

## Pigmented Nevus

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### Abstract

**Background:** Pigmented nevi develop at approx. 6 months after birth, and the number of pigmented nevi often increases until middle age. Pigmented nevi evolve with age and finally disappear.

**Materials and methods:** We studied 300 nevi of 78 male and 222 female Japanese patients. We analyzed the patients' histopathological findings, the locations of their nevi, and their gender and age. We divided the nevi into three groups (1. all three histopathological-group, 2. junctional and compound group, 3. compound and intradermal group) based on their locations and pathological findings. Sun-exposed areas were the head, face, neck, limbs and hands. Other areas were classified as the non-sun-exposed areas.

**Results:** There were 41 junctional nevi, 73 compound nevi, and 186 intradermal nevi. The number of pigmented nevi peaked at middle age. The average age of the patients with intradermal nevi was significantly ( $P < 0.05$ ) older than those of the patients with junctional or compound nevi. The peaks in the numbers of junctional (30's) and compound nevi (20's) were lower than that of intradermal nevi. All three histopathological groups were observed on the face and back. The junctional and compound nevi groups were observed on the hands, feet and soles. The compound and intradermal nevi groups were observed at the head, neck, chest, upper limb, abdomen, lumbar and buttock.

The face had the largest number of compound nevi and intradermal nevi; 28 and 93 cases, respectively. Junctional nevi were observed more commonly in the non-sun-exposed areas compared to the sun-exposed areas, whereas for the compound and intradermal nevi, the number of nevi at the sun-exposed areas was larger than that in the non-sun-exposed areas. The number of nevi arising at sun-exposed areas was greater than that at non-sun-exposed areas in all generations.

**Conclusions:** Pigmented nevi often appear as junctional nevi and then migrate or evolve with age.

**Keywords:** Nevus; Nevi; Evolution; Age; Junctional; Compound; Intradermal

### Introduction

There are several types of nevi: congenital, acquired, pigmented (melanotic), spitz, blue, sebaceous, and others. Baelz first reported the presence of pigment cells in the pre- and postnatal dermis [1]. Pigmented nevi originate from a proliferation of melanocytes or nevomelanocytes [2]. Nevomelanocytes are melanocytes in the neural crest, and these cells differentiate after migration to the skin [3]. Usually, pigmented nevi arise about 6 months after birth, and the number of pigmented nevi increases with age. Nevomelanocytes differentiated in the skin are developed as nevi cells by some factors (e.g., ultraviolet light). Pigmented nevi begin to evolve at the dermis with age [2]. Pigmented nevi stop increasing at middle age and then regress and fade. There are three types of pigmented nevi, classified based on histopathological findings: the junctional, compound and intradermal types. In the junctional type, nevi cells are observed at the junctional area. Compound nevi are located at both the junctional area and the dermis layer. Intradermal nevi are in the dermis (papillary and reticular) layer.

It is important to distinguish pigmented nevi from malignant melanoma. A dermoscope is useful and precise, but this tool is not sufficient compared to histopathology for the final diagnosis. A histopathological diagnosis is more accurate, and an immunohistopathological diagnosis improves the accuracy of identifying a pigmented nevus or melanoma.

In the present study, we focused on three types of acquired pigmented nevi and verified the evolution of pigmented nevi with age from our histological analysis.

### Materials and Methods

This was a retrospective study of the cases of 300 Japanese patients (78 males, 222 females) with nevi examined between June 2003 and December 2013. The number of cutaneous surgery was about 100 cases for one year in our clinic; the ratio of nevi was about 20-30% every year. We elected 300 benign melanotic nevi, then we excluded other skin tumor and suspected malignant tumor. There was not any bias in this study, all our case were pigmented nevi from histopathological findings in this studying period. The patients' ages ranged from 5 to 81 yrs. All nevi were removed under local anesthesia after the patients provided written consent. All of the nevi specimens

were stained with hematoxylin and eosin. Using the patients' medical records, we analyzed their histopathological findings, the location of their nevi, and age. We divided the nevi into three groups (1. all three histopathological-group, 2. junctional and compound group, 3. compound and intradermal group) based on their locations and pathological findings. The nevi locations were as the head, face, neck, limbs (upper and lower), hands, chest, abdomen, lumbar, buttocks, feet and soles. The sun-exposed areas were considered the head, face, neck, limbs and hands. All other parts of the body were considered as the non-sun-exposed areas. We divided the patients into three generations: 0–25 yrs, 26–50 yrs, and ≥51 yrs [4].

**Statistics**

The statistical analysis was performed using Student's t-test and p-values <0.05 were considered significant.

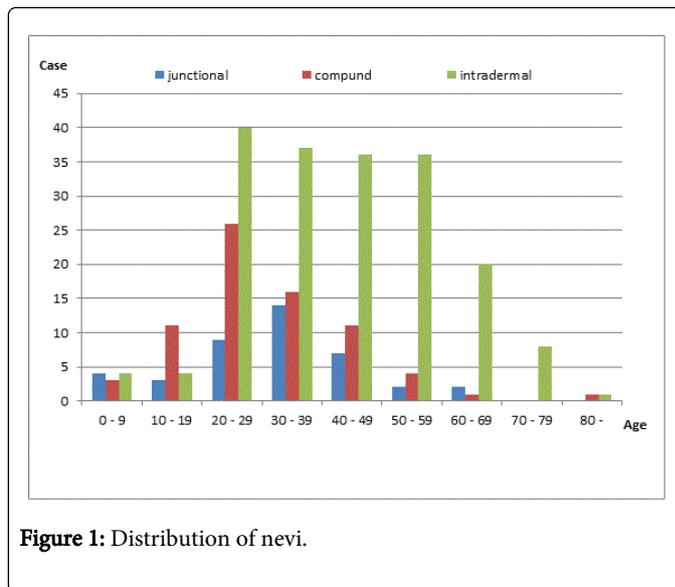
**Results**

There were 41 junctional nevi (female: 29, male: 12), 73 compound nevi (female: 55, male: 18) and 186 intradermal nevi (female: 138, male: 48). The average ages of these junctional, compound and intradermal nevi were 32.85, 30.27 and 42.95 yrs old; the average age of the intradermal nevi was significantly (P<0.05) older than those of the other two nevi (Table 1). The average ages of the female patients with a junctional nevi or compound nevi were older than the corresponding ages of the males, whereas the average age of the females with the intradermal type was younger than that of the males (Table 1).

	Junctional	Compound	Intradermal
<b>Cases</b>	41	73	186
	29	55	138
	12	18	48
<b>Average age</b>	<b>32.85</b>	<b>30.27</b>	<b>42.95</b>
	33.79	30.71	42.35
	30.58	28.94	44.46
<b>Max age</b>	65	81	81
<b>Min age</b>	5	7	8

**Table 1:** Numbers of cases, gender and patient ages for each nevus type.

The number of patients with intradermal nevi strongly increased at the 20's, and intradermal nevi were very often seen in 20's to 50's. The peaks in the numbers of junctional (30's) and compound nevi (20's) were lower than that of intradermal nevi (Figure 1). Junctional nevi were not observed in any patient 70 years or older. The average age of each nevus type among all locations except for the lower limbs was oldest in intradermal nevi (Table 2).



**Figure 1:** Distribution of nevi.

As summarized in Table 2, based on our findings, we divided the locations of nevi into three groups: {a} the all three-histological group, {b} the compound and intradermal nevi group, and {c} the junctional and compound group. The all three-histological group nevi were on the face and back. The junctional and compound group nevi were observed on the hands, feet and soles. The compound and intradermal group nevi were observed in the head, neck, chest, upper limb, abdomen, lumbar and buttock.

		Junctional	Compound	Intradermal	Cases
<b>All three-histological group</b>	<b>Face</b>	33.3	33.3	47.3	127
	<b>Back</b>	31	26.7	41	36
<b>Compound and intradermal nevi group</b>	<b>Head</b>		28.5	38.3	15
	<b>Neck</b>		29.3	38.1	19
	<b>Chest</b>		22	28.1	14
	<b>Upper limb</b>		28.9	42.2	19
	<b>Abdomen</b>		31	34.9	11
	<b>Lumbar</b>			29	2
	<b>Buttock</b>			49	6
<b>Junctional and compound group</b>	<b>Hands</b>	35.5			7
	<b>Lower limb</b>	49		31.8	8
	<b>Feet</b>	33.9	28		14
	<b>Soles</b>	28.9	34.3		22

**Table 2:** The three nevus groups and their locations.

Junctional nevi were seen most often on the soles, 12 cases. The face had the largest numbers of compound nevi and intradermal nevi; 28 and 93 cases, respectively (Figure 2). There were little number of

intra dermal nevi at the end of the limbs, hands, feet or soles, and junctional nevi were not observed on the trunk (Table 2, Figure 2).

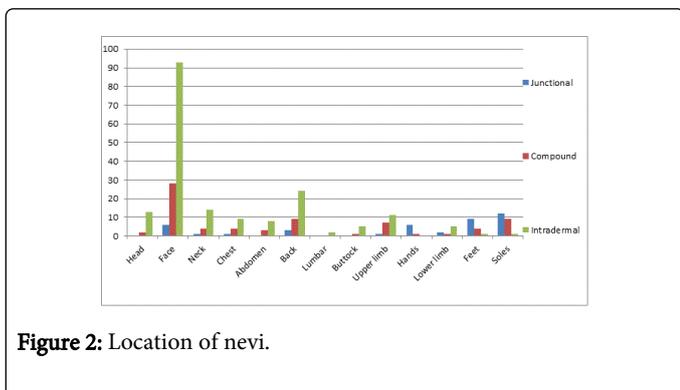


Figure 2: Location of nevi.

Our analysis of the three generation groups revealed that the number of nevi peaked during the ages 26 to 50 yrs, and then the number decreased (Figure 3). The number of nevi arising at sun-exposed areas was higher than that at non-sun-exposed area in all generations (Figure 3).

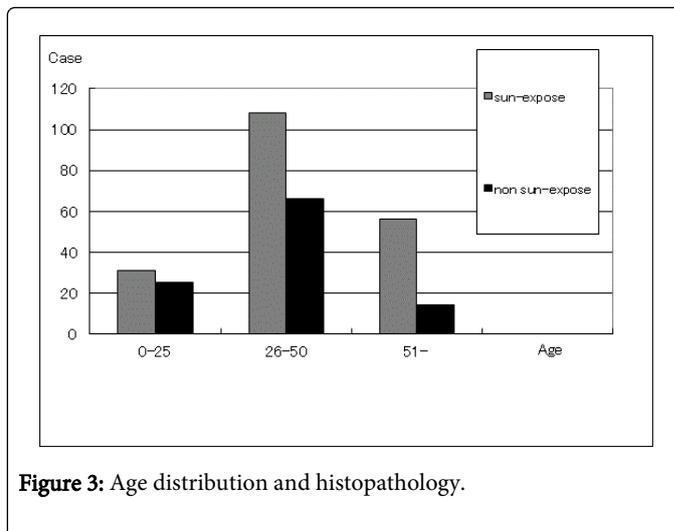


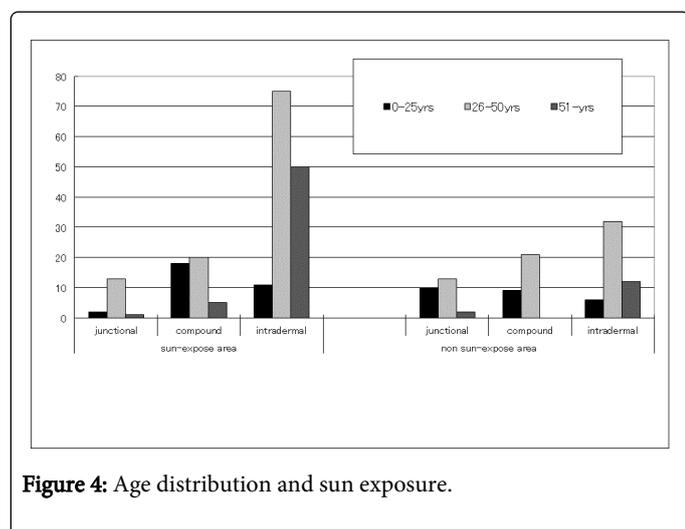
Figure 3: Age distribution and histopathology.

Each histopathological type peaked in number at 26–50 years in both the sun-exposed and non-sun-exposed areas (Figure 4). Among the patients ≥ 51 yrs old, the intra dermal type of nevi was the most common (Table 3, Figure 4). Junctional nevi were observed more frequently in the non-sun-exposed areas compared to the sun-exposed areas, although for the compound and intra dermal nevi, the number of nevi at the sun-exposed areas was larger than that in the non-sun-exposed areas (Table 3, Figure 4).

	Junctional	0-25 yrs	26-50 yrs	51+ yrs	Case number	Compound	0-25 yrs	26-50 yrs	51+ yrs	Case number	Intra dermal	0-25 yrs	26-50 yrs	51+ yrs	Case number
Sun exposed area	Head					Head	1	1			Head	1	10	2	
	Face		6			Face	10	15	3		Face	7	43	43	
	Neck		1			Neck	2		2		Neck	3	8	3	
	Upper limb		1			Upper limb	3	4			Upper limb		9	2	
	Hands	2	3	1		Hands	1				Hands				
	Lower limb		2			Lower limb	1				Lower limb		5		
					16					43					136
Non-sun exposed area	Chest	1				Chest	1	3			Chest	2	7		
	Abdomen					Abdomen		3			Abdomen	2	5	1	
	Back	1	2			Back	3	6			Back	2	16	6	
	Lumbar					Lumbar					Lumbar		2		
	Buttock					Buttock	1				Buttock		1	4	
	Feet	2	6	1		Feet	1	3			Feet			1	
	Soles	6	5	1		Soles	3	6			Soles		1		
					25					30					50

					41					73					186
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**Table 3:** Nevi types by location and age groups.



**Figure 4:** Age distribution and sun exposure.

## Discussion

Pigmented (melanotic) nevi develop in the skin and are divided into three histological types: junctional, compound and intradermal type. In the late 19<sup>th</sup> century, Unna described ‘Abtropfung,’ which indicates that junctional nevi progress to compound and then to intradermal nevi [5]. Previous reports [6,7] noted that the number of nevi peaks in middle age and then begins to decrease. One report described that in a British population, the peak time in the number of nevi was in the 20s, the children  $\leq 10$  yrs old generally had two or three nevi, the subjects in their 20s had 22–33 nevi, and those in their 60s had 4–6 nevi [8].

Generally, non-Caucasians have twice the number of nevi compared to Caucasians. The present investigation showed that our Japanese patients at 26–50 yrs old showed the peak in the number of all pigmented nevi and of each histopathological type, and we found that these Japanese patients developed a greater number of pigmented nevi compared to the British population in the previous report [8].

The life of a pigmented nevus cell is as follows. (1) The nevus develops as a swelling with color (brown or light black) in the skin. (2) The nevus grows and develops a deep color with aging. (3) The nevus evolves and migrates, and eventually the color of the nevus fades with further aging. (4) The nevus becomes flat with a light color. Finally (5), the nevus disappears and then melanin granules stay in the dermis.

A decrease in number and disappearance of nevi indicate that the nevi progressed from the upper (junction) area to lower (intradermal) layer and then regressed. There are three hypotheses concerning the progression or migration of nevi. The first is evolution from the basement line to the dermal layer. The second is protection from sunlight (i.e., ultraviolet light). The third finding is simply escape or migration from the epidermis.

Our present findings indicate that the period of evolution of most of the nevi was approx. 20–40 yrs. Nevi cells could migrate with age; the origin of nevi might be the junctional type. All nevi might not develop

as only junctional nevi; some might develop as the compound or intradermal type and regress at developing sites without evolution. Because our patients  $\geq 70$  yrs old did not have any junctional nevi, it appears that new pigmented nevi do not develop and that most pigmented nevi progress as a compound or intradermal nevus in older individuals. In light of the lifespan of nevi, our results confirmed that the number of intradermal nevi, especially at the sun-exposing areas among people  $\geq 51$  yrs old was large.

A previous report [4] described that junctional nevi were common in all age groups, but our present analysis of 300 nevi revealed that the average age of the patients with a junctional nevi was younger than that of the patients with an intradermal nevi, and the age range of the junctional nevi patients was small. These differences between previous studies and our results might be related to race, ultraviolet light exposure and the origin of nevi.

The locations of the developing nevi in our patient population are characteristic. Junctional nevi were often observed at the end of a limb, but intradermal nevi were not seen at these locations. Most of the intradermal nevi were on the trunk. There were no intradermal nevi on the feet or soles. Our hypothesis is as follows. {A} there are four origins of nevi: the face, back, hands and soles based on the data of age (Table 2). {B} Nevi in these locations might migrate to other locations. {C} Nevi in the face and back might move more slowly than nevi in other locations, since the average age of the patients with nevi in these locations was older.

The face had the largest number of developing nevi. The reasons for this may be identifiable based on the change of nevi and from cosmetology; generally the number of melanocytes in the face and genital area is largest, and sun-exposed areas (e.g., the face) have twice the number of melanocytes as non-sun-exposed areas.

Factors that affect the development of nevi are sun exposure (ultraviolet light) [9,10] aging, puberty [2], pregnancy [2], and the use of systemic corticosteroids [11]. Ultraviolet light is well-known as a factor in melanocyte migration, and it might be related to the evolution and change of nevi. Our hypothesis before we conducted the present study was that the number of nevi in sun-exposed locations (e.g., the face) would be greater than that in non-sun-exposed locations. This hypothesis was well supported by some of our results. From the average ages of the female patients with the three different types of nevi, it appears that the age of the developing nevi could be older but the evolution of nevi might be younger compared to those in males. In particular, the migration of nevi in females could be related to and affected by pregnancy. The life of nevi in females could be of shorter duration than in males. Ultraviolet light might cause the development of junctional-type nevi in sun-exposed areas, and we suspect that they may evolve or migrate to the dermis, since in the present study the number of compound- and intradermal-type nevi in sun-exposed areas was larger than that of the nevi in the non-sun-exposed areas. Studying the location of nevi and age of developing nevi from the new born age possess scientific value and meaningful.

There might be two reasons why the number of intradermal nevi is larger than those of the junctional and compound type, as follows. One reason is the evolution of nevi from the junctional layer to the dermis,

which might start from the individual's teen years to their 30s, which is the peak time for the number of nevi. The other reason is that some origins of nevi might be the intradermal type, with nevi cells developing in the dermis (de novo development) or from the hair follicles. The numbers of junctional nevi on the feet and soles were greater than those at other locations. Nevi in non-sun-exposed areas (hands, feet and soles) might appear at an older age than those in sun-exposed areas. Our hypothesis is that these locations (hands, feet and soles) might be one original location of developing nevi. Because the number of nevi in sun-exposed areas was greater than those in the non-sun-exposed areas, the evolution and development of nevi in non-Caucasian people such as Japanese could be easily affected by ultraviolet light.

## Conclusion

It is of interest that pigmented nevi migrate and evolve, and that the increase in the number of pigmented nevi does not continue into old age.

## References

1. Baelz E (1885) Die Körperlichen Eigenschaften der Japaner. MDGNVO 4: 40.
2. Jay Kincannon and Christine Boutzale (1999) The physiology of pigmented nevi. Pediatrics 104: 1042-1045.
3. Holbrook KA, Underwood RA, Vogel AM, Gown AM, Kimball H (1989) The appearance, density and distribution of melanocytes in human embryonic and fetal skin revealed by anti-melanoma monoclonal antibody, HMB-45. Anat Embryol (Berl) 180: 443-455.
4. Westhafer J, Gildea J, Klepeiss S, Clarke L, Helm K (2007) Age distribution of biopsied junctional nevi. J Am Acad Dermatol 56:825-827.
5. Unna P (1893) Zur epithelialen Abkunft der Naevuszellen. Virchows Arch [A] 143: 224.
6. Grichnik J, Rhodes A, Sober A (2003) Benign hyperplasias and neoplasias of melanocytes. In Cooke D, Noujaim S, Silverman L, Boyle P, editors. Fitzpatrick's dermatology in general medicine. New York: McGraw Hill, USA.
7. MacKie RM (1998) Melanocytic nevi and malignant melanoma. In: Champion RH, Rook, Wilkinson, Ebling (Eds.), Textbook of dermatology. Malden (MA): Blackwell Science Ltd, USA.
8. MacKie RM, English J, Aitchison TC, Fitzsimons CP, Wilson P (1985) The number and distribution of benign pigmented moles (melanocytic naevi) in a healthy British population. Br J Dermatol 113: 167-174.
9. Kennedy C, Bajdik CD, Willemze R, De Gruijl FR, Bouwes Bavinck JN (2003) Leiden Skin Cancer Study. The influence of painful sunburns and lifetime sun exposure on the risk of actinic keratoses, seborrheic warts, melanocytic nevi, atypical nevi, and skin cancer. J Invest Dermatol 120: 1087-1093.
10. Valiukeviciene S, Miseviciene I, Gollnick H (2005) The prevalence of common acquired melanocytic nevi and the relationship with skin type characteristics and sun exposure among children in Lithuania. Arch Dermatol 141: 579-586.
11. Goldman L, Richfield DF (1951) Effect of corticotropin and cortisone on development and progress of pigmented nevi. JAMA 147: 941-943.