Journal of Cutaneous Pathology 1975: **2**: 265–283

Human Orf

JAN VINCENTS JOHANNESSEN[1], HANS-KRISTIAN KROGH[2], INGVAR SOLBERG[3], ARE DALEN[2], HANS VAN WIJNGAARDEN[4] AND BJØRN JOHANSEN[3]

[1]The Norwegian Radium Hospital, Department of Pathology, Montebello, Oslo; [2]Departments of Dermatology and Microbiology, Haukeland Sykehus, University of Bergen, Bergen; [3]National Institute of Public Health, Virus Department B and Department of Methodology, Oslo, Norway; and [4]N. V. Philips Gloeilampenfabrieken, Application Laboratory, Electron Optics, Eindhoven, The Netherlands

Human orf is usually considered a rare disease caused by a virus belonging to the paravaccinia subgroup of pox viruses and transmitted to man from sheep and goats. This paper presents 119 new human cases with epidemiological, clinical, histopathological and ultrastructural findings. Erythema multiforme was found to be a common complication of human orf. Other complications tended to be caused by overtreatment. Electron microscopy of negatively stained suspensions from lesions was found to be the best and most rapid diagnostic method available.

(Received for publication October 9, 1975)

Human ecthyma contagiosium or "orf" is usually considered a rare disease (Leavell et al. 1968) and relatively few cases have been reported (Schmidt 1967). It is not even mentioned in some major textbooks of dermatology (Hellerstrøm 1962) and dermal pathology (Graham et al. 1972). The largest material published includes 19 cases collected in the U. S. A. over a 7-year period (Leavell et al. 1968). Orf is found all over the world where sheep and goats are raised.

The word "orf" is an Anglo-Saxon name for cattle, and the disease is most often seen in sheep and goats. Although orf is the most common name, more than 83 others have been used (Nürnberg 1942). In sheep it was first reported by Steeb in 1787 (cited by Schmidt 1967) and in 1879 the Norwegian veterinarian G. Hansen described its occurrence in goats. Between 1867 and 1875 he alone treated more than 1000 cases. He has also mistakenly been credited with the first report on human orf (Laurent 1927, Blakemore et al. 1948, Hodgson-Jones 1951, Nagington & Whittle 1961, Schmidt 1967) occurring in two women handling infected goats. His report, however, deals with goats only and he stresses that "pox disease was not seen in sheep, cows or humans". In his paper he mentions that dairymaids milked both goats and cows without transmitting the disease to the latter (Hansen 1879). His article was written in Norwegian and this obviously explains the false citations given in later works.

In 1923 the disease was shown to be transmitted by a filterable agent (Aynaud 1923) and 11 years later it was immunologically separated from the vaccinia-variola group of human viruses (Boughton & Hardy 1934). The first report on human orf was published in the same year (Newsom & Cross 1934).

The orf virus has a DNA genome and

is classified as belonging to the paravaccinia subgroup of the pox viruses (Büttner et al. 1964, Peters et al. 1964, Joklik 1968). Several authors have dealt with the human infection. Most of them, however, deal with isolated cases (see review by Schmidt 1967). The limited number of microscopic examinations of human lesions of ecthyma contagiosum has made a complete description of the disease impossible for any one observer (Wheeler & Cawley 1956). Three cases have previously been presented from Norway (Høvding 1957) and one from Sweden (Lindgren & Skogh 1973). These are the only previous reports from Scandinavia.

The present work is based on 119 of our own cases of human orf, including clinical observations, histopathology and electron microscopy.

Material and Methods

Material

A. Sixty patients, 18 female and 42 male, were examined at the Outpatients Clinic, Department of Dermatology, University of Bergen, from 1957 through 1973. In two cases electron microscopy was performed. Biopsies were taken from two other cases for light microscopy. In one case lambs were inoculated with infectious material. In nine cases bacteriological investigations were made.

B. Fifty-four cases were diagnosed on biopsies sent to The Norwegian Radium Hospital, Department of Pathology, between 1972 and 1975. In 10 cases electron microscopy was performed on material fixed in acid non-buffered formaldehyde and embedded in paraffin for light microscopy (see below). In two cases material primarily fixed in glutaraldehyde was used, and in two cases dry scales were used for negative staining.

C. Material from five cases sent to the National Institute of Public Health were studied by electron microscopy using the negative staining technique.

Methods

Light microscopy: Biopsies were fixed in acid non-buffered 4 % formaldehyde and embedded in paraffin. Sections were stained with hematoxylin and eosin, periodic-acid Schiff (PAS), Feulgen or methyl green pyronine.

Electron microscopy:

a) Tissue cubes 2 mm in diameter, were immersed in 2 % phosphate-buffered glutaraldehyde, postfixed in osmium-tetroxide, dehydrated in graded alcohols and embedded in Epon 812 using propylene oxide as an intermedium. Semithin sections were cut with glass knives mounted on a LKB Pyramitome and stained with toluidine blue for light microscopical orientation. Ultrathin sections were cut with an LKB Ultrotome III also equipped with glass knives, mounted on naked or formvar/carbon-coated copper grids and examined with a Philips EM 201 electron microscope or a Philips EM 301 equipped with ordinary high resolution stage, goniometer stage or scanning electron microscope attachment operated in the scanning transmission electron microscopy mode (STEM).

b) Paraffin-embedded material was also used for electron microscopy after removal of paraffin by xylol, post-fixation in osmium-tetroxide and processing for electron microscopy as described above.

c) Crusts from lesions were put in a glass tube with about 0.5 ml of distilled water and ground and emulsified with a tight-fitting glass rod. One drop of this crude suspension was mixed with an equal amount of acid or alkalic 0.8 % sodium

silicotungstate (SST) or 1 % phosphotungstic acid (PTA) and transferred to a formvar/carbon-coated copper grid. These cases were examined with a Jeol 100 B electron microscope.

Results

Geographical Distribution of Patients

This is shown in Fig. 1. The distribution of human orf does not reflect the number of sheep and goats in the different counties (Fig. 2 & Table 1). The Fig. is not representative of the true incidence since most specimens were from the Bergen area. The Fig. shows, however, that the disease is mainly located in the coastal area when comparing Finnmark (coastal) and Oppland (inland). There are three times as many sheep in the county of Oppland as there are in the county of Finnmark. Despite this, no case of human orf was received from Oppland, while seven positive specimens were obtained from Finnmark. Because of this, an enquiry was made among the general practitioners in Oppland. They claimed that orf did not occur in this county, neither in sheep nor in man, in

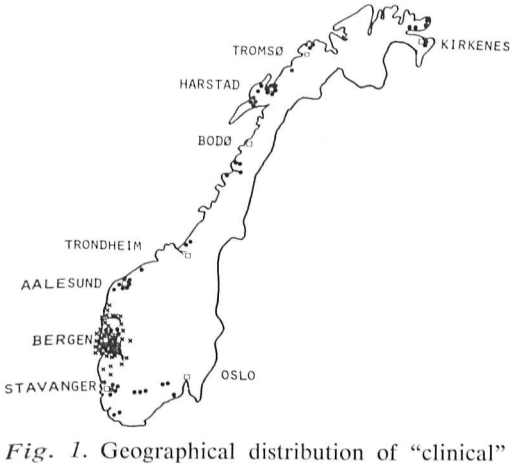


Fig. 1. Geographical distribution of "clinical" (×) and "histopathological" (O) cases of orf.

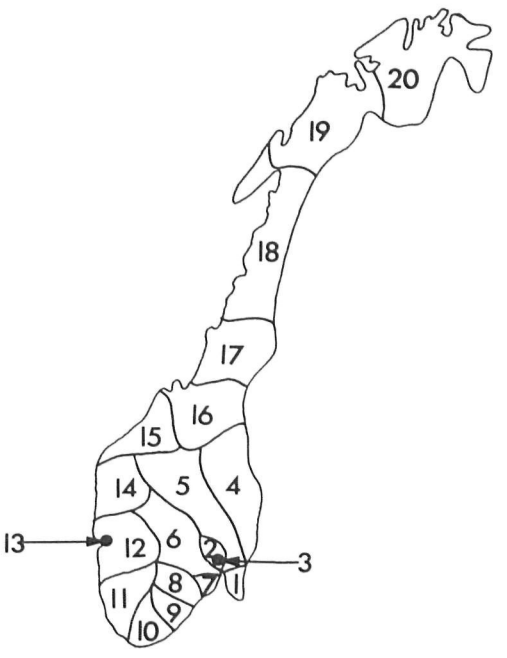


Fig. 2. Counties of Norway. Arabic figures refer to Table 1.

Table 1

Thousands of sheep (goats) per county 1973

1	Østfold	3.3(–)
2 and 3	Oslo and Akershus	13.5(–)
4	Hedmark	85.5(2.0)
5	Oppland	99.6(6.6)
6	Buskerud	66.8(1.3)
7	Vestfold	4.1(–)
8	Telemark	38.8(1.1)
9	Aust-Agder	28.1(–)
10	Vest-Agder	41.5(–)
11	Rogaland	289.0(1.9)
12 and 13	Bergen and Hordaland	201.0(4.6)
14	Sogn and Fjordane	222.3(13.3)
15	Møre and Romsdal	122.2(7.8)
16	Sør-Trøndelag	89.0(0.8)
17	Nord-Trøndelag	47.2(1.0)
18	Nordland	149.7(9.9)
19	Troms	112,2(21.7)
20	Finnmark	33.9(–)

Statistical Yearbook of Norway, 93rd Issue, Central Bureau of Statistics of Norway, Oslo 1974.

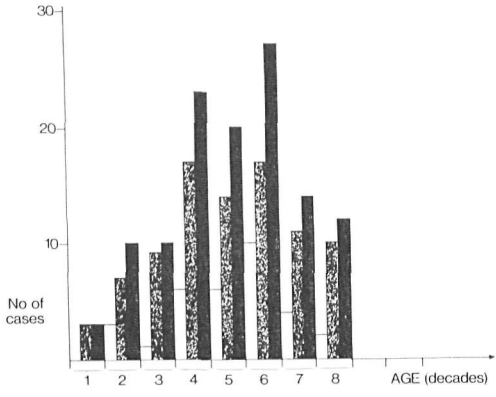


Fig. 3. Age distribution of orf cases, white columns representing females, grey males and black both.

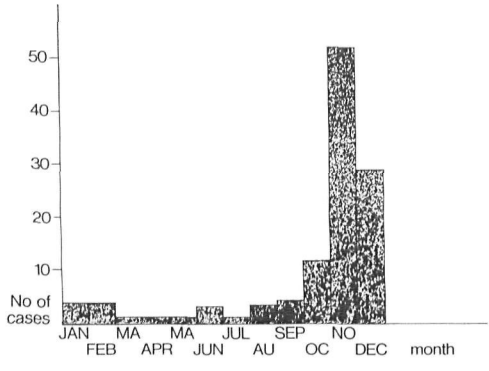


Fig. 4. Seasonal distribution of orf cases.

contrast to Milkers nodules which were seen occasionally. Some of the doctors were familiar with orf from their earlier practice.

Age of Patients

Most patients were in their fourth to sixth decade (Fig. 3). The youngest patient was 3 and the oldest 76 years of age.

Time of the Year

The majority of cases were registered in the three last months of the year, during the shearing and slaughtering season (Fig. 4).

Mode of Infection

Most patients had been in contact with sheep, directly or indirectly. Eight patients had been in contact with goats as well. In three of these only the goats showed signs of infection. One patient had been in contact only with goats, which showed clinical evidence of orf infection.

Seven of the patients were not sheep raisers themselves. They had, however, handled mutton bought from the butcher. Six were infected as a result of preparing sheep heads, which is a gastronomic speciality in the fjords of western Norway. The rest of those directly infected had handled sheep or played with them.

Six patients were infected indirectly. One had been playing in the sheep pen; one hit his head against the door frame of the sheep pen; one got a wooden splinter from the sheep pen under his skin; one was wounded by barbed wire from a sheep fence; one was wounded by a knife which had been used for sheep-slaughtering, and one hit himself on a tractor used for sheep transportation.

Six others were uncertain whether they had been directly infected by handling sheep, or indirectly through implements.

Localization of Lesions

The majority of lesions were located on the hands (Table 2). In female patients, lesions were twice as often located on the right hand as on the left; while the left hand was more often affected in male patients. Infections of head and neck were almost exclusively seen in male patients.

Number of Lesions

Of the 60 cases observed in the Department of Dermatology, 21 patients showed two to 10 lesions. The rest of the cases were not so closely observed clinically, and probably because of this, the number of lesions was not specified.

Table 2

Localization and number of orf lesions

Localization	Males	Females
Head	19	1
Neck	2	–
Right arm	1	1
Left arm	3	2
Arm (unspec.)	1	–
Right hand	39	24
Left hand	49	12
Hand (unspec.)	10	1
Left leg	1	1
Unknown	2	2
Total	127	44

Incubation time varied from three to six days. Most cases were seen three to four weeks after infection.

Natural History

The lesions were similar to those seen in sheep and goats (Fig. 5). They started as macules which after a couple of days passed through a papulous to a target stage which was seen 1–2 weeks after the infection. This was characterized by a red center surrounded by a white ring and a red halo. It was followed by a nodular stage with lesions showing red, weeping surface and often a central umbilication (Figs. 6 and 8a). Three to four weeks after infection a granulomatous or papillomatous stage was seen (Figs. 7 and 8b). Most patients were seen and also biopsies taken during the last two stages. The lesions had a diameter of 0.5 to 5 cm, usually 1–3 cm. In some cases this stage was followed by ulceration and superinfection. In all cases spontaneous

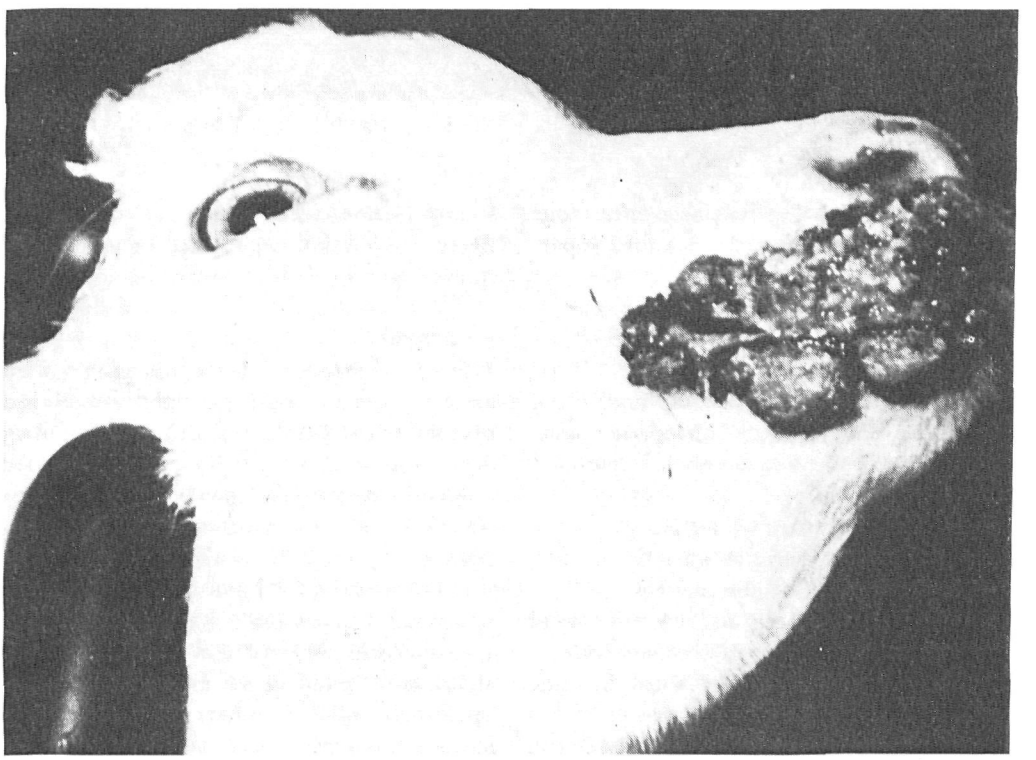


Fig. 5. Orf infection in goat.

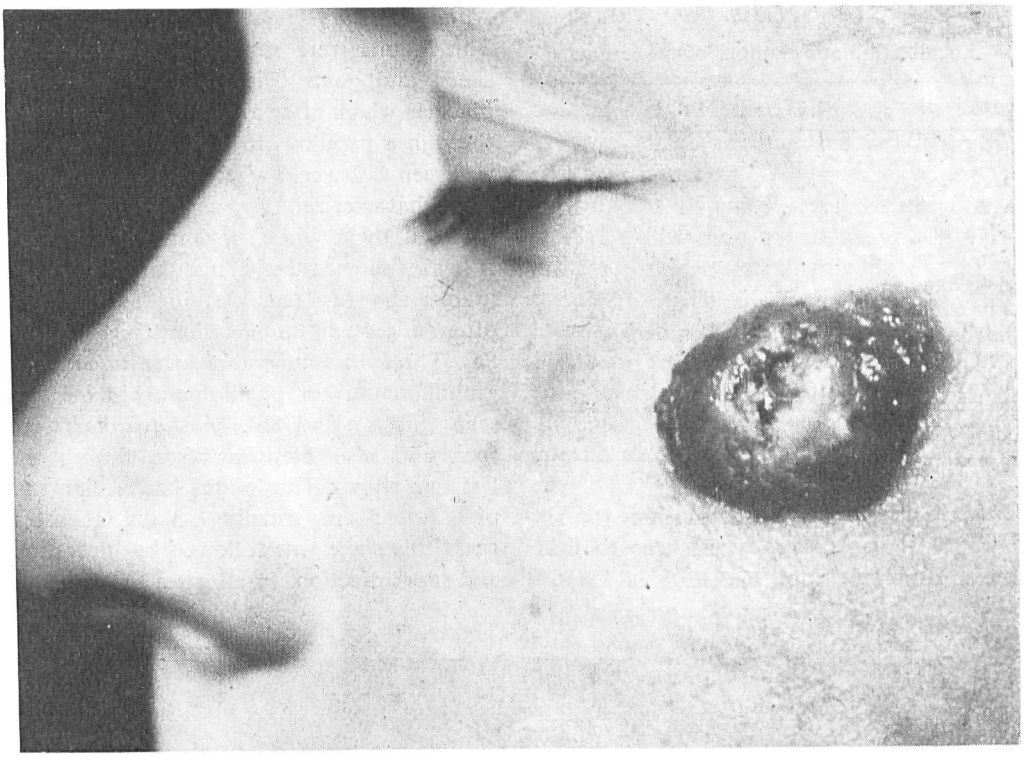


Fig. 6. Orf lesion with central umbilication.

regression and healing was seen after four to 24 weeks. Lesions without heavy superinfection healed without scars within four to 28 weeks, usually within seven weeks.

Complications

Only the clinical material has been used in this connection, as the histopathological material is too heterogeneous and partially lacking in follow-up.

Regional adenitis was found in 17 of 42 male patients (suppurative adenitis in one), and in three of 18 female patients.

Lymphangitis was seen in two males and one female. One male showed *urticaria.*

Erythema multiforme was seen in nine males and seven females (Fig. 9).

Erythema multiforme bullosum was seen in one of each sex (Fig. 10).

Superinfection was seen relatively often. Bacterial isolation carried out in nine cases showed common bacterial pathogens.

Histopathological Findings

1–2-week-old lesions. The epidermis showed moderate acanthosis with light vacuolated cytoplasm in the keratinocytes (ballooning degeneration) (Fig. 11a). The dermis showed dilated and partially newly-formed, thin-walled blood vessels between which an inflammatory infiltrate was seen. The latter was composed of lymphocytes, eosinophils and macrophages.

2–3-week-old lesions. Intraepidermal vesicles were found in some cases and intraepidermal bullae in others (Fig. 11b). Skin surface was sometimes covered by keratotic or parakeratotic material. The rete pegs

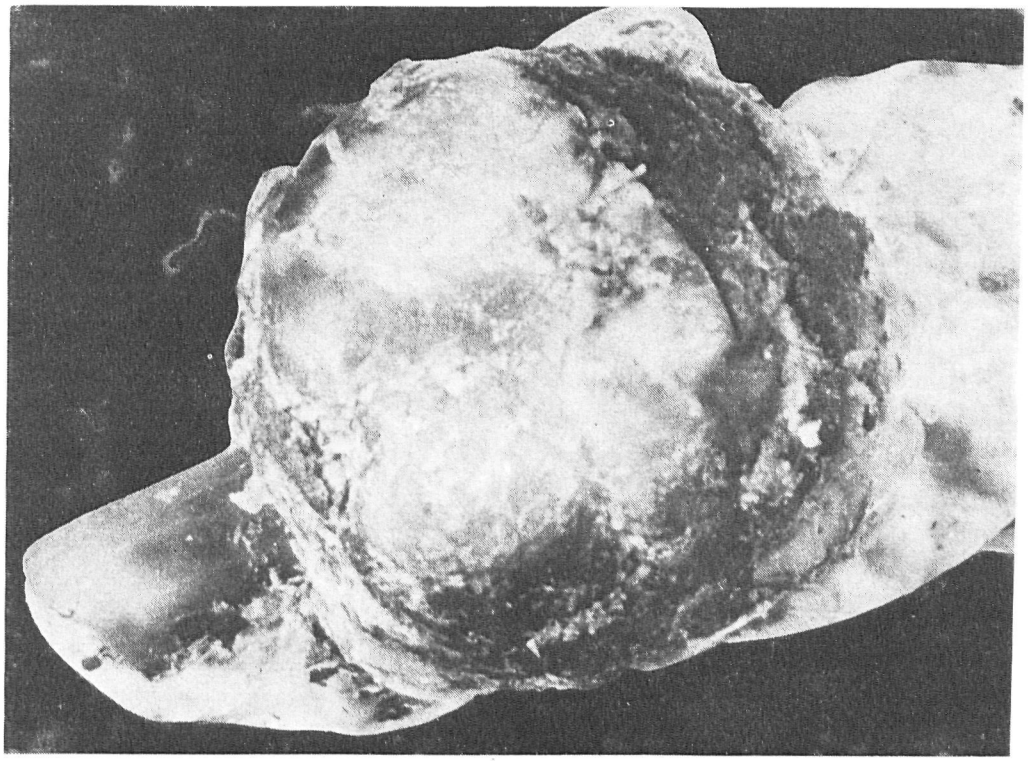


Fig. 7. Amputated finger with giant orf lesion clinically misdiagnosed as malignancy.

showed active proliferation with numerous mitosis and penetrated deep into the underlying dermis. The dermis had the appearance described above (Figs. 11c & d, 12).

Later stages. During the following couple of weeks the lesions gradually involuted. The epidermal hyperplasia disappeared as did the underlying dermal inflammatory reaction.

Typical histological pictures were not seen in cases with massive superinfection.

An epidermal collarette at the base of the lesions like that seen in granuloma pyogenicum was not observed.

Special staining methods gave little additional information.

Ultrastructural Findings

Biopsies. The light microscopical findings were confirmed. During the first week the epidermis showed intra- and extracellular edema (Figs. 12 & 13). In all cases viral particles were found in epidermis when scrutinized. The ease (or difficulty) of detection was the same whether biopsies were primarily fixed in glutaraldehyde or in acid non-buffered formaldehyde and embedded in paraffin for light microscopy and later re-embedded in Epon for electron microscopy, or sent unfixed to the laboratory. The ultrastructural preservation of the cells harbouring the viral particles was, however, superior in those specimens primarily fixed in glutaraldehyde.

The number of viral particles found in different patients varied enormously, even in biopsies taken at the same stage of the disease process. The number of virus-con-

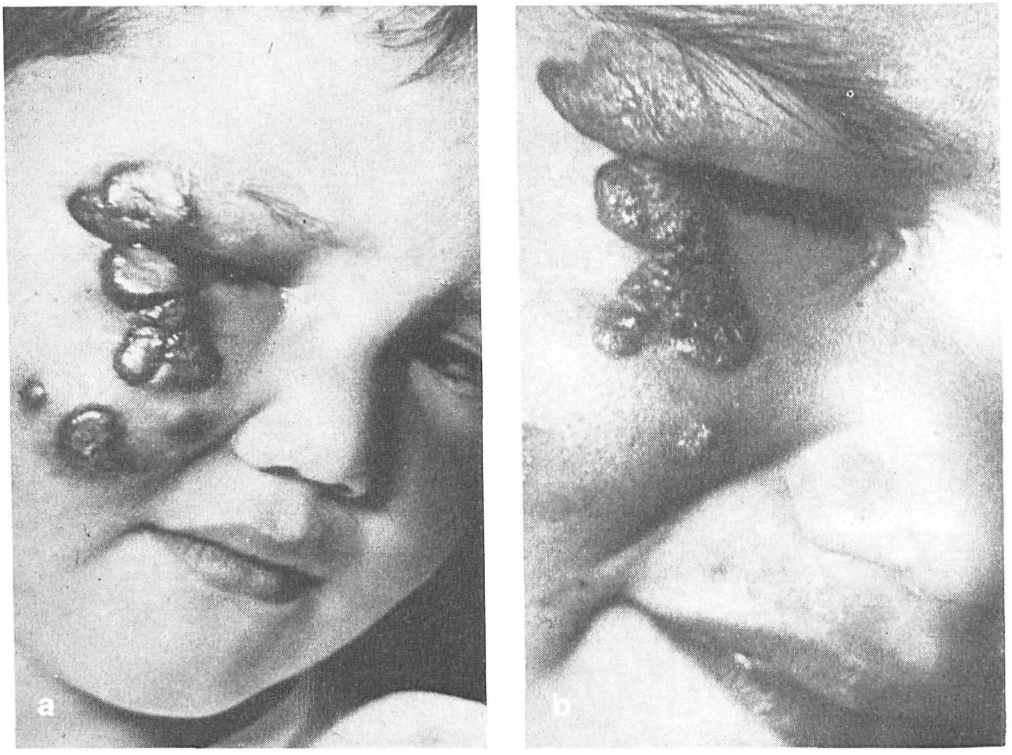


Fig. 8. Orf in nodular (a) and papillomatous stage (b).

taining cells was greatest in the first two weeks after infection. Viral particles were found in epidermis only (Fig. 14).

Viral particles were almost exclusively found in cells showing moderate or marked degenerative changes and always in cytoplasm or extracellularly around damaged keratinocytes (Fig. 14).

In the first two weeks after infection a higher proportion of immature forms were seen.

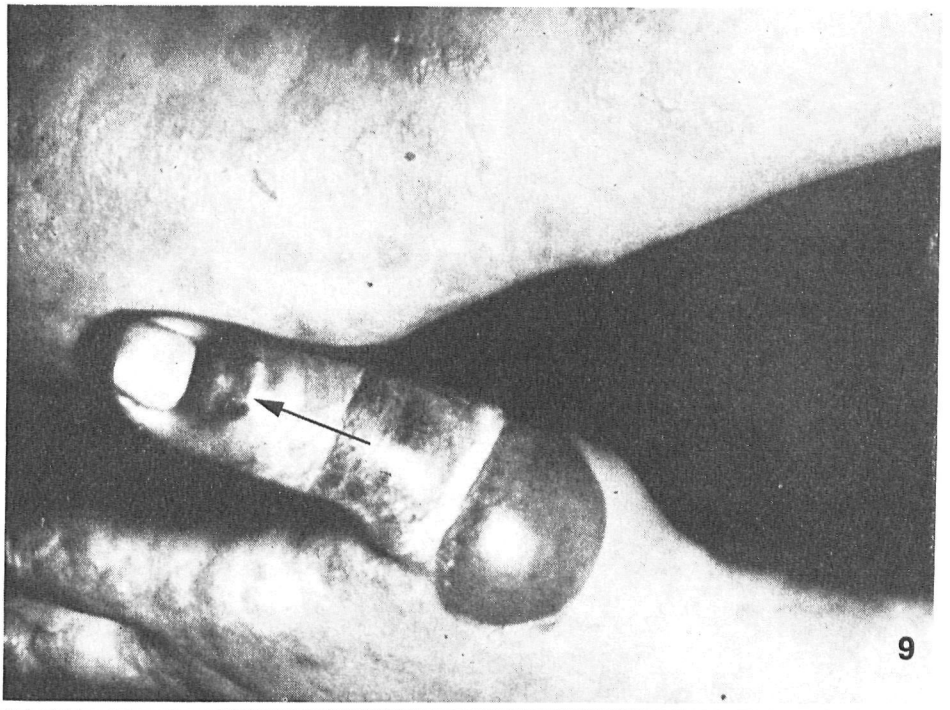
The Orf Virus

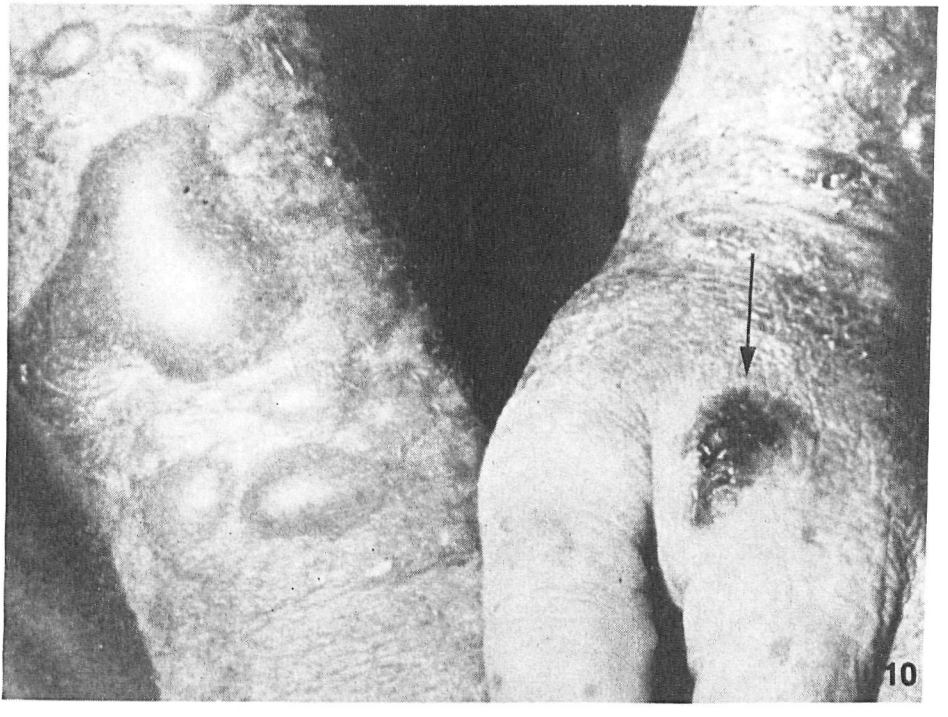
The inner structures of the virus particles were revealed in ultrathin sections (Fig. 14) and in specimens negatively stained at alkaline reaction. The surface structures were best observed in specimens negatively stained at acid reaction (Figs. 15 & 16).

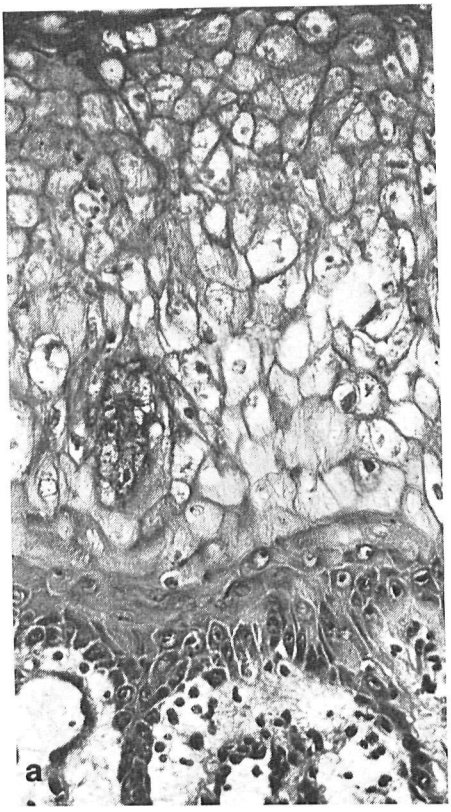
The immature virus particles were ball-shaped, and 1800 Å in diameter (Fig. 14b). The nucleoid was small and eccentric. We were not able to resolve an unequivocal striated nucleoid substructure in these particles even when tilting the specimen stage.

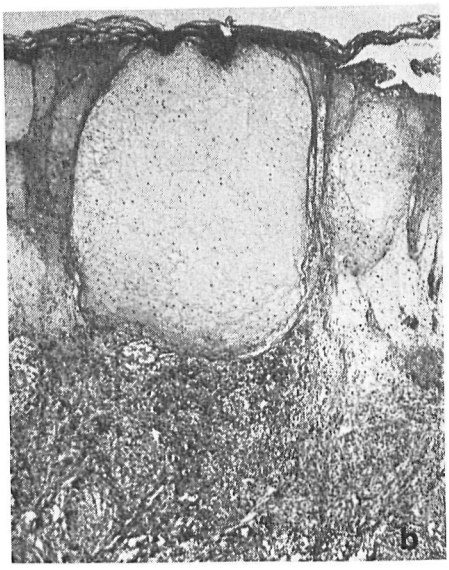
The mature particles contained a central electron dense core with a length varying from 2200 to 3700 Å, a breadth varying from 850 to 1400 Å, and a thickness varying from 280 to 1100 Å, depending upon mode of fixation and staining (Fig. 14). Sometimes a triplet and sometimes a duplet

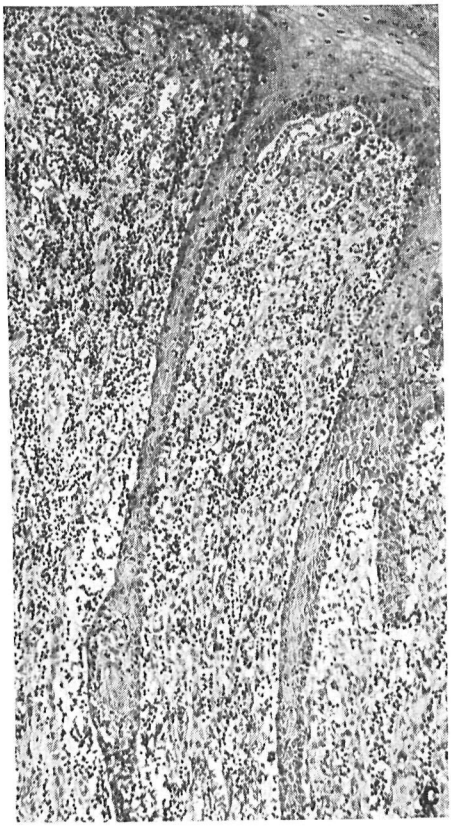
Fig. 9 and 10. Orf complicated by erythema multiforme bullosum. The primary lesion is in the regressive stage (arrow).

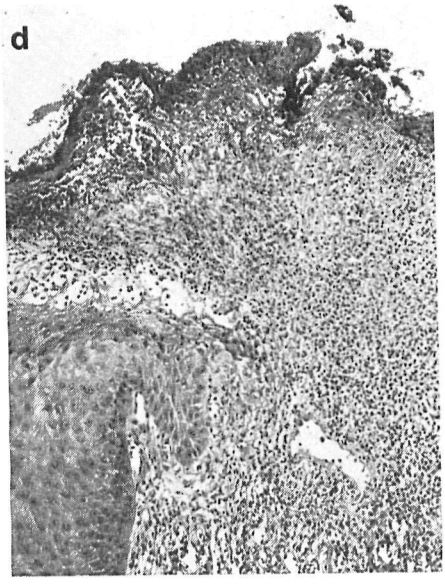

9


10


a


b


c


d

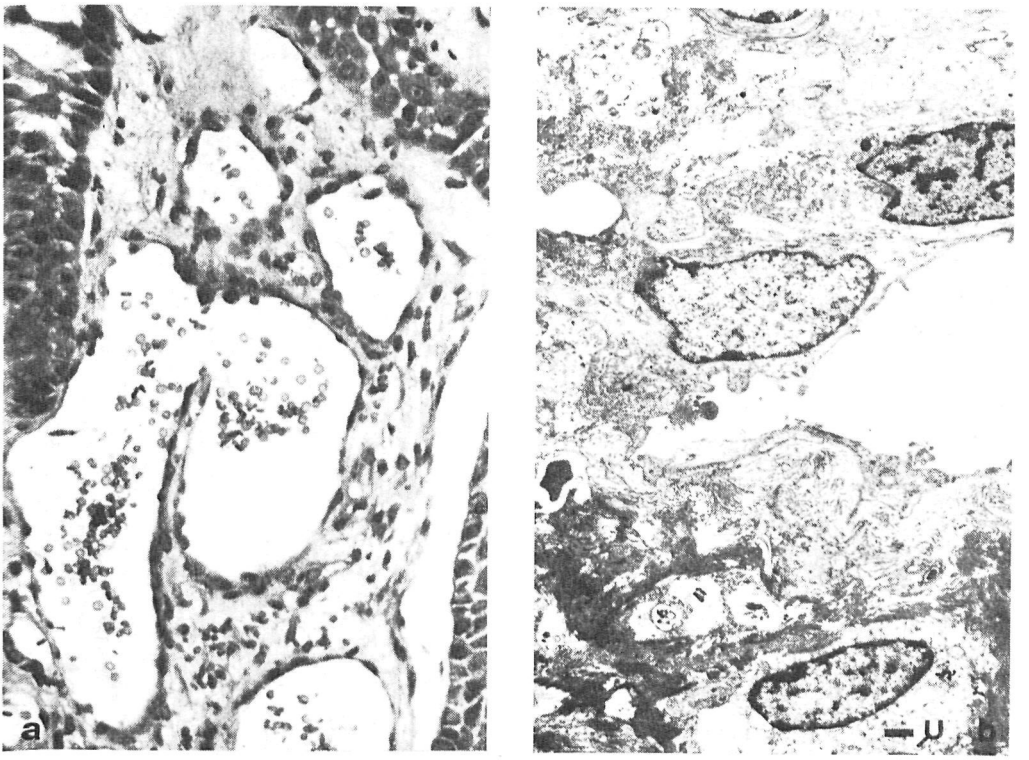


Fig. 12. Light (a) and electron micrograph (b) of angiomatous dermal stroma in orf. (a) H & E × 250. (b) Uranyl acetate and lead citrate stain, × 3600.

substructure was seen. Each substructure seemed tube-like with a central portion with low electron density and surrounded by a shell with increasing electron density towards the periphery. These seemed to be linked together, giving rise to an S- or U-like formation. Some viral particles showed only one central structure with the same size as the combined substructures seen in others. This may be due to artificial changes during processing. In some particles the central structure showed a periodicity of up to 10 alternating light and electron-dense lines arranged parallel to the length axis when observed in ultrathin sections.

The central core was wrapped in a medium electron-dense material which, in some viral particles, seemed homogeneous and in some laminated. A 40 Å zone of low electron density separated this area from the surrounding band-like structures.

These band-like structures were discernible in ultrathin cross-sections (Fig. 14c), but best visualized in suspensions negatively stained at an acid pH. They were 100 Å broad and gave rise to a criss-cross pattern (Figs. 15 & 16). Tilting of the specimen

Fig. 11. Histopathological appearance of orf in early stage with ballooning degeneration of keratinocytes (a), and later stages with intraepidermal bullae (b), penetrating rete ridges (c), and ulceration (d). H & E × 250, × 40, × 100, × 100, respectively.

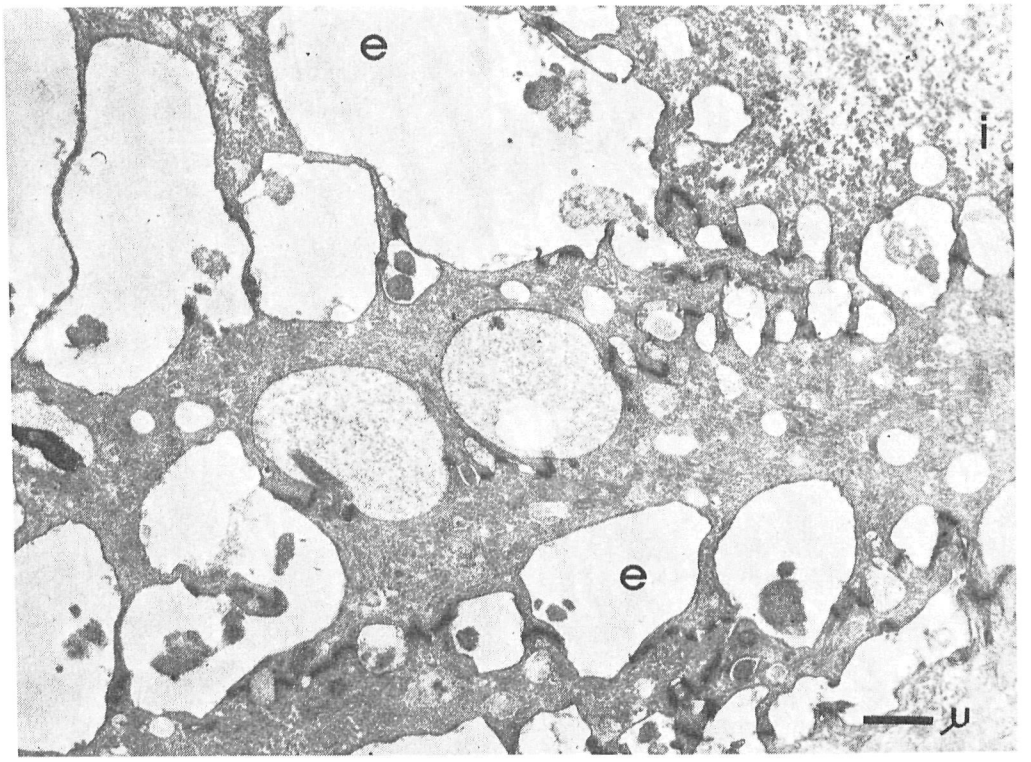


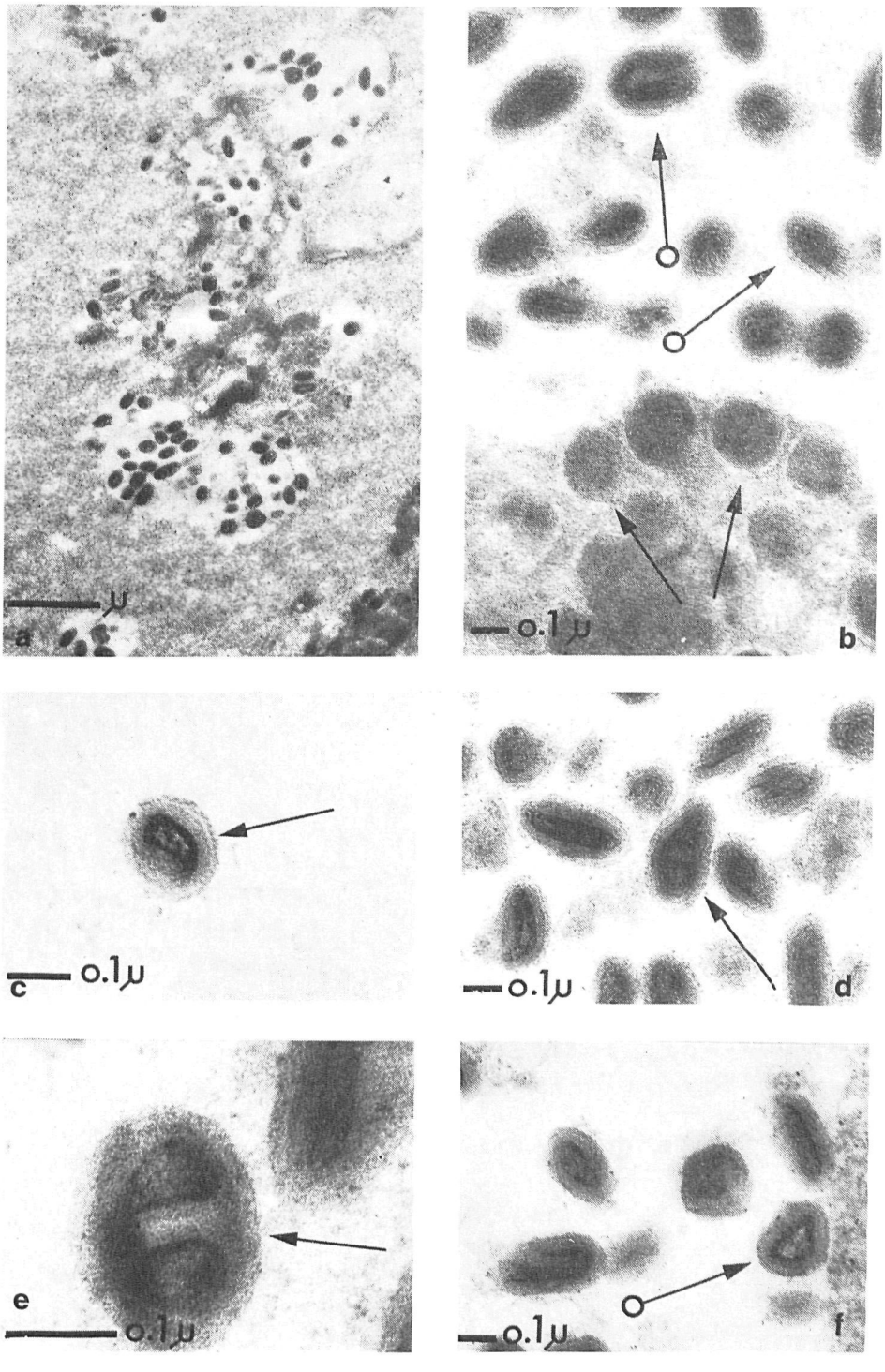
Fig. 13. Intra- (i) and extracellular (e) epidermal edema in early orf lesion. Electron micrograph stained with uranyl acetate and lead citrate, × 9000.

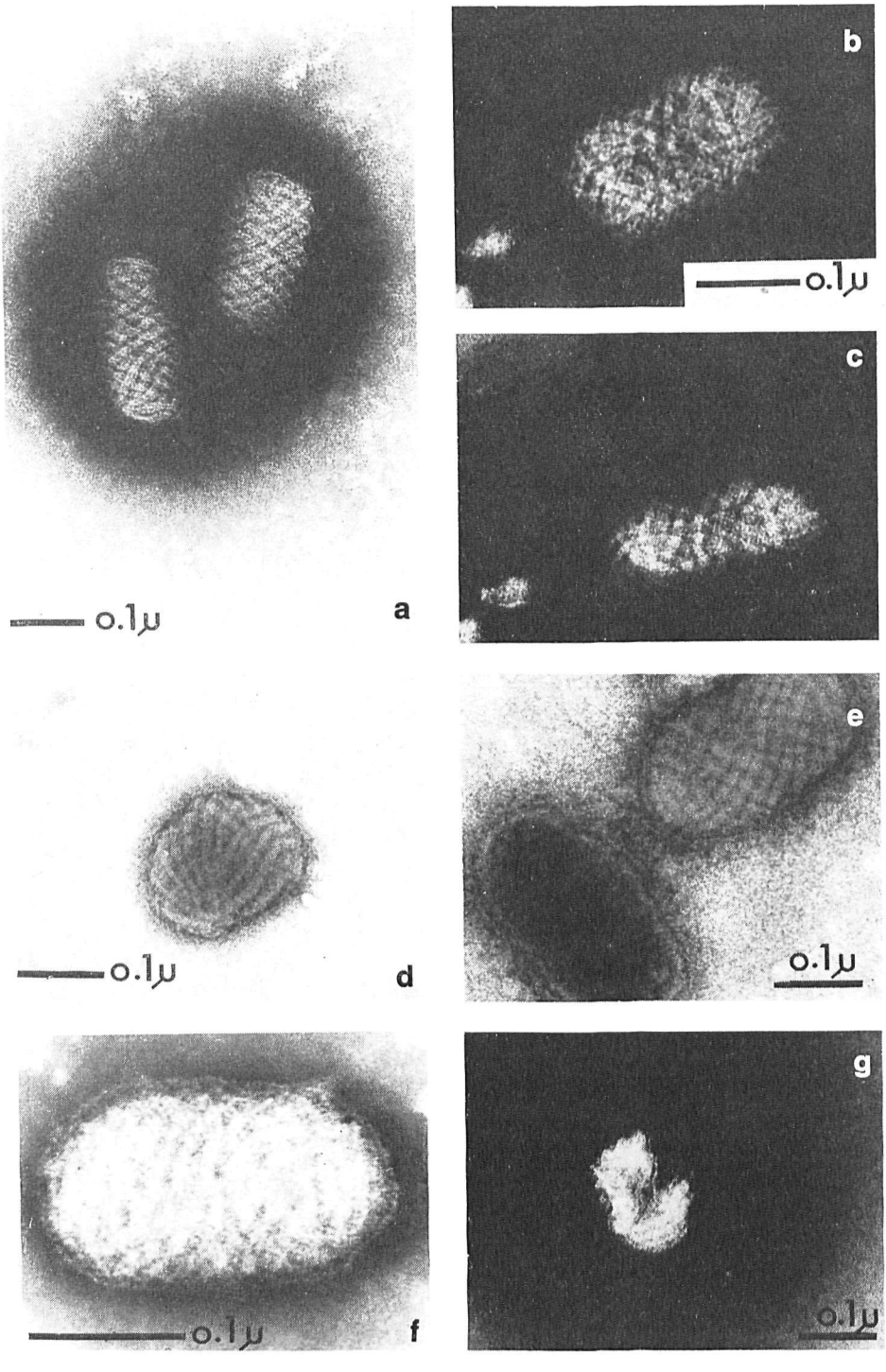
stage showed that this pattern was a result of superimposition of top and bottom images (Figs. 15a–c & 16a–f) and this was also shown when using a scanning attachment operated in the scanning transmission mode on negatively stained viral particles (Fig. 16a–h). When focused at the center of the viral particle a criss-cross pattern was obtained (Fig. 16g), but when focused at top, bands ran in one direction only (Fig. 16h).

The windings deviated 30 to 70° from the length axis of the virus. The bands were flattened and showed a periodicity of approximately 55 Å in their length axis with alternating light and dark areas slightly tilted towards the axis, and with a three-layered appearance in the breadth axis, suggesting a helical substructure.

The outermost portion of the viral particle was 20 Å thick enveloping membrane (Fig. 15e–g) giving the total mature virus

Fig. 14. Electron micrographs showing the appearance of orf in ultrathin sections. Survey picture (a) and larger magnification (b) showing immature (arrow) and mature (labelled arrow) virions. (c) Shows band-like structures of surface in cross-section (arrow), (d), (e) and (f) show virions with anomalous cores appearing U-shaped (arrows) or triangular (labelled arrow) in sections. Uranyl acetate and lead citrate stain, × 14,000, 56,000, 90,000, 56,000, 160,000 and 60,000, respectively.


μ
a
o.1μ
b
c
o.1μ
o.1μ
d
e
o.1μ
o.1μ
f


a
0.1μ
b
0.1μ
c
d
0.1μ
e
0.1μ
f
0.1μ
g
0.1μ

a dimension of approximately 2600 × 1400 × 1000 Å, and the form of a slightly flattened cylinder. Thickness varied up to 1700 Å, breadth up to 2000 Å and length up to 4200 Å. A bigger variation in size was found in ultrathin sections compared to negative stained specimens, probably reflecting artificial changes caused by preparation procedures.

Discussion

Human orf is considered an uncommon disorder (Nagington & Whittle 1961, Leavell et al. 1968, Yeh & Soltani 1974). This report shows that it is fairly common in Norway and we believe, as do Gray (1949), Kewish (1951) and Farmer & Perry (1960) that it is a common occupational disease all over the world.

In sheep, orf is mostly of economic interest because the localization to nostrils, lips and buccal mucose of the lambs and to the udders of their dams interferes with suckling. Reports on high mortality usually reflect secondary invasion of pathogenic micro-organisms.

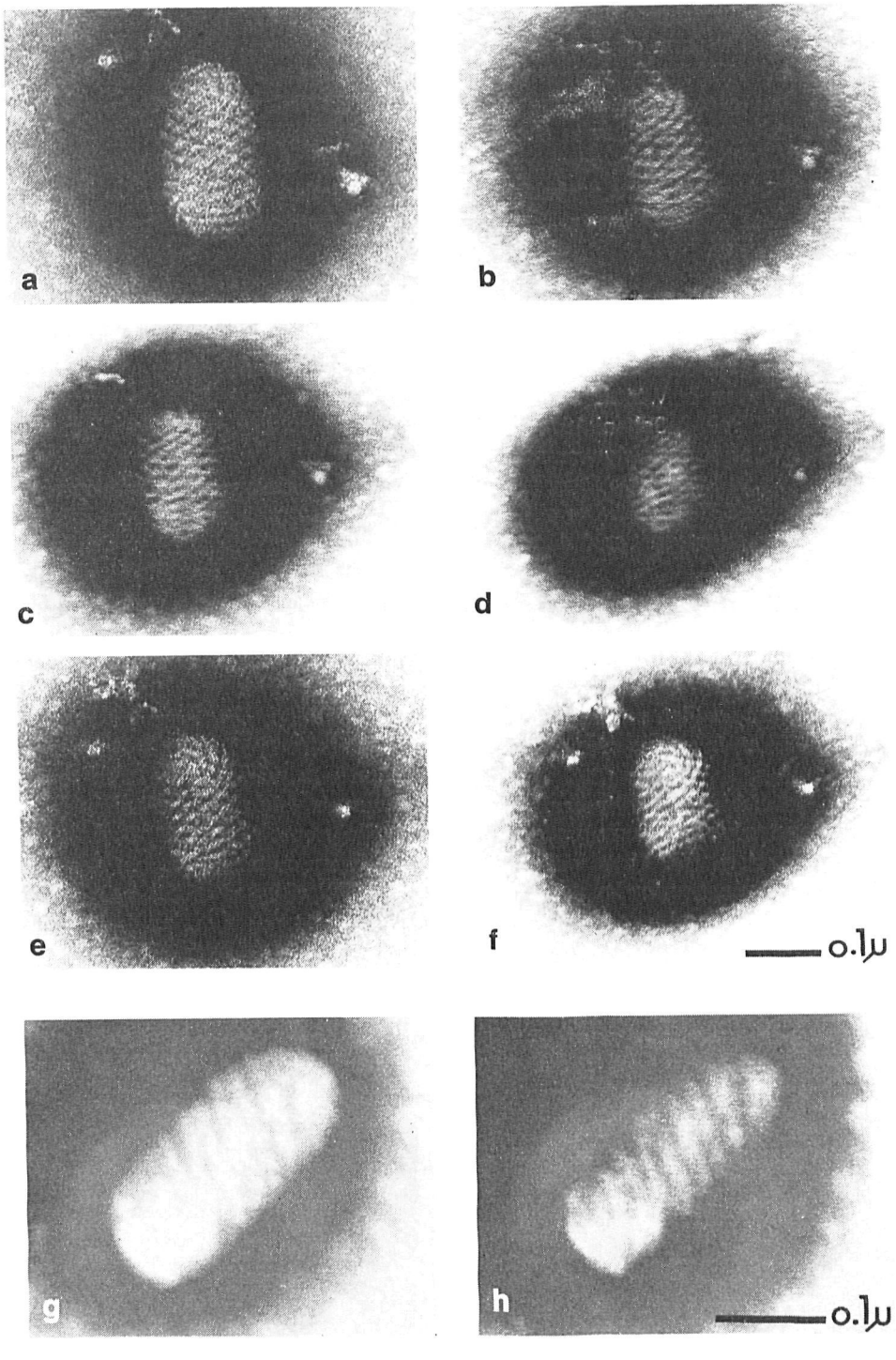
In man, the disease is usually benign and heals spontaneously, and many patients do not seek medical advice. Those unfamiliar with the clinical picture may be alarmed by its rapid growth and mistake it for malignancy. In one of our cases a finger was amputated for this reason (Fig. 7). More often it is misdiagnosed as a keratoacanthoma or a granuloma pyogenicum. In the nodular stage the lesion may resemble a giant molluscum contagiosum. The tendency to central umbilication is characteristic of the human infection (Schmidt 1967). When the disease affects the eye, permanent blindness may be the result (Royer et al. 1970). Metastatic lesions have been reported in humans (Kewish 1951), but would probably be difficult to differentiate from multiple primary lesions.

Apart from superinfection, lymphadenitis and ocular damage, complications in humans have seldom been reported. Secondary erythema multiforme has been reported only once (Blakemore et al. 1948). In our material erythema multiforme was rather a frequent complication and in these cases it was the main reason for seeking medical advice.

Indirect infections through knives, barbed wire, etc. have been reported previously (Leavell et al. 1968) and were common in our study. This is not surprising, as the virus has been found to remain infective for more than 15 years at room temperature and more than 22 years when refrigerated (Schmidt 1967). It does however become inactivated after exposure to ultraviolet light (Schmidt 1967). Natural transmission from man to man has not been reported. Immunity is only partial in both sheep and man (Blakemore et al. 1948, Beck & Taylor 1974). Sheep outbreaks are not confined to any particular period of the year, but seem to be more prevalent during the spring and summer months (Glover 1928) and to decrease with the approach of winter (Král & Schwartzman 1964). This is, however, the high season for human orf, mainly due to the wool shearing and slaughtering taking place at that time (Fig. 4).

The relatively high frequency of lesions

Fig. 15. Electron micrographs showing band-like surface structures of negatively stained orf virions tilted − 18° (a), 0° (b) and + 45° (c). (b) and (c) show same particle. (d) shows the arrangement of the band-like structures at the end of a virion tilted on the specimen grid. (e), (f) and (g) show enveloping membrane of intact (e and f) and damaged (g) virions, acid 1 % PTA stain (a–c, f–g) or acid 0.8 % SST stain (d,e), × 110,000, 150,000, 150,000, 120,000, 120,000, 230,000 and 110,000, respectively.


a
b
c
d
e
f
0.1μ
g
h
0.1μ

in head and neck in male patients probably reflects their more active role in the handling of sheep, as does their higher overall incidence of orf. The occurrence of twice as many lesions on the right hand as on the left in female patients, contrasting with a slight over-representation of left hand lesions in males, may perhaps reflect a difference in working procedure.

Orf has caused industrial trouble among shearers in Australia (Fenner & White 1970). We have witnessed similar difficulties in Norway. In the autumn of 1974 the slaughterhouse workers in Norway went on strike. This delayed slaughtering, which when resumed was carried out at a forced pace. During this an epidemic of human orf, partially complicated by erythema multiforme, broke out and almost led to panic (these cases are not included in the present report).

Although the clinical picture may mislead the observer to a diagnosis of malignancy, no histopathological signs of malignancy have been found. The lesion may, however, be mistaken for other benign lesions such as pyogenic granuloma, but differing from this in the lack of epidermal collarette and the presence of penetrating epidermal fingers running through a full thickness of the dermis.

Our findings do not support the view that the histopathological picture of orf is different in sheep and man (Wheeler & Cawley 1956), or the claims of Abdussalam (1957) that the epidermal cell vacuolation remains restricted to individual cells and that the cell boundaries do not break to form a large vesicle as in other pox diseases. Furthermore, our findings are contrary to those of Leavell et al. (1968) which suggest that the orf lesion is vaguely reminiscent of precancerous lesions.

Our ultrastructural observations support and extend those of Peters et al. (1964), Büttner et al. (1964), Nagington et al. (1964), Kluge et al. (1972) and Yeh & Soltani (1974). Slight differences in the dimensions of the virus reported in different papers probably reflect differences in preparation. The orf virus was found to be strictly epidermiotrophic. Leavell et al. described inclusion bodies in the endothelial cells of small intradermal vessels (Leavell et al. 1965). These inclusions were intranuclear, and as we did not find intradermal viral particles in any of our specimens and no intranuclear particles even in heavily infected keratinocytes, we have no reason to believe that the described inclusions harbored viruses.

Our clinical findings are in accordance with those of Leavell and coworkers (1968). To the physician familiar with orf, the clinical diagnosis is usually simple, particularly when it is known that the patient has been in contact with sheep or goats.

Formerly, the diagnosis in doubtful cases was confirmed by inoculation of material from lesions into newborn lambs. When older lambs were used, a false negative result might have been caused by acquired immunity. Passive immunization from dam may also represent a diagnostic pitfall. The method of inoculation is therefore not only expensive and time-consuming, it is also unreliable.

Isolation of the virus by tissue culture is possible, but difficult (see review by Schmidt 1967). Serum analysis for anti-

Fig. 16. Arrangement of band-like surface structures demonstrated in a tilting series of one single orf virion observed at 0° (a), + 30° (b), + 42° (c), + 51° (d), − 24° (e) and + 42° (f) and in scanning transmission electron micrographs of the same virion focused on center (g) and top (h) of particle. Negatively stained with acid 1 % PTA, × 110,000 (a–f) and 160,000 (g–h), respectively.

bodies to orf virus is also possible, but seldom used.

The best and most rapid diagnostic method is electron microscopy of negatively stained suspensions from lesions. This is somewhat more difficult in later stages of the disease, both because of a lower number of viral particles and because of masking of these by bacteria and cellular debris. The viral particles of orf and Milkers nodules have a similar ultrastructural appearance. It is therefore crucial that the ultrastructural findings are correlated to clinical information and the type of animal contact.

The importance of knowing the benign nature of this condition is obvious, since complications tend to be caused by overtreatment.

Acknowledgements

The authors are grateful for the expert technical assistance of Inga Finseth and Inger Bakken Holmefjord.

Fig. 5 was kindly placed at our disposal by Johan Krogsrud, Department of Virology, National Veterinary Institute, Oslo, and Fig. 7 by the Gade Institute, Department of Pathology, University of Bergen.

References

Abdussalam, M. (1957) Contagious pustular dermatitis II. Pathological histology. *Journal of Comparative Pathology and Therapeutics 67,* 217–222.

Aynaud, M. (1923) La stomatite pustuleuse contagieuse des ovins (chancre du mouton). *Annales de l'Institut Pasteur 37,* 498–527.

Beck, C. C. & Taylor, W. B. (1974) Orf: it's awrful. *Veterinary Medicine/Small Animal Clinician 69,* 1413–1417.

Blakemore, F., Abdussalam, M. & Goldsmith, W. N. (1948) A case of orf (contagious pustular dermatitis): Identification of the virus. *British Journal of Dermatology and Syphilis 60,* 404–409.

Boughton, I. B. & Hardy, W. T. (1934) Contagious ecthyma, sore mouth of sheep and goats. *Journal of the American Veterinary Medical Association 85,* 150–178.

Büttner, D., Giese, H., Müller, G. & Peters, D. (1964) Die Feinstruktur reifer Elementarkörper des Ecthyma contagiosum und der Stomatitis papulosa. *Archiv für die gesamte Virusforschung 14,* 657–673.

Farmer, J. L. & Perry, H. O. (1960) Orf: An occupational disease. *Minnesota Medicine 43,* 818–821.

Fenner, F. & White, D. O. (1970) Poxviruses. In: *Medical Virology,* pp. 250–263. New York and London: Academic Press.

Graham, J. H., Johnson, W. C. & Helwig, E. B. (1972) *Dermal Pathology.* Hagerstown, Maryland: Harper & Row.

Gray, E. H. (1949) Contagious ecthyma in man. *California Medicine 70,* 417–418.

Glover, R. E. (1928) Contagious pustular dermatitis of the sheep. *Journal of Comparative Pathology and Therapeutics 41,* 318–340.

Hansen, G. (1879) Om en egen sygdom (Kopper?) hos Geden i Norge. *Tidsskrift for Veterinairer 9,* 298–302.

Hellerstrøm, S. (1962) *Hudsjukdomar.* Lund: Håkan Ohlssons Boktryckeri.

Hodgson-Jones, I. S. (1951) Orf in London. *British Medical Journal 1,* 795–796.

Høvding, G. (1957) Ecthyma contagiosum, en virussykdom overført fra sau til menneske. *Nordisk Medicin 25,* 1089–1090.

Joklik, S. K. (1968) The large DNA animal viruses: The pox virus and herpes virus group. In: *Molecular Basis of Virology,* ed. Fraenkel-Conrat H., pp. 576–582. ACS monograph, New York, Amsterdam, London: Reinhold Book Corporation.

Kewish, O. K. (1951) Sheep shearers get orf. *British Medical Journal 1,* 356.

Kluge, J. P., Cheville, N. F. & Peery, T. M. (1972) Ultrastructural studies of contagious ecthyma in sheep. *American Journal of Veterinary Research 33,* 1191–1200.

Král, F. & Schwartzman, R. M. (1964) Contagious ecthyma of sheep and goats. In: *Veterinary and Comparative Dermatology,* pp. 223–244. Philadelphia: J. B. Lippincott Co.

Laurent, M. (1927) Contribution à l'étude des formes atypiques de la maladie ovine décrite sous le nom d'ecthyma contagieux des lèvres. *Bulletin Médicale Véterinaire de France 80,* 267–273.

Leavell, U. W., McNamara, M. J., Meulling, R. J. & Landrum, F. (1965) Ecthyma contagiosum (orf). *Southern Medical Journal 58,* 239–243.

Leavell, U. W., McNamara, M. J., Muelling, R., Talbert, W. M., Rucker, R. C. & Dalton, A. J. (1968) Orf: Report of 19 human cases with clinical and pathological observations. *Journal of the American Medical Association 204,* 657–664.

Lindgren, S. & Skogh, M. (1973) Orf – nu i Sverige? Summary of a lecture held at the 30th Congress of the Swedish Medical Association.

Montgomery, H. (1967) Viral diseases. In: *Dermatopathology I,* pp. 531–567. New York: Harper & Row.

Nagington, J. & Whittle, C. H. (1961) Human orf: Isolation of the virus by tissue culture. *British Medical Journal 18,* 1324–1327.

Nagington, J., Newton, A. A. & Horne, R. (1964) The structure of orf virus. *Virology 23,* 461–472.

Newsom, I. E. & Cross, F. (1934) Sore mouth in sheep transmissible to man. *Journal of the American Veterinary Medical Association 84,* 799–801.

Nürnberg, H. (1942) Über den ansteckenden Maulgrind der Schafe und Ziegen, pp. 5–47. Doctoral thesis at Institut für Veterinär-Pathologie der Universität Berlin.

Peters, D., Müller, G. & Büttner, D. (1964) The fine structure of paravaccinia viruses. *Virology 23,* 609–611.

Royer, J., Joubert, L. & Prave, M. (1970) Grave ocular damage in man due to ovine contagious pustular dermatitis. *Bulletin de la Société des sciences vétérinaires et de médecine comparée Lyon 72,* 93–104.

Schmidt, D. (1967) Die Dermatitis Pustulosa des Schafes. In: *Handbuch der Virusinfektionen bei Tieren,* ed. Röhrer H., pp. 713–761. Jena: Gustav Fischer Verlag.

Wheeler, C. E. & Cawley, E. P. (1956) The microscopic appearance of ecthyma contagiosum (orf) in sheep, rabbits and man. *American Journal of Pathology 32,* 535–545.

Yeh, Hsu-Po & Soltani, K. (1974) Ultrastructural studies in human orf. *Archives of Dermatology 109,* 390–392.

Address:
Jan Vincents Johannessen, M. D.
Department of Pathology
The Norwegian Radium Hospital
Montebello, Oslo 3, Norway