

Report

Seasonal effect upon excision of acquired melanocytic proliferations

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Abstract

Background Acquired melanocytic proliferations (AMPs) are excised throughout the year. Questions exist concerning seasonal variation in these excisions.

Objective To investigate whether AMPs are removed more often during the spring–summer seasons than in the fall–winter and whether the percentage of benign nevi, dysplastic nevi and melanoma varies according to season.

Design Retrospective analysis of 4794 histologically confirmed biopsies of AMPs was performed.

Results A total of 2802 of the 4794 lesions (58%) were removed during the spring–summer season. These results confirm that seasonal variation in removal of AMPs does occur, and that removal peaks during the warmer months. In addition, the increased numbers of removals were accounted for by increases in benign pigmented lesion removals.

Conclusions Many etiologic factors can be suggested for increased removal of AMPs during the warmer months. Reasons may include the cosmetic desires of the patient and clothing choices resulting in increased awareness of pigmented lesions. Increases in the number of skin cancer prevention programs offered by dermatologists in the spring also have a large impact on the awareness of the general population and potentially contribute to the seasonal variation.

Introduction

Several studies have demonstrated seasonal variation in the incidence of skin cancers, with melanoma being most commonly studied.^{1–3} Many etiologic factors have been implicated. Heavy exposure to sunlight during childhood is generally accepted as an important risk factor for melanoma. However, the effect of UV exposure immediately prior to diagnosis is unclear. Armstrong *et al.*⁴ have suggested that exposure to sunlight is relevant to the etiology of common nevi, not just melanoma. Short-term promotional effects of sunlight on the cells in the junctional zone of nevi have also been reported.⁵ These effects on acquired melanocytic proliferations (AMPs) removed during the summer months have since been supported by studies utilizing DNA histograms and digital epiluminescence microscopy (D-ELM), which showed increased proliferation fractions and increased pigment networks, brown globules and pigment dots, respectively.^{6–8} If valid, these results indicate that AMPs of any type become more apparent with the increased sun exposure that occurs during warmer months, thus potentially creating a seasonal variation. No study to date, however, has investigated the seasonal incidence of all diagnostic categories of

AMP – benign nevi, dysplastic nevi and melanoma. In our clinics, we noticed that more patients presented requesting removal of AMPs during the spring and summer months. As a result, we set out to determine if the number of excised AMPs increased during the warmer months and, if so, if these increases were accounted for by benign nevi, dysplastic nevi or melanoma. We also wanted to determine if the relative percentages of benign nevi, dysplastic nevi and melanoma stayed the same throughout the year or if there was seasonal variation, with increased dysplastic lesions and melanoma being removed during the warmer months of the year.

Methods

We performed a retrospective case review of 4794 biopsies that had been submitted to the Pathology Department of the University of Arkansas for Medical Sciences (UAMS) between October 1997 and September 2001. All diagnoses were made by two board-certified dermatopathologists (Bruce R. Smoller MD and Thomas D. Horn MD). The biopsies reviewed consisted of those with diagnoses of compound nevus, junctional nevus, intradermal nevus (IDN), blue nevus, cellular blue nevus, halo nevus, spitz nevus, dysplastic nevus of mild, moderate, or severe type, melanoma *in situ* (MIS),

and melanoma. To compare the incidence of benign pigmented lesions with that of dysplastic nevi or melanoma, some diagnostic groups were combined. The benign nevi group consisted of compound nevus, junctional nevus, IDN, blue nevus, cellular blue nevus, halo nevus, and spitz nevus. The dysplastic nevi group included all levels of dysplasia (mild, moderate and severe). The melanoma group included melanoma and melanoma *in situ*. Each diagnostic group was then divided into four quarters based on the month of removal. Lesions removed during January to March were placed in the first quarter, those removed during April to June in the second quarter, those removed during July to September in the third quarter, and those removed during October to December in the fourth quarter. Warmer months (referred to here as April to September) were compared with cooler months (referred to here as October to March). The Pearson chi-square test was employed to assess AMP removals for imbalance, both with respect to warmer vs. cooler months and with respect to arbitrary inequality across the four quarters of the calendar year. Cochran-Mantel-Haenszel methods,⁹ specifically the tests for general association and for differences in row mean scores, were deployed to detect changes in the distribution of AMPs among pathologic classes, both with respect to warmer vs. cooler months and with respect to the four quarters of the calendar year. The average temperature for Arkansas during the warmer months is 22.92 °C, the warmest month being July with an average temperature of 26.89 °C; the average temperature for Arkansas during the cooler months is 8.97 °C, the coolest month being January with an average temperature of 4.33 °C (average temperatures for Arkansas, www.ncdc.noaa.gov).

Results

Of the 4794 cases, benign melanocytic lesions comprised 74% (3560); dysplastic melanocytic lesions comprised 15% (693); and the melanoma group comprised 11% (541). Dysplastic nevi growths, when divided into their respective levels of severity, consisted of 417 mild cases, 187 moderate cases, and 89 severe cases.

Analysis of the data showed that, of the 4794 cases, 58% (2802) occurred during the warmer months, vs. 42% (1992) in the cooler months ($P < 0.0001$). The seasonal breakdown was 22, 27, 31 and 20% in the first through fourth quarters, respectively ($P < 0.0001$). These results supported our first hypothesis that seasonal variation of AMPs does occur and that there are peaks during the warmer months (Table 1).

To further investigate this hypothesis, we looked at the occurrence per quarter of individual groups. For benign pigmented lesions, approximately 60% were removed during the warmer months, vs. 40% during the cooler months ($P < 0.0001$); the seasonal breakdown was 21, 27, 33 and 19% in the first through fourth quarters, respectively ($P < 0.0001$). For dysplastic melanocytic proliferations, about 56% were removed during the warmer months, vs. 44%

Table 1 The number of total combined AMPs removed per quarter and season

	Quarter				Total	P-value
	1st	2nd	3rd	4th		
Lesions	1043	1303	1499	949	4794	< 0.0001
Per cent	21.75	27.18	31.27	19.80	100.00	

	Warm (2nd + 3rd)		Cool (1st + 4th)		Total	P-value
	Lesions	2802		1992		
Per cent	58.45		41.55		100.00	

Table 2 Number of AMPs removed per quarter/season by pathologic class

	Quarter				Total	P-value
	1st	2nd	3rd	4th		
Benign nevi						
Number	754	968	1163	675	3560	< 0.0001
Per cent	21.18	27.19	32.67	18.96	100.00	
Dysplastic nevi						
Number	158	199	187	149	693	0.02
Per cent	22.80	28.72	26.98	21.50	100.00	
Melanoma						
Number	131	136	149	125	541	0.51
Per cent	24.21	25.14	27.54	23.11	100.00	

	Warm (2nd + 3rd)		Cool (1st + 4th)		Total	P-value
	Benign nevi	2131		1429		
Per cent	59.86		40.14		100.00	
Dysplastic nevi						
Number	386		307		693	0.003
Per cent	55.70		44.30		100.00	
Melanoma						
Number	285		256		541	0.21
Per cent	52.68		47.32		100.00	

during the cooler months ($P = 0.003$); the seasonal breakdown was 23, 29, 27 and 22% during the first through fourth quarters, respectively ($P = 0.02$). The percentage of the melanoma-grouped lesions removed was 53% during the warmer months vs. 47% during the cooler months ($P = 0.21$), with a seasonal breakdown of 24, 25, 28 and 23% in the first through fourth quarters, respectively ($P = 0.51$) (Table 2 and Fig. 1).

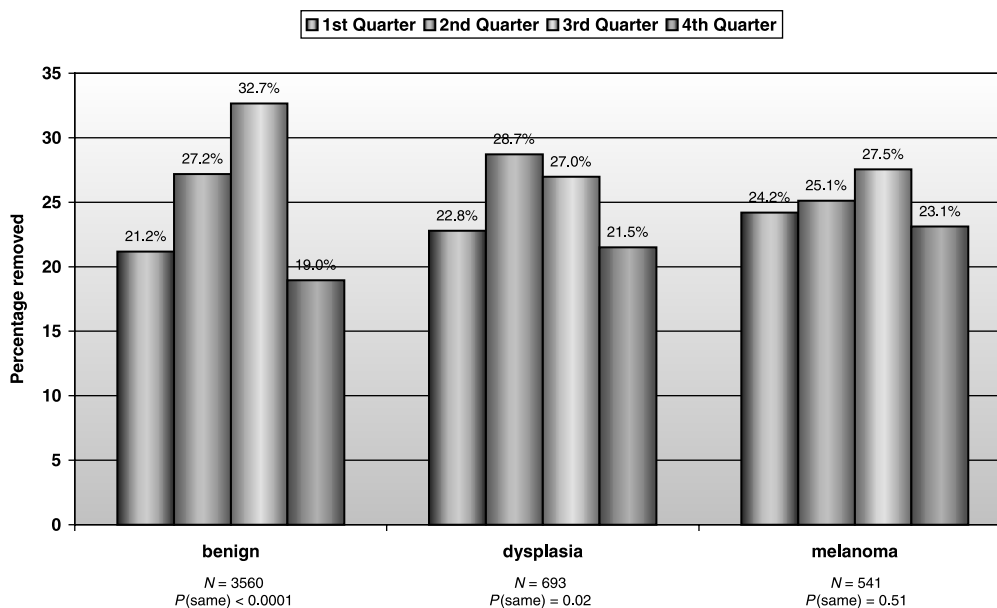


Figure 1 The percentage of AMPs removed in each quarter, grouped by pathologic class

Once increased removal of AMPs during the warmer months had been established, we investigated whether the relative percentages among the three groups (benign nevi, dysplastic nevi and melanoma) remained constant or varied between quarters. To achieve this goal, we looked at each quarter separately to determine the percentage of each diagnostic grouping (Table 3). Then, we compared those percentages obtained for each grouping among the four quarters. To evaluate the significance of the differences found, two statistical tests were performed. The test for difference in row mean scores (TDRMS) was used to detect a net shift in proportions towards one end of the scale or the other, so that an increase in benign nevi growths would be accompanied by a decrease in melanomas, or vice versa. The test for general association (TGA) was used to look for arbitrary changes in proportions between quarters or from cooler to warmer months. The TGA indicated that an association existed ($P = 0.007$). The

TDRMS ($P = 0.002$) indicated that the association took the form of a net shift in proportions towards benign nevi growths and away from melanoma growths during the second and third quarters. When quarters were combined into warmer months vs. cooler months, the statistical significance of these trends was emphasized: the TGA gave $P = 0.002$ while the TDRMS gave $P = 0.0004$. During the warmer months, 76% of AMPs were benign nevi, vs. 14% dysplastic nevi and 10% melanoma; during the cooler months, 72% of AMPs were benign nevi, vs. 15% dysplastic nevi and 13% melanoma (Fig. 2). This finding indicates that the increased removals occurring during the warmer months were accounted for by increases in benign lesion removals.

Lastly, we specifically looked at the three levels of the dysplastic nevi growths to determine whether any association between severity and quarter existed. Both the TGA ($P = 0.39$) and the TDRMS ($P = 0.82$) indicated the absence

	Quarter			
	1st	2nd	3rd	4th
Benign nevi	72.29 (754)	74.29 (968)	77.59 (1163)	71.13 (675)
Dysplastic nevi	15.15 (158)	15.27 (199)	12.47 (187)	15.70 (149)
Melanoma	12.56 (131)	10.44 (136)	9.94 (149)	13.17 (125)
Total	100.00 (1043)	100.00 (1303)	100.00 (1499)	100.00 (949)

Table 3 Percentage of pathologic class within each quarter

TGA: $P = 0.007$; TDRMS: $P = 0.002$.

Numbers in parentheses represent the numbers of each lesion. See Fig. 2 for representation by season.

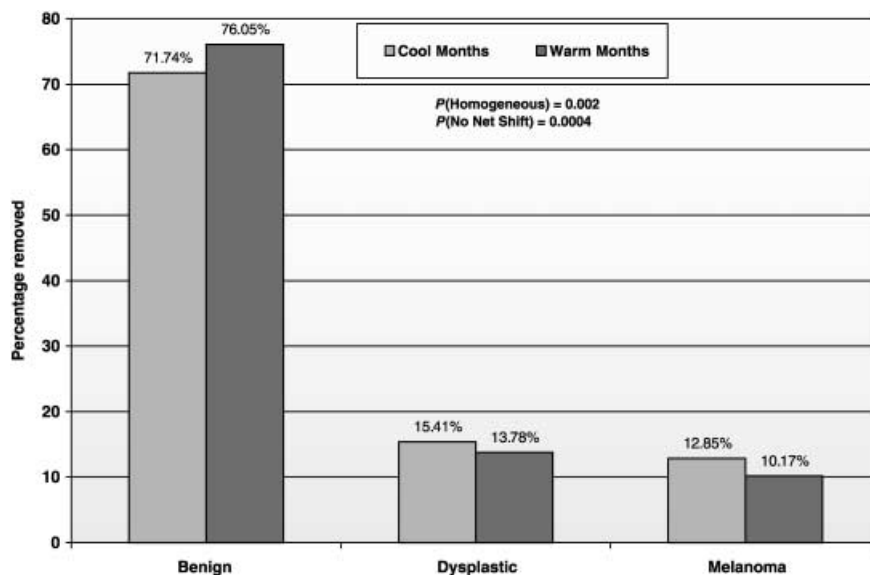


Figure 2 The percentage of AMPs removed in each pathologic class, grouped by season. TGA: $P = 0.002$; TDRMS: $P = 0.0004$

of any association with quarter. When quarters were combined into warmer vs. cooler months, the TGA indicated a possible trend that failed to reach statistical significance ($P = 0.09$), while the TDRMS indicated no net shift in severity ($P = 0.86$). The change that one sees in the data is an increase in the proportion of both mild and severe dysplastic nevi at the expense of moderate dysplastic nevi during the warmer months, but not a shift from one extreme to the other.

Discussion

The results support our initial clinical observation that more pigmented lesions are removed during the warmer months of the year. In addition, we found that the increased removal during those months is mostly accounted for by the increased removal of benign pigmented lesions. Our findings also show that, of all the benign and dysplastic lesions, a greater percentage are excised in the April–September half-year, with melanomas showing no statistically significant variation.

We were surprised by the lack of seasonal variation in the melanoma grouping. Previous studies have demonstrated seasonal variation in melanoma presentations.^{1–3} However, this lack of variation could represent a trend towards patients and physicians becoming more attuned to this important melanocytic proliferation. Another cause of the lack of variation could be the combining of melanoma and MIS for the statistical analysis. Akslen *et al.*¹⁰ report that seasonal variation in melanoma exists but that MIS is evenly distributed throughout the year. Looking at these two classes separately, melanoma comprised 380 of the 541 cases and MIS 161 of the 541 cases. Fifty-six per cent of our melanoma cases occurred during the warmer months ($P = 0.02$) while only

Table 4 Percentage of melanoma and MIS considered separately by season

	Warm	Cool	Total	P-value
Melanoma ($P = 0.02$)				
Number	212	168	380	0.02
Per cent	55.79	44.21	100.00%	
MIS ($P = 0.24$)				
Number	73	88	161	0.24
Per cent	45.34	54.66	100.00	

45% of MIS occurred at that time ($P = 0.24$), consistent with the results of Akslen *et al.*¹⁰ (Table 4). In addition, however, our population may differ substantially in pattern and degree of sun exposure from the population for which statistical significance of seasonality of melanoma has previously been demonstrated. Many of those studies were carried out in regions such as Australia and Hawaii, where individuals have significantly more sun exposure and different clothing habits than those living in Arkansas.

A possible reason for increased removal of lesions during the warmer months relates to increased visualization of AMPs resulting from the short-term promotional effects of sunlight,^{5–8} as mentioned above. Because seasonal increases in pigmentation and thickening of the epidermis are just beginning in the early spring, thus making the skin less effective at screening out UV radiation at that time, this theory seems reasonable. Interestingly, however, we did not find any statistically significant difference in the percentage of more severe dysplastic lesions amongst the four quarters. We must, nevertheless, acknowledge that the DNA histograms in the study of

Fleming *et al.*,⁶ showing increased proliferation fractions are more sensitive than the human eye, and thus more likely to detect small changes that would reflect increased activity of the nevi cells and thus potentially pinpoint those lesions with a high likelihood of increased levels of dysplasia. However, Akslen *et al.*¹¹ reported that sunlight stimulation could not be confirmed as the sole cause of melanocytic proliferation.

Changes in clothing habits have been suggested as yet another plausible mechanism. However, studies performed in Hawaii, where clothing styles are unchanged throughout the year, have also demonstrated seasonal variation.¹² In addition, Swerdlow *et al.*³ demonstrated seasonality of skin cancers of the face whose visibility is not affected by seasonal variation in dress. Diet and hormone theories have been mentioned in passing as a possible contributing factor to the seasonal variation.¹³ Seasonal variations in serum levels of melatonin, 25 hydroxyvitamin D, and other pituitary-gonadal axis hormones have been reported.^{13,14} Current evidence for either a diet or a hormone hypothesis is insufficient at this time, but this area could warrant future exploration.

Other possible etiologies for increased summer removals include increased personal self-awareness, increased cosmetic desires and the intensified primary prevention campaigns that occur during these months, as well as seasonal changes in the utilization of medical resources.^{3,15} Primary prevention campaigns against skin cancer impact a large proportion of the general population, most likely through increased visits to primary care physicians and dermatologists. Of interest, Del Mar *et al.*¹⁶ have reported that primary prevention campaigns may be adding considerable costs in the form of increased excision of benign skin lesions. Notably, there are many American Academy of Dermatology skin cancer screenings held in May of every year by the UAMS Dermatologists. This theory could serve as a further avenue of investigation for future studies. In conclusion, many etiologic factors can be suggested for increased removal of AMPs, especially benign pigmented lesions, during the warmer months.

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