

Possible Influence of Age on the Expression of the Heterozygous Cerumen Phenotype

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ABSTRACT The relationship of cerumen (earwax) phenotype and age was examined in 2,618 women. An increasing proportion of white women with dry or unclassifiable cerumen was found with advancing age, ranging from 2.0% in women under 30 years to 13.3% in women 70 years and older. No statistically significant change with age was found in other racial groups. It is suggested that the increase of dry or unclassifiable cerumen in white women represents a change in the expressivity of alleles that determine cerumen type occurring with advancing age in women who are heterozygous for the trait.

Cerumen (earwax) occurs as two phenotypic traits that can be identified by either wet (sticky) or dry consistency. Matsunaga (1962) showed that cerumen type is based on simple mendelian inheritance. The wet type is dominant homozygous (WW) or heterozygous (Ww); the dry type is homozygous recessive (ww). The heterozygous wet type cannot be clinically differentiated from the homozygous dominant type. A striking variation in this polymorphism is related to racial origin. The wet-type cerumen is highly prevalent in Europeans and Africans; the dry-type cerumen is highly prevalent in Chinese, Japanese, Mongols, and American Indians (Matsunaga, 1962; Petrakis et al., 1967; Petrakis, 1969, 1971, 1983). The selective forces that maintain this polymorphism have not been identified. The cerumenous glands are part of the system of apocrine glands that includes the sweat glands and the mammary glands (Hurley and Shelley, 1960; Bloom and Fawcett, 1962). In reviewing reports on cerumen in populations, it is apparent that, with the exception of the studies of Nakajima and Hirano (1969) and Hayashi (1958) in Japan, cerumen phenotype and age have not been examined. These investigators reported no change in the proportions of wet and dry cerumen with age. We have examined 2,618

women of various racial groups and present data that indicate that among white women a significant increase in the dry phenotype is associated with advancing age.

METHODS

Wet or dry cerumen type was classified in 2,618 women (1,822 white, 345 black, 320 Chinese, and 81 Japanese) who attended the Breast Screening Clinic at the University of California, San Francisco between 1975 and 1980. Women diagnosed with breast cancer were excluded from the study. Wet or dry cerumen type was determined in both ears by otoscopic examination, using the criteria of Matsunaga (1962) and Petrakis et al. (1967). An unclassifiable category was established in instances where the observer was unable to classify cerumen type. In each racial group, the women with wet or dry cerumen were studied by 10-year age group. The linear trend in the proportion of dry cerumen type occurring with age was determined by chi-square.

RESULTS

The percentage of white women with dry cerumen was found to increase with advanc-

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TABLE 1. Number and proportion of women with dry cerumen by age and racial group

Age in years, (group decade)	White		Black		Chinese		Japanese	
	No. dry/total	% dry	No. dry/total	% dry	No. dry/total	% dry	No. dry/total	% dry
≤29	4/204	2.0	2/44	4.5	25/45	55.6	3/5	60.0
30-39	17/352	4.8	0/66	0.0	40/71	56.3	9/12	75.0
40-49	46/585	7.9	2/91	2.2	47/96	49.0	22/25	88.8
50-59	46/474	9.7	2/88	2.3	29/51	56.9	25/31	80.6
60-69	22/212	10.4	2/42	4.8	20/37	54.1	7/8	87.5
70+	6/45	13.3	0/14	0.0	7/20	35.0	—	—
Total	141/1872	7.5	8/345	2.3	168/320	52.5	66/81	81.5

χ^2 trend: 19.6, $P < 0.0001$; 0.03, $P = 0.43$ (NS); 1.01, $P = 0.15$ (NS); 1.00, $P = 0.16$ (NS)

TABLE 2. Number and proportion of unclassifiable type cerumen by race and age

Age group	White		Black		Chinese		Japanese	
	No./total	%	No./total	%	No./total	%	No./total	%
20-29	1/204	0.5	0/44	0	1/45	2.2	0/5	0
30-39	5/352	1.4	1/66	1.5	1/71	1.4	1/12	8.3
40-49	16/585	2.7	0/91	0	1/96	1.0	0/25	0
50-59	8/574	1.4	1/88	1.1	0/51	0	0/31	0
60-69	1/212	0.5	0/42	0	0/37	0	0/8	0
70+	1/45	2.2	0/14	0	0/20	0	—	—
Total	32/1,872	1.7	2/345	0.6	3/320	0.9	1/81	1.2

ing age, beginning with 2% in the age group ≤29 years and reaching 13.3% in the 70+ years age group (Table 1). A rapid increase occurred between 30 and 50 years; the increase was slower above 50 years. Similar age-associated increases were observed for the dry allele frequency (q). Chi-square test for linear trend was highly significant ($\chi^2 = 19.6$; $P < 0.0001$). Among white women, the overall frequency of unclassifiable cerumen type was 32/1,872 (1.7%). The numbers and proportions of unclassifiable cerumen type in the various racial groups is shown in Table 2.

In contrast to the findings in white women, no statistically significant age-related increase in the proportion with dry cerumen, in dry allele frequency, or in unclassifiable cerumen frequency was found among black, Chinese, and Japanese women; however, the latter samples were relatively small.

DISCUSSION

The increase in proportion of white women observed to have dry cerumen type with advancing age offers several interpretations. The first interpretation is that the increase is due to misclassification of cerumen pheno-

type by the examiners. This, however, is not likely because each of the three examiners who obtained these data has had several years experience in classifying cerumen type. In addition, our findings in Chinese and Japanese women in the United States are similar to those reported from Asia, including the overall proportion of unclassifiable subjects.

The second interpretation is that an increasing frequency of external ear infections occurs with advancing age that might alter or suppress secretion and result in misclassification of wet as dry cerumen. This is also unlikely in view of the progressive increase in dry cerumen with age. Further, it is unlikely that over 10% of women have chronic bilateral external ear canal infections.

A third interpretation is that in this population sample we may be detecting a selection process against women with wet-type cerumen. However, the effect appears to be confined to white women inasmuch as we observed no statistically significant change with age in other racial groups. In similar earlier data from Japan, no age-related change in frequency of cerumen type was found (Nakajima and Hirano, 1968; Hayashi, 1958).

TABLE 3. Frequency of dry cerumen in European populations

Population	Number tested	% dry	Frequency of dry allele (q)	Reference
German	514	3.10	0.176	Matsunaga and Ebbing (1956)
English	125	2.25	0.150	Petrakis (unpublished)
Icelandic	322	1.20	0.111	Lehmann et al.
Finnish (NE)	323	2.50	0.157	Eriksson et al. (1980)
Spanish-Basque	491	5.09	0.225	Calderon (1977)
Castilian	308	2.27	0.151	Calderon (1977)
Andalusian	209	0.96	0.098	Calderon (1977)
Greek	81	6.17	0.248	Spanidu and Petrakis (unpublished)

Forces that change gene frequency include gene flow (migration), drift, and mutation. Mutation is extremely unlikely in this situation. Similarly, it would be necessary to demonstrate that our sample of white women had experienced an in- or out-migration of a cohort of women with higher proportions of dry or wet cerumen, respectively, resulting in a progressively increasing proportion of dry cerumen among older women. We have no way to rule out this possibility. But the regularity observed in the increase of dry cerumen frequency, and the data from European countries that contributed the bulk of the U.S. white population (England, Germany, Scandinavia), which show few differences by nationality in the proportion of wet and dry cerumen types, make this explanation, as well as that of drift, unlikely. Table 3 is a summary of currently available data for European populations, showing an overall low frequency of dry cerumen. No data were found for other European countries.

Because wet and dry cerumen phenotypes are also present in nonhuman primates, the two earwax types probably arose early in primate evolution (Matsunaga, 1962). One can only speculate as to what selective forces in the past were responsible for the persistence of the cerumen dimorphism and its present-day racial distribution. No conclusive evidence for a differential rate of external ear infections in either type has been found (Petrakis et al., 1971; Gregg, 1985). A further argument against the selection hypothesis as an explanation for our findings is that the reported increase in age-specific mortality from all causes in women in the younger age groups is significantly lower than the rate of increase of the dry phenotype (State of California, 1979-1980).

The fourth interpretation, which appears the most likely, is that some of the heterozy-

gous wet phenotypes are becoming heterozygous dry. The expressivity of the allele for wet cerumen may become repressed with advancing age, resulting in an increasing proportion of dry phenotype that is detectable in women of the heterozygous phenotype. No effect would be detectable in women of the homozygous dominant genotype. Examples of such age-related changes in the expression of a dominant gene are male pattern baldness and Huntington chorea (Stern, 1973). Possibly, modifier genes that influence the final phenotypic expression of cerumen alleles exist that might be more readily expressed with advancing age and in response to altered physiologic states or medications in heterozygous subjects. We did not observe a similar change in the proportion of dry cerumen with age among the Asian women. This may be a result of the estimated lower proportion of heterozygous women among Asian compared to white populations (e.g., Japanese [2 pq] = 0.175 vs. white [2 pq] = 0.390), making it more difficult to detect a small effect in a population with a high proportion of dry phenotypes.

On the basis of the data presented here, further studies are warranted on the possible influence of age and other factors on the pleiotropic expression of the alleles affecting cerumen phenotype as well as other apocrine glands, including the breast and apocrine sweat glands in presumably heterozygous subjects. It would also be of interest to determine if men show a similar change with age.

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