Acta Dermatovener (Stockholm) 56: 429–434, 1976

NUCLEAR BODIES IN CELLS OF NORMAL HUMAN SKIN

Bent Hentzer and Takasi Kobayasi

From the Department of Dermatology, University of Copenhagen, Rigshospital, Copenhagen, Denmark

Abstract. The frequency of nuclear bodies in the cells of normal human skin has been studied. Three different types were observed in most cells. The frequency of nuclear bodies varied according to cell type. The average frequency in our material was 15%. A significantly lower frequency was found in epidermal cells and a higher frequency in endothelial cells. These observations should be kept in mind when nuclear bodies in abnormal skin are evaluated.

Key words: Nuclear body; Human skin

Nuclear bodies have been observed in most tissues under both normal and pathological conditions. Experimentally induced nuclear bodies have also been reported (6, 13). The function of nuclear bodies remains unknown, although de Thé et al. (6) described their morphology as long as 15 years ago. Many authors came to the conclusion that the nuclear body is a normal organelle in most cells, but their frequency and degree of differentiation varies (2, 10, 12).

To the best of our knowledge, the appearance and frequency of nuclear bodies in different cell types of normal adult human skin have not been described previously. This knowledge is necessary to interpret findings of nuclear bodies in pathological skin lesions.

MATERIAL AND METHODS

Skin specimens from healthy individuals were obtained from the Department of Plastic Surgery of this hospital. Eight were females aged 20 to 54, one was a man aged 45. Eight of the specimens were taken under general anesthesia, one under local anesthesia.

The specimens were fixed in a 6% solution of glutaraldehyde in Veronal acetate buffer, pH 7.4, with 7.5% sucrose. After osmification and dehydration, the specimens were embedded in Epon 812. Ultrathin sections were stained with uranyl acetate and lead citrate or periodic acid–silver proteinate *ad modum* Thiéry (24). A Siemens electron microscope (Elmiskop IA) was operated at 80 kV with a double condensor system.

RESULTS

Nuclear bodies were present in all samples studied. Three types of ultrastructure could be distinguished.

Type I

In type I, 46.3% of all nuclear bodies consisted of a homogeneous matrix with sparse fibrillar material. The body was surrounded by a lucent halo and had an average diameter of 0.3 μm. The body appeared with the same frequency in all cell-types except in the basal epidermal cells, which rarely contain this type (Table I).

Type II

This type was composed of several concentrically arranged fibrils. The individual fibrils were 50–100 Å across. Frequently a central, dense core without granules was observed. This body was also surrounded by a lucent halo. It measured 0.6 μm across and was observed in 34.7% of all cells with nuclear bodies. A similar frequency was found in most cells except basal epidermal cells.

Type III

Type III was the most complex and rare nuclear body of the three types. It was composed of several concentrically arranged fibrils and a central lucent core. Varying numbers of dense granules were de-

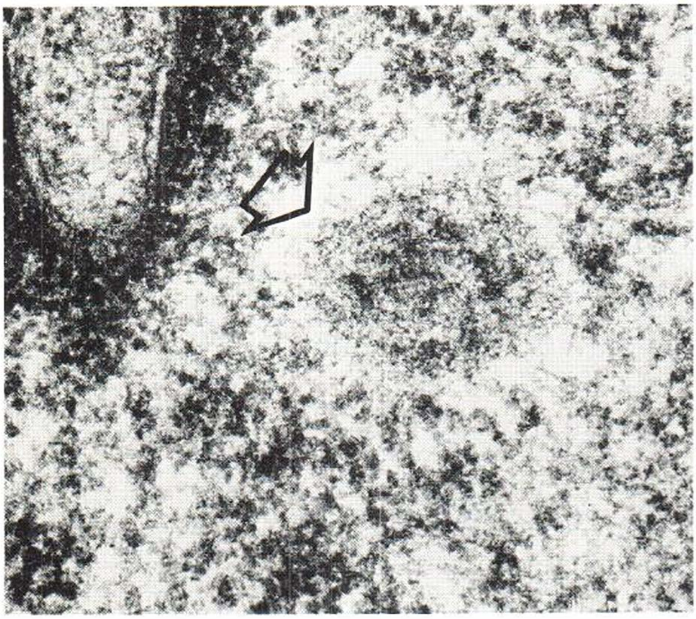

Fig. 1. Nuclear body type I. The body consists of a homogeneous matrix with sparse fibrillar material. Note the surrounding clear halo (arrow). ×73 000.

monstrated in the core. The size of the individual granule was 100–200 Å. Type III was the largest of the bodies, reaching 0.8 μm across. The size increased proportionally with the number of granules. When there were several granules in the core, fewer concentric fibrils were seen. This body was demonstrated in 19.0%. A low frequency was found in all cell types except the basal epidermal cells, in which this type was rather common.

All nuclear bodies were randomly distributed in the nuclei, without relation to nucleoli. When nuclear bodies were found in sections of nuclei, usually only one nuclear body could be seen. However, some nuclei contained more than one. All

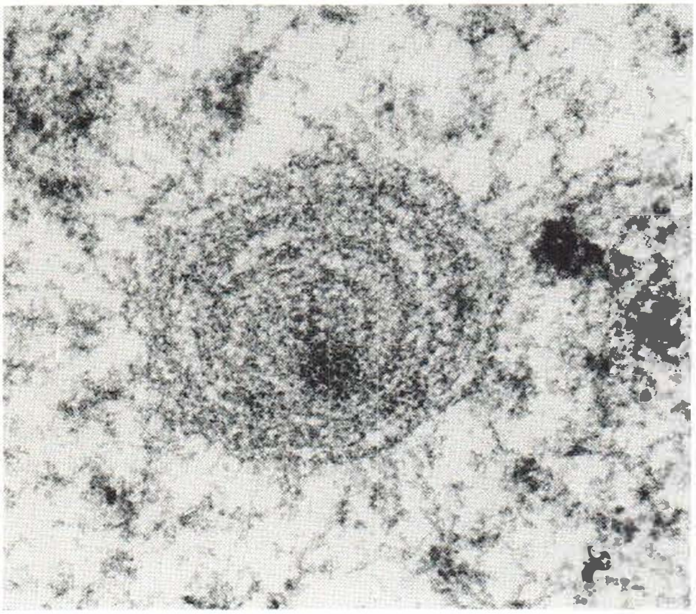

Fig. 2. Nuclear body type II. The body consists of several concentrically arranged fibrils and a non-granular central core. ×73 000.

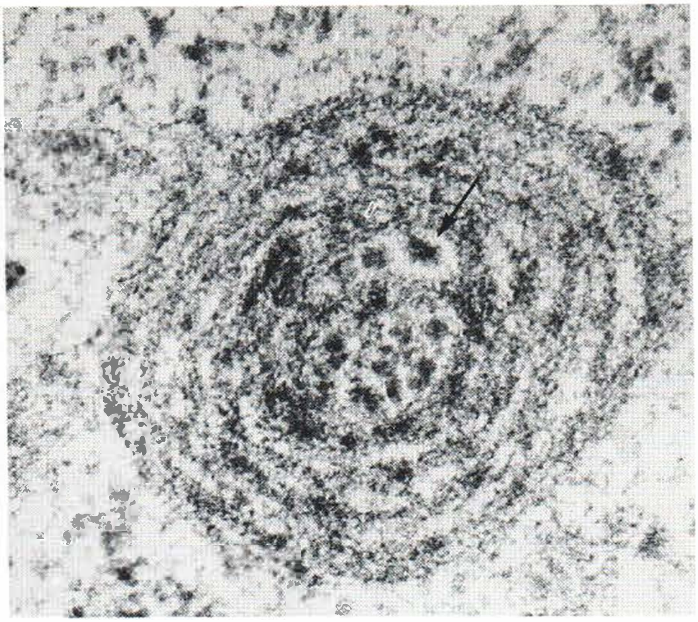

Fig. 3. Nuclear body type III. This large complex body consists of five concentrically arranged fibrils and a granular core (arrow). ×73 000.

three types of nuclear bodies may occur within the same nucleus. In this study, 7.5 % of nuclear body containing nuclei had more than one body.

The distribution of the nuclear bodies in different cell types is shown in Table II. All nuclei of cells in full thickness skin biopsies were examined for nuclear bodies. We encountered 865 nuclei in different cells of full thickness skin and found that 132 (15.3 %) of these contained one or more nuclear bodies. Nuclear bodies occurred much more frequently in the cells of the corium than in epidermal cells. Basal epidermal cells showed slightly more nuclear bodies than did prickle or granulosa cells. In the corium, 35.3 % of the endothelial cells of blood vessels contained nuclear bodies. Actually, this frequency was the highest as compared with all

Table I. *Distribution of nuclear body types in different cells of normal human skin*

	Type I		Type II		Type III		Types I, II, III (total numbers)
	Counted numbers	%	Counted numbers	%	Counted numbers	%	
Clear cells	0	–	0	–	0	–	0
Langerhans cells	0	–	0	–	0	–	0
Melanocytes	1	–	1	–	0	–	2
Epidermal basal cells	2	18.2	6	54.5	3	27.3	11
Epidermal squamous and granulosa cells	7	46.7	6	40.0	2	13.3	15
Fibroblasts	12	44.4	9	33.3	6	22.2	27
Macrophages	6	50.0	4	33.3	2	16.7	12
Mast cells	3	–	0	–	1	–	4
Pericytes	1	–	1	–	2	–	4
Endothelial cells	30	47.6	23	36.5	10	15.9	63
Muscle cells	0	–	0	–	0	–	0
Lymphocytes	6	–	1	–	0	–	7
Monocytes	0	–	0	–	0	–	0
Schwann cells	0	–	0	–	0	–	0
Unclassified cells	0	–	0	–	2	–	2
	68	46.3	51	34.7	28	19.0	147

Table II. *Frequency of nuclear bodies in different cells of normal human skin*

	Total numbers of nuclei	Nuclei with nuclear bodies	Nuclei with nuclear bodies (%)
Clear cells	1	0	–
Langerhans cells	6	0	–
Melanocytes	16	2	–
Epidermal basal cells	140	11	7.9
Epidermal squamous and granulosa cells	237	15	6.3
Fibroblasts	133	23	17.3
Macrophages	51	10	19.6
Mast cells	19	4	–
Pericytes	46	4	–
Endothelial cells	156	55	35.3
Muscle cells	3	0	–
Lymphocytes	44	6	–
Monocytes	1	0	–
Schwann cells	5	0	–
Unclassified cells	7	2	–
	865	132	15.3

other skin cells. Sex and age seemed not to influence the presence of nuclear bodies.

When the sections were PAS-stained with Thiéry's technique, nuclear bodies became lightly stained, as did chromatin granules. Both the granular material in the core and the surrounding fibrillar structures remain unstained.

DISCUSSION

Dupuy-Coin et al. (8) suggested that nuclear bodies are cell organelles and that they are always present. Statistical studies demonstrated at least one body per nucleus in canine epididymis. Nuclear bodies in various normal tissues have been reported by Ellis (11) in human sebaceous cells, by Wier et al. (27) in human keratinocytes, by Henry & Petts (12) in human thymus, by Dixon (7) in rabbit sympathetic neurons, and by Weber & Frommes (25) in calf adrenals. However, it is well known that nuclear bodies occur with a greater frequency in pathological conditions (8). They have been observed in most tissues under pathological conditions, e.g. brain (10, 18), sympathetic neurons (7, 20), liver (5), thymus (12, 14), skin (1, 2, 3, 4, 16, 23, 28), prostate (22), and various other tissues (2).

Nuclear bodies have also been induced by different experimental techniques (19). Increased numbers of nuclear bodies develop in skin explants grown in vitro (13). In calves treated with corticotrophic hormone, nuclear bodies were found to multiply in the adrenals (26). These authors suggested that the nuclear bodies are hormonal receptors in the adrenals of the calf. The hormonal hypothesis tallies with the observation that nuclear bodies decrease in canine epididymis after castration or estrogen therapy (21). Increased numbers of nuclear bodies have been related to cell hyperactivity (2). However, in the present study, there was no significant difference between the frequency of nuclear bodies in the mitotically active basal cells and other cells of the epidermis. Nuclear bodies of normal and pathological tissues showed the same morphology (10).

Ultrastructural cytochemistry of nuclear bodies showed that the capsule was proteinaceous and that the granules in the core of some bodies contained ribonucleoprotein (10).

Like previous authors (12), we too found no relation between sex and the frequency of nuclear bodies. However, the frequency was lower in young individuals than in adults (12, 15).

The average frequency of nuclear bodies in our material was 15%. Previous publications report, 15% in canine epididymis (8) and 33.5% in the cells of sclerosing subacute panencephalitis (9). The frequency in our study varied according to cell type. It is worth noting the low frequency in epidermal cells and the frequent occurrence in endothelial cells. This uneven distribution remains a mystery. In human thymus, nuclear bodies were most commonly seen in epithelial cells. In other cell types of thymal tissue, they were most frequent in the endothelial cells (12). The classification of nuclear bodies proposed by Bouteille et al. (2) was applied in this study. The significance of the different distributions of nuclear body types in basal cells is impossible to evaluate because of the relatively low numbers. Most previous works on nuclear bodies have shown that type I is the most common and type III the rarest. Dupuy-Coin & Bouteille (9) found that out of 100 nuclear bodies, 90 were of types I and II, and 10 of other types. Some authors have claimed that the different types reflect a difference in the degree of differentiation (2).

Agglomerates of glycogen particles have been reported (5) in the core of nuclear bodies of liver cells of diabetic patients. As has been recorded previously (17), nuclear bodies stained slightly positive with PAS in the present study too.

The present study has demonstrated that nuclear bodies of types I, II, and III are commonly found in most cell nuclei in normal adult skin. However, their frequency varies according to cell type. This finding is important and must be kept in mind when diseased or experimentally altered skin is studied.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge the expert technical assistance of Miss Lise Fredebo and Mrs Birthe Brøbeck.

REFERENCES

1. Bellone, A. G., Caputo, R. & Clementi, F.: Sulle presenza di microcorpi intranucleri in cellule epidermiche di dermatosi bollose del gruppo pemfigo. G Ital Dermatol *105:* 13, 1964.
2. Bouteille, M., Kalifat, S. R. & Delarue, J.: Ultrastructural variations of nuclear bodies in human diseases. J Ultrastruct Res *19:* 474, 1967.
3. Brody, I.: The ultrastructure of the epidermis in psoriatis vulgaris as revealed by electron microscopy. J Ultrastruct Res *6:* 324, 1962.
4. Caputo, R. & Bellone, A. G.: On a new type of intranuclear microbodies observed in bullous mucosynechial and atrophic dermatitis (ocular pemphigus). J Invest Dermatol *47:* 141, 1966.
5. Caramia, F., Ghergo, G. F. & Menghini, G.: A glycogen body in liver nuclei. J Ultrastruct Res *19:* 573, 1967.
6. De Thé, G., Riviere, M. & Bernhard, N.: Examen au microscope électronique de la tumeur VX2 du lapin domestique dérivée du papillome de Shope. Bull. Cancer *47:* 569, 1960.
7. Dixon, J. S.: Nuclear bodies in normal and chromatolytic sympathetic neurons. Anat Rec *168:* 179, 1970.
8. Dupuy-Coin, A. M., Lazar, P., Kalifat, S. R. & Bouteille, M.: A method of quantitation of nuclear bodies in electron microscopy. J Ultrastruct Res *27:* 244, 1969.
9. Dupuy-Coin, A. M. & Bouteille, M.: Developmental pathway of granular and beaded nuclear bodies from nucleoli. J Ultrastruct Res *40:* 55, 1972.
10. Dupuy-Coin, A. M., Kalifat, S. R. & Bouteille, M.: Nuclear bodies as proteinaceous structures containing ribonucleoproteins. J Ultrastruct Res *38:* 174, 1972.
11. Ellis, R. A.: Eccrine, sebaceous and apocrine glands. *In* Ultrastructure of Normal and Abnormal Skin (ed. Zelickson, A. S.), p. 151. Lea and Febiger, Philadelphia, 1967.
12. Henry, K. & Petts, V.: Nuclear bodies in human thymus. J Ultrastruct Res *27:* 330, 1969.
13. Hentzer, B. & Kobayasi, T.: Personal observation, 1975.
14. Krishan, A., Uzman, B. G. & Hedley-Whyte, E. T.: Nuclear bodies: a component of cell nuclei in hamster tissues and human tumors. J Ultrastruct Res *19:* 563, 1967.
15. Lemaire, R.: Recherches morphologiques, cytochimiques et expérimentales sur les inclusions nucléaires dans l'épididyme du chien. Arch Biol (Liège) *14:* 341, 1963.
16. Nasemann, T.: Elektronenoptische Beobachtungen an einem Akanthom mit sicherer Virusätiologie in Analogie zu den Befunden am Keratoakantom. Hautarzt *16:* 156, 1965.
17. Nicander, L.: Fine structure and cytochemistry of nuclear inclusions in the dog epididymis. Exp Cell Res *34:* 533, 1964.
18. Popoff, N. & Steward, S.: The fine structure of nuclear inclusions in the brain of experimental golden hamsters. J Ultrastruct Res *23:* 347, 1968.
19. Recher, L., Chan, H. & Sykes, J. A.: Comparative study of microspherules and acridine orange reaction products. J Ultrastruct Res *44:* 347, 1973.
20. Seïte, R.: Etude ultrastructurale de divers types d'inclusions nucléaires dans les neurones sympathiques du chat. J Ultrastruct Res *30:* 152, 1970.
21. Simar, L. & Lemaire, R.: Etude ultrastructurale des inclusions nucléaires de l'epididyme du chien. C R Acad Sci *262:* 1455, 1966.
22. Smetana, K., Gyorkey, F., Gyorkey, P. & Busch, H.: Compact filamentous bodies of nuclei and nucleoli of human prostate gland. Exp Cell Res *64:* 133, 1971.
23. Swanbeck, G. & Thyresson, N.: Electron microscopy of intranuclear particles in lichen ruber planus. Acta Dermatovener (Stockholm) *44:* 105, 1964.
24. Thiéry, J. P.: Mise en évidence des polysaccharides sur coupes fines en microscopie électronique. J Microsc *6:* 987, 1967.
25. Weber, A. F. & Frommes, S. P.: Nuclear bodies: their prevalence, location, and ultrastructure in the calf. Science *141:* 912, 1963.
26. Weber, A., Whipp, S., Usenik, E. & Frommes, S.: Structural changes in the nuclear body in the adrenal

zona fasciculata of the calf following the administration of ACTH. J Ultrastruct Res *11:* 564, 1964.
27. Wier, K. A., Fukuyama, K. & Epstein, W. L.: Nuclear changes during keratinization of normal human epidermis. J Ultrastruct Res *37:* 138, 1971.
28. Zelickson, A. S.: Virus-like particles demonstrated in keratoacanthomas by electron microscopy. Acta dermatovener (Stockholm) *42:* 23, 1962.

Received November 27, 1975

B. Hentzer, M.D.
Department of Dermatology
Rigshospital
Blegdamsvej 9
DK-2100 Copenhagen
Denmark