An earlier age of breast cancer diagnosis related to more frequent use of antiperspirants/deodorants and underarm shaving

K G McGrath

Breast cancer incidence suggests a lifestyle cause. A lifestyle factor used near the breast is the application of antiperspirants/deodorants accompanied by axillary shaving. A previous study did not support a link with breast cancer. If these habits have a role in breast cancer development, women using antiperspirants/deodorants and shaving their underarms frequently would be expected to have an earlier age of diagnosis than those doing so less often. An earlier age of diagnosis would also be expected in those starting to use deodorants and shaving at an earlier age. This is the first study to investigate the intensity of underarm exposure in a cohort of breast cancer survivors. Four hundred and thirty-seven females diagnosed with breast cancer were surveyed. Once grouped by their frequency of underarm hygiene habits, the mean age of diagnosis was the primary end point. Secondary end points included the overall frequency of these habits, and potential usage group confounding variables were evaluated. All statistical tests were two-sided. Frequency and earlier onset of antiperspirant/deodorant usage with underarm shaving were associated with an earlier age of breast cancer diagnosis. Combined habits are likely for this earlier age of diagnosis. In conclusion, underarm shaving with antiperspirant/deodorant use may play a role in breast cancer. It is not clear which of these components are involved. Reviewed literature insinuates absorption of aluminium salts facilitated by dermal barrier disruption. Case-controlled investigations are needed before alternative underarm hygiene habits are suggested. ***European Journal of Cancer Prevention*** **12:479–485 © 2003 Lippincott Williams & Wilkins.**

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Key words: Aluminium, antiperspirants, breast cancer, deodorants, lifestyle, underarm shaving

Department of Medicine, Saint Joseph Hospital-Resurrection Health Care, Mail Box 285, 2900 N Lake shore Drive, Chicago, IL 60657, USA.
E-mail: k-mcgrath@northwestern.edu.

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Introduction

The cause of over 50% of female breast cancer remains unexplained, and is probably a consequence of environmental or lifestyle factors (Carroll, 1975; Dupont and Page, 1985; Harris *et al.*, 1992; Madigan *et al.*, 1995; Collman *et al.*, 1996; Coogan *et al.*, 1996; Zheng *et al.*, 1998; Holmes *et al.*, 1999; Abeloff *et al.*, 2000; Clemons and Goss, 2001). An environment close to the breast is the axilla and a lifestyle factor close to the breast, especially in the United States, is the axillary application of antiperspirants/deodorants, often associated with shaving. Ninety per cent of the United States population regularly uses antiperspirants and deodorants, with their daily use ($ sales) only exceeded by toothpastes (Laden, 1999). Figure 1 plots over time the US incidence of female breast cancer versus antiperspirants/deodorants sales (Roush *et al.*, 1987; SEER Cancer Incidence Public-Use Database, 2001; US Cosmetic and Toiletries Market, 2001). If this environment–lifestyle factor plays a role in breast cancer, a relationship should exist between the age of diagnosis and the degree of practice of these hygiene habits.

One previous study by Mirick *et al.* (2002) determined that these habits were not associated with an increased risk of breast cancer. That study did not fully address the intensity of these habits. An example, with another lifestyle exposure, is the clear dose–response relationship between duration of smoking and daily consumption of cigarettes with an increased risk of lung cancer (Doll and Peto, 1978).

This study addresses the frequency (intensity) of underarm hygiene habits within a cohort of breast cancer survivors with their age of diagnosis. Results with biological and epidemiological evidence are presented to link these habits to breast cancer.

Methods

Study design

This was a retrospective study using a written questionnaire sent to surviving female breast cancer patients (1 January 1993 to 31 December 2001) to evaluate their underarm hygiene practices of antiperspirant/deodorant use and underarm shaving. Institutional Review Board approval was granted for a confidential and anonymous survey by informed consent of female breast cancer survivors from the tumour registry of two Chicago hospitals. The patients received and returned the

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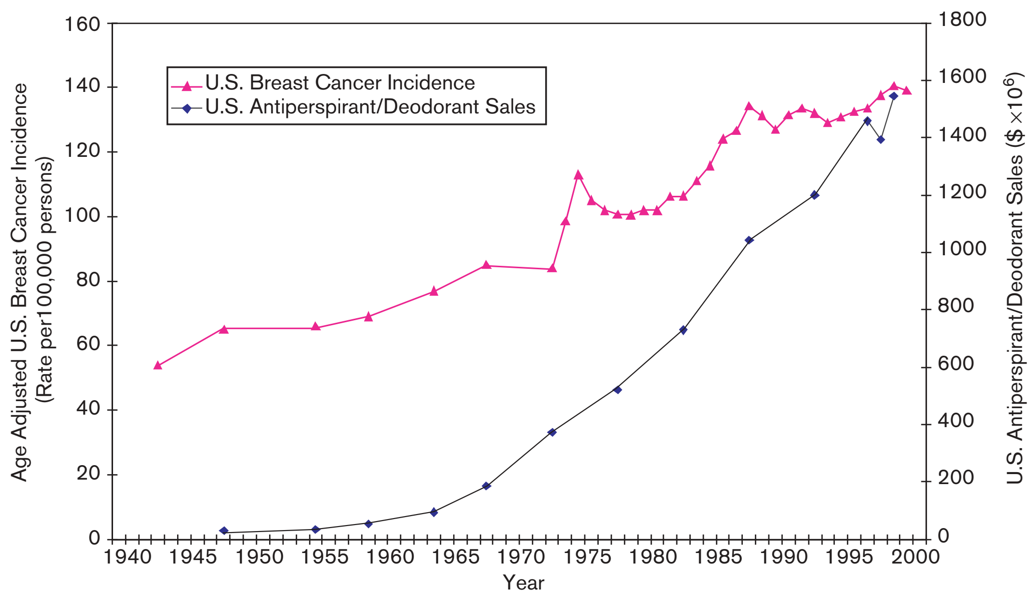
Fig. 1



USA breast cancer incidence and antiperspirant/deodorant sales (Roush *et al.*, 1987; SEER Cancer Incidence Public-Use Database, 2001; US Cosmetic and Toiletries Market, 2001).

Table 1 Usage groups defined

Habit responses	Max	Mid	Min	Non
Antiperspirant and/ or deodorant use	2–5 × /week or 1 × /day or > 1 × /day and…	2–5 × /week or 1 × /day and…	Never/rare or 0–< 2 × /month and…	No and…
Underarm shaving	> 3 × /week	1 × /week or 1–< 2 × /week or 2 × /week	Never/rare or < 1 × /week	No

All user group = Max + Mid + Min.

questionnaire by mail. On the survey there was an optional confidential section for contact information for investigator interview use only. Data collected included patient demographics (age, racial origin, birth country, country of residence), extent of disease at diagnosis, age at menarche, number of live childbirths, fibrocystic breast disease history and family breast cancer history. Using a categorical scoring scale, other risk factors for breast cancer (dietary fat, alcohol intake, oestrogen usage, exercise), and frequency of antiperspirant/deodorant (A/D) use and underarm shaving (S) were recorded. The ages of onset of these underarm hygiene habits were recorded.

Respondents were instructed to check their product labels to properly record if they used antiperspirants, deodorants, or a combined product. This cohort was subdivided into usage groups. The primary end point was the mean age of breast cancer diagnosis compared between the usage groups. The usage groups are as follows: Maximum (Max), Middle (Mid), Minimum (Min), None (Non), and All. The criteria for each group are listed in Table 1. The mean age of breast cancer diagnosis was also compared between subjects starting these habits before the age of 16 and those subjects starting these habits at or after the age of 16. This start age was defined as the mean of the start age of antiperspirant use, deodorant use, and start age of underarm shaving. Secondary end points included the overall frequency of these habits and the effect of potential confounding variables.

Statistical analysis

Results from this study were aggregated for analysis, and Stat Works, Inc. (Carrboro, NC, USA) assisted the investigator in performing the data management procedures and statistical analysis, utilizing Version 8.1 of the SAS statistical software package. Categorical data are reported as numbers and percentages of subjects in each category, and continuous measures as number of subjects, means, standard deviations, standard errors of the mean, medians, minimum and maximum values, or confidence intervals as appropriate. For all pair-wise comparisons between the usage groups, the two-sample t-test was used. While categorical outcome variables (e.g. exercise amount) were tested for between user groups, differences were tested using the Cochran Mantel Haenszel test with modified ridit scoring. All statistical tests were two-sided and all statistical testing were declared statistically significant if the calculated *P*-value is ≤ 0.050.

Results

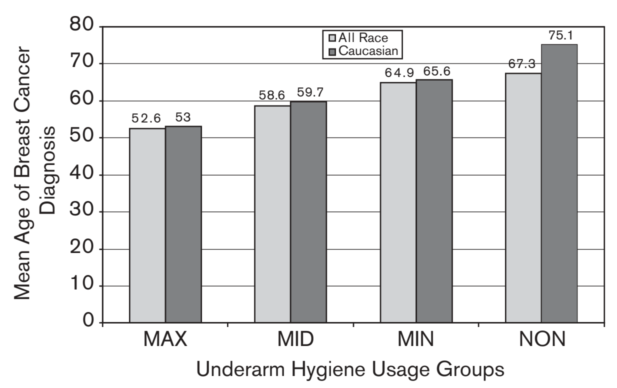
Of the 1344 questionnaires sent, 437 were returned. The general characteristics of the respondents are shown in Table 2. As presented in this table the age distribution of the respondents was not skewed. Not all respondents had usage group designation, due to missing or incomplete responses. Within all race respondents, the mean age at diagnosis of the Max group was 52.6 years ($n = 35$) compared with: the Mid group 58.6 years ($n = 120$), the Min group 64.9 years ($n = 50$), and the Non group 67.3 years ($n = 32$). The mean differences were: 6 years/$P = 0.0121$, 12.3 years/$P < 0.0001$, 14.7 years/$P < 0.0001$, respectively. The mean age at diagnosis of the Min group was 2.4 years. earlier than the Non group ($P = 0.4243$). Of Caucasian respondents the mean age at diagnosis of the Max group was 53 years ($n = 30$), compared with: the Mid group 59.7 years ($n = 105$), the Min group 65.6 years ($n = 44$) and to the Non group 75 years ($n = 20$). The differences were: 6.8 years/$P = 0.0104$, 12.5 years/$P < 0.0001$, 22 years/$P < 0.0001$, respectively. The mean age at diagnosis of the Min group was 9.5 years earlier than the Non group, $P = 0.0014$. The mean age at diagnosis of the USA-born Max group (all races, $n = 29$) was 16 years earlier than the USA-born Min group (all races, $n = 41$), $P < 0.0001$. Figure 2 summarizes the mean age at diagnosis of all four groups.

Table 3 presents the pair-wise comparisons of each usage group followed by the usage group's summary statistics in Table 4. As presented in Figure 3, within the all-race Max group, those that began use at an age of < 16 ($n = 24$) had a mean age at diagnosis of 46.3 years, 19 years earlier than those starting at age ≥ 16 with a mean age at diagnosis of 65.3 years ($n = 10$, 1 subject omitted A/D/S start age), $P < 0.0001$. Of All users (Max + Mid + Min), those that began these habits at age < 16 ($n = 193$, 12 omitted A/D/S start age) had a mean age of diagnosis of 57 years, 9.6 years earlier than those beginning at age ≥ 16 with a mean age of diagnosis of 66.6 years ($n = 127$), $P < 0.0001$. The All group (Max + Mid + Min, $n = 205$), had a mean age of diagnosis of 59.1 years, 8.2 years earlier than the Non use group's mean age of diagnosis of 67.3 years, ($n = 32$), $P = 0.0012$. There was no significant difference in the mean age of diagnosis of those who responded: 'Did not to never/rarely shave but used A/Ds at any frequency' ($n = 142$) compared with those who responded: 'Did not to never/rarely used A/Ds but did shave at any frequency' ($n = 62$), $P = 0.9201$. Those who used antiperspirants, but not deodorants, and shaved at any frequency ($n = 31$) had a mean age of diagnosis 3 years earlier than those who used deodorants, but not antiperspirants, and shaved at any frequency ($n = 63$), $P = 0.2688$ (Figure 4).

Table 2 **Breast cancer survey, respondent's general characteristics**

Number of questionnaires sent/received	1344/437
Race beakdown:	
Caucasian	85%
African–American	4%
Asian/Asian American	7%
Hispanic	3%
Native American	1%
Age distribution:	
31–40 years	11
41–50 years	52
51–60 years	87
61–70 years	109
71–80 years	97
81–90 years	65
91–100 years	4
Mean age	65.7 years
Median age	66.0 years
Standard deviation	13.26
25th and 75th percentiles	56 and 76 respectively
Minimum age	31 years
Maximum age	94 years
Missing age data	12
Percentage of subjects using antiperspirants/deodorants combined or separately	85.58%
Percentage of subjects who shaved underarms at all	79.86%
Percentage of shavers who use antiperspirants/deodorants combined or separately	93.41%
Percentage of subjects who did not shave or use antiperspirants or deodorants	9.15%
Mean age of menarche/mean number of live childbirths (all races)	
Max group	12.26/1.86
Mid group	12.69/2.13
Min group	12.94/2.23
Non group	13.23/1.87

Fig. 2



Usage group's mean age of breast cancer diagnosis. $P < 0.05$ All race: Max versus Mid (0.0121), Min (<0.0001), Non (<0.0001); Mid versus Min (0.0028), Non (0.0006). $P < 0.05$ Caucasian: Max versus Mid (0.0104), Min (< 0.0001), Non (<0.0001); Mid versus Min (0.0060), Non (<0.0001); Min versus Non (0.0014). $P > 0.05$ All race: Min versus Non (0.4243).

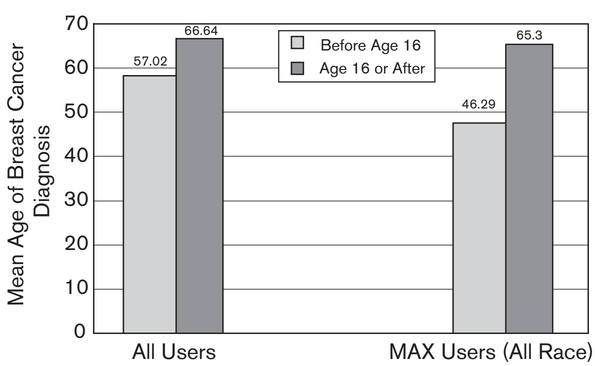
Table 3 Pair-wise comparisons of usage groups

	Mean difference in age of diagnosis	95% Confidence interval	*P*-value (*t*-test)
All races			
Max versus Mid	−6.03	(−10.73, −1.34)	0.0121
Max versus Min	−12.32	(−18.05, −6.60)	<0.0001
Max versus Non	−14.74	(−21.44, −8.05)	<0.0001
Mid versus Min	−6.29	(−10.38, −2.20)	0.0028
Mid versus Non	−8.71	(−13.63, −3.79)	0.0006
Min versus Non	−2.42	(−8.44, 3.59)	>0.05 (0.4243)
Caucasian only			
Max versus Mid	−6.68	(−11.76, −1.599)	0.0104
Max versus Min	−12.54	(−18.34, −6.73)	<0.0001
Max versus Non	−22.02	(−29.16, −14.87)	<0.0001
Mid versus Min	−5.86	(−10.00, −1.70)	0.0060
Mid versus Non	−15.34	(−20.93, −9.745)	<0.0001
Min versus Non	−9.48	(−15.17, −3.80)	0.0014

Table 4 Usage group's summary statistics (all races/Caucasian only)

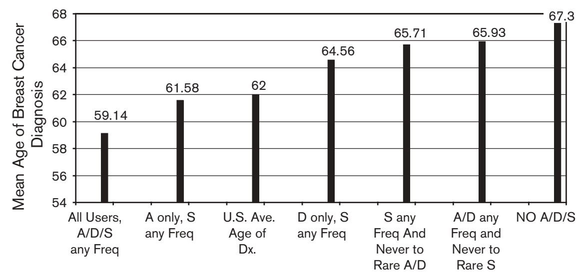
Statistic	Max	Mid	Min	Non
Mean age of diagnosis	52.6/53.03	58.63/59.71	64.92/65.57	67.34/75.05
Standard deviation	13.34/13.95	12.08/11.95	12.86/11.06	14.10/9.28
Sample size	35/30	120/105	50/44	32/20
SE of mean	2.25/2.55	1.10/1.17	1.82/1.67	2.49/2.08
Lower 95% conf. limit	48.02/47.82	56.45/57.40	61.26/62.21	62.26/70.71
Upper 95% conf. limit	57.18/58.24	60.82/62.03	68.58/68.93	72.43/79.39
Minimum age	35/35	35/35	30/37	40/48
Median age	47/48.5	59/60	67/67	72.5/77.5
Maximum age	79/79	84/84	92/92	87/87

Fig. 3



Age-related differences in mean age of breast cancer diagnosis related to onset of underarm antiperspirant/deodorant use and shaving. All users: difference 9.62 years, $P<0.0001$; Max users: difference 19.01 years, $P<0.0001$. Note: Start age = mean start age of antiperspirant use, deodorant use and underarm shaving.

Fig. 4



Additional usage group's mean age of breast cancer diagnosis and average age of breast cancer diagnosis in USA (SEER Cancer Incidence Public-Use Database, 2001). A, antiperspirant; D, deodorant; S, underarm shaving; Freq, frequency.

There was no significant difference between each usage group's family history of breast cancer, mean age of menarche and number of live childbirths, dietary fat, oestrogen use, amount of exercise or hard liquor consumption ($P > 0.05$). However, the mean beer/wine consumption was not similar between the usage groups ($P = 0.0113$). The responses to the beer/wine 'none to rare' category were as follows: Non ($n = 30$, 94%) > Min ($n = 36$, 77%) > Max ($n = 25$, 71%) > Mid ($n = 75$, 62%).

Discussion

Circumstances involving a woman's environment and lifestyle clearly play a role in the incidence of breast cancer. Environmental and lifestyle investigations have included diet (fat, alcohol, charred meat and fibre), exercise, body habitus, hormones, breastfeeding, reproductive history, smoking, radiation exposure, electromagnetic fields, viruses, and pesticides. None of these have fully explained such a common female cancer. Five to ten per cent of breast cancer has a genetic basis and over 50% of women with breast cancer have yet to be linked to a major risk factor (Carroll, 1975; Dupont and Page, 1985; Harris *et al.*, 1992; Madigan *et al.*, 1995; Collman *et al.*, 1996; Coogan *et al.*, 1996; Zheng *et al.*, 1998; Holmes *et al.*, 1999; Abeloff *et al.*, 2000; Clemons and Goss, 2001). This study suggests that a woman's underarm hygiene habits may provide such a link. The data from this study are consistent with the hypothesis that the degree of antiperspirant/deodorant usage and axillary shaving is associated with an earlier age of breast cancer diagnosis. The age distribution of the 437 respondents was not skewed towards younger individuals. The mean age of breast cancer diagnosis was progressively lower proceeding from the Non to Max usage groups (Figure 2). In addition, beginning these habits at an earlier age was associated with a significantly earlier age of diagnosis (Figure 3). These results suggest that combined habits were necessary. Separately done, these habits were not associated with a significant earlier age of diagnosis (Figure 4).

Ninety per cent of the United States population uses daily antiperspirants and deodorants (Laden, 1999), and in women, this use is frequently associated with underarm shaving. Figure 1 plots the annual incidence of female breast cancer with the annual sales of antiperspirants/deodorants in the United States (Roush *et al.*, 1987; Harris *et al.*, 1992; SEER Cancer Incidence Public-Use Database, 2001; US Cosmetic and Toiletries Market, 2001). Often used in combination, antiperspirants (for dryness and malodour) and deodorants (for malodour) contain numerous components, including aluminium and other metal salts, antimicrobials, aliphatic alcohols and glycols, and fragrances (Maken *et al.*, 1999; Benohanian, 2001). Adverse events from these topically applied products have included clothing damage, skin irritation/inflammation, contact dermatitis and granulomas. There has been no correlation to breast cancer (Montemarano *et al.*, 1997; Laden, 1988; Maken *et al.*, 1999; Jones, 2000; Scheman, 2000; Benohanian, 2001; Robb-Nicholson, 2001; Mirick *et al.*, 2002).

The most consistently used components since the commercial introduction of antiperspirants in 1903 are aluminium salts to promote underarm dryness (Laden, 1999). Aluminium-based compounds persist in today's antiperspirants. Daily transdermal exposure over long periods of time of metal-containing compounds in personal-care products has raised some health concerns but data are lacking regarding bioavailability (Hostynek *et al.*, 1993; Exley, 1998; Darbre, 2001). In studies involving intact human skin, dermal absorption of aluminium reveals only shallow epidermal penetration secondary to the metal's avid formation of complexes with skin proteins (Hostynek *et al.*, 1993). Experiments with adult mice, naked mouse pups and excised skin patches taken from adult mice have shown that the shaved skin was not a barrier to the absorption of topically applied aluminium salts (Anane *et al.*, 1995). Transplacental passage of aluminium from pregnant mice to fetus organs occurred after maternal transcutaneous exposure to aluminium salts (Anane *et al.*, 1997). Aluminium appeared in the milk of lactating rabbits following subcutaneous injections of aluminium lactate (Yokle and McNamara, 1985).

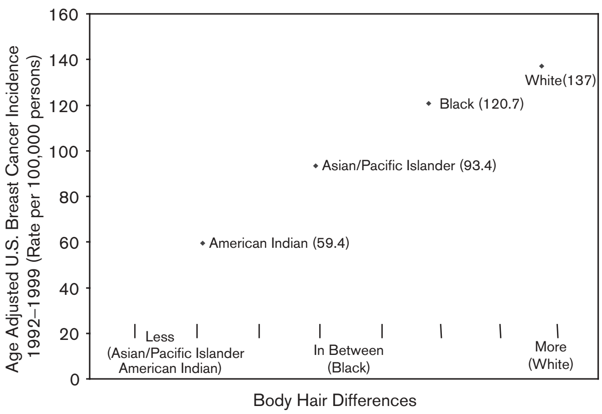
There are numerous animal and plant studies suggesting an adverse role of aluminium, especially when present in its active moiety (Al^{3+}), affecting a number of biological processes, including cross-linking of DNA strands and enzyme system modification (DeBoni *et al.*, 1980; Karlik *et al.*, 1980; Wenk and Stemmer, 1982). Al^{3+} has an extremely high charge ($3+$) to ionic radius (0.05 nm) causing it to rapidly penetrate nuclear compartments, bind tightly to nucleic acids, ATP and heterochromatin, and inhibit or adversely affect DNA template activity, linker histones, and DNA and RNA polymerase enzyme systems (DeBoni *et al.*, 1974, 1980; Crapper *et al.*, 1980; Crapper McLachlan and DeBoni, 1977, 1980; Matsumuto and Morimura, 1980; Wen and Wisniewski, 1985; Wedrychowski *et al.*, 1986). Associated with elevated concentrations of aluminium are a decreased rate of DNA synthesis, an increase in DNA replication errors, and an increase in the affinity of linker histones for DNA (Berlyne *et al.*, 1972; Laussac and Commenges, 1983). These studies provide circumstantial evidence that Al^{3+} has oncogenic potential.

Experimental data indicate that both depth of penetration, which determines duration of antiperspirant effect, and relative antiperspirant efficacy are significantly dependent on ionic mobility (size and charge). Thus, the prevailing pH is crucial and small pH changes within a relatively narrow range lead to formation of $Al^{3+}/H_2O/OH^-$ complexes of markedly different solubility and bioavailability. In aluminium hydroxide solutions, for example, concentrations of free Al^{3+} at pH 4.2 are 100–1000 times greater than at pH 6.2. Generally, decreases in solution pH below 5.5 result in exponential increases in Al^{3+} concentrations (Kaehny *et al.*, 1977; Martin, 1991; Borak and Wise, 1998). An analogy is acid rain releasing Al^{3+} from rocks and soil into lakes and streams (Dyearssen *et al.*, 1987; Martin, 1991, 1994). Axillary sweat has a normal pH of 4.5–7.4, with increased sweating rates associated with higher pH values (Herrmann and Sulzberger, 1958; Jakubovic and Ackerman, 1985; Quinton *et al.*, 1999). However, the lower pH of some aluminium salts (e.g. aluminium chloride pH <4, aluminium chlorhydrate pH 4.38) and the sweat reduction that antiperspirants cause, along with microbial action on axillary apocrine sweat, could cumulatively contribute to an acidic underarm environment, 'axillary acid rain' (Hermann and Sulzberger, 1958; Lansdown, 1995; McGee *et al.*, 1998; Labows *et al.*, 1999; Quinton *et al.*, 1999. This may explain, at least in part, why world breast cancer incidence is lower in countries with different cultural habits or less disposable income for western axillary hygiene practices or in areas with less media exposure, as in some rural areas (Donegan *et al.*, 1988; Cancer Facts and Figures, 1998; Laden, 1999).

Unique valveless and bi-directional lymphatic flow exists between the breast and axillae. Shared is a rich anastomoses, which could easily provide direct and chronic exposure of breast tissue to Al^{3+} or other applied axillary substances (Taylor, 1959; Moore and Dalley, 1999). This may also explain the most frequent tumour location occurring in the upper-outer breast (Lester and Cotran, 1999). If topical absorption occurs, normal plasma clearing of Al^{3+} by transferrin and citrate binding may be insufficient with daily exposure, especially over decades (Martin, 1997; Ohman and Martin, 1994).

Al^{3+} clearance through human breastfeeding has not been studied, yet the longer women breastfeed the more they are protected against breast cancer (Collaborative Group on Hormonal Factors in Breast Cancer, 2002). Less frequent underarm shaving may be necessary in

Fig. 5



USA breast cancer incidence by race/ethnicity versus body hair (Jakubovic and Ackerman, 1992; Dawber *et al.*, 1998; Anon., 1998; Freinkel, 2000; SEER Cancer Incidence Public-Use Database, 2001; Collaborative Group on Hormonal Factors in Breast Cancer, 2002).

individuals with less body hair (Caucasian > Black > Asian/Native American), and the US incidence of breast cancer is higher in Caucasians followed by Blacks and then Asians and Native Americans (Figure 5) (Jakubovic and Ackerman, 1992; Dawber *et al.*, 1998; Anon., 1998; Freinkel, 2000; SEER Cancer Incidence Public-Use Database, 2001; Collaborative Group on Hormonal Factors in Breast Cancer, 2002). The Japanese have less mean number of axillary hairs with less daily growth than Caucasians, and notably, a lower incidence of breast cancer (Jakubovic and Ackerman, 1992; Cancer Facts and Figures, 1998).

These underarm hygiene habits are lifestyle factors, influenced by culture, and passed down from mother to daughter. This may also explain a 'familial' predisposition for breast cancer. Until further studied, alternative hygiene and cultural habits should be considered to possibly reduce the risk of breast cancer. Figure 1, plotting the annual incidence of female breast cancer with the annual sales of antiperspirants/deodorants in the United States, leads towards an intersection, perhaps a 'saturation point'. This could be a contributing component in the slowing of breast cancer incidence trends.

A small retrospective study such as this cannot conclusively link a woman's underarm habits to breast cancer, however, as a pilot and exploratory investigation it raises suspicion about the underarm hygiene habits practiced by American women. Case–control investigations are now necessary to further evaluate such an association. As with tobacco and lung cancer studies, the intensity of exposure is paramount.

Acknowledgements

Tumor Registry, Resurrection Health Care, Chicago, IL. Section of Oncology, Resurrection Health Care, Chicago, IL. Department of Medicine, Saint Joseph Hospital/ Resurrection Health Care, Chicago, IL.

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