

## ON A NEW TYPE OF INTRANUCLEAR MICROBODIES OBSERVED IN BULLOUS MUCO-SYNECHIAL AND ATROPHIC DERMATITIS (OCULAR PEMPHIGUS)\*

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Intranuclear microbodies with a spiral structure have been described in numerous dermatological conditions of viral or of unknown etiology. According to some workers these microbodies are virus-like particles, while to others, they represent a non-specific reaction to a pathogen, not well-identified.

Keratoacanthoma has been the subject of many such studies. In the nuclei of keratoacanthoma cells, numerous workers (1-4) have described rounded and oval-shaped microbodies varying in size from 0.2 to 0.6  $\mu$ , and surrounded by a lighter ring. Similar microbodies have also been observed in bullous dermatoses of the pemphigus group (5), in lichen ruber planus (6), in psoriasis (7), in "self-healing epithelioma" (8) and in conditions of established viral etiology (5, 9).

In one case of bullous muco-synechial and atrophic dermatitis (ocular pemphigus), in addition to the microbodies with typical spiral structure, there was present another type of microbody which contained distinguishable particles about 200 Å in diameter and staining strongly with osmic acid. These particles partially or totally occupy the microbodies. The larger the number of particles contained in these microbodies, the smaller is the number of membranes present in them.

Study of these intranuclear particles was done in an attempt to contribute to the elucidation of the significance of these microformations.

### MATERIALS AND METHODS

In five cases, clinically and histologically diagnosed as bullous muco-synechial and atrophic dermatitis, biopsy specimens were obtained from bullous lesions, from atrophic-cicatricial lesions and from apparently healthy skin. The specimens were fixed in 1% osmic acid in Millonig's buffer (10) for 4 hours at 4° C. Dehydration in acetone and inclusion in Vestopal (11) were performed according to the technic described by Caputo and Lombardi (12). The ultrathin sections obtained

with an "Ultratome" microtome were stained with uranyl acetate and observed under a Hitachi HU 11 microscope.

### RESULTS

In all five cases studied we observed a great number of spiral-shaped microbodies, varying in size from 0.2 to 1  $\mu$ , in the sections of epidermal cell nuclei. These formations occurred both singly and in groups and were in all instances were surrounded by a lighter ring (Fig. 1).

In one of the five cases considered, microbodies with a distinctive structure were noted in the specimens of both the bullae and the atrophic skin. These microbodies in fact contained a notable quantity of particles which stained intensely with osmic acid and were about 200 Å in diameter ("inhabited microbodies"). Such particles were found in the central portion of the microbody (Fig. 3) or at its periphery; and at times they completely occupy the microbody (Figs. 4, 5). In the former case, the particles form a sort of central "nucleoid" spherical or tetrahedric shape. Occasionally it is also possible to see two "nucleoids" located at the poles of the microbody (Fig. 2).

The mass of osmiophilic particles is surrounded by a varying number of spiral membranes (Fig. 3), being less numerous when the aforesaid particles occupy a large part of the microbody (Figs. 4, 5). When the particles completely occupy the microbody, there appear to be only two membranes (Figs. 4, 5). Occasionally septa are also observed within the microbodies (Figs. 4, 5).

In most sections the particles are almost spherical and are separated by small lighter spaces. However, in some cases the particles may assume a tubular aspect (Fig. 3).

The "inhabited" microbodies vary in size from 0.4 to 1.5  $\mu$  and are usually round or oval-shaped; but some were observed with varied shapes (Fig. 2). These "inhabited" microbodies are surrounded by a lighter ring. In some instances both "inhabited" and simple spiral microbodies were observed within the same nucleus.

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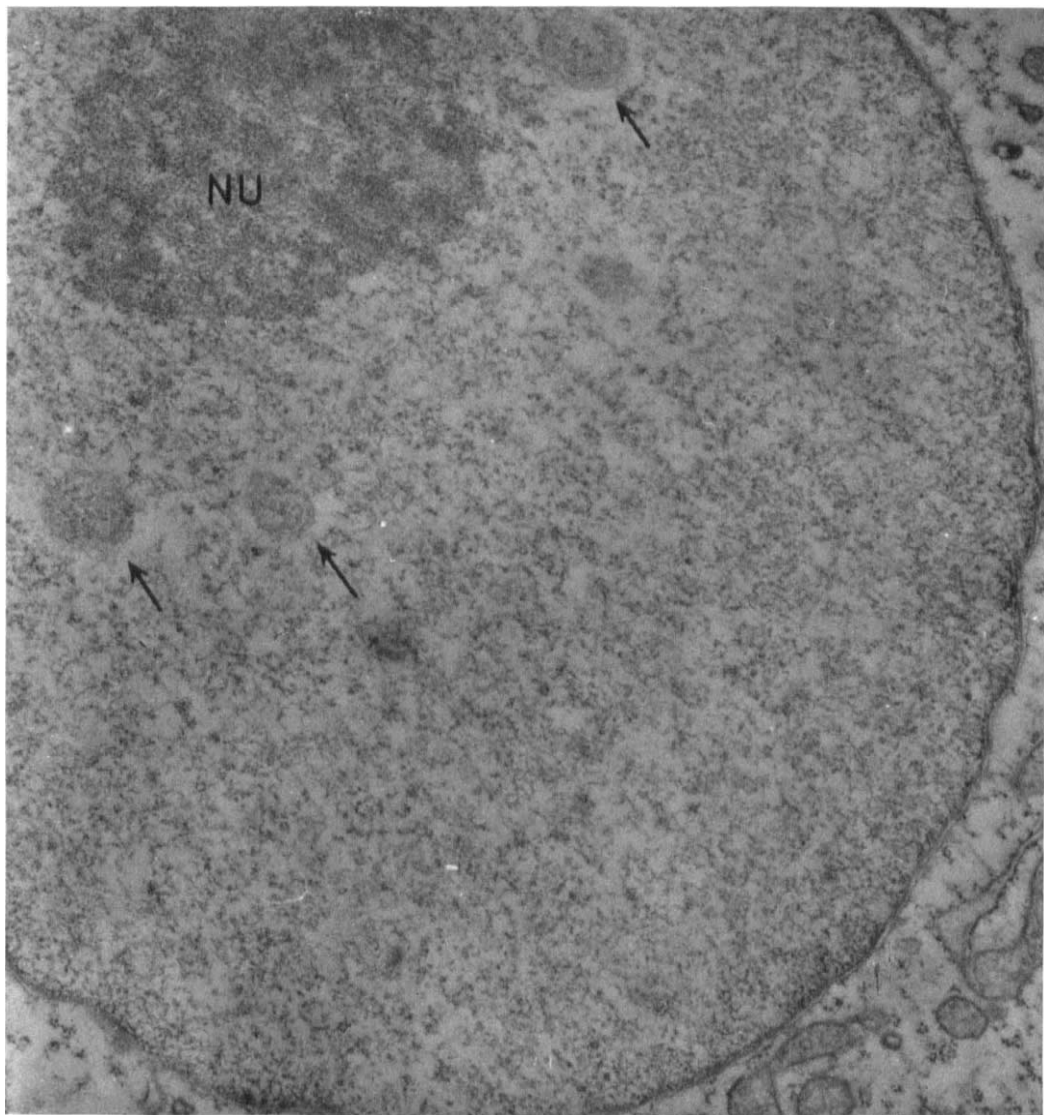


FIG. 1. Intranuclear "non-specific" spiral microbodies (→). NU = nucleolus.  $\times = 15,000$ .

#### DISCUSSION

There have been numerous reports on the presence of intranuclear microbodies in various cutaneous diseases. Zelikson and Lynch (1) were the first to observe in the nuclei of keratoacanthoma intranuclear microbodies composed of an amorphous central nucleoid surrounded by a various number of membranes. These microbodies, varying in size from 250 to 600  $m\mu$ , could be single or multiple, and were interpreted by the authors to be "virus-like particles". Simi-

lar observations were reported by Gay Prieto and co-workers (4).

In a recent report on the viral etiology of keratoacanthoma, Forck, Fromme and Jordan (3) confirmed the findings of Zelikson and Lynch, and also noted the presence in the nuclei of other rounded particles, surrounded by membranes and varying in size from 35 to 60  $m\mu$ , not unlike the herpes zoster virus.

Microbodies very similar to those observed by Zelikson and Lynch in keratoacanthoma

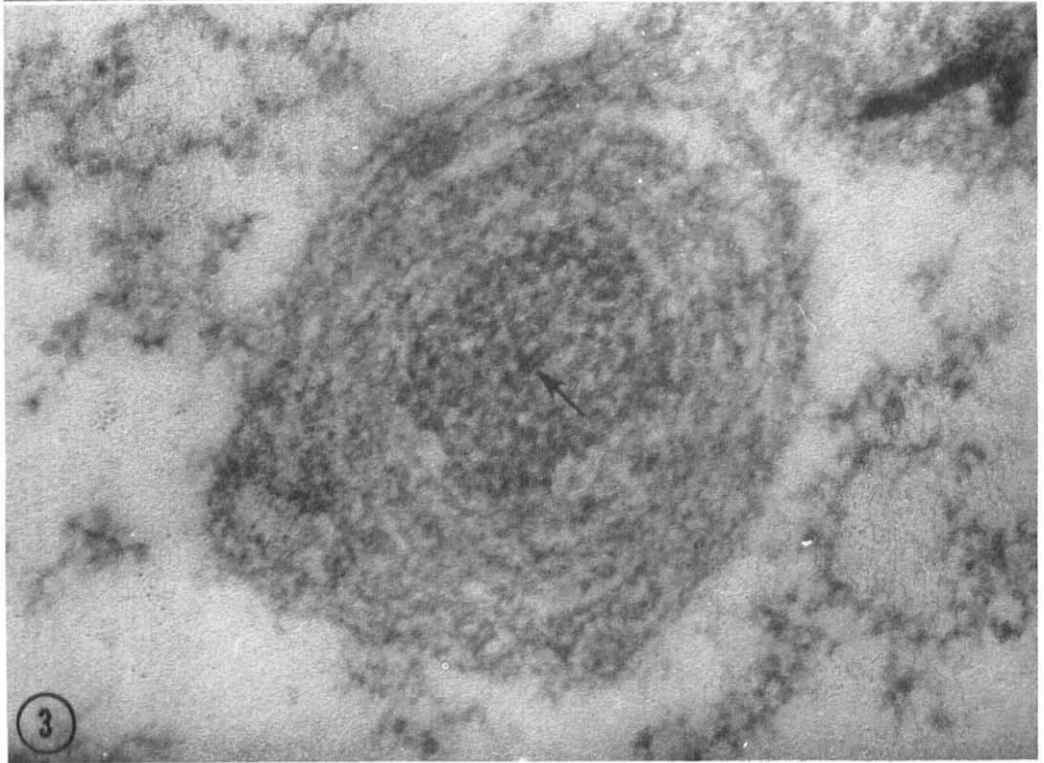
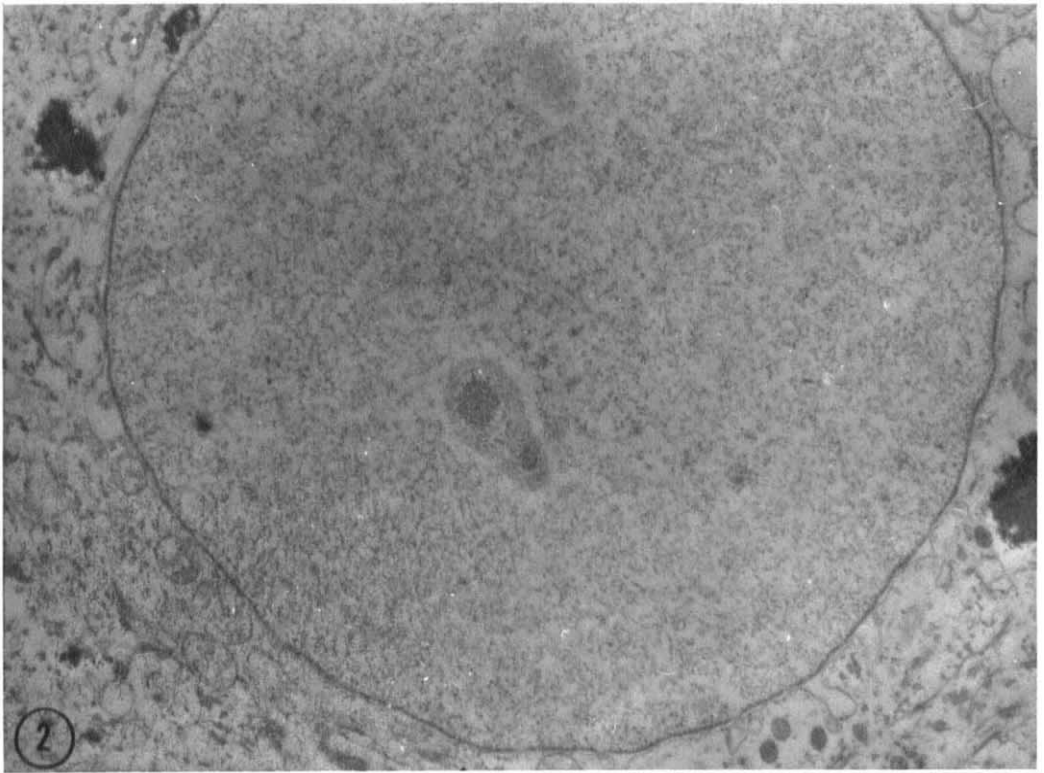


FIG. 2. "Inhabited" intranuclear microbody of irregular aspect containing two nucleoids of osmiophilic particles at the two poles.  $\times 12,500$ .

FIG. 3. Intranuclear microbody presenting a tetrahedral central nucleoid surrounded by spiral membranes. At the center of the nucleoid a particle of tubular aspect can be observed, ( $\rightarrow$ ),  $\times 75,000$ .

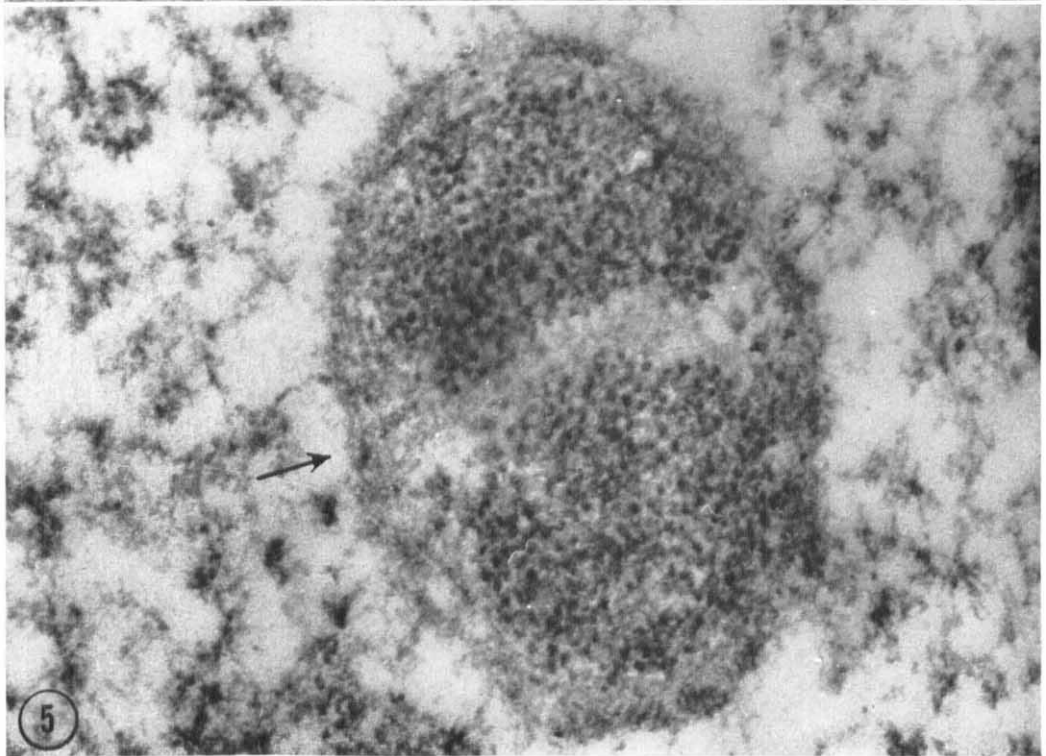
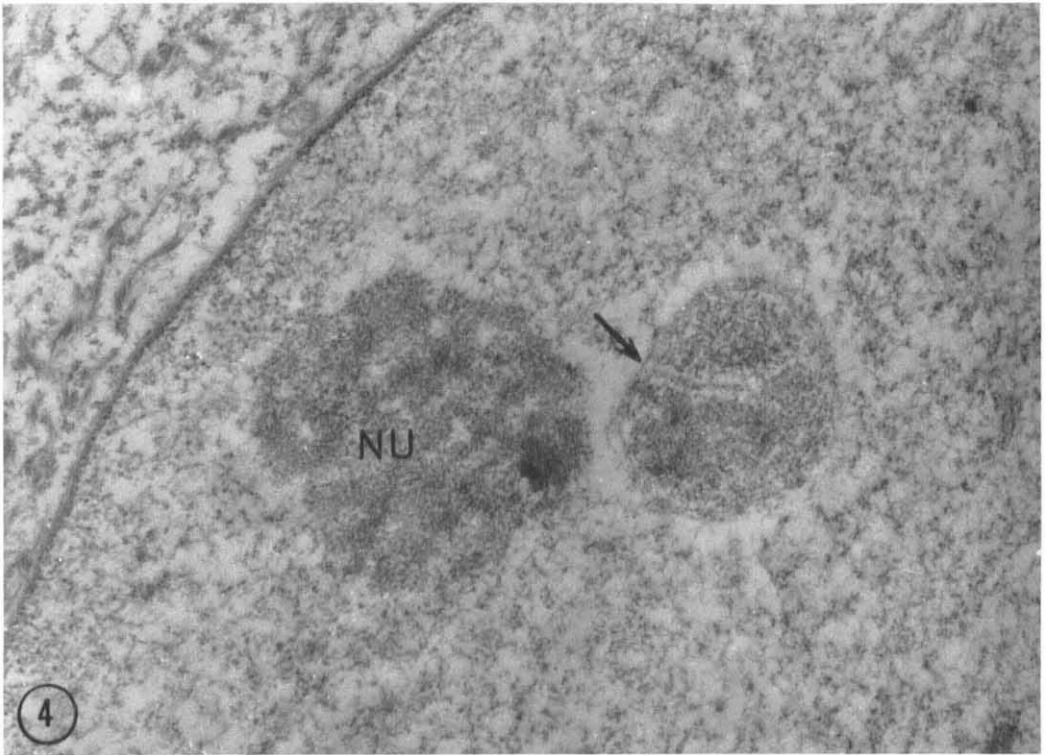


FIG. 4. Intranuclear microbody completely occupied by osmiophilic particles. It is surrounded by two membranes and presents a septum at the center. ( $\rightarrow$ ). NU = nucleolus.  $\times 35,000$ .

FIG. 5. Intranuclear microbody totally occupied by particles surrounded by two membranes and with a septum. ( $\rightarrow$ ).  $\times 75,000$ .

have been observed by Brody (7) in the nuclei of psoriatic subjects.

Swambeck and Thyresson (6) observed intranuclear microbodies in lichen ruber planus. In their opinion these formations may have some relationship to a viral etiology of the disease. Burket and Caplan (8) reported similar findings in the study of the ultrastructure of that which they call "multiple self-healing epithelioma". These workers consider that the intranuclear microbodies are non-specific reactions, without altogether excluding a viral etiology.

Bellone, Caputo and Clementi (5) found numerous microbodies with analogous characteristics in the nuclei of dermatoses of the pemphigus group, as well as in warts and in herpes zoster. They are of the opinion that this may be a reaction of the nuclear components to a "noxa" of probable viral origin.

Recently Nasemann (9) also observed intranuclear microbodies in condyloma acuminatum. However, he considers them as non-specific reactions to products of altered cellular metabolism.

In reviewing the above-mentioned observations, two points can be made: a) The intranuclear microbodies encountered in the above-mentioned diseases are almost identical (spiral aspect with or without an amorphous central nucleoid). b) The diseases in which intranuclear microbodies have been observed either have a well-ascertained viral etiology or are of unknown origin.

These observations lead one to inquire if the microbodies do not always represent an analogous nonspecific reaction of the nuclear components to a pathogenic noxa of viral nature.

In all five cases of bullous muco-synechial and atrophic dermatitis in this study, a notable quantity of "non-specific" microbodies was observed. But in one case, in addition to these microbodies, we also noted a great quantity of "inhabited" microbodies—that is microbodies occupied in part or totally by osmiophilic particles about 200 Å in size.

While we cannot define the nature of these particles, we may, however, point out that they are very similar both in size and in shape to the granules of RNA described in the nuclei of cells infected by polio virus during the earliest phase of the infection (13).

In our opinion, the observation that the number of membranes surrounding the "inhabited"

microbody increases as the number of particles contained in the microbody diminishes is worthy of interest.

This observation may indicate that the osmiophilic particles represent a kind of early reaction of the nuclear material to viral invasion, and furthermore that, at a later stage, the osmiophilic granules disappear, to be followed by the appearance of spiral membranes similar to those observed in the majority of nuclear microbodies described by us as non-specific.

#### SUMMARY

The authors studied five cases of bullous muco-synechial and atrophic dermatitis (ocular pemphigus). In one case they observed several "inhabited" intranuclear microbodies containing particles staining strongly with osmic acid, about 200 Å in size, surrounded by membranes.

The number of membranes is inversely proportional to the number of particles contained in the microbody.

It is hypothesized that the nuclear microbodies composed solely of membranes ("non-specific microbodies") are residues of the original "inhabited microbodies" in which the presence of a transient pathogenic noxa (virus?) may be distinguishable.

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