INFLUENCE OF HYDROCORTISONE, CORTISONE AND ACTH ON THE LEPROMIN REACTION [1]

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In a preliminary note (1) we reported on the influence which Compound F (hydrocortisone), applied locally, exerts upon the reactions to lepromin, tuberculin and the antigens of Frei and Ducrey. In the present report we deal with the effects of that drug, cortisone and ACTH on the lepromin reaction, extending the data and completing the observations.

Harris and Harris (8) studied the influence of general treatment with cortisone and ACTH on the tuberculin reaction in guinea-pigs and rabbits. They found that these hormones inhibit the local and general reactions to tuberculin but do not prevent the Arthus phenomenon. As soon as the treatment was stopped, the hypersensitivity reappeared within 4 days.

Derbes and collaborators (4) found that cortisone and ACTH administered in large doses to guinea-pigs infected with virulent tubercle bacilli diminished but did not inhibit the skin reactions to tuberculin. The modifications of the histopathological changes consisted of a quantitative diminution of the inflammatory exudate, with no major modifications of the cytological structure.

Sheldon and collaborators (12) found, in guinea-pigs with progressive tuberculosis submitted to treatment with cortisone and ACTH for 6 days, that the cutaneous reaction to tuberculin did not disappear, although it was less marked than in the control animals.

Osgood and Favour (10) investigated the effect of the adrenocorticotropic hormone on the tuberculin reaction and the inflammatory reaction induced by turpentine. They found that the treatment inhibited the tuberculin hypersensitivity reactions in guinea-pigs sensitized with heat-killed tubercle bacilli, and also stopped the inflammation but not the necrosis provoked by oil of turpentine.

Long and Favour (9) observed modifications of the reactions to tuberculin (PPD) and to the hemolytic streptococcus in a group of 34 patients given cortisone and ACTH treatment. These modifications depended upon the degree of sensitivity of the patients, the dosage of the hormone, and the duration of the treatment. With respect to the tuberculin reaction, it was found that there was a marked inhibitory effect on the necrosis, somewhat less effect on the infiltration, and least on the erythema. The treatment also acted on the general phenomena that usually accompany the reaction, but on the other hand it did not alter the reaction to histamin.

Goldman and collaborators (7) hold that the tuberculin type of inflammation can be inhibited to a certain extent by means of local injection of Compound F.

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[1] This report, in a briefer form and in the Spanish language, was presented at the VI International Congress of Leprology, Madrid, October 1953. This is a translation, approved by the authors, of the final report.

PERSONAL INVESTIGATIONS

Program of study.—At the suggestion of Wade, who at the time was studying the influence of cortisone on the lepromin reaction in dogs, we started these investigations in February 1953. We were especially interested to ascertain the influence of the hormones, especially hydrocortisone (Compound F), on the two responses, early and late, which are induced by the intradermal injection of lepromin in positive reactors.

It being widely believed that the Fernandez 48-hour reaction is one of allergic nature, whereas the Mitsuda 3-weeks reaction is the expression of a state of resistance or relative immunity, it was particularly desired to ascertain if the hormone has an inhibitory effect only on the former, or also affects the latter. With this end in view we performed, first, a series of experiments to determine the local effect of Compound F by injecting it simultaneously with the antigen. In a few cases we also injected the hormone into the Mitsuda reaction lesion some weeks after the lepromin had been administered. In another experiment, we observed the evolution of the lepromin reaction in patients who were receiving general treatment with cortisone and ACTH.

MATERIALS AND METHODS

In these experiments we used the following materials:

Saline suspension of hydrocortisone acetate (Hydrocortone acetate, Merck), each cubic centimeter containing the equivalent of 25 mgm. of the drug.

Cortisone acetate (Cortone acetate, Merck) and ACTH (Armour Laboratories).

Lepromin suspensions prepared by one of us (J.M.M.F.).

PPD tuberculin (Sharp and Dohme), first concentration.

Lygranum, Squibb, for the Frei reaction.

Ducrey vaccine.

The intradermal injections were given in the dorsal region in the following manner: 0.2 cc. of the hydrocortisone suspension was injected on the left side, immediately followed by 0.2 cc. of the antigen under study into the plaque caused by the injection of the drug. Symmetrically on the right side was given an injection of the corresponding antigen alone. As a further control an injection of hydrocortisone alone was given to ascertain the skin reactivity to the drug. In a small number of cases the procedure was modified by filling the syringe with equal parts of hydrocortisone and the antigen under study, the mixture being injected intradermally.

The readings of the reactions were made after 24 and 48 hours and after 1, 2, 3 and 4 weeks, but only the 48-hour and 3-week responses were recorded as the final results. The lepromin reactions were read according to the criteria recommended by the Second Pan-American Leprosy Conference ([11]), which are essentially the same as those recommended by the WHO Expert Committee ([15]). For the other reactions the usual gradings were used, taking into account both erythema and infiltration.

For the interpretation of the results with the lepromins we adopted the following criteria: 1. For the Fernandez reaction, (*a*) total inhibition, where there was complete absence of erythema and infiltration; (*b*) partial inhibition, when there was less erythema and infiltration than in the control reaction; and (*c*) lack of inhibition, when there was no difference in the skin response from that of the control. 2. For the Mitsuda reaction, (*a*) total inhibition, when after three weeks no papule or nodule could be seen at the site of injection; (*b*) partial inhibition, when the papule or nodule was smaller than the control reaction.

RESULTS

EFFECT OF COMPOUND F INJECTED SIMULTANEOUSLY WITH LEPROMIN

This investigation was made with 21 adults, 15 of them natives of Boston who had had no contact with leprosy patients, and 6 of Rosario who had had household contact with patients. We were able to observe the early reaction in all of these individuals, but the late reaction in only 20 of them.

Fernandez reaction.—In 3 cases the early reaction was negative in the control sites. Of the 18 positive reactors, 14 of them 1+, the others 2+ to 3+, 14 showed total inhibition of the reaction by the hydrocortisone, and in the other 4 there was partial inhibition. Complete inhibition of this reaction is illustrated in Fig. 1 (site 1, compared with 1').

Mitsuda reaction.—Of the 20 cases observed at the end of three weeks, 3 were nonreactors, these being the same ones in which the early reaction was negative. Of the 17 reactors 8 were 1+, 8 were 2+ and 1 was 3+. In all of these cases the Compound F had an evident inhibitory effect. In 14 cases the inhibition was total, for after 5 weeks there was to be seen only an atrophic plaque, very similar to that provoked by the injection of the drug alone. In the other 3 cases the inhibition was partial.

Hydrocortisone controls.—With respect to the control injections with Compound F alone, it was observed that in all cases it provoked a condition of cutaneous atrophy, which was confirmed histologically. In the center of the atrophic area there were small yellowish nodules which persisted for several weeks.

Histological study.—Biopsies were made, after 48 hours and after 7, 14 and 21 days, of the reactions induced by the antigen alone and of the sites of injection of the combination of antigen and Compound F.

The Fernandez reaction: A representative section, shown in Fig. 3, shows the histological picture of a positive 48-hour lepromin reaction. There are capillary dilatation, edema and fibrinoid imbibition of the collagen, and a cellular infiltrate with lymphocytes predominant, together with some polynuclears, especially eosinophiles. This infiltrate is perivascular, periglandular and perifollicular.

The site of the injection of Compound F and lepromin in the same case, also after 48 hours, is shown in Fig. 2. Here are seen only slight perivascular lymphocyte infiltration, the hydrocortisone having inhibited all the reactional phenomena which were induced by the antigen alone.

The Mitsuda reaction: The structure of a lepromin reaction after 14 days is shown in Fig. 4. One can see the formation of a follicular infiltrate in the deeper dermis, with epithelioid cells in the center surrounded by a dark halo of lymphocytes.

The site of injection of Compound F and lepromin in the same case, also after 14 days, is shown in Fig. 5. The action of the drug has inhibited the formation of the tuberculoid granuloma characteristic of the Mitsuda

reaction. There is to be seen, however, a marked atrophy of the epidermis, which confirms histologically the clinical observation. Lastly, there is demonstrated the presence of a basophilic substance of granular aspect, consisting of the deposit of the injected drug.

Fig. 6 shows the typical histological picture of a 21-day Mitsuda reaction, the infiltrate of distinctly follicular tuberculoid structure. Fig. 7 is of the site of injection of Compound F and lepromin, in the same case and also after 21 days. The inhibitory effect of the drug is quite evident, there being only a slight perivascular lymphocytic infiltrate accompanied by atrophy of the epidermis. There are also seen here, in the upper levels, basophilic masses which are deposits of the hydrocortisone.[2]

In synthesis, the histological study confirms as a whole the clinical observations, showing how hydrocortisone inhibits the tissue reactions, early and late, induced by lepromin in positive reactors.

EFFECT OF COMPOUND F ON THE MITSUDA REACTION LESION

In two cases we infiltrated the nodules of the positive Mitsuda reactions, after 21 days of evolution, with 0.2 cc. of hydrocortisone.

Clinically, 48 hours after the injection the lesion had the appearance of a yellowish-violaceous plaque, replacing the Mitsuda nodule. On the sixth day there was a slightly atrophic plaque of yellowish color, and the nodular infiltration had disappeared.

Biopsy of these elements, six days after the injection of the Compound F, showed that the drug had disorganized and partially eliminated the tuberculoid infiltrate which characterizes the Mitsuda reaction. In its place there were found masses of basophilic material, without any cellular reaction.

EXPERIMENTS WITH OTHER ANTIGENS

Tuberculin reaction.—Twelve cases were tested with PDD (first concentration), and 2 were found negative. Of the 10 positive cases, Compound F injected locally produced total inhibition of the reaction in 6, and partial inhibition in 2, while in 2 there was no inhibition. These last cases were persons highly hypersensitive to tuberculin.

Frei reaction.—Of 10 cases tested by intradermal injection of Lygranum (Squibb), 5 gave negative reactions. Of the 5 positive cases, 4 showed total inhibition by Compound F, and in 1 the inhibition was only partial.

Ducrey reaction.—Out of 9 cases tested, 1 was negative. In the positive group of 8 cases, the inhibition was total in 4 and partial in 2, while in the remaining 2 there was no inhibition.

The results obtained in these groups of patients are summarized in Table 1. The results with the lepromin reactions are also included, for purposes of comparison and to make complete the data on the tests involving intradermal injection of hydrocortisone.

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[2] The authors supplied another photomicrograph to show the hydrocortisone deposit at higher magnification, but because of limitations of space it cannot be used.—EDITOR.

EFFECT OF GENERAL TREATMENT WITH CORTISONE AND ACTH ON THE LEPROMIN REACTION

This second part of our investigation was incomplete, due to conditions beyond our control. The program called for performing the lepro-

TABLE 1.—*Effects on various skin reactions of the intradermal injection of hydrocortisone.*

Antigen	Cases, total	Cases non-reactive	Inhibition by hydrocortisone		
			Total	Partial	Nil
Tuberculin, PPD, first	12	2	6	2	2
Frei (Lygranum)	10	5	4	1	0
Ducrey	9	1	4	2	2
Lepromin, early reaction	21	3	14	4	0
Lepromin, late reaction	20	3	14	3	0

min test before, during and after the hormone treatment. However, it takes at least three weeks to complete the evolution of the reaction lesion, and in the majority of the cases (severe pemphigus, disseminated lupus

TABLE 2.—*Results of the lepromin test in patients with Cortone or ACTH.*

Case	Diagnosis	Drug used	Dose /[a]		Reaction	
			48 hours	21 days	Early	Late
1	Sarcoidosis	ACTH gel	700	900	—	1+
2	Toxiderma	Cortone	300	400	1+	3+
3	Pemphigus	Both	1000	5000	—	±
4	Toxiderma	Cortone	1000	3600	—	—
5	Pemphigus	ACTH	400	1200	—	—
6	Pemphigus	Both	1600	2200	—	?
7	Toxiderma	Cortone	760	960	±	1+
8	Pemphigus	Both	3000	5200	±	1+
9	Urticaria	Cortone	500	500	—	?
10	Sarcoidosis	Actar gel	800	1300	—	1+
11	Sarcoidosis	Actar gel	720	920	—	—
12	Arthritis, rheumatoid	Cortone	1300	2500	1+	1+
13	Lupus disseminatus	Cortone	2100	4000	+	1+
14	Alopecia areata	Cortone	1500	2000	—	—

a Total dosage in milligrams received at the time of reading the reaction.

erythematosus and toxiderma) it was impossible to wait so long a time before beginning treatment. We therefore limited ourselves to performing the test in cases already subjected to treatment with the drug. The results obtained are given in Table 2.

Because of lack of knowledge of the natural reactivity of these patients, we can simply point out here that only 2 of the 14 gave definitely positive early reactions, although 4 others showed some response, while 7 of the 14 gave positive late reactions. One of the early positives (Case 2) had received only 300 mgm. of cortisone at the time the reaction was read, and he gave a strong (3+) late reaction at the end of 3 weeks—at which time he had received only 100 mgm. more of the hormone. The other early reactor (Case 12) also gave a definite, if weak (1+), late reaction. More will be said of this matter in the discussion.

DISCUSSION

Mentioning first the tests with tuberculin and the Frei and Ducrey antigens, to dispose of the subject, our results agree to a large extent with those of Goldman and collaborators (7) with respect to the influence of Compound F on the reactions. This drug tends to inhibit, partially or totally, the reaction of hypersensitivity which they provoke. Inhibition depends upon the dose of the drug and the degree of reactivity of the individual. According to our experience, when the sensitivity is high the inhibition is only partial, and sometimes there is none with the dose that we used.

With respect to the influence of hydrocortisone on the lepromin reaction, the major part of this study, it can be said that it exercises a total or partial inhibitory effect on both the early (Fernandez) and late (Mitsuda) responses.

In the early reaction this hormone impeded the formation of the infiltrated erythematous halo, which is its distinguishing feature. In the majority of the cases the inhibition was complete, and this could be confirmed histologically. This phenomenon was observed by Baliña, Wilkinson and Gatti (2) in one case, in which they used the drug in the form of an ointment.

In 1939 Büngeler and Fernandez (3) demonstrated that this early reaction corresponds in both its clinical evolution and its histological structure, to the type of allergic reactions. These authors found, after 24 hours, changes in the collagen (fibrinoid imbibition and necrosis) which characterizes the reactions of hypersensitivity. Dharmendra (5) and Fernandez (6) demonstrated, further, that this reaction is provoked by protein elements of the lepromin.

The inhibitory effect which hydrocortisone exerts on the early lepromin reaction is explained by the fact that this hormone possesses the property of interfering with the phenomena of hypersensitivity, lessening or abolishing them. Osgood and Favour (10) deduced from their experi-

ments that the adrenocorticotropic hormone acts in these cases by limiting the tissue reaction secondary to the cellular aggression. This mechanism explains the suppression of the cutaneous activity against tuberculin in animals sensitized with heat-killed bacilli.

Hydrocortisone was also found to have an inhibitory action on the late or Mitsuda reaction. In 14 out of 17 reactive cases the inhibition was total, and in the other 3 it was partial. The histological findings were confirmatory, showing that the hormone impedes the formation of the tuberculin granuloma.

In a recent article Sullivan and collaborators (13) reported that if hydrocortisone is injected locally into the cutaneous lesions of sarcoidosis it provokes a complete regression of the tuberculoid infiltrate. In its place only masses of basophilic material are seen, situated in the deep corium without any cellular reaction. We observed a similar phenomenon after injecting hydrocortisone in the late nodule induced by lepromin. Clinically the nodule was resorbed within a week, and histologically there was partial regression of the tuberculoid infiltrate, which was substituted by masses of basophilic material composed of deposits of the drug.

Regarding the effect of general treatment with ACTH and cortisone on the lepromin reaction, little can be said because of lack of a control lepromin test before the patients were put under treatment, or after that treatment had been discontinued. It is of interest, however, and possibly significant, that in the first experiment 18 (or 86%) of the group of 21 patients gave positive early reactions, whereas of the 14 under hormone treatment only 2 (14%) were definitely positive and 9 were entirely negative. The difference with the late reaction was not as great, but it was nevertheless substantial. Of the first group, only 3 of the 20 (15%) were negative after 3 weeks, whereas 7 of the 14 (50%) of those receiving the general hormone treatment were negative, and in only one of the positives —the patient who had received a total of only 400 mgm. of cortisone—was the reaction of more than the 1-plus grade.

The exact relationship of the early and late lepromin reactions is as yet unknown. Some authors regard them as two stages of one and the same phenomenon, while for others they are two independent phenomena. In actual practice we find with some frequency a dissociation of these reactions, it being not uncommon for the early one to be negative in persons who react positively in the third week.

In the work here reported we found a close correlation of the inhibitory phenomena exhibited by the two reactions under the influence of hydrocortisone injected intradermally. In other words, in all instances when the drug interfered with the early reaction, it also interfered with the late one, although sometimes in a different degree of intensity. In four of the cases there was partial inhibition of the early response and total inhibition of the late one, while in three cases the reverse condition was seen; in the 10 remaining cases there was total inhibition of both

reactions. The question remains: Does this parallelism of the results mean that these phenomena are two stages of one and the same process, or does it simply mean that the hormone inhibits all tissue reactions *in situ* regardless of their nature?

Long and Favour (9) observed in many cases in which the tuberculin reaction was partially or totally inhibited by general treatment with ACTH or cortisone, that within 36 hours after the treatment was interrupted the reactions became positive. Sometimes this reactivation occurred in spite of the fact that the tuberculin had been injected as much as three weeks before.

Wade (14) observed, in dogs subjected to systematic treatment with cortisone (intramuscular injections), that the Mitsuda reaction remained negative while the treatment was continued, but that after it was suspended positive reactions appeared and evolved in the same length of time and the same way as if the lepromin had been injected when the treatment was stopped. In our experience, on the other hand, the influence of the hydrocortisone injected locally was more lasting, and we gained the impression that it was definitive. Five months after the injections of the antigen and drug were made there was to be seen at the site only an atrophic plaque without the least sign of activity. This difference of effect might be attributed to the route of administration of the hormone, the local injection provoking a greater inhibition because it was in higher concentration where the antigen was located, but for another observation by Wade (14). In tests made in a group of healthy laboratory personnel the Mitsuda reaction was inhibited for several weeks by hydrocortisone injected with the antigen, but ultimately—apparently after the drug had been absorbed—reactions occurred, although modified in appearance and slower than normal in healing. Why no such phenomenon was observed in our cases we are unable satisfactorily to explain.

CONCLUSIONS

1. The local injection of hydrocortisone acetate provokes partial or total inhibition in the reactions of hypersensitivity to lepromin (i.e., the early or Fernandez reaction), to tuberculin and to the Frei and Ducrey antigens.

2. The late (Mitsuda) reaction to lepromin is also inhibited, the drug impeding the formation of the tuberculoid granuloma which characterizes it.

3. In cases receiving general treatment by cortisone and ACTH the Fernandez reaction occurred with much less frequency than in cases not so treated, and the Mitsuda reaction was positive, usually in low degree, in only 50 per cent of the cases.

RESÚMEN

Los A.A. estudian la influencia del Compuesto F, cortisona y ACTH sobre la lepromino reacción en sus respuestas precoz y tardía.

Investigan la acción del acetato de hidrocortisona inyectando por vía intradérmica 0.2 cc. de esta droga e inoculando de inmediato y en el mismo lugar 0.2 cc. de lepromina. Comprueban que la hormona inhibe total o parcialmente la reacción precoz así como también las reacciones a la tuberculina, antígeno de Frei y antígeno de Ducrey en la gran mayoría de los casos estudiados. Comprueban que también inhibe frecuentemente la reacción de Mitsuda impidiendo la formación del nódulo de 3a semana. El estudio microscópico confirma la observación clínica, mostrando cómo la droga provoca atrofia epidérmica e impide la formación del infiltrado histológico que individualiza a estas reacciones.

Infiltrando intradérmicamente con hidrocortisona el nódulo correspondiente a una reacción de Mitsuda de 3a semana observan una reabsorción clínica e histológica de dicho nódulo.

La influencia del tratamiento general con cortisona y ACTH sobre la lepromino reacción no pudo establecerse en forma concluyente por resultar incompleta la experiencia realizada. Sólo cabe señalar que en 2 casos sobre un total de 14, el tratamiento general no inhibió la reacción de Fernández y que en 7 casos sobre 14, tampoco inhibió la reacción de Mitsuda.

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REFERENCES

1. Appel, B., Fernandez, J. M. M. and Dougherty, E. The influence of the local injection of hydrocortisone (Compound F) on the reactions to tuberculin, lepromin, and the Frei and Ducrey antigens. J. Investig. Dermatol. (In press.)
2. Baliña, L., Wilkinson, F. and Gatti, J. La hidrocortisona, su aplicación dermatológica. Día Med. **25** (1953) 1683.
3. Büngeler, W. and Fernandez, J. M. M. Estudo clínico e histopatológico das reações alérgicas na lepra. Rev. brasileira Leprol. **8** (1940) 157-170; 231-241; 355-366.
4. Derbes, V. J., Dent, J. H., Weaver, N. K. and Vaughan, D. D. Response of tuberculin skin test to ACTH and cortisone in tuberculous guinea pigs. Proc. Soc. Exper. Biol. & Med. **75** (1950) 423-426.
5. Dharmendra. Studies of the lepromin test. (5) The active principle of lepromin is a protein antigen of the bacillus. Leprosy India **13** (1941) 89-103.
6. Fernandez, J. M. M. The early reaction induced by lepromin. Internat. J. Leprosy **8** (1940) 1-14.
7. Goldman, L., Preston, R. H., Rockwell, E. and Baskett, J. Inhibition of tuberculin reaction by local injection of Compound F. J. American Med. Assoc. **150** (1952) 30-31.
8. Harris, S. and Harris, T. N. Effect of cortisone on some reactions of hypersensitivity in laboratory animals. Proc. Soc. Exper. Biol. & Med. **74** (1950) 186-189.

9. LONG, J. B. and FAVOUR, C. B. The ability of ACTH and cortisone to alter delayed type bacterial hypersensitivity. Bull. Johns Hopkins Hosp. **87** (1950) 186-202.
10. OSGOOD, C. K. and FAVOUR, C. B. Effect of adrenocorticotropic hormone on inflammation due to tuberculin hypersensitivity and turpentine and on circulating antibody levels. J. Exper. Med. **94** (1951) 415-430.
11. PAN-AMERICAN LEPROSY CONFERENCE, SECOND. Rio de Janeiro, 1946. Rev. brasileira Leprol. **14** (1946) 281-355; also, Internat. J. Leprosy **15** (1947) 91-119.
12. SHELDON, W. H., CUMMINGS, M. M. and EVANS, L. D. Failure of ACTH and cortisone to suppress tuberculin skin reactions in tuberculous guinea pigs. Proc. Soc. Exper. Biol. & Med. **75** (1950) 616-618.
13. SULLIVAN, R. D., MAYCOCK, R. L., JONES, R. JR. and BEERMAN, H. Local injection of hydrocortisone and cortisone into skin lesions of sarcoidosis. J. American Med. Assoc. **152** (1953) 308-312.
14. WADE, H. W. Personal communication.
15. WHO EXPERT COMMITTEE ON LEPROSY, First Report. WHO Technical Report Series No. 71, Geneva, September 1953.

DESCRIPTION OF PLATES

PLATE (10)

FIG. 1. This picture exemplifies the influence of locally-injected hydrocortisone on the lepromin and tuberculin reactions at 48 hours. At 1 (upper left), intradermal injection of lepromin and hydrocortisone; at 1′ (upper right), lepromin alone. Note the virtually complete suppression of the erythema and infiltration (Fernandez reaction) in the former of these two sites. At 2, intradermal injection of tuberculin (PPD) and hydrocortisone; at 2′, tuberculin alone. Note that at the former site there is little more than the immediate effect of the injection itself, whereas in the control the tuberculin reaction is positive.

FIG. 2. Showing the suppressive effect on the Fernandez reaction of hydrocortisone injected at the same time as the lepromin. Compare Fig. 3.

FIG. 3. Photomicrograph showing the effects of an intradermal injection of lepromin after 48 hours, in a strongly positive early or Fernandez reaction.

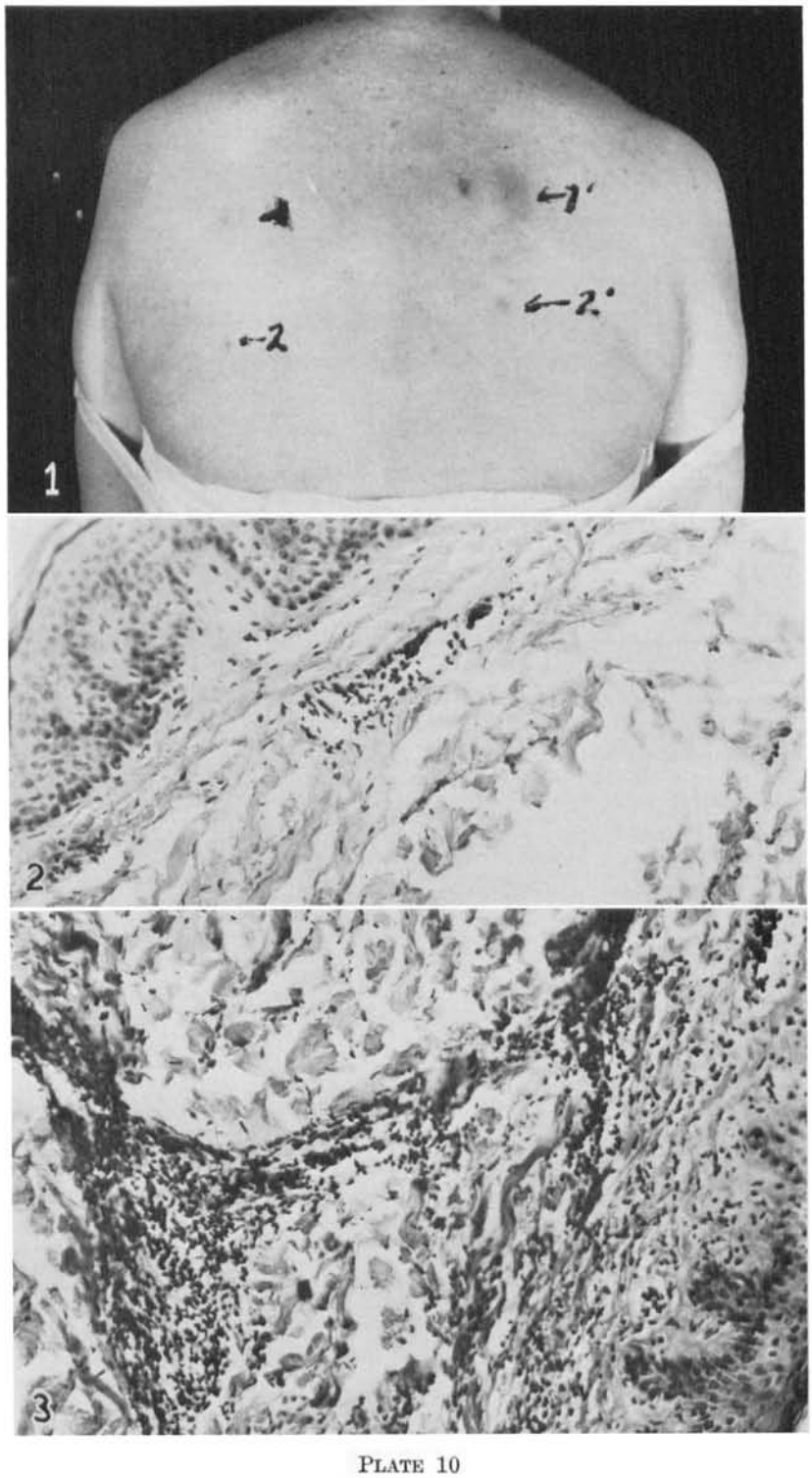

PLATE 10

PLATE (11)

FIG. 4. The condition at 14 days resulting from the intradermal injection of lepromin in a positive late or Mitsuda reactor. Note in the deeper levels the follicular infiltrate of epithelioid cells, surrounded by a dark halo of lymphocytes.

FIG. 5. Showing the lack of response at 14 days to lepromin when hydrocortisone was injected at the same time. Specimen removed from the same patient as the one shown in Fig. 4, at the same time.

FIG. 6. The follicular tuberculoid condition typical of a positive lepromin reaction (Mitsuda lesion) at 21 days.

FIG. 7. Specimen removed from the same patient and at the same time as the one shown in Fig. 6. Note the lack of reaction.

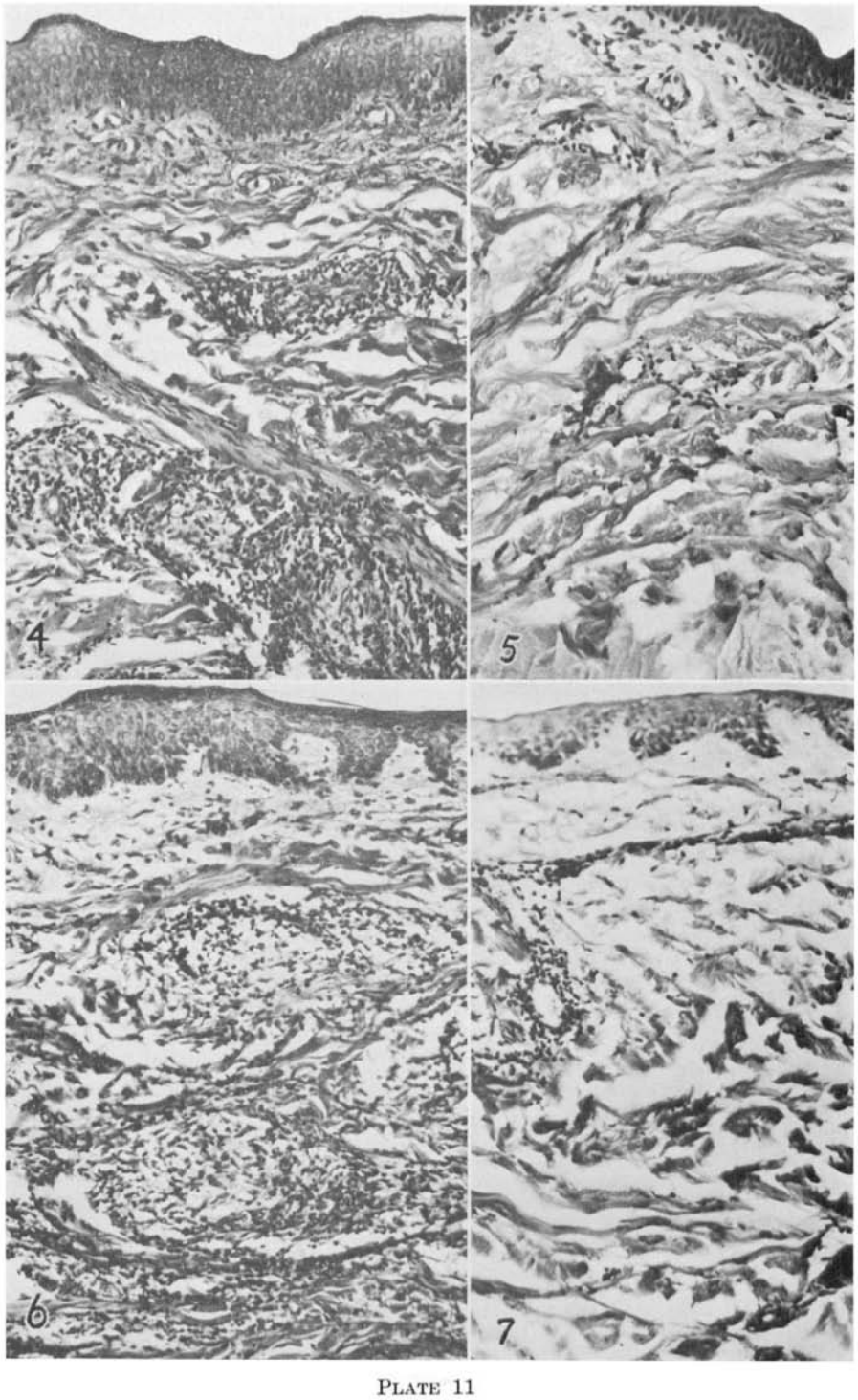

PLATE 11