptability to parasitic behaviour might lead to a greatly increased knowledge of human leprosy.

LEPROSY-LIKE DISEASES IN ANIMALS

SUSCEPTIBILITY OF OTHER ANIMALS TO RAT LEPROSY

Rat leprosy, discovered in *Rattus norvegicus*, is readily transmissible to the albino rat, which is of the same species, and to mice. Numerous workers have attempted, without success, to transmit it to such animals as rabbits, guinea-pigs, hamsters, etc. Local lesions with acid-fast bacilli are produced, and bacilli may be found at the site of inoculation for many months, but there is no generalized infection.

Laigret (53) reported that by inoculating guinea-pigs and rabbits with rat leprosy material and later injecting them with acetone extracts of B.C.G. cultures, he obtained the development of leprous lesions. Ota and Asami claim to have produced lesions in the same animals by inoculating their cultures of *M. leprae muris*.

An interesting question arises regarding the susceptibility of man to rat leprosy. Marchoux (68) described a patient suffering from leprosy of a rather unusual form.

> The visible lesions were brown, circinate, merging spots on the limbs and face. There was no alteration of cutaneous sensibility on the spots or elsewhere. From time to time there appeared pemphigoid blisters with small, round, slow healing ulcers at the edges of the blisters. The macules were the scars of such lesions. From the lesions and also the nasal mucosa there were obtained masses of fine, short "cocciform" and acid-fast bacilli which Marchoux named *Mycobacterium pulviforme*. At autopsy masses of these bacilli were found in the skin, glands, liver and, above all, the spleen. Spleen pulp was inoculated into rabbits, guinea-pigs and rats. Five out of six of the rats developed an infectious process which spread like rat leprosy; the other animals developed no disease. Infection was kept going in white rats in series; it showed all the characteristics of true rat leprosy, macroscopically and microscopically.

Marchoux concluded that this case was probably one of rat leprosy affecting a human, the only case of its kind on record. Incidentally, he considered the production of the disease in the animals as demonstrating that the "granular" forms of bacilli are living and not dead. Laigret (52) investigated the susceptibility of man to rat leprosy by inoculating a leprosy patient, but the results were inconclusive.

SUSCEPTIBILITY OF RATS AND MICE TO OTHER ACID-FAST ORGANISMS

Most workers have found *M. leprae muris* to be the only acid-fast organism capable of producing a generalized infection in the rat, though several workers have claimed successful transmission of human

leprosy to that animal. It would profit little to attempt to deal fully with the literature of experimental inoculations of animals by various acid-fast organisms of doubtful pathogenicity, but a few illustrative examples may be cited.

Bayon reported that injection into rats of (*a*) human leprosy organisms from patients, (*b*) his cultures obtained from human leprosy, (*c*) rat leprosy organisms from a spontaneously affected rat, and (*d*) his cultures from rat leprosy all produced the same lesions, which were identical with those of natural rat leprosy.

Fraser (35) pointed out that bacilli from human leprosy, the supposed cultures of that organism grown by Bayon and by Kedrowsky, and also *B. phlei*, could produce in animals local inflammatory lesions, but that the bacilli in them gradually disappeared and they then subsided. Exactly the same lesions could be produced by killed bacilli, which showed that these organisms were not really pathogenic to the animal.

Lowe verified these findings in the rat. Injection of large numbers of human leprosy bacilli, of tubercle bacilli of the supposed rat leprosy cultures of Uchida and that of Cilento and North, all produced marked local and slight general lesions but no progressive disease. The same results can be produced with almost any acid-fast organism killed by heat in the autoclave. Thus the local lesions appear to be produced mechanically and not by any true process of infection. The bacilli can be found in the tissues for over a year, which may lead to the false conclusion that the animal has really been infected. Similar findings had been reported by de Souza-Araujo (28).

In recent years numerous attempts have been made to transfer human leprosy to rats and mice.

Franchini and Cendali (34) reported the production of local lesions in the peritoneum of white rats by injecting emulsions of Hansen's bacillus. On the other hand Cilento and North reported failure to transmit human leprosy to rats.

Cantacuzene and Langhin (18) inoculated intraperitoneally with leprosy material rats that had received two days previously an intraperitoneal injection of a mixture of 5 percent each of sodium diphosphate and calcium chloride, as in the method of van Diense for securing the rapid development of the "ultra-virus" of tuberculosis into the acid-fast bacillus. They reported the production of a chronic leprous infection fatal in five or six months, with general glandular and splenic enlargement. These authors (19) also inoculated rats that had received the same preliminary treatment with a filtrate (Chamberland L3) of leprosy material. The rats, killed at intervals varying from two weeks to two months, showed a thickened and adherent omentum containing acid-fast bacilli and granules. Nodenot and Berny (89) were unable to confirm these findings.

Ota and Asami injected rats with Hansen's bacilli which had been seeded and had multiplied on the media of Lowenstein and Petragnini for one month and

fed them on a diet deficient in vitamin B. In two of seven animals nodules full of acid-fast bacilli appeared on the cheek and nose.

Tisseuil and Berny (117) reported that injections of human leprosy material into the liver of rats gave negative results, and Tisseuil and Gillier (119) found that similar inoculations into the testes produced some local inflammation, with acid-fast bacilli which could be found there up to two years, but that no generalization took place.

Lepine, Markianos and Bilfinger (59) injected leprosy material with finely powdered glass into the peritoneum of white rats and produced extensive lesions containing acid-fast bacilli, the appearances suggesting multiplication. On passage the virulence decreased greatly, and increasing numbers of the bacilli became acid-sensitive.

Row, Dalal and Gollerkerji (103), injected white mice intraperitoneally and obtained minute nodules in the omentum or mesentery that persisted for over a year, were rich in acid-fast bacilli, and showed typical lepromatous cell-changes. Heat-killed bacilli did not produce such nodules, although bacilli were recovered for some time afterward. They regarded their lesions as evidence of multiplication and pathogenicity of the bacilli in mice; with guinea-pigs and rats their experiments were negative.

Nakamura and Kobashi (88) found that human leprosy could be conveyed to rats by inoculation after the nasal mucous membrane had been damaged by acid, and also by intratesticular inoculation after removal of the thyroid gland.

Watanabe (132) inoculated rats with leprous emulsions and inserted fragments of nodules subcutaneously. Local lesions and acid-fast bacilli were found for over one year. Intraperitoneal injections produced nodules in the mesentery which persisted for several months. Intravenous injections produced no lesions. He considered that the injected bacilli increased up to a point and then died out. Injections of potassium iodide given after the inoculations caused a reaction in the infected tissues (133) but did not increase the animals' susceptibility and the infection died out.

LEPROSY-LIKE DISEASES IN OTHER ANIMALS

A good survey of this subject was made by Klingmüller (49), from whose book some of the following section is quoted. Leprosy-like diseases have been reported in fish, fowls, ducks, pigs, cattle, horses, sheep and buffaloes. Many years ago various workers reported leprosy-like lesions in animals and birds in leprosaria—Brosse (16) in parrots, dogs, cats, and pigs; Simond (108) in an ass; van Es and Martin (124) in pigs. Such findings have not been reported in recent years, probably as the result of increased knowledge of bacteriology and pathology.

Domestic Fowls—Several reports have been made, chiefly in China, of leprosy-like lesions in domestic fowls. The Chinese are said to attribute this condition to their eating material infected by lepers. Barbezieux (9) recorded two fowls that showed nodules and loss of toes. Vardon (122) failed to verify this, and Fayrer (32)

in India found that such changes were due to the legs having been tied tightly with string. Guild failed to confirm the reported occurrence of a leprosy-like disease in ducks in Africa.

Birds.—Sibley (107) reported the occurrence in siskins of a disease caused by an acid-fast organism which produced leprosy-like lesions in the spleen, the tissue showing masses of bacilli with little tissue reaction. Noller (90) confirmed this, finding lesions in the spleen, liver, skin and lungs and to a slight extent in the cerebellum and the intestines.

Cattle, horses, sheep.—Several workers, including Bang (8), Meyer (83), Pallaske (96), Lienaux (60), Stockmann (111), and Lange and Berge (55) have reported the occurrence in these animals of an infectious disease caused by an acid-fast organism found in masses in the walls of the small intestine and in the mesenteric glands. The animal suffers from chronic diarrhoea and wasting, and dies in about a year. The bacillus is reported to have been cultured by Twort's method (on a killed culture of tubercle bacilli). Some of the writers consider this disease to be allied to tuberculosis, but others consider it to be more closely allied to leprosy.

Buffaloes.—Kok and Roesli (51) reported a skin disease in buffaloes, of which they had seen five cases, manifested by nodules in which acid-fast bacilli were found. They thought that it was skin tuberculosis, but suggested that it might be a form of leprosy. Lobel (61) made a thorough investigation of this disease, which he considers to be a form of leprosy, and recorded 21 cases. The disease is very chronic and produces nodules varying from 5 to 60 millimeters in diameter, sometimes discrete and sometimes massed, usually hard but sometimes soft and fluctuating and occasionally ulcerating. The affected areas are depigmented and depilated. Nasal lesions were seen in two cases. The lesions show masses of acid-fast bacilli. Attempts to cultivate them and to transmit the infection experimentally failed.

Opossum—Boyé (14) described leprosy-like lesions of the opossum (*Philander cancrivor*) with acid-fast bacilli in the inguinal glands. Jordan (46) examined a large number of opossums but failed to find any with such an infection, and also failed to infect these animals with human leprosy.

REFERENCES

(1) Afanador, A. Inoculation du bacille de Stéfansky dans les veines de rats bloqués. Compt. rend. Soc. Biol. **116** (1934) 1260–1261.

(2) Afanador, S. and Bernard, P. Evolution de la lèpre des rats après inoculations intraveineuses. Compt. rend. Soc. Biol. **116** (1934) 1257.
(3) Alexandrescu, J. "Lepra Sobolanilor." Thèse de Jasi, 1908.
(4) [Anonymous.] Report on plague investigations in India. Jour. Hyg. **7** (1907) 911.
(5) Asami, S. Rat leprosy in Northeastern Japan; cultivation of the organism; animal experiments with the cultures. La Lepro **3** (1932), No. 4.
(6) Asami, S. Histological investigations of spontaneous and experimental leprosy in rats. La Lepro **4** (1933), No. 1.
(7) Azevedo. (Rat leprosy in Brazil.) (*Quoted by* Leger.)
(8) Bang. (*Quoted by* Klingmüller, p. 135.)
(9) Barbezieux, G. Le lèpre en Indo-Chine. Presse Med. **53** (1911) 635.
(10) Bayon, H. The present position of leprosy research. Lepra **14** (1914) 50–62.
(11) Bernard, P. Localisation des bacilles de Stéfansky injectés dans la veine du rat. Bul. Soc. Path. exot. **27** (1934) 117–120.
(12) Berny, P. Effet comparatif de l'iode sur le rat lépreux. Bull. Soc. Path. exot. **26** (1933) 1237–1239.
(13) Berny, P. La bacilluria chez les rats lépreuses. Bull. Soc. Path. exot. **27** (1934) 910–912.
(14) Boye. Sur une maladie de la sarigue de Guane presentant de grandes analogies avec la lèpre humaine. Bull. Soc. Path. exot. **24** (1931) 637–639.
(15) Brinckerhoff, W. R. Rat Leprosy. United States Pub. Health Bull. No. 30, 1910.
(16) Brosse, E. La lèpre est-elle contagieuse? (*Quoted by* Klingmüller.)
(17) Bull, R. J. Leprosy-like disease of a rat. Intercolon. Med. Jour. Australasia **12** (1907) 263.
(18) Cantacuzene, J. and Longhin, S. Transmission expérimentale de la lèpre humaine au rat blanc. Compt. rend. Acad. Sci. **195** (1932) 533–535.
(19) Cantacuzene, J. and Longhin, S. De l'existence d'un ultra-virus chez le bacille de la lèpre humaine. Compt. rend. Soc. Biol. **109** (1932) 1003–1004.
(20) Chapin. United States Publ. Health Rep. **27** (1912) 161. (*Quoted by* Wolbach and Honeij.)
(21) Chorine, V. Conservation du bacille de Stéfansky. Bull. Soc. Path. exot. **27** (1934) 222–224.
(22) Chorine, V., Guilliny and Montestruc, E. Inoculation de bacilles de Stéfansky dans la chambre antérieure de l'oeil du rat. Compt. rend. Soc. Biol. **116** (1934) 1261.
(23) Cilento, R. W. and North, E. A. Human and murine leprosy in Tropical Australia. Preliminary notes and observations. Med. Jour. Australia **2** (1931) 767-775.
(24) Cook, C. The epidemiology of leprosy in Australia. Commonwealth of Australia, Dept. of Health Service Publication No. 38, 1927, p. 275.
(25) Currie, D. H. and Hollmann, H. T. Further observations on rat leprosy. Lepra **13** (1913) 17–24.
(26) Dean, G. A disease of rats caused by an acid-fast bacillus. Centralbl. f. Bakt., Orig. **34** (1903) 222–224.
(27) Dean, G. Further observations on a leprosy-like disease of the rat. Jour. Hyg. **5** (1905) 99–112.

(28) DE SOUZA-ARAUJO, H. C. Experimental leprosy. Trans. Roy. Soc. Trop. Med. and Hyg. **24** (1931) 577–598.

(29) EHLERS, E., BOURRET, G. and WITH. Recherches sur le mode de propagation et les procédés de diagnostic bacteriologique de la lèpre. Bull. Soc. Path. exot. **9** (1911) 253.

(30) EMERSON, G., ANDERSON, H. H. and LEAKE, C. D. Lipolytic activity of rat tissues in experimental leprosy. Proc. Soc. Exp. Biol. and Med. **30** (1932) 150–152.

(31) EMERSON, G., ANDERSON, H. H. and LEAKE, C. D. Lipolytic activity of rat lepromata during treatment with various antileprotics. Proc. Soc. Exp. Biol. and Med. **31** (1933) 18–20.

(32) FAYRER. (*Quoted by* Klingmüller, p. 135.)

(33) FIELDING, J. W. Observations on rodents and their parasites. Jour. and Proc. Roy. Soc. New South Wales **41** (1927) 115.

(34) FRANCHINI, G. and CENDALI, G. (Experimental leprosy in the monkey and the white rat.) Arch. Italiano Sci. Med. Colon, Tripoli **8** (1927) 3–6.

(35) FRASER, H. Fourteenth Annual Report of the Institute for Medical Research, Kuala Lumpur, Federated Malay States.

(36) FRIEDHEIM, E. A. H. L'origine de la cellule lépreuse étudiée en culture de tissu. Compt. rend. Soc. Biol. **100** (1929) 163–165.

(37) FUKAMACHI, T. (Application of rat leprosy to the study of therapy of human leprosy. Pathological and histological study of rat leprosy.) Nippon no Ikai **7** (1927), No. 46.

(38) GERBINIS, P. Essai de culture du bacille de Stéfansky. Bull. Soc. Path. exot. **26** (1933) 1135–1137.

(39) GILLIER, R. and TISSEUIL, J. Essai de traitement de la lèpre du rat. Troisieme serie. Bull. Soc. Path. exot. **27** (1934) 189–199.

(40) GUILLINY, R. and MONTESTRUC, E. Étude sur la lèpre oculaire murine. Bull. Soc. Path. exot. **26** (1933) 901–905.

(41) HENDERSON, J. M. A contribution to the pathology of cutaneous rat leprosy. Indian Jour. Med. Res. **16** (1928) 1–5.

(42) HOLLMANN, H. T. Cultivation of an acid-fast bacillus from a rat suffering with rat leprosy. United States Publ. Health Rep. **27** (1912), No. 3.

(43) HONDA, I. Sur une maladie ressemblant á la lèpre de l'homme chez les rats. Tokyo Igakukwai Zashi **22** (1908), No. 20.

(44) IITOYO, K. and SAKAI, G. Sur la lèpre du rat. Saikingaku Zasshi. *Also* Centralbl. f. Bakt. **48** (1910) 690.

(45) ISHAWARA, T. Ueber die Rattenlepra. Centralbl. f. Bakt. **67** (1913) 446–450.

(46) JORDAN, P. (A preliminary note on the opossum as an experimental animal in leprosy.) Folia. Clin. et Biol. São Paulo **3** (1934) 85–88.

(47) KAWAMURA. (*Quoted by* Kitasato, 1910).

(48) KITASATO. Die lepra in Japan. Proc. 2nd Internat. Conf. on Lep., Bergen, 1909. (1910).

(49) KLINGMÜLLER. Die Lepra. Berlin, 1930, pp. 134–141.

(50) KOCH, F. Die Rattenlepra und ihre Bedeutung fur klinik Pathogenese und Therapie der menschlichen Lepra. Centralbl. f. Haut- u. Geschlechtskrankh. **40** (1932) 433–440.

(51) KOK, J. and ROESLI, M. Huid-tuberculose (?) bij buffels. Ned. Ind. Bl. Diergeneesk. (1926) 465.

(52) LAIGRET, J. Sensibilité de l'homme au bacille de la lèpre murine. Arch. Inst. Past. Tunis **21** (1932) 290–293.

(53) LAIGRET, J. Réproduction de la lèpre murine chez le cobaye at chez le lapin, traités par un extrait acétonique de bacilles tuberculeux. Compt. rend. Acad. Sci. **197** (1933) 1468–1470.

(54) LAMPE, P. H. J. and DE MOOR, C. E. Ratten-lepra. Geneesk. Tijdschr. v. Nederlandsch-Indië **8** (1935) 634–654.

(55) LANGE and BERGE. (*Quoted by* Klingmüller.)

(56) LEBOUF, A. Existence de *lepra murium* en Nouvelle-Calédonie. Bull. Soc. Path. exot. **5** (1912) 463.

(57) LEGER, M. Lepra murium à la Guyane française. Bull. Soc. Path. exot. **12** (1919) 169.

(58) LE GUYON, R. Sur l'étiologie de la lèpre des rats. Allaitement croise par des mères saines de jeunes rats issus de mères lépreuses et inversement. Compt. rend. Soc. Biol. **108** (1931) 792–794.

(59) LEPINE, P., MARKIANOS, J. and BILFINGER, F. Essais d'adaptation du bacille de Hansen a l'organisme du rat blanc. Bull. Soc. Path. exot. **27** (1934) 373–384.

(60) LIENAUX. (*Quoted by* Klingmüller, p. 135.)

(61) LOBEL, L. W. M. Lepra Bubalorum. Utrecht, 1934.

(62) LOWE, J. A note on the action of chaulmoogra (Hydnocarpus) preparations on *M. leprae muris*. Lep. in India **9** (1934) 79–83.

(63) LOWE, J. Studies in rat leprosy. Indian Jour, Med. Res. **22** (1934) 187–198.

(64) LOWE, J. A note on the staining of *Mycobacterium leprae* in tissue sections. Indian Jour. Med. Res. **22** (1934) 313–315.

(65) LOWE, J. The application of tissue culture methods to leprosy research. Lep. in India **7** (1935) 19–22.

(66) MARCHOUX, E. Rôle des infections secondaires dans le dévelopment de la lèpre du rat. Bull. Soc. Path. exot. **5** (1912) 466–468.

(67) MARCHOUX, E. Transmission de la lèpre par les mouches. Ann. Inst. Past. **30** (1916) 61–68.

(68) MARCHOUX, E. La lèpre du rat et de l'homme. Proc. 3rd. Int. Conf. on Lep. Strasbourg, 1923.

(69) MARCHOUX, E. and CHORINE, V. Résistance du bacille de la lèpre du rat aux acides et aux alcalis. Bull. Soc. Path. exot. **25** (1932) 1025–1026.

(70) MARCHOUX, E., MARKIANOS, J. and CHORINE, V. Le bacilles de la lèpre a-t-il été obtenu en cultures artificielles? Compt. rend. Soc. Biol. **106** (1931) 1191–1192.

(71) MARCHOUX, E. and SOREL, F. La lèpre des rats. Ann. Inst. Past. **26** (1912) 675–700.

(72) MARCHOUX, E. and SOREL, F. La lèpre des rats. Recherches étiologiques et réflexions qu'elles suggerent à propos de la lèpre humaine. Ann. Inst. Past. **26** (1912) 778–801.

(73) MARKIANOS, J. Filtration du virus de la lèpre des rats. Bull. Soc. Path. exot. **22** (1929) 410–411.

(74) MARKIANOS, J. Le developpement du virus filtrant avant sa transformation en bacilli de la lèpre des rats. Bull. Soc. Path. exot. **22** (1929) 537–538.

(75) MARKIANOS, J. Le rôle des poux dans la transmission de la lèpre. Bull. Soc. Path. exot. **22** (1929) 633–635.

(76) MARKIANOS, J. Developpement rapide du virus filtrant de la lèpre des rats après inoculation aux jeunes rats. Bull. Soc. Path. exot. **22** (1929) 758–759.
(77) MARKIANOS, J. L'ultra-virus de la lèpre des rats. Bull. Soc. Path. exot. **22** (1929) 896–897.
(78) MARKIANOS, J. Essai de traitement de la lèpre des rats pas les bacilles degraissés. Bull. Soc. Path. exot. **23** (1930) 145–148.
(79) MARKIANOS, J. Recherche sur l'action preventive sur la lèpre des rats d'antigene de bacilles degraissés. Bull. Soc. Path. exot. **23** (1930) 149–150.
(80) MARKIANOS, J. Essai de traitement de la lèpre murine. Bull. Soc. Path. exot. **22** (1930) 268–272.
(81) MARKIANOS, J. Lèpre et virus filtrable. Ann. Inst. Past. **46** (1931) 292–295.
(82) MCCOY, G. W. Leprosy-like disease in rats. United States Publ. Health Rep. (1908), July 10.
(83) MEYER, K. F. Proc. Path. Soc. Philadelphia. (*Quoted by* Klingmüller, p. 135.)
(84) MEZINESCU. Maladie lépreuse des rats et ses relations avec la lèpre humaine. Compt. rend. Soc. Biol. **64** (1908) 514.
(85) MUIR, E. and HENDERSON, J. M. Rat Leprosy. Indian Jour. Med. Res. **15** (1928) 807–817.
(86) MUIR, E., HENDERSON, J. M. and LANDEMAN, E. Tumour-like growths caused by intraperitoneal inoculation of *B. leprae murium*. Indian Jour. Med. Res. **15** (1927) 15–19.
(87) MUIR, E. The leprolin test. Lep. in India **5** (1933) 204–218.
(88) NAKAMURA, K. and NOBASHI, S. Inoculation of human leprosy into rats. Keijo Jour. Med. **5** (1934) 184–189.
(89) NODENOT, L. and BERNY, P. Inoculation du bacille de Hansen dans le péritoine de rats après blocage. Bull. Soc. Path. exot. **26** (1933) 989–990.
(90) NOLLER, W. Centralbl. f. Bact. **84** (1927) 476.
(91) NORTH, E. A. Investigation in Rockhampton into the possible relationship between human and rat leprosy. Health (Canberra) **8** (1930) 67–74.
(92) OHTAWARA, T. and ICHIHARA, T. Studien der Lepra. I. Mitteilung. Statistische Betrachtung der Rattenlepra. Centralbl. f. Bact. **123** (1932) 495–503.
(93) OHTAWARA, T. and ICHIHARA, T. Studien der Lepra. III Mitteilung. Das Verhatten der Geschlechlsdrusen den Rattenleprabazillen gegenuber. Centralbl. f. Bakt. **134** (1935) 316–318.
(94) OLIVER, J. The origin of the lepra cell. Jour. Exp. Med. **43** (1926) 233–239.
(95) OTA, M. and ASAMI, S. Culture du *Mycobacterium leprae muris* Compt. rend. Soc. Biol. **111** (1932) 287–289.
(96) PALLASKE, S. Virchow's Arch. **263** (1927) 189. (*Quoted by* Klingmüller, p. 135.)
(97) PERRIE and MCALISTER. (*Quoted by* Klingmüller, p. 135.)
(98) PRIESTLEY, H. Rat leprosy in North Queensland. Australasian Med. Gaz. **34** (1913) 405.
(99) PRUDHOMME, R. Actions de rayons X sur les lepromes des rats. Bull. Soc. Path. exot. **27** (1934) 917–920.
(100) RABINOWITSCH, L. Ueber eine durch saurefeste Bacterien hervorgerufene Hauterkrankung. Centrabl. f. Backt. **33** (1903) 755–580.
(101) RICHARDS, R. E. Rat leprosy in Rockhampton. Health (Canberra) **5** (1927) 117.

(102) RIDLONG, J. R. Notes on leprosy in rats. United States Publ. Health Rep. **28** (1913) 1447–1448.

(103) ROW, R., DALAL, N. P. and GOLLEKERI, G. V. On some experimental studies on leprosy. Indian Jour. Med. Res. **21** (1934) 545–552.

(104) SALLE, A. J. Acid-fast organisms from leprous lesions. Cultivation in tissue cultures and other mediums. Jour. Inf. Dis. **54** (1934) 347.

(105) SALLE, A. J. and MOSER, J. R. Bacteriology of leprosy. II. Growth and staining reactions of organisms inoculated into minced chick embryo medium. Proc. Soc. Exp. Biol. and Med. **31** (1934) 725–726.

(106) SALLE, A. J. and MOSER, J. R. Bacteriology of leprosy. III. Growth and staining reactions of acid-fast organisms inoculated into minced animal tissues. Proc. Soc. Exp. Biol. and Med. **31** (1934) 727–728.

(107) SIBLEY, W. Lancet (1890). (*Quoted by* Klingmüller, p. 135.)

(108) SIMOND. La lèpre et ses modes de propagation à la Guyane française. Thèse de Bordeaux, 1887. (*Quoted by* Klingmüller, p. 135.)

(109) SOULE, M. H. The relationship of human and rat leprosy. Internat. Jour. Lep. **3** (1934) 291–310.

(110) STEFANSKY, W. Eine lepra-ähnliche Erkranking der Haut und der Lymphdrusen bei Wanderratten. Centralbl. f. Bakt. **22** (1903) 481–487.

(111) STOCKMANN, S. Rept. Chief. Vet. Off., Board. Agriculture, London. 1909. (*Quoted by* Klingmüller, p. 135.)

(112) TAKEUCHI. (*Quoted by* Klingmüller, p. 136.)

(113) THEZE. (*Quoted by* Leger.)

(114) TIDSWELL, F. Note on a leprosy-like disease in rats. Report of the Board of Health on Leprosy in New South Wales. 1904.

(115) TISSEUIL, J. Première serie d'essais de traitement de la lèpre chez le rat. Bull. Soc. Path. exot. **25** (1932) 969–976.

(116) TISSEUIL, J. Nouvelle serie de traitement de la lèpre du rat. Bull. Soc. Path. exot. **26** (1933) 579–584.

(117) TISSEUIL, J. and BERNY, P. Inoculation du bacille de Hansen directement dans le foie des rats. Bull. Soc. Path. exot. **26** (1933) 990.

(118) TISSEIUL, J. and CHORINE, V. La coloration par la fuchsine ne tue pas le bacille de Stéfansky. Bull. Soc. Path. exot. **27** (1934) 12–17.

(119) TISSEUIL, J. and GILLIER, R. Inoculation testiculaire de la lèpre humaine au rat. Bull. Soc. Path. exot. **26** (1933) 1134–1135.

(120) UCHIDA, M. Sur les microbes acido-resistants isolés des rats lépreux. Saikingaku Zasshi (1923), No. 328.

(121) UCHIDA, M. A study of the diseases of the eyes in cases of rat leprosy. Histological examination of the eyes of the leprous rat. La Lepro **3** (1932), No. 4.

(122) VADON. Ann. Hyg. Med. Colon. (1914) 512.

(123) VALTIS, J. and MARKIANOS, J. Influence du B.C.G. sur la lèpre murine. Compt. rend. Soc. Biol. **103** (1930) 483–485.

(124) VAN ES., L. and MARTIN. Nebraska Exper. Stat. Res. Bull. No. 30. (*Quoted by* Klingmüller, p. 135.)

(125) WALKER, A. A report of some cases of rat leprosy. Jour. American Med. Assn. **51** (1908) 1153.

(126) WALKER, E. L. Some new aspects of the etiology and endemiology of leprosy. Jour. Prev. Med. **3** (1929) 167–195.

(127) WALKER, E. L. and SWEENEY, M. A. The chemotherapeutics of the chaulmoogric acid series and other fatty acids in leprosy tuberculosis. Jour. Inf. Dis. **26** (1920) 238–264.

(128) WALKER, E. L. and SWEENEY, M. A. The identity of human leprosy and rat leprosy. Jour. Prev. Med. **3** (1929) 325–333.

(129) WALKER, E. L. and SWEENEY, M. Microscopic demonstration of acid-fast bacilli in tuberculous filtrates. Jour. Infec. Dis. **54** (1934) 182–193.

(130) WALKER, E. L. and SWEENEY, M. Cultivation of facultative acid-fast bacteria from filtrates of leprosy. Proc. Soc. Exp. Med. and Biol. **31** (1934) 1162–1163.

(131) WALKER, E. L. and SWEENEY, M. Culture of lepra bacillus from filtrates from bacterial filters. Jour. Infec. Dis. **57** (1935) 97.

(132) WATANABE, Y. Experimental studies on animals concerning leprosy. Report II. Inoculation tests with human leprosy. Part I. Kitasato Arch. Exp. Med. **12** (1935) 139–153.

(133) WATANABE, Y. Experimental studies on animals concerning leprosy. Report III. The effect of potassium iodide on animals inoculated with leprosy. Kitasato Arch. Exp. Med. **12** (1935) 304–312.

(134) WAYSON, N. E. Personal communication.

(135) WELLMAN, C. and HAND, A. Experiments with culture media suitable for use in the tropics. Jour. Trop. Med. and Hyg. **15** (1912) 300–307.

(136) WHERRY, W. B. The leprosy-like diseases among rats on the Pacific coast Jour. American Med. Assn. **50** (1908) 1903.

(137) WHERRY, W. B. Further notes on rat leprosy and on the fate of human and rat lepra bacilli in flies. United States Publ. Health Rep. (1908), October 16; *also*, Jour. Inf. Dis. **5** (1908) 507–514.

(138) WHERRY, W. B. Experiments in vaccination against leprosy. Jour. Inf. Dis. **6** (1909).

(139) WILSON. Tuberculous bacillaemia. Special report, series No. 182, Medical Research Council. 1933.

(140) WOLBACH, W. B. and HONEIJ, J. A. A critical review of the bacteriology of human and rat leprosy. Jour. Med. Res. **29** (1914) 367–423.

(141) ZINSSER, H. and CAREY, E. G. A contribution to the study of rat leprosy. Jour. American Med. Ass. **58** (1912) 692–695.

DESCRIPTION OF PLATES

PLATE 43

FIG. 1. Naturally acquired rat leprosy. Alopecia. (Photograph from Dr. P. H. J. Lampe.)

FIG. 2. Rat leprosy, showing involvement of cervical, axillary and inguinal lymph nodes, and of internal organs. (Photograph from Dr. P. H. J. Lampe.)

FIG. 3. Rat leprosy produced by intraperitoneal inoculation. Marked lesions of liver and spleen and great thickening of omentum.

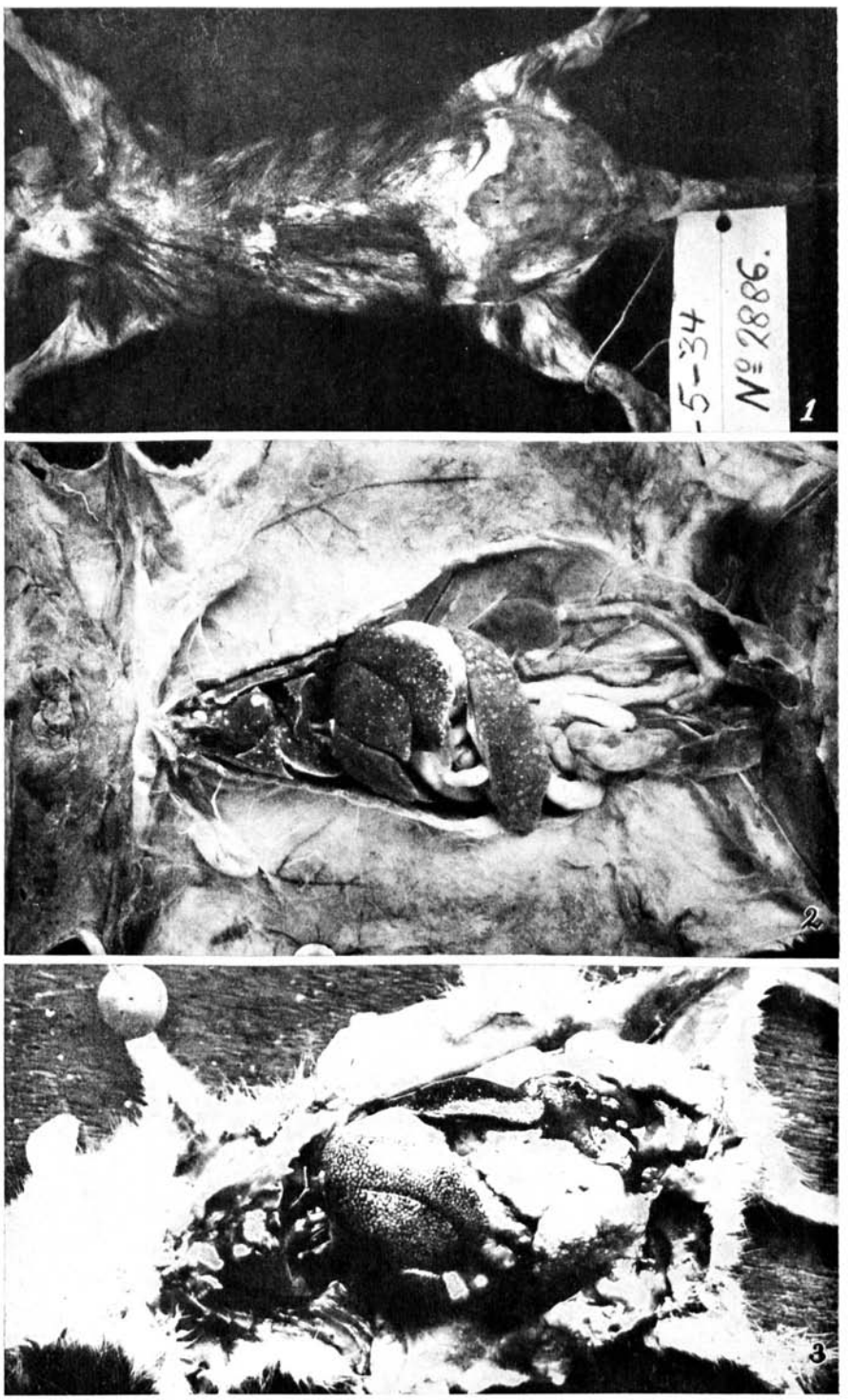

PLATE 43

PLATE 44

FIG. 4. Rat leprosy. Enormously enlarged omentum and involvement of liver and spleen after intraperitoneal inoculation.

FIG. 5. Rat leprosy. Marked involvement and enlargement of liver.

FIG. 6. Rat leprosy. Breaking down and ulceration of inguinal lymph nodes after subcutaneous inoculation in the thigh.

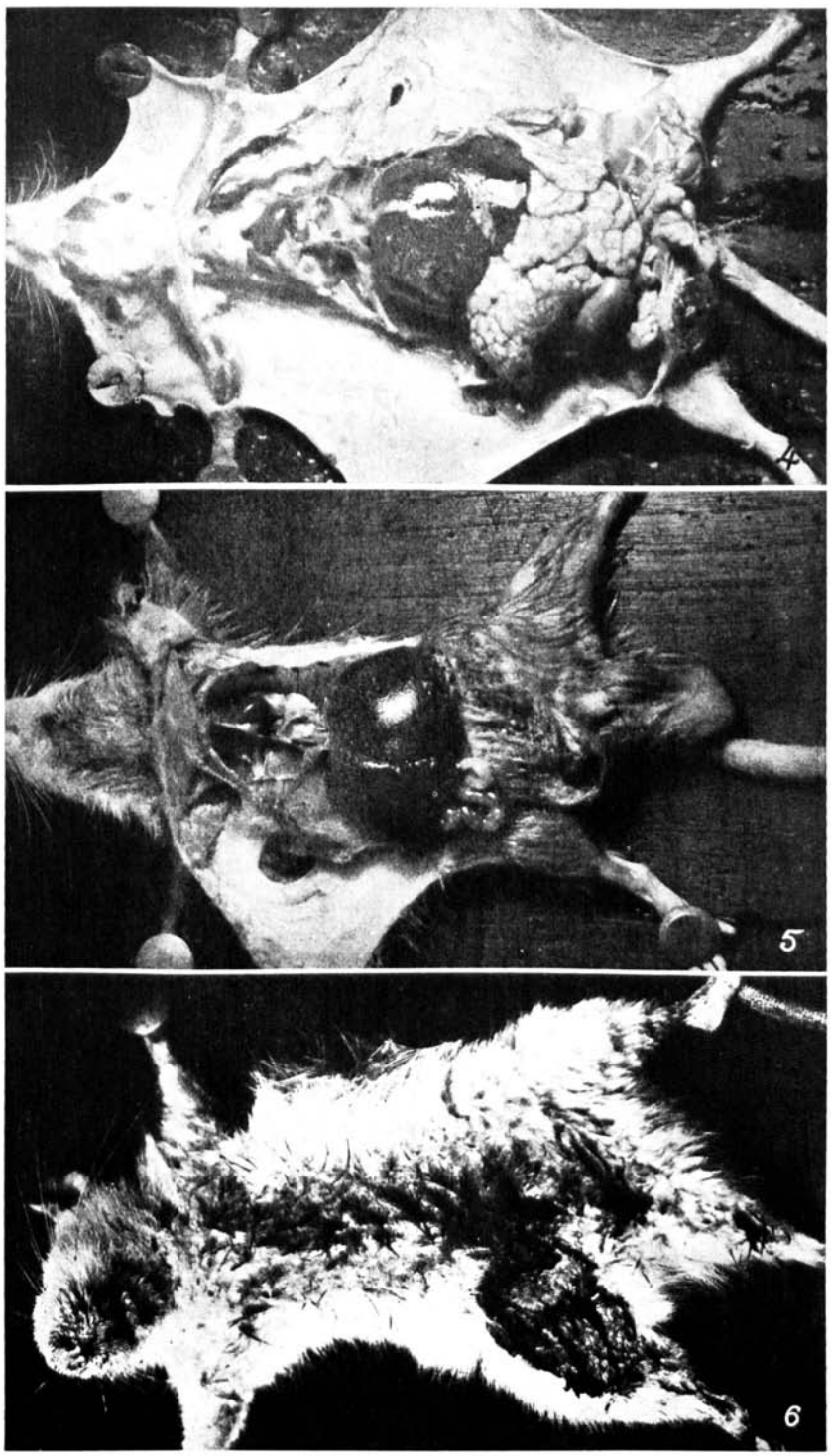

PLATE 44