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HISTOLOGICAL STUDY OF AN EARLY CASE OF LEPROSY IN A YOUNG CHILD OF LEPROUS PARENTS

REPORT OF A CASE, WITH AUTOPSY *

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So far as the writers are aware, no autopsy reports on early leprosy in very young children of leprous parents have been recorded. Most of the available reports of the disease in children concern clinical cases; those which have been found are summarized below. The present case is placed on record because of the unusual circumstance that the child died and was autopsied at the early age of a little over 17 months, only two months after the infection was discovered. A detailed study of the autopsy material has been made to determine the possible manner of infection.

PREVIOUS REPORTS OF EARLY LEPROSY IN CHILDREN

Goodhue and McCoy (2), in 1916, reported the case of a female child, 19 months old, born of leprous parents and removed to clean surroundings six hours after birth. The only affection from which she suffered was scabies. At the age of 19 months she had a triangular leucodermic area on the right cheek, and on the back of each thigh a few irregularly shaped similar areas of doubtful nature, not anesthetic. On the flexor surface of the left forearm was a reddish brown nodule, 12 × 8 mm., projecting about 2 mm. above the surface, said to have appeared two weeks before the day of the examination. This lesion was excised and found positive for acid-fast bacilli, in both smears and sections. The histology was that of a lepromatous nodule.

In a subsequent report on the same case, by Goodhue and Hasseltine (1), in 1924, it was stated that the biopsy scar was free from acid-fast bacilli four months after the operation, but three months later a few atypical acid-fast organisms were obtained from it and the child was then declared leprous. When 10 years of age she was reexamined, with negative findings, and was considered to be free from the disease. The authors attributed the clearing up of the disease to the surgical removal of the nodule eight years before.

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In their report Goodhue and McCoy stated that they had not found an authentic record of a case as young as theirs, except one observed in Japan by Nakajo (8) the report of which was available to them only as an abstract, cited as follows:

The writer reports the case of a 3-months-old child whose parents were lepers. Sections of the skin showed typical leprosy infiltrations and lepra bacilli. When the child was born the writer looked for lepra bacilli in the umbilical and placental blood with negative results.

Tardieu (16), also in 1916, reported the case of a child nursed by its leprosy mother for three months. At the age of one month there were observed over the body several pimples and erythematous patches which were confirmed to be leprosy. Numerous nodules developed, and Hansen's bacilli were found in the nasal mucous membrane when the child was five months old. The possibility that this was an "instance of heredity" was discussed. If it was one of contagion, the evolution was considered extremely rapid.

Henry (3), in 1924, reported the case of a child three years old who had been separated from his leprosy parents two months after birth. The first sign of the disease was a red patch on one thigh. Two months later this lesion had become larger and showed anesthesia, and two further patches had appeared on the limbs. The exposure to infection was only two months, the "incubation period" three years.

Neff (9), in 1926, reported a case in a 14-months-old child who developed a papulo-nodule on the cheek, in which numerous acid-fast bacilli were found. The nasal mucus was found negative on several occasions, until four months later when other nodules appeared on the face. Treatment by moogrol checked the progress; the original nodule was absorbed, leaving a scar the size of a shilling, but the small nodules left very small scars. The case was bacteriologically negative after seven months and had remained so for several months at the time of the report.

Montero (7), in 1927, reported the case of a child born prematurely in the eighth month and removed immediately from leprosy surroundings. It was not suckled once by the mother. He demonstrated leprosy bacilli in the placental tissues and blood of the umbilical cord, and also in serum obtained by dry cupping. The child died six weeks later with diarrhoea and generalized pemphigus, and the bacillus was also found in the fluid of those lesions.

Tisseuil and Berny (18) reported a 10-months-old child who showed on the right leg a tawny spot that rapidly developed into a nodule the size of a kidney bean and that contained numerous bacilli.

Lara and de Vera (5, 6), in 1935, reported cases of very early leprosy in children born at Culion and pointed out the occurrence of an unrecognized characteristic leprosy papule which is usually positive for *M. leprae*.

Souza Campos (14), in 1937, reported on the clinical aspects of tuberculoïd leprosy in 28 children of leprosy parents varying in age from 13 months to 13 years. He classified the lesions observed into four types: (a) nodular, (b) papulate, (c) lichenoid, with miliary papules, and (d) Boeck's sarcoid. He called attention to the scars left by these le-

sions, whose peculiar features permit a retrospective diagnosis when the cases give a strongly positive lepromin reaction.

Tisseuil (17), also in 1937, reported four children aged 2, 3, 6 and 7 years and a girl of 15 years in each of whom he observed a single lesion on the face. This consisted of a red, raised nodule which spread in the healthy skin and cicatrized centrally. The structure was tuberculoid. These lesions were regarded as "primary leprous chancres."

One of us (C.B.L.) reported in 1938 (4) 35 cases of very early leprosy in children born at Culion and described—in addition to the leprotic papules previously described by Lara and de Vera—lesions with a rather marked resemblance to minute wheals: urticariform, or of mosquito—or ant-bite appearance. Some of these wheal-like, maculo-papular lesions were so minute that they would have been overlooked except for the use of a hand lens. It was pointed out that lesions of this type when first noticed may be smaller than an ordinary pinhead or several millimeters in diameter; they may be either distinctly papular, but not acuminate, or almost imperceptibly raised; they feel slightly infiltrated, or distinctly indurated, or shotty, as the finger is stroked over them. Usually faint pinkish or purplish, they are sometimes of a deep red color.

Souza Campos (15) reported very recently two cases of leprosy in children, 20 and 30 months old, with papuloid lesions that rapidly underwent suppuration. He classified these cases as of reactional tuberculoid leprosy, the evolution of which is toward spontaneous cure. The author emphasized the benignity of certain forms of leprosy in infancy, mainly the lesions of tuberculoid nature, which always heal spontaneously since they are not exposed to superinfection. He again called attention to the cicatricial aspect of the healed lesions.

In a more recent report by Nolasco and Lara (12) on a histological study of 14 cases of leprosy in very young children it was pointed out that the early, papular, thickened lesions noted in such cases might, because of their multiple localization and their tendency to show bacilli very early—as soon as they are discovered clinically—be considered primary inoculation lesions, comparable to the primary focal lesions of tuberculosis in the lung parenchyma of children (10).

REPORT OF CASE

The present report deals with the case of a child 17 months and 8 days old at the time of death, who two months previously had been found to have a heavily bacillated (4+) wheal-like lesion about the middle of the right knee.

A male child born normally on July 2, 1937, weight 5 lbs. 5 oz. Not separated from the leprous parents, both of whom were LI-N1 cases. Hospitalized for cough and fever on November 26, 1938, robust, weight 22 lbs. 6 oz. Died of empyema following lobar pneumonia on December 10th, after 14 days in the hospital. Autopsy performed on December 11th, about nine hours after death.

The following is an abstract of the protocol of previous skin blemishes as observed by one of us (C.B.L.) in the regular bimonthly physical examinations.

First examination, August 9, 1937: Free from active skin eruptions. Second examination, October 16, 1937: Pin-point to pin-head or larger reddish vesico-papules on abdomen, chest and back; a few on arms, groin, ankles and legs. Depigmented mottlings laterally on abdomen and on both legs from the knees to the ankles, said to be previous sites of vesicular eruptions. Third examination, December 8, 1937: Fairly numerous, fresh, pinkish, thickened, small scars on feet and lower legs, left forearm and hand, right thigh and left shoulder. Some of those on the hands and feet are still crusted. Fourth examination, February 10, 1938: Fairly numerous small to large pea-sized, drying, superficial vesico-papules scattered on face, trunk and extremities, more numerous on the feet and ankles; many still crusted, some already healed but still thickened. A few crusted eruptions on superior scalp. All of the lesions described are probably scabitic.

Fifth examination, April 12, 1938: Fairly numerous pale scars with dark borders on trunk and extremities. A number of pin-head to pea-sized vesiculated papules, upper back, anterior left shoulder. Bean-sized superficial ulcer, upper external right knee. No definitely suspicious lesions. Sixth examination, June 10, 1938: Numerous depigmented scars, probably of scabies, on trunk, and forehead. In the right lower dorsal region is a small hypo-pigmented area, 15×5 mm. *Bacteriological smear* from this area, negative for acid-fast bacilli. Seventh examination, August 1, 1938: A number of drying pea-sized scabies lesions, posterior upper right thigh, left buttock, posterior legs, both knees, and around both ankles. Two small pea-sized vesico-papules, anteriorly on right thigh. Thickened scar on left elbow. No definite suspicious lesions.

Eighth examination, October 8, 1938: On the right knee, about the center, is a thickened, slightly shiny, pale, wheal-like area, 6×5 mm., rather suspicious in appearance; no other suspicious lesions. *Bacteriological smear*: bacilli found, abundant (4+), with many globi.

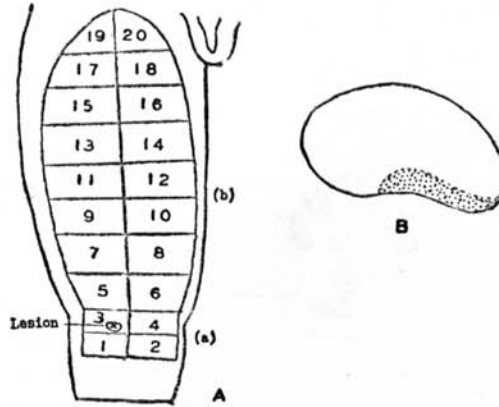
Final examination, December 8, 1938, two days before death: Child in the hospital, very ill and quite weak, suffering from lobar pneumonia. The previously positive lesion on the right knee is now a brownish, slightly depressed, nonindurated scar, not distinguished from other scars of similar size and appearance around it. No new suspicious lesions.

AUTOPSY FINDINGS

The principal condition found with respect to the cause of death was lobar pneumonia of the right basal and middle lobes with secondary seropurulent pleuritis, the quantity of fluid being about 200 cc.

As regards the leprous lesion on the right knee discovered two months before, nothing could be identified in this region except the nonindurated scars which have been mentioned. Because of this fact, the following procedure was followed in searching for the unidentifiable lesion.

Procedure.—A rectangular transverse piece of skin 1.7×3 cm. was excised from the middle of the right knee, extending in depth to the patella (see diagram Aa, Text-fig. 1). For histological demonstration of the possible upward extension of the leprotic infection along the nerve trunks or lymphatics another piece of skin, pyramidal in shape, 8×5 cm., was excised above the knee up to the middle of the fold of the groin, including all of the subcutaneous fat (Ab, Text-fig. 1). The inguinal lymph nodes on both sides were excised *en masse* and fixed without sectioning to avoid warping and possible loss of tissue in preparing them for embedding. The axillary and peribronchial lymph nodes were similarly preserved. The ulnar, superficial and deep peroneal, and posterior tibial nerves on both sides were dissected as far as their limits would permit. Pieces of the visceral organs (heart, lung, spleen, liver, kidney, adrenals and testes) were also taken for routine histological examination. All tissues were fixed in Zenker's fluid, preserved in 80 percent alcohol until studied, and sectioned in paraffin.



TEXT-FIG. 1. A, diagram of right thigh, showing (a) the site of the skin specimen removed from the knee and (b) that of the thigh; also the blocks into which they were cut for examination and the one in which the clinically vanished lesion was found histologically. B, diagram of the largest of the right inguinal lymph nodes, the shaded part representing the region in which acid-fast bacilli were found in the largest numbers.

The specimens were prepared for embedding as follows: (a) The rectangular piece of skin from the knee (Aa) was divided into four approximately equal pieces and marked 1, 2, 3 and 4, as shown in the diagram. They were embedded separately in such a way as to produce the usual transverse skin sections, beginning with their lower or inferior edges and passing upward. Each specimen was cut serially and completely, from three to seven sections being mounted on each slide. Every twentieth slide (1st, 20th, 40th, etc.) of each series was stained with eosin and hematoxylin, to locate the site of the clinically vanished lesion.

(b) The pyramidal piece of skin from the thigh (Ab) was cut longitudinally and each strip divided transversely into eight more or less rectangular pieces, making a total of 16 blocks which were numbered from 5 to 20 as shown in the diagram. From the lower edge of each of these blocks

a few sections were cut with the object of studying the possible centripetal manner of spread of the infection.

(c) The groups of lymph nodes were carefully dissected from the enveloping tissue and each was split longitudinally, parallel to its flat surface. There were 9 right inguinal nodes, 8 left inguinals, 9 right axillaries, 8 left axillaries, and 4 peribronchials, or 38 nodes in all. Only a few sections from each of these specimens were examined, particularly for acid-fast microorganisms.

(d) Cross sections of the upper and lower ends of each nerve, together with longitudinal sections of the main pieces also taken from the ends, were studied.

Representative slides from all of the skin blocks were stained with eosin and hematoxylin, Voerhoff's elastic tissue stain, Mallory's aniline blue stain, and for acid-fast bacilli. Sections from all of the lymph nodes, nerves and visceral organs were stained with eosin and hematoxylin and for acid-fast microorganisms.

HISTOLOGICAL FINDINGS

Specimen from the knee.—The sections of three blocks—taken at 20-slide intervals, as described—showed no important histological changes, except the presence of superficial scars. In block 1 (8 slides examined) there were two long scars; in block 2 (10 slides) one small scar near one end of the section; and in block 4 (9 slides) two long scars, one located near one end of the section and another long one at about the middle of the section. In block 3, however, round cells were found about sweat-gland coils in the first slide, and pathological changes were also found in the next five slides (Nos. 20 to 100); slides 120, 140, and 166 showed no important changes.

The histological changes found in this block at 5-slide intervals (Nos. 25 to 70) are as follows: Moderate to marked collections of small and large round cells around blood vessels, hair follicles, sweat gland coils and ducts, distributed in all layers of the corium and in places extending to the superficial layer of the subcutaneous fat (Plate 11, Fig. 1). A very few faint, pinkish, large monocytes in the round-cell collections. The cytoplasm of some of the large monocytes in the larger collections deep in the corium is vacuolated (Fig. 2). Portions of the corium between the round-cell collections are quite cellular, due to large monocytic infiltration. The smooth muscles about three hair shafts are split far apart into smaller bundles by the cellular reaction. A small nerve trunk deep in the corium, close to the subcutis, shows slight lymphocytic and large monocytic infiltration. The greater portion of the lesion is located in the

deep corium, but a small portion of it in one slide is in contact with the epidermis. There are no epithelioid or tuberculoid foci and no giant cells. This lesion is apparently a very young, heavily bacillated leproma, with early formation of foamy cells.

Concerning the presence of scars, four are found, two very old and two fairly cellular and apparently more recent. One is small, cellular, 0.2 mm. wide, in relation to one end of the cellular collections in the deeper corium (Fig. 3). Another is superficial, very long (3.2 mm.), one-half of it over the perivascular round-cell collections in the corium. A third is recent, cellular and relatively large (1.4 mm. long and 0.2 mm. thick), located over the middle of the lesion; it probably resulted from the incision made in the last bacteriological examination. The fourth scar is a stretch of markedly atrophic thin epidermis, 1 mm. long over the border of the lesion.

In a slide stained for acid-fast microorganisms, abundant bacilli and globi were found in the lesion, the globi within vacuoles in the large monocytes. In the connective tissue trabeculae of the deep subcutaneous fat, as far as 2.1 mm. below the surface of the epidermis, isolated bacilli and some globi were also demonstrated within large monocytes (Plate 12, Fig. 4). The thickness of the corium is only 0.6 mm. Sections from blocks 1, 2 and 4 were all negative for bacilli.

Specimen from the thigh.—From each of the sixteen blocks into which this specimen was divided, one eosin-hematoxylin stained slide was examined. No important changes could be found, though in one block (No. 11) there were some apparently insignificant collections of small round cells in the corium. Sections from this block were examined for bacilli, but none could be demonstrated. The nerve trunks in the subcutis appeared in all instances to be normal and undisturbed, without cellular collections.

Lymph nodes.—Right inguinal group (18 sections from 9 nodes): In the largest node of this group acid-fast bacilli in small groups, with a few globi (Fig. 5), were found within large monocytes mixed together with pigment. The bacilli were most numerous in the cortical portion of the gland, beneath the capsule near one end of the organ at the hilum (Text-fig. 1, B). Rare isolated bacilli were also found in other parts of the same node (Fig. 6). The other nodes of this group were negative, except one much smaller one in which only one bacillus was found,

within a large monocyte. Histologically all of these nodes show a general, uniform disturbance of the lymphoid architecture; the germinal centers are indistinct. The one containing numerous bacilli is similar to the others, showing no histological change that would indicate the presence of the infection, except that it was the largest organ in the group.

In none of the other groups examined—left inguinal, 16 sections from 8 nodes; right axillary, 18 sections from 9 nodes; left axillary, 16 sections from 8 nodes; and peribronchial, 8 sections from 4 nodes—could any acid-fast bacilli be demonstrated. Histologically they are all similar to the infected right inguinal group.

Nerves.—One section of the right ulnar nerve (out of 6 sections, 2 transverse and 4 longitudinal), shows a few loosely-arranged small round-cell collections around a small-sized blood vessel in the nerve trunk. This area proved negative for acid-fast bacilli. No abnormal histological changes were found in the sections of the other nerves examined.

Visceral organs.—Spleen: lymph follicles inconspicuous, splenic pulp diffusely infiltrated with leukocytes and cellular debris; negative for acid-fast bacilli. Liver: cells show cloudy swelling and a little fatty infiltration; portal areas show some loosely-arranged round cells and some monocyte collections; negative for bacilli. Kidney, adrenal and heart: all show cloudy swelling. Testes, right and left: apparently normal, without any cellular collections. Lung: consolidation of lobar pneumonia; fibrin, leukocytes, red cells and cellular debris matted together in alveoli whose walls have disappeared in places.

DISCUSSION

The appearance of a single isolated lesion in this child, with abundant acid-fast bacilli in both smears and sections, the demonstration of the bacilli in fairly large numbers in the lymphatic nodes of the region of drainage of the single lesion, most conspicuous in the hilar portion of one of the two nodes found to be infected, and the failure to demonstrate bacilli in any of the other organs examined, indicate that the knee lesion in this case was very probably the one of primary inoculation.

The four isolated cases reported by Goodhue and McCoy (2), Henry (3), Neff (9) and Tisseuil and Berny (18), and the several others recorded by Lara and de Vera (6), Souza Campos (14), Tisseuil (17), Lara (4) and Nolasco and Lara (12) might

be regarded as instances of probable primary inoculation lesions of leprosy. Points in favor of this conclusion are the ages of the children when the lesions were discovered, the tendency of the lesions to appear as definitely isolated papular, nodular, or papulo-nodular elements which may be single or of multiple localization, and their tendency to show *M. leprae* very early, or as soon as they are discovered clinically. Evidence brought forward in the present report tends to substantiate the belief that the skin lesion is the primary inoculation lesion, comparable to the primary lesion or chancre of syphilis and to the primary focal lesions of tuberculosis in the lung parenchyma of children (10).

Although the possibility of "hereditary" or congenital leprosy, as reported by Tardieu (16) and Montero (7), cannot be denied, such congenital cases have apparently never been observed at or reported from Culion. In 58 children under 2 years of age that have been autopsied here, search being made for the leprosy bacilli in the deep organs (spleen, liver, lymph nodes and nerves), none could be demonstrated (11). It would appear that, if congenital leprosy ever occurs at all, its occurrence must be extremely rare.

Analyzing the protocol of the bimonthly clinical observations made of the present case by one of us (C.B.L.), after the fifth examination on April 12, 1938, and the seventh examination on August 1st, note was made of a bean-sized superficial ulcer on the upper external surface of the right knee and of drying, pea-sized scabies lesions on both knees; and two days before death "the four-plus positive lesion on the right knee was a brownish slightly depressed scar which could not be distinguished from similar scars around it." Serial histological sections of the four blocks of skin from the knee (Text-fig. 1, Aa) also revealed the presence of scars. In block 3, in which the lesion was located, three scars—aside from the distinctive one produced by the incision made in the bacteriological examination—were identified, all in apparent relation to the lesion in the corium below them. It is evident from these observations that the inoculation lesion in this case is in close association with previous breaches of the surface continuity of the skin, presumably due to scabies.

Rodriguez (13) has observed three cases in which enlarging macules started from scabies scars. Lara (4) has also mentioned a type of early leprotic skin manifestation in children that is

scar-like, slightly thickened and distinctly indurated, and which may be indistinguishable from neighboring scars of skin diseases; and he mentioned one undoubted case of the 35 in the series dealt with in which a wheal-like lesion developed from a scar-like depigmented area. Skin biopsy specimens from 14 of these cases were studied by Nolasco and Lara (12) and two lesions originally discovered clinically as scar-like areas were identified histologically as leprotic conditions in association with definite scars.

Concerning the spread of the infection from the skin in early leprosy, the present case definitely demonstrates spread by way of the lymphatics. In the skin lesion isolated bacilli within large monocytes were found in the connective tissue trabeculae of the subcutaneous fat as far as 2.1 mm. below the surface of the epidermis, or 1.5 mm. below the lowermost limits of the corium (Figs. 1 and 4). Since many bacilli were also found in one of the related lymph nodes of drainage, mostly within large monocytes, but not in any of the other lymph-node groups examined, it is obvious that the microorganisms were spread passively by way of the lymphatics presumably through the agency of the large monocytes.

With regard to the findings in the nerves of the skin specimens, there was slight lymphocytic and large monocytic infiltration, without bacilli, in small nerve trunks in the sections of the skin lesion (block 3), but no histological changes were demonstrated in those of the nineteen other blocks of skin examined. The several specimens of deeper nerves examined were all essentially negative.

SUMMARY

1. An autopsied case of very early leprosy in a 17-months-old child of leprous parents is reported.
2. The single, isolated, heavily bacillated lesions discovered two months before death, no longer identifiable clinically two days before death, was found in histological sections after a systematic search for it.
3. Histologically the lesion was a very young leproma with beginning formation of foamy cells and numerous bacilli, in close association with three scars that presumably were due to scabies.
4. Evidence is presented which tends to corroborate the belief that the early skin lesion of leprosy is the primary inoc-

ulation lesion. This conclusion is based on the finding of bacilli in considerable numbers only in the corresponding regional lymphatic nodes of drainage, with none in the other groups of lymph nodes, the nerves, or the other organs examined.

5. The spread of the infection in this case of early leprosy by way of the lymphatics is discussed.

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DESCRIPTION OF PLATES

PLATE 11

FIG. 1. Low-power view of the lesion found in block 3 (section No. 60), showing extension into the subcutaneous fat. Hematoxylin and eosin.

FIG. 2. High-power view of the lesion, showing a part of one of the larger cell collections, containing monocytes with faint pinkish, vacuolated cytoplasm loaded with bacilli (see Fig. 4). Eosin and hematoxylin.

FIG. 3. A small, cellular scar, 0.2 mm. wide (slide No. 2), in relation to one end of a cellular collection in the corium. Voerhoff's elastic tissue stain.

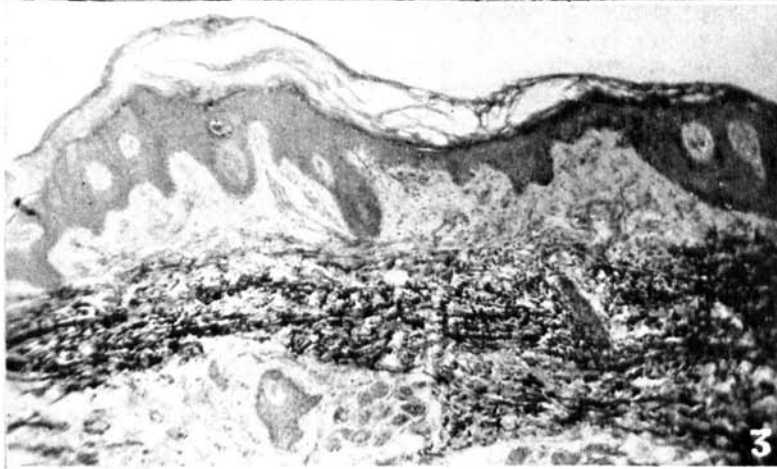
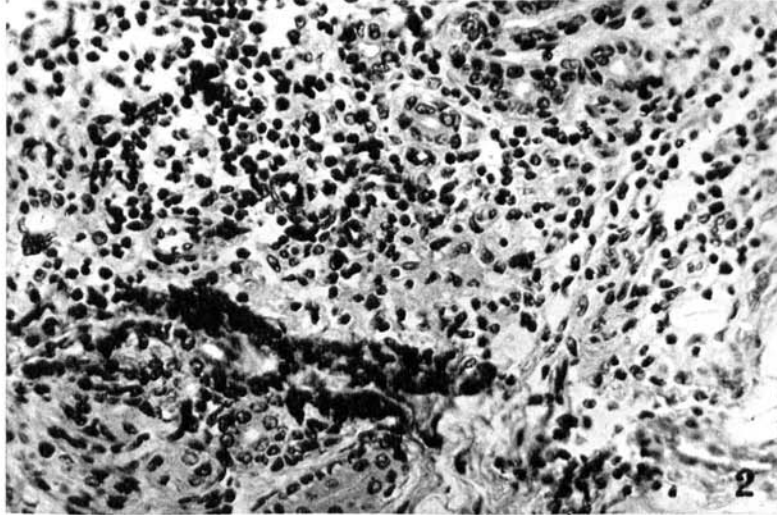


PLATE 11

PLATE 12

FIG. 4. Acid-fast bacilli and globi within vacuolated large monocytes in the connective-tissue trabeculae of the subcutis.

FIG. 5. Section of the most heavily bacillated portion of the largest of the right inguinal lymph nodes, showing a globus of acid-fast bacilli.

FIG. 6. Another portion of the same lymph node, showing isolated bacilli.

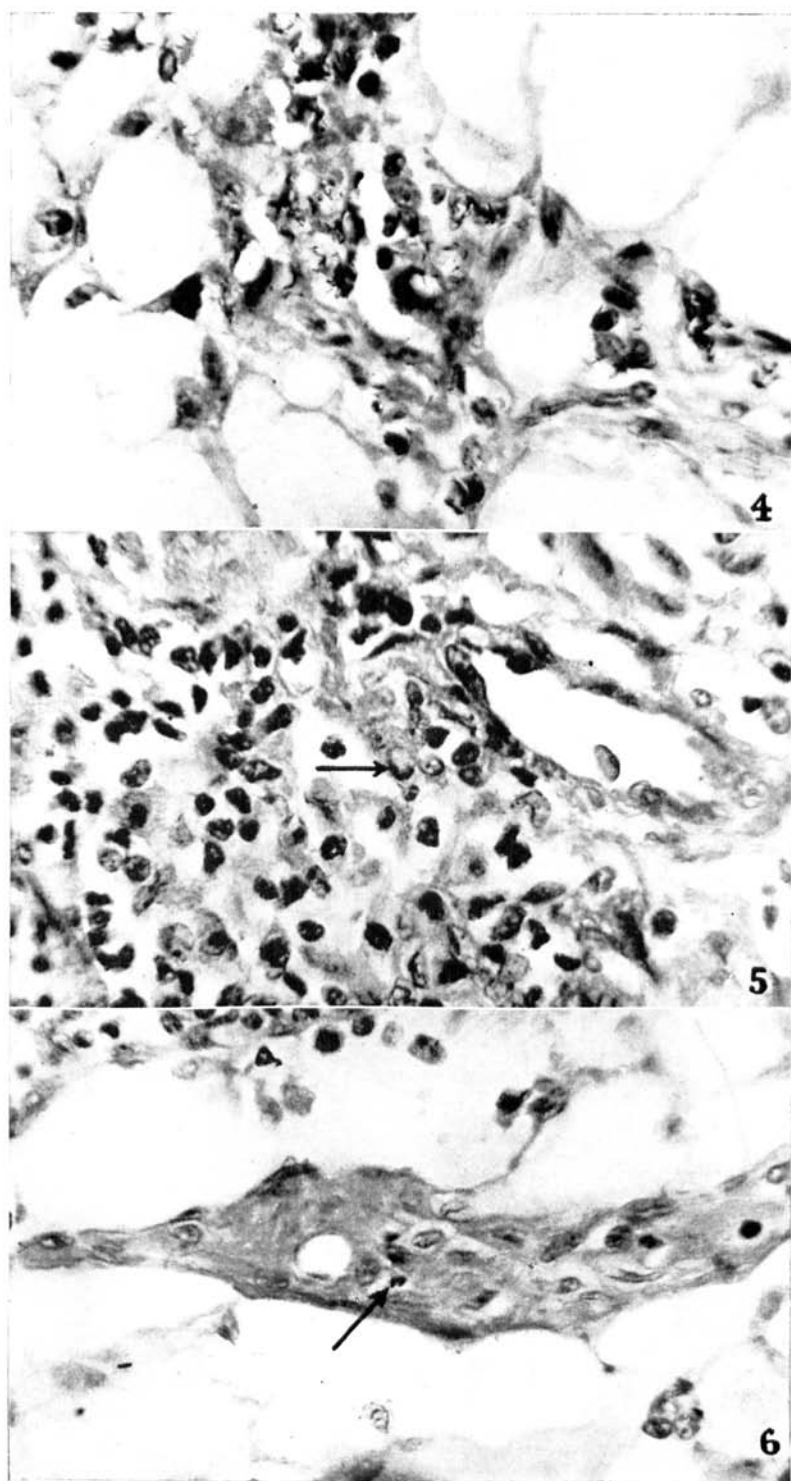


PLATE 12