

THE MICROSCOPIC APPEARANCE OF ECTHYMA CONTAGIOSUM (ORF) IN SHEEP, RABBITS, AND MAN *

CLAYTON E. WHEELER, M.D., and EDWARD P. CAWLEY, M.D.

*From the Department of Dermatology, University of Virginia School of Medicine,
Charlottesville, Va.*

Ecthyma contagiosum, otherwise known as orf and contagious pustular dermatitis, is a virus disease of sheep which is occasionally transmitted to man. The microscopic appearance of the lesions of ecthyma contagiosum presents several unusual features which merit detailed description. The lesions will be described as they appear in sheep, rabbits, and man.

ECTHYMA CONTAGIOSUM IN SHEEP

The microscopic appearance of the lesions of ecthyma contagiosum in sheep has been reported by Aynaud,¹ Lloyd *et al.*,² Pask *et al.*,³ Asakawa *et al.*,⁴ and Glover.⁵ The descriptions of these authors are essentially in agreement with our own except they are not as detailed and do not stress the granulomatous and papillomatous features of the disease as much as would seem indicated.

The description of the disease that follows is based upon the inoculation of the virus of ecthyma contagiosum into the scarified skin of 6 sheep. Tissue was removed for biopsy on 80 occasions, ranging from the 4th to the 42nd day after inoculation of the virus.

On the fourth day after inoculation there was essentially no change in the epidermis and the dermis showed a small amount of vascular dilatation. By the fifth and sixth days the epidermis was mildly acanthotic and the uppermost four or five layers of cells in the prickle cell layer were undergoing ballooning degeneration. The dermal infiltrate was prominent and was composed largely of round cells and reticulo-endothelial cells. There were many newly formed blood vessels and their walls showed well developed, proliferative endothelial changes. The vascular changes remain a prominent feature of the disease throughout its course and they will not be mentioned again.

On the seventh and eighth days the ballooning degeneration of the uppermost portion of the prickle cell layer resulted in almost complete loss of nuclei and cytoplasm of the cells, and the remaining cell walls produced a "basket-weave" appearance. A few tiny, superficial vesicles were produced by the process of reticular degeneration. The

* Received for publication, August 31, 1955.

underlying prickle cell layer presented mild pseudo-epitheliomatous hyperplasia and there was considerable dissolution of the basal layer. The dermal infiltrate was increased and there was edema of the upper portion of the dermis. At times there was enough fluid in the dermis to produce small subepidermal vesicles. By the eleventh day the surface of the lesion was composed of a superficially placed, multilocular pustule, whose roof was a thin horny layer, and whose base was the proliferating prickle cell layer. At the base of the pustule there remained a few scattered balloon cells. The underlying epidermis was moderately pseudo-epitheliomatous and the basal layer presented marked dissolution. The dermal infiltrate was very dense and composed largely of round cells and reticulo-endothelial cells or young fibroblasts. A few polymorphonuclear cells could be seen in the upper portion of the dermis.

Between the 11th and 17th days the cells of the pustule disintegrated and the surface of the lesion became covered with a heavy layer of hyperkeratotic and parakeratotic material. The epidermis showed marked pseudo-epitheliomatous hyperplasia and dissolution of the basal layer. The dense dermal infiltrate persisted. Between the 17th and 22nd days the lesion was covered with a dense crust which became progressively less parakeratotic and more hyperkeratotic. The rete pegs grew downward and the dermal papillae grew upward to produce a finger-like papillomatous appearance. The dermal infiltrate was composed of the same cell types but it was decreased slightly in amount. Less edema was evident and there was very little dissolution of the basal layer of the epidermis.

Between the 22nd and 40th days the lesion gradually involuted. The papillomatous character gradually disappeared and the dermal infiltrate gradually resolved. At the time the crust separated, the epidermis showed mild acanthosis and the dermis contained a minimal cellular infiltrate which was largely perivascular and periappendageal. Slight increase in connective tissue was present but this was not sufficient to be evident grossly as scar.

In summary, the early phases of the disease are characterized by ballooning degeneration of the uppermost portion of the prickle cell layer, which results in multiloculated, superficially placed vesicles and pustules which are replaced late in the disease by a heavy crust. The middle phase of the disease is characterized by pseudo-epitheliomatous hyperplasia and granuloma formation which gives way near the end of the disease to a papillomatous phase. The corresponding phases of the disease present grossly as red macules which develop successively

into red papules, gray pustules, and brown crusts which overlie warty, papillomatous bases.

Re-inoculation of the virus of ecthyma contagiosum into sheep (partially immune animals) produces essentially the same lesions grossly and microscopically. The re-inoculation disease lasts for a much shorter period. The pustular, crusted, and granulomatous phases appear much earlier and in most animals the papillomatous phase is not seen. When it does occur it is inconspicuous and of short duration.

ECTHYMA CONTAGIOSUM IN RABBITS

Most authors^{1,4,5} have failed to observe evidence of disease in rabbits after the inoculation of the virus of ecthyma contagiosum, but a few^{6,7} have reported the production of a mild disorder. We have observed the appearance of tiny (1 to 2 mm.), erythematous maculopapules in rabbit skin after intradermal inoculation.⁸ The lesions appeared after an incubation period of 7 to 9 days and the duration of the disease was 3 to 5 days. We performed three serial passages in rabbit skin and produced typical ecthyma contagiosum in a sheep inoculated with third passage rabbit material. The dilutions in these serial passages were great enough to make it seem quite certain that the virus was able to proliferate in the skin of the rabbit.

There is only one microscopic description of ecthyma contagiosum in rabbits to be found in the literature, to the best of our knowledge, and there is some doubt whether the disease described in that instance is ecthyma contagiosum.⁹

Our description of the microscopic appearance of ecthyma contagiosum in rabbits is based upon the intradermal inoculation of the virus in 8 animals. During three serial passages of the virus the microscopic appearance of the lesions did not change. Under low magnification the lesions usually appeared flat, but an occasional section showed very mild papillomatosis. Higher magnification showed no specific change in the epidermis (occasional insignificant crusting and slight spotty decrease in thickness). The dermis contained a round-cell infiltrate which varied in amount from moderately dense to very dense. Some edema and vascular dilatation were evident and there was a moderate amount of new blood vessel formation and proliferation of the endothelial lining of these vessels.

The lesions in rabbits are characterized microscopically by mild chronic inflammatory changes in the dermis and lack of ballooning degeneration and the prominent granulomatous and proliferative character of the disease in sheep. One might expect such findings from the

gross appearance of the lesions which are tiny, evanescent, erythematous maculopapules.

ECTHYMA CONTAGIOSUM IN MAN

Descriptions of the microscopic appearance of ecthyma contagiosum in man can be found in the writings of Robert and Orbaneja,¹⁰ Kingery and Dahl,¹¹ Percival *et al.*,¹² and Pask *et al.*³ It is probable, too, that Stark *et al.*¹³ have described the disease in some detail under the term milkers' nodules. The limited number of microscopic examinations of human lesions of ecthyma contagiosum make a complete description of the disease impossible for any one observer, but a good idea of the histologic picture can be gained from a compilation of the findings of the several authors, including an analysis of the material available to us.¹⁴

The epidermis became thickened, largely through proliferation of the cells of the prickle layer. The cells of this layer underwent ballooning degeneration and, by an extension of the process (reticular and colliquative degeneration), vesicles were formed in the epidermis. A considerable degree of parakeratosis often developed and at times pseudo-epitheliomatous hyperplasia was found. Inclusion bodies might or might not be seen in smears prepared from the vesicles.^{2,3,6}

The dermis presented edema and dilatation of the blood vessels and lymphatics. New blood vessel formation was prominent and the endothelial cells of many of the vessels showed active proliferation. Varying amounts of dermal infiltrate were seen, but usually there was a dense collection of lymphocytes and reticulo-endothelial cells among which could be found a few polymorphonuclear leukocytes and plasma cells.

The microscopic picture, therefore, resembles lesions produced by the pock viruses (ballooning degeneration leading to vesiculation) with added findings that usually are associated with a chronic granuloma. The microscopic picture is consistent with the appearance of the gross lesions which are often multiloculated vesicles and at other times resemble pyogenic granulomas.

SUMMARY

The inoculation of the virus of ecthyma contagiosum into the skin of sheep, rabbits, and man produces lesions which are different in many respects. In sheep, ballooning degeneration and the formation of superficial, multiloculated vesicles and pustules are characteristic of the early phases of the disease and granulomatous and papillomatous

features predominate in the later phases. The disease in rabbits does not show ballooning degeneration and it lacks the pronounced granulomatous or papillomatous character of the lesions in sheep. Lesions in man usually are characterized by vesiculation, which is a result of ballooning degeneration of the cells of the prickle layer, but a granulomatous character occasionally dominates the microscopic appearance. These differences in the microscopic features in the three species constitute an excellent example of the important part the reaction of the host plays in the disease picture produced by an infectious agent.

The virus of ecthyma contagiosum usually is classified with the pock-producing dermatropic viruses (herpes simplex, herpes zoster, vaccinia, variola, varicella). There is some justification for this classification because ballooning degeneration is a prominent feature of the lesions in sheep and man. The consistent granulomatous and papillomatous features of the lesions in sheep, the lack of a pock-like picture in rabbits, and the tendency of the lesions to become granulomatous in man, however, set ecthyma contagiosum apart from the usual pock disorders.

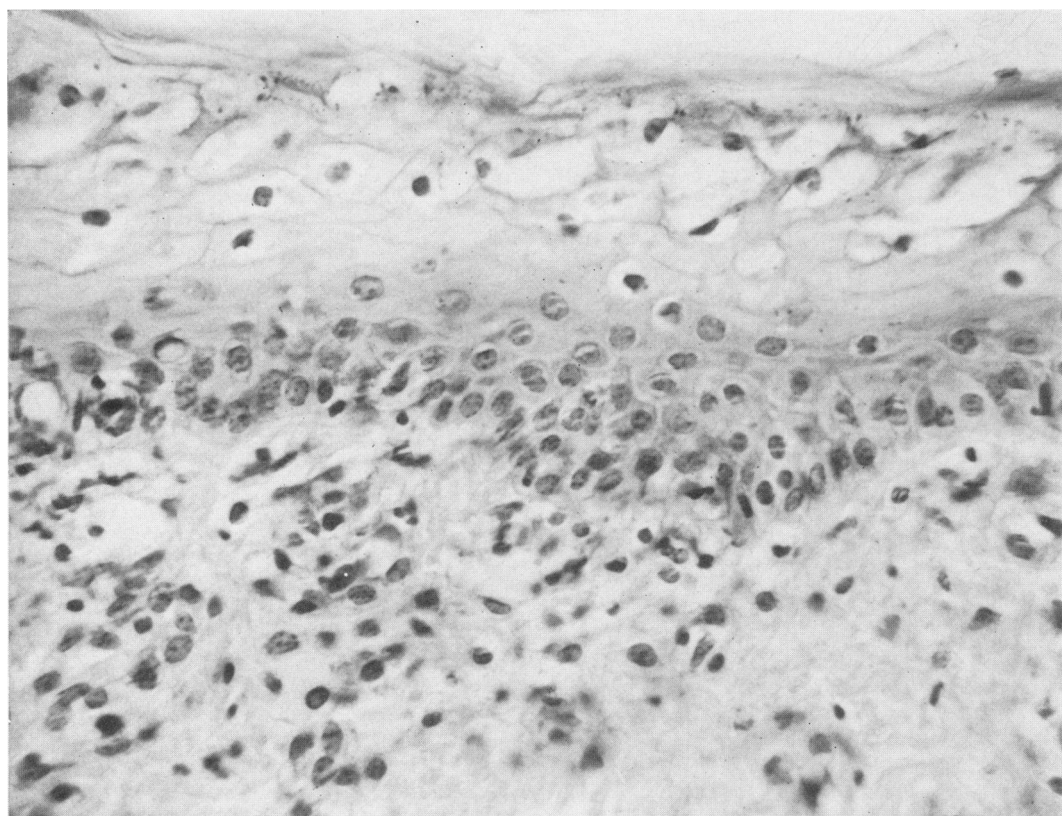
REFERENCES

1. Aynaud, M. La stomatite pustuleuse contagieuse des ovins (chancre du mouton). *Ann. Inst. Pasteur*, 1923, 37, 498-527.
2. Lloyd, G. M.; MacDonald, A., and Glover, R. E. Human infection with the virus of contagious pustular dermatitis. *Lancet*, 1951, 1, 720-721.
3. Pask, V. M.; Mackerras, I. M.; Sutherland, A. K., and Simmons, G. C. Transmission of contagious ecthyma from sheep to man. *M. J. Australia*, 1951, 2, 628-632.
4. Asakawa, Y.; Imaizumi, K.; Tajima, Y., and Endo, M. Studies on a contagious ecthyma-like disease observed among the sheep. *Jap. J. M. Sc. & Biol.*, 1952, 5, 475-486.
5. Glover, R. E. Contagious pustular dermatitis of the sheep. *J. Comp. Path. & Therap.*, 1928, 41, 318-340.
6. Blakemore, F.; Abdussalam, M., and Goldsmith, W. N. A case of orf (contagious pustular dermatitis): identification of the virus. *Brit. J. Dermat.*, 1948, 60, 404-409.
7. Blanc, G., and Martin, L. A. Sensibilité du lapin et de l'homme au virus de la stomatite des ovins. *Compt. rend. Acad. d. sc.*, 1933, 197, 586-587.
8. Wheeler, C. E.; Potter, M., and Cawley, E. P. Experimental ecthyma contagiosum. *J. Invest. Dermat.* In press.
9. Selbie, F. R. Shope papilloma and sheep dermatitis in the rabbit: mutual interference, superinfection and effects of chemical pre-treatment of the skin. *Brit. J. Exper. Path.*, 1946, 27, 143-154.
10. Robert, P., and Orbaneja, G. Trois cas de granulomes angiopapillomateux éruptifs infectieux. *Ann. de dermat. et syph.*, 1937, 8, 45-55.
11. Kingery, L. B., and Dahl, J. Ecthyma contagiosum in man. Data concerning its incidence in several Western states; report of a case. *Arch. Dermat. & Syph.*, 1945, 51, 359-364.

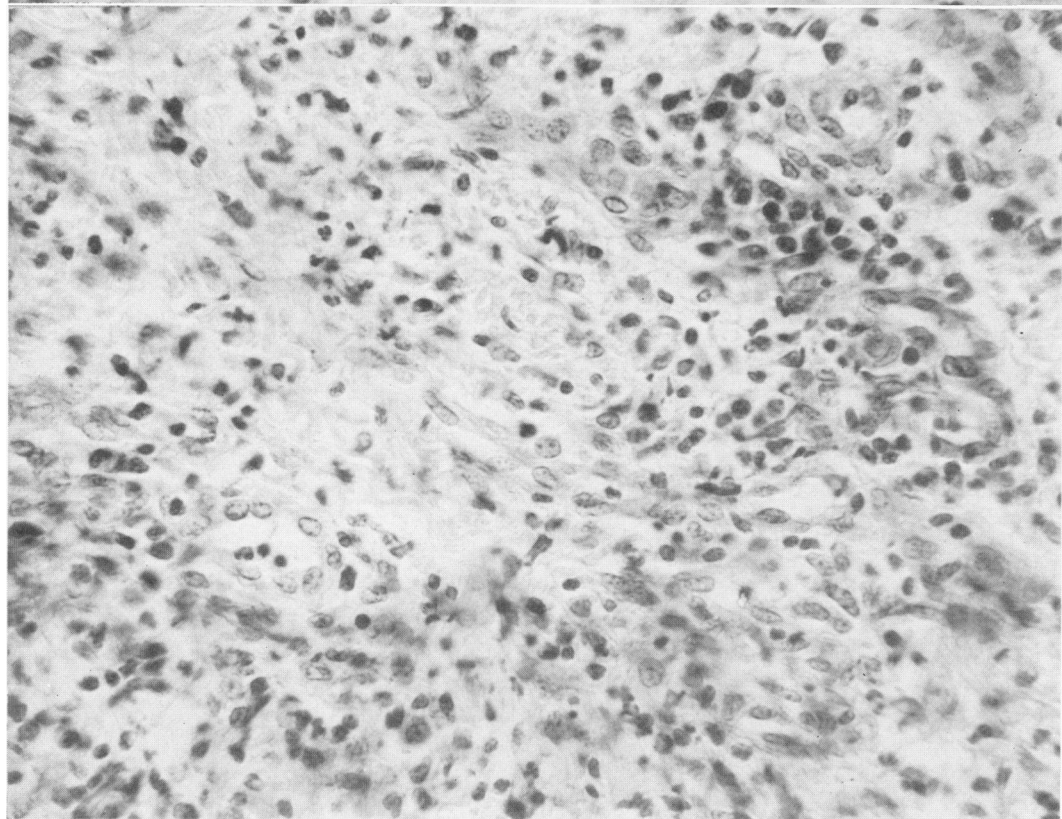
12. Percival, G. H.; Drennan, A. M., and Dodds, T. C. Atlas of Histopathology of the Skin. E. & S. Livingstone, Ltd., Edinburgh, 1947, pp. 187 and 197.
 13. Stark, A. M.; Tresenhausen, M. M.; Gozanskaja, N. M.; Skrozky, D.; Shtastny, D. S., and Zuk, W. A. Über die Pockenätiologie der sog. Melkerknoten. *Arch. f. Dermat. u. Syph.*, 1934, 170, 38-60.
 14. Wheeler, C. E.; Cawley, E. P., and Johnson, H. A. Ecthyma contagiosum (orf). *A. M. A. Arch. Dermat.*, 1955, 71, 481-485.
-

LEGENDS FOR FIGURES

- FIG. 1. Sheep V. Five days after inoculation of the virus of ecthyma contagiosum. Ballooning degeneration is present in the uppermost cells of the prickle layer and vascular changes and a sparse round-cell infiltrate can be seen in the dermis. $\times 445$.
- FIG. 2. Sheep II. Ten days after inoculation of the virus. The granulomatous changes in the dermis are well developed. $\times 445$.



1



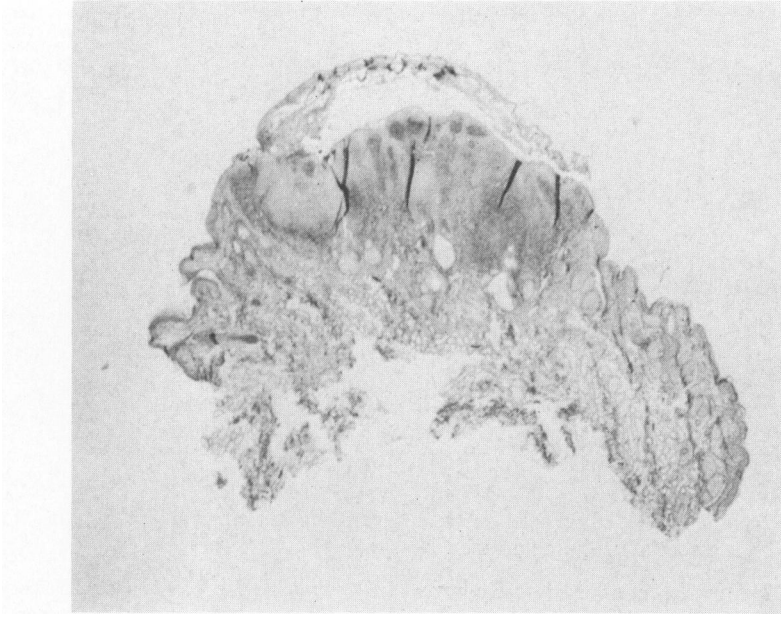
2



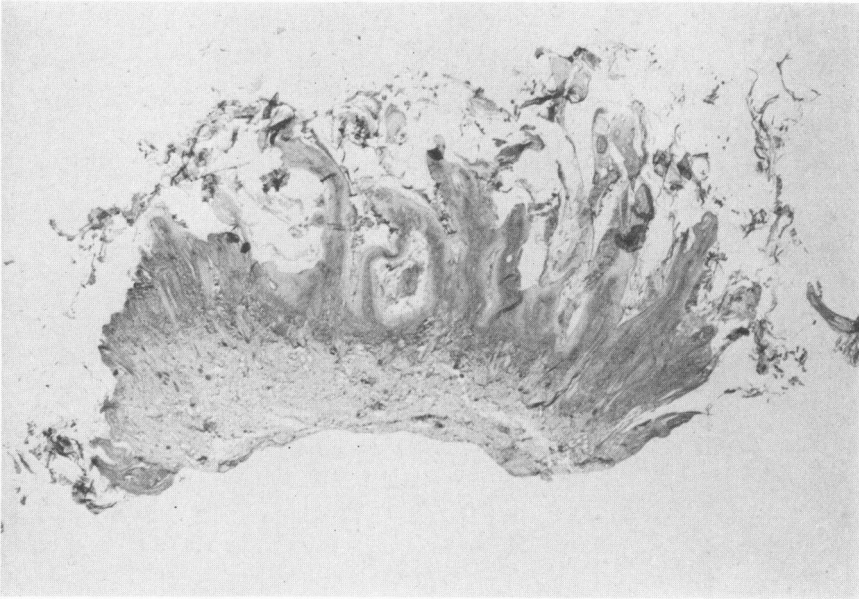
FIG. 3. Sheep V. Twelve days after inoculation of the virus. Pseudo-epitheliomatous hyperplasia is a prominent feature. $\times 110$.

FIG. 4. Sheep II. Ten days after inoculation of the virus. This low-power photomicrograph ($\times 11$) shows the superficial position of the pustule. Most of the pus cells have been lost in preparing the specimen.

FIG. 5. Sheep I. Seventeen days after inoculation of the virus. The low-power photomicrograph ($\times 9$) shows the pronounced papillomatosis characteristic of the lesion at this age.



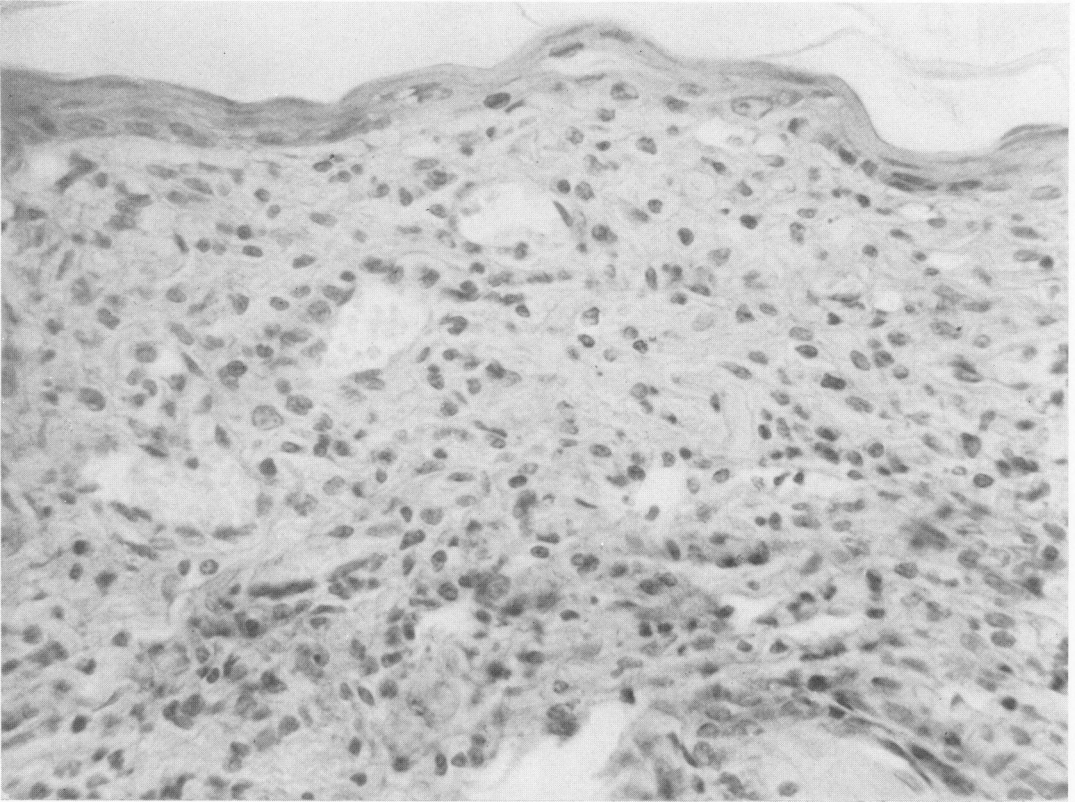
4



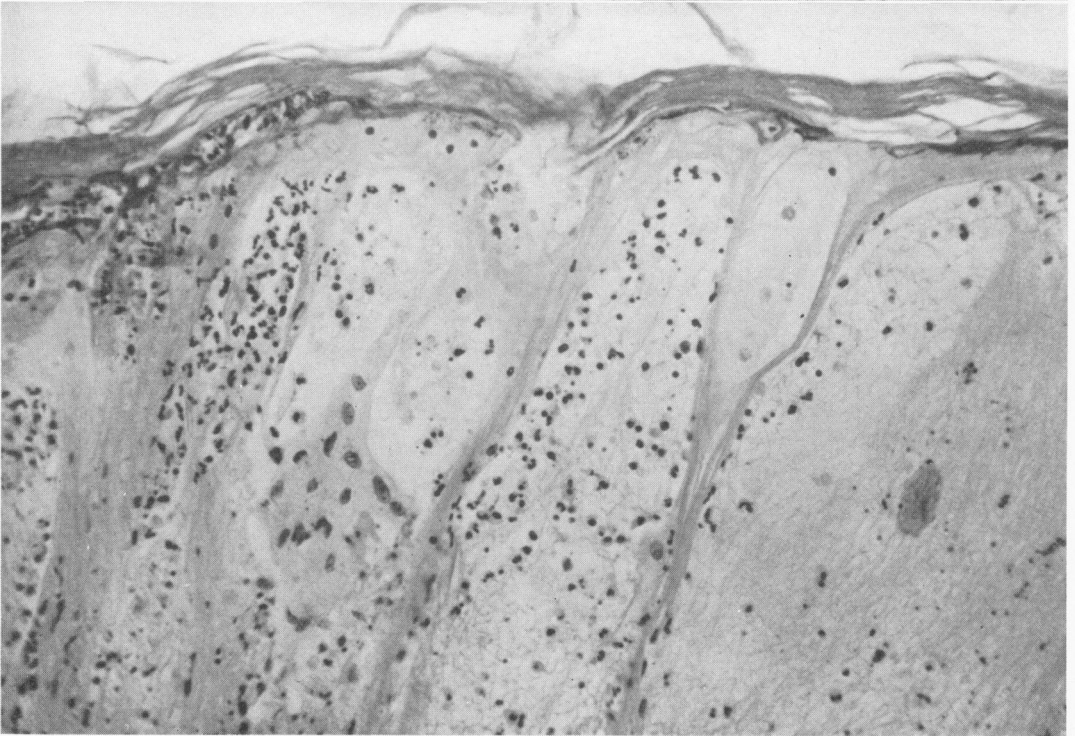
5

FIG. 6. Rabbit V. Third-passage lesion 9 days after inoculation of the virus. The lesion is essentially a granuloma. $\times 445$.

FIG. 7. Human lesion approximately 3 weeks after inoculation of the virus. Ballooning and reticular degeneration have resulted in a multilocular vesicle. $\times 270$.



6



7