Night Shift Work, Light at Night, and Risk of Breast Cancer

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Background: **Exposure to light at night may increase the risk of breast cancer by suppressing the normal nocturnal production of melatonin by the pineal gland, which, in turn, could increase the release of estrogen by the ovaries. This study investigated whether such exposure is associated with an increased risk of breast cancer in women.** ***Methods:*** **Case patients (n = 813), aged 20–74 years, were diagnosed from November 1992 through March 1995; control subjects (n = 793) were identified by random-digit dialing and were frequency matched according to 5-year age groups. An in-person interview was used to gather information on sleep habits and bedroom lighting environment in the 10 years before diagnosis and lifetime occupational history. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated by use of conditional logistic regression, with adjustment for other potential risk factors.** ***Results:*** **Breast cancer risk was increased among subjects who frequently did not sleep during the period of the night when melatonin levels are typically at their highest (OR = 1.14 for each night per week; 95% CI = 1.01 to 1.28). Risk did not increase with interrupted sleep accompanied by turning on a light. There was an indication of increased risk among subjects with the brightest bedrooms. Graveyard shiftwork was associated with increased breast cancer risk (OR = 1.6; 95% CI = 1.0 to 2.5), with a trend of increased risk with increasing years and with more hours per week of graveyard shiftwork (*P* = .02, Wald chi-squared test).** ***Conclusion:*** **The results of this study provide evidence that indicators of exposure to light at night may be associated with the risk of developing breast cancer. [J Natl Cancer Inst 2001;93:1557–62]**

It has been proposed that exposure to light at night and power frequency (50–60 Hz) magnetic fields may increase the risk of breast cancer by suppressing the normal nocturnal production of melatonin by the pineal gland, which, in turn, could increase the release of estrogen by the ovaries *(1,2)*. Studies of breast cancer and measures of magnetic field exposure have led to conflicting results [reviewed in *(3)*]. To date, no study has investigated the relationship between the risk of breast cancer and exposure to light at night as estimated from characteristics of sleep habits or bedroom environment. Shiftwork has also been proposed to increase the risk of breast cancer *(1)*, and four studies *(4–7)* investigating this have all reported increased risk among women who work during the night.

The purpose of this study was to investigate whether the risk of breast cancer is associated with exposure to light at night as characterized by sleep habits, bedroom lighting environment, and shiftwork in the 10 years before diagnosis and/or residential exposure to power frequency magnetic fields. Results regarding magnetic field exposure are described elsewhere *(8)*. This report presents the primary findings regarding indicators of light at night exposure.

Subjects and Methods

Case patients were women aged 20–74 years with a new diagnosis of breast cancer (ICD-O site codes 174.0–174.9) *(9)* from November 1992 through March 1995. Case patients were identified by the Cancer Surveillance System of the Fred Hutchinson Cancer Research Center, Seattle, WA, one of 10 population-based cancer registries funded by the National Cancer Institute, Bethesda, MD, as part of the Surveillance, Epidemiology, and End Results (SEER)[1] Program. Of the 1039 eligible case patients identified, 813 (78%) agreed to participate. Control subjects were women between the ages of 20 and 74 years with no history of breast cancer, selected to

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be equal in number to the case patients and frequency matched according to 5-year age groups. Control subjects were identified by random-digit dialing with the use of a modification of the method described by Waksberg *(10).* Of the 20 148 phone numbers dialed, 95% were successfully resolved in terms of determining whether the phone was residential and whether an eligible woman lived in the household. Of 1053 eligible women selected as control subjects, 793 (75%) agreed to participate.

Data Collection

Data collection took place from April 1993 through December 1995. An in-person interview was used to ascertain information on known or suspected risk factors for breast cancer, such as reproductive history, family history of breast cancer, and lifestyle factors (e.g., alcohol consumption and cigarette smoking). In addition, questions were included to obtain details on sleep patterns and habits in the 10 years before diagnosis (or reference date), lighting characteristics of the subject's bedroom for all homes occupied in the 10 years before diagnosis (or reference date), and lifetime occupational history. Questions on sleep habits and bedroom characteristics included the following: 1) the time the subject usually turned off the lights to go to sleep and the time she woke up, for each of the 7 days of the week; 2) the usual number of times the subject's sleep was interrupted; 3) when sleep was interrupted, whether the subject typically turned on a light and, if so, for how long; and 4) ambient light level in the bedroom while sleeping. Subjects were asked to classify the typical bedroom ambient light level according to the following six levels of darkness: 1) The subject wore a mask to keep out light; 2) she could not see her hand in front of her face; 3) she could see to the end of her bed; 4) she could see across the room; 5) she could barely read; and 6) she could read comfortably. Subjects were allowed to report multiple patterns of sleep habits and bedroom characteristics for each residence occupied in the 10 years before diagnosis. The lifetime occupational history consisted of every job the subject held for 6 months or longer, including volunteer and military service. Details included beginning and end dates for each job, job title, full-time or part-time status, and the percentage of time worked at day, evening, or graveyard shift, using specific start and stop times in defining each shift.

The Fred Hutchinson Cancer Research Center Institutional Review Board approved the procedures for contacting potential participants, obtaining informed consent, and all data collection procedures; all participants signed written informed consent before participation.

Statistical Methods

Nine variables were defined before analysis to characterize various aspects of a subject's exposure to light at night via sleep habits, bedroom lighting environment, and shiftwork. Using information on sleep habits, three variables were constructed to characterize potential exposure to light-at-night by not sleeping during the period of the night when nocturnal melatonin levels are typically at their highest. For the purposes of these analyses, the peak period was defined to be between 1:00 and 2:00 AM, based on evidence that suggests nocturnal melatonin levels increase throughout the evening to peak at approximately the midpoint of the dark period at night *(11).* For ease of presentation, the sleep pattern that reflects *not* sleeping during this period will be referred to henceforth as "nonpeak sleep." The three variables included the following: 1) the number of nights per week the subject experienced nonpeak sleep, weighted over all sleeping patterns in the 10 years before diagnosis; 2) ever having a sleep pattern in the 10 years before diagnosis in which the subject frequently experienced nonpeak sleep (frequent = three or more nights per week); and 3) the number of years during the 10 years before diagnosis that the subject had a pattern of frequent nonpeak sleep. For each day of the week, the subject was considered to have experienced nonpeak sleep if she reported the following: 1) turning off the lights to go to sleep at or after 2:00 AM, 2) rising for the day at or before 1:00 AM, or 3) not going to bed at all (i.e., she slept fewer than seven times per week, not including naps).

Three variables characterized exposure to light during the subject's night from either interrupted sleep or the self-reported ambient light levels of the bedroom: 1) reported number of times during the night that the subject got up and turned on a light, 2) percentage of the subject's night that the light was on, and 3) self-reported ambient light level of the subject's bedroom during the night. Night was defined as the time between turning off the lights to go to sleep and waking up; thus, night was unique to each subject and sleeping pattern and was not associated with clock time. Bedroom ambient light level was considered to be a continuous variable with values 1–6, corresponding to the six levels of increasing ambient light described above. All three variables were weighted over all sleeping patterns in the 10 years before diagnosis (reference date).

Three variables characterized exposure to light at night from working the graveyard shift in the 10 years before diagnosis: 1) ever worked during the graveyard shift, 2) hours per week worked during the graveyard shift based on a weighted average of all jobs in the 10 years before diagnosis (reference date), and 3) number of years worked at least one graveyard shift per week (one shift = 8 hours). Graveyard shift was defined as beginning work after 7:00 PM and leaving work before 9:00 AM.

All continuous measures of exposure were also analyzed as categorical variables to investigate whether an exposure effect (or lack thereof) was dependent on the form of the dose–response relationship with breast cancer. Except for bedroom ambient light level and the number of years worked at least one graveyard shift per week, continuous exposure variables were categorized using quartiles of the distributions of the control subjects who had nonzero values. Bedroom ambient light levels were categorized into three groups: 1) The subject reported wearing a mask or could not see hand in front of face (reference group), 2) the subject reported seeing the end of the bed or across the room, and 3) the subject reported being almost able to read or read comfortably. Because of the low number of exposed subjects, the number of years worked at least one graveyard shift per week in the 10 years before diagnosis was divided according to the median rather than quartiles, creating three groups: 1) no years worked at least one graveyard shift per week (reference group), 2) worked at least one graveyard shift per week for fewer than 3 years (the median value of the control subjects for which the number of years ≠ 0), and 3) worked at least one graveyard shift per week for 3 or more years.

Previous analyses revealed that the following were each statistically significant ($P<.05$, Wald chi-squared test) risk factors for breast cancer in this study *(8):* family history of breast cancer (mother or sister), parity (number of full-term pregnancies), ever use of oral contraceptives, and recent (within the last 5 years) discontinued use of hormone replacement therapy. Other breast cancer risk factors investigated in earlier analyses *(8)* included age at first pregnancy, duration of lactation, early (<40 years old) bilateral oophorectomy, ever having undergone an upper gastrointestinal x-ray series, alcohol consumption, and ever having been a smoker. Each of these factors was associated with slight, marginally statistically significant effects ($.05<P\leqslant.10$, Wald chi-squared test) on the risk of breast cancer, but they were not included in the present analyses because of the relatively low numbers of exposed subjects to minimize the number of risk factor combinations not present in all of the exposure categories. Odds ratios (ORs) and 95% confidence intervals (CIs) were used to evaluate relative risks using conditional logistic regression *(12)* (SAS/STAT Release 6.11; SAS Institute, Inc., Cary, NC). All models were conditional on 5-year age strata, with no adjustment for any covariates and with adjustment for the four factors listed above. The results from the crude (unadjusted) and adjusted analyses were essentially the same; therefore, only adjusted ORs are presented. Statistical significance was determined by the Wald chi-squared test.

RESULTS

Descriptive Characteristics

The in-person interview was completed for all 813 case patients and 793 control subjects. Complete information on sleep habits and bedroom characteristics was obtained for 808 case patients and 788 control subjects (99% for both). History of graveyard shiftwork in the 10 years before diagnosis (reference date) was obtained for 813 case patients and 792 control subjects. A more detailed description of the characteristics of case patients and control subjects is provided elsewhere *(8).* In brief, control subjects were slightly younger than case patients and less likely to have a family history of breast cancer. Control subjects were more likely to have used oral contraceptives and to have had four or more full-term pregnancies (although the mean number of full-term pregnancies was similar among case patients and control subjects: 2.2 for case patients and 2.5 for control subjects). A lower proportion of control subjects had discontinued hormone replacement therapy in the 5 years before the reference date (diagnosis).

Sleep Habits and Bedroom Environment

Results of analyses between sleep habits involving nonpeak sleep and breast cancer risk are shown in Table 1. Overall, most subjects (87.2% of the case patients and 88.5% of the control subjects) never experienced a pattern of nonpeak sleep in the 10 years before diagnosis. Of those subjects who did, the case patients reported more nights of nonpeak sleep per week than the control subjects (mean = 2.2 nights/week for the case patients and 1.7 nights/week for the control subjects). Of the subjects who reported having a sleep pattern of frequent (three or more nights/week) nonpeak sleep, case patients reported spending more years of the 10 before diagnosis experiencing this sleep pattern than did the control subjects (4.2 years for the case patients and 3.4 years for the control subjects). Subjects who had at least one pattern of frequent nonpeak sleep were more likely to have ever used oral contraceptives (70%) than subjects who never experienced such a pattern (61%) and were more likely to be nulliparous (16% versus 13%, respectively), although the mean number of full-term pregnancies was similar among both groups (2.2 versus 2.4, respectively) (data not shown). Both those who had at least one pattern of frequent nonpeak sleep and those who did not had identical proportions of family history of breast cancer (15%) and nearly identical proportions of recently discontinuing hormone replacement therapy (5% for the frequent nonpeak sleep group versus 6%).

Based on the measure of nights per week of nonpeak sleep, there is an increased risk of breast cancer with each additional night of experiencing this sleep pattern (OR = 1.14 for each night; 95% CI = 1.01 to 1.28). When this exposure measure was analyzed as a categorical variable, there was some indication that those who experienced at least 2.6 nights per week of nonpeak sleep were at an increased risk for breast cancer (OR = 1.7; 95% CI = 1.0 to 3.1), but there is no evidence of a trend of increasing risk with increasing number of nights (P = .12, Wald chi-squared test). Table 1 also shows that ever having a pattern of frequent nonpeak sleep in the 10 years before diagnosis was associated with a slight increased risk (OR = 1.4; 95% CI = 1.0 to 2.0) of breast cancer, but this effect was not statistically significant. However, breast cancer risk was statistically significantly associated with the number of years in the 10 years before diagnosis that the subject frequently experienced nonpeak sleep (OR = 1.09 for each year; 95% CI = 1.02 to 1.18). When the number of years was treated as a categorical variable, experiencing at least 4.6 years of frequent nonpeak sleep is associated with a twofold increase in the risk of breast cancer. Although the third quartile contained relatively few case patients and the point estimate of the OR was below unity, there was evidence of a trend of increasing risk with increasing number of years of frequent nonpeak sleep (P = .04, Wald chi-squared test).

Table 1. Odds ratios for breast cancer risk among women who did not sleep when the nocturnal peak melatonin level typically occurs

Exposure	Case patients		Control subjects		Odds ratio†	95% confidence intervals
	No.	%*	No.	%*		
No. of nights/wk‡						
Continuous	763	100	741	100	1.14§ P = .03	1.01 to 1.28
Quartiles‖						
Reference	665	87.2	656	88.5	—	—
<0.6	22	2.9	23	3.1	1.0	0.5 to 1.8
0.6–1.2	23	3.0	22	3.0	1.1	0.6 to 2.1
1.2–2.6	20	2.6	21	2.8	1.0	0.5 to 1.9
⩾2.6	33	4.3	19	2.6	1.7	1.0 to 3.1
At least 3 nights/wk						
Ever¶						
No	682	89.4	680	91.8	—	—
Yes	81	10.6	61	8.2	1.4	1.0 to 2.0
No. of years¶						
Continuous	763	100	741	100	1.09§ P = .02	1.02 to 1.18
Quartiles#						
Reference	682	89.4	680	91.8	—	—
<1.0	19	2.5	17	2.3	1.2	0.6 to 2.3
1.0–3.0	20	2.6	15	2.0	1.4	0.7 to 2.8
3.0–4.6	9	1.2	14	1.9	0.6	0.3 to 1.5
⩾4.6	33	4.3	15	2.0	2.3§ P = .01	1.2 to 4.2

*Percentage calculated from total number of case patients/control subjects with complete sleep and risk factor data (n = 763 case patients and 741 control subjects).

†Logistic regression models conditional on 5-year age strata; odds ratios were adjusted for parity, family history of breast cancer (mother or sister), oral contraceptive use (ever), and recent (<5 years) discontinued use of hormone replacement therapy.

‡Weighted average over 10 years before reference date.

§Statistical significance determined by the Wald chi-squared test.

‖Quartiles computed from all control subjects for which sleep data were available and number of nights/week ≠ 0. Reference level is number of nights/week = 0. P_{trend} = .12, Wald chi-squared test.

¶During the 10 years before reference date.

#Quartiles computed from all control subjects for which sleep data were available and number of years ≠ 0. Reference level is number of years = 0. P_{trend} = .04, Wald chi-squared test.

Results of analyses between indicators of light exposure during the subject's night and breast cancer risk are shown in Table 2. Among subjects who reported having at least one sleep pattern in the 10 years before diagnosis in which they got up and turned on a light, both case patients and control subjects reported approximately one episode per night (weighted average of the 10 years before diagnosis). When they did get up and turn on a light, case patients and control subjects reported similar proportions of the night with the light on (3% of the night for both, weighted average of the 10 years). Ten-year weighted average bedroom ambient light levels were similar for case patients and control subjects (ambient light level = 3 for both, i.e., able to see the end of the bed during the night).

There was no association between the risk of breast cancer and any of the following indicators of light exposure during the subject's night: 1) reported number of times during the night that the subject got up and turned on a light, 2) percentage of the subject's night that the light was on, and 3) reported ambient light level of the subject's bedroom during the night. Analyzing either the number of times that the subject got up and turned on a light

Table 2. Odds ratios for breast cancer risk and light at night

Exposure	Case patients No.	Case patients %*	Control subjects No.	Control subjects %*	Odds ratio†	95% confidence intervals
Reported No. of times light on						
Continuous	763	100.0	741	100.0	1.03	0.90 to 1.18
Quartiles‡						
Reference	429	56.2	414	55.9	—	—
<0.3	67	8.8	83	11.2	0.8	0.6 to 1.2
0.3–0.8	94	12.3	84	11.3	1.1	0.8 to 1.5
0.8–1.3	93	12.2	78	10.5	1.1	0.8 to 1.6
⩾1.3	80	10.5	82	11.1	1.0	0.7 to 1.4
Reported % time light on, %						
Continuous	762	100.0	741	100.0	0.99	0.97 to 1.02
Quartiles§						
Reference	435	57.0	416	56.1	—	—
<0.4	86	11.3	83	11.2	1.0	0.7 to 1.4
0.4–0.9	76	10.0	81	10.9	0.9	0.6 to 1.2
0.9–2.9	79	10.4	80	10.8	1.0	0.7 to 1.4
⩾2.9	86	11.3	81	10.9	1.0	0.7 to 1.4
Reported ambient light levels						
Continuous	762	100.0	740	100.0	1.1	0.9 to 1.2
Groups‖						
1	94	12.3	88	11.9	—	—
2	633	83.1	627	84.7	1.0	0.7 to 1.4
3	35	4.6	25	3.4	1.4	0.8 to 2.6

*Percentage calculated from total number of case patients/control subjects with complete sleep, light at right, and risk factor data (n = 763 case patients and 741 control subjects).

†Logistic regression models conditional on 5-year age strata; odds ratios were adjusted for parity, family history of breast cancer (mother or sister), oral contraceptive use (ever), and recent (<5 years) discontinued use of hormone replacement therapy.

‡Quartiles computed from all control subjects for which sleep and light-at-night data were available and number of times ≠ 0. Reference level is number of times = 0.

§Quartiles computed from all control subjects for which sleep and light-at-night data were available and percent time ≠ 0. Reference level is percent time = 0.

‖Group 1: subject reported wearning a mask or could not see hand in front of face (ambient light levels 1 and 2); group 2: subject reported seeing end of bed or across the room (ambient light levels 3 and 4); and group 3: subject reported being almost able to read or read comfortably (ambient light levels 5 and 6).

or the percentage of the night the light was on as a categorical variable did not change the results. When bedroom ambient light level was considered as a categorical variable, there was an indication of an increased risk of breast cancer among subjects with the brightest bedrooms, but this result was not statistically significant (OR = 1.4; 95% CI = 0.8 to 2.6).

Graveyard Shiftwork

Results of analyses between graveyard shiftwork and breast cancer risk are shown in Table 3. Most subjects never worked the graveyard shift in the 10 years before diagnosis. Of those subjects who worked at least some time during the graveyard shift, the case patients worked more hours per week than the control subjects (7.2 hours/week for the case patients and 4.6 hours/week for the control subjects, 10-year weighted average over all jobs). During the 10 years before diagnosis, the case patients reported working more years at jobs that required at least one graveyard shift (one shift = 8 hours) per week (4.5 years for the case patients and 3.1 years for the control subjects). Relative to subjects who never worked at least one graveyard shift per week, subjects who did were more likely to have ever used oral contraceptives (76% versus 62%), less likely to have recently discontinued hormone replacement therapy (3% versus 6%), and less likely to have a family history of breast cancer (10% versus 15%). The mean number of full-term pregnancies was similar among both groups (2.3 in the shiftwork group versus 2.4 in the group who never worked at least one graveyard shift per week), but the graveyard shiftworkers were more likely to be nulliparous (16% versus 14%).

Women who worked the graveyard shift at least once in the 10 years before diagnosis are at an approximately 60% increased risk (OR = 1.6; 95% CI = 1.0 to 2.5) for breast cancer compared with those who did not work the graveyard shift. Furthermore, the risk of breast cancer significantly increased with each additional hour per week (10-year weighted average) of graveyard shiftwork (OR = 1.06 for each hour; 95% CI = 1.01 to 1.13). Based on an analysis that treats hours per week as a categorical variable, there was a trend of increasing risk with more hours per week of graveyard shiftwork (P = .02, Wald chi-squared test). Women who worked at least 5.7 hours per week had more than a twofold increase in the risk of breast cancer (OR = 2.3; 95% CI = 1.0 to 5.3). Breast cancer risk statistically significantly increased with increasing number of years of working at least one graveyard shift per week (OR = 1.13 for each year; 95% CI = 1.01 to 1.27). Based on an analysis of this measure as a categorical variable, there was evidence of a trend of increasing risk with more years of working at least one shift per week in the 10 years before diagnosis, but this trend was not statistically significant (P = .14, Wald chi-squared test).

Discussion

An increased risk of breast cancer was found among subjects who reported not sleeping during the period of the night when nocturnal melatonin levels are typically at their highest. This increased risk was found particularly among those subjects in the highest exposure groups. Breast cancer risk was also increased in subjects who reported working the graveyard shift at least some time in the 10 years leading up to a diagnosis of breast cancer, and there was clear evidence of a trend of increasing risk with increasing years of graveyard shiftwork and with more hours per week of work during the graveyard shift. No relationship was found between the risk of breast cancer and the number of times the subject reported getting up and turning on a light or the proportion of the night that this light was on. There was, however, some indication of an increased risk among subjects with the brightest bedrooms.

To date, no study of breast cancer and light at night has used measures based on sleep habits or bedroom lighting environment as estimates of exposure to light at night. Our findings are consistent with results obtained from four studies *(4–7)* showing a relationship between the risk of breast cancer and shiftwork, two of which *(4,6)* also reported increased risk with duration of night work. Our findings are also consistent with those from six studies *(13–18)* that investigated the relationship

Table 3. Odds ratios for breast cancer risk and graveyard shiftwork* in the 10 years before diagnosis (reference date)

Exposure	Case patients No.	Case patients %†	Control subjects No.	Control subjects %†	Odds ratio‡	95% confidence intervals
Ever worked graveyard						
No	713	93.0	706	95.0	—	—
Yes	54	7.0	37	5.0	1.6§	1.0 to 2.5
					$P = .04$	
Hours/wk						
Continuous	767	100	743	100	1.06§	1.01 to 1.13
					$P = .03$	
Quartiles‖						
Reference	713	93.0	706	95.0	—	—
<1.2	11	1.4	9	1.2	1.3	0.5 to 3.1
1.2–2.7	13	1.7	10	1.4	1.4	0.6 to 3.2
2.7–5.7	13	1.7	9	1.2	1.5	0.6 to 3.6
⩾5.7	17	2.2	9	1.2	2.3§	1.0 to 5.3
					$P = .04$	
At least one shift/wk¶						
No. of years						
Continuous	767	100	743	100	1.13§	1.01 to 1.27
					$P = .04$	
Median (3 ys)#						
Reference	733	95.6	718	96.6	—	—
<3	15	2.0	11	1.5	1.4	0.6 to 3.2
⩾3	19	2.5	14	1.9	1.6	0.8 to 3.2

*Graveyard shift defined as beginning work after 7:00 PM and leaving work before 9:00 AM.

†Percentage calculated from total number of case patients/control subjects with complete occupational and risk factor data (n = 767 case patients and 743 control subjects).

‡Logistic regression models conditional on 5-year age strata; odds ratios were adjusted for parity, family history of breast cancer (mother or sister), oral contraceptive use (ever), and recent (<5 years) discontinued use of hormone replacement therapy.

§Statistical significance determined by Wald chi-squared test.

‖Quartile computed from all control subjects for which occupational data were available and hours/week ≠ 0. Reference level is hours/week = 0. $P_{trend} = .02$, Wald chi-squared test.

¶One shift = 8 hours.

#Median computed from all control subjects for which occupational data were available and number of years ≠ 0. Reference level is number of years = 0. $P_{trend} = .14$, Wald chi-squared test.

between breast cancer risk and light at night by use of an alternative approach that examined whether blind women, who generally do not perceive light at night, are at a reduced risk of breast cancer. Using U.S. hospital discharge records, Hahn *(13)* reported a statistically significantly reduced risk of breast cancer among women who had profound bilateral blindness. Although an immediate attempt to replicate these findings in a smaller dataset found no reduction in breast cancer risk for blind women *(14)*, the association was subsequently confirmed in four other studies *(15–18)*.

The variables used to define exposure to light at night in this study are based on questionnaire data collected after the breast cancer diagnosis for the case patients. Thus, it is possible that a woman's recall of prior sleep habits could be affected by her more recent disease experience, resulting in differential recall for case patients relative to control subjects. This is unlikely for several reasons. First, the subjects were not asked about restlessness or sleeplessness *per se* nor were they asked about sleep during the specific time of the night when melatonin levels are thought to be highest. Rather, the subjects were asked when they went to bed and when they got up. Second, sleep questions were asked in the context of each residence occupied in the 10 years before diagnosis, and the subjects were allowed to report multiple sleep patterns at each residence. Third, the subjects were not asked to focus specifically on the graveyard shift. Instead, they were provided start and stop times for each shift period and were asked to report the percentage of time worked days, evenings, and graveyard for each occupation. Finally, if there was differential recall because a subject's disease status could have altered her perception of sleep quality, it would most likely have been reflected in the question most directly addressing sleep quality: reported number of times a subject got up during the night and turned on a light. There was no association between breast cancer risk and this measure.

It should also be recognized that, because the light at night indicators used in this study are imperfect, there is likely to be misclassification of the primary exposure measures among study subjects. This could arise for a number of reasons: 1) Details of prior sleep habits are dependent on subject recall; 2) analyses regarding "nonpeak" sleep and graveyard shiftwork were limited to the 10 years before diagnosis, and thus exposure would have most likely been underestimated if a subject's cumulative exposure over her lifetime is the more relevant time period; 3) if there is a window of time in which exposure is most important in breast cancer development, this study would be limited in its ability to assign individuals to the appropriate exposure levels; and 4) the definition of nonpeak sleep was based on the assumption that the time period between 1:00 AM and 2:00 AM reasonably reflects the portion of the night when melatonin levels are typically highest. In all of the instances noted above, the general effect of exposure misclassification would be to bias the risk estimates toward unity.

It should also be noted that subjects who report frequent graveyard shiftwork may be more likely to also experience nonpeak sleep. If so, these two exposure measures will be correlated to some extent, and it could be that the increased risk of breast cancer associated with nonpeak sleep is accounted for primarily by those subjects who also worked the graveyard shift. To assess this possibility, additional analyses were conducted in which both graveyard shiftwork and nonpeak sleep variables were evaluated simultaneously. The estimated ORs for either exposure indicator and breast cancer risk did not appreciably change in magnitude nor did the associated levels of statistical significance. Nonpeak sleep was also analyzed with the graveyard shiftworkers removed, and the results did not change appreciably. These results indicate that, although graveyard shiftwork and nonpeak sleep are associated (as would be expected), one indicator is not merely a surrogate for the other. Subjects could experience nonpeak sleep for many reasons, and graveyard shiftwork is only one. Indeed, twice as many subjects reported nonpeak sleep than graveyard shiftwork (183 subjects reported at least one pattern of nonpeak sleep and 91 subjects reported ever working graveyard shift).

To the extent that graveyard shiftwork and nonpeak sleep reflect exposure to light at night, the results of this study add to a growing body of evidence that such exposure, for whatever reason, may be linked to breast cancer risk. It is well established that light at night exposure reduces nocturnal melatonin levels [reviewed in *(19)*], providing a mechanism by which such exposures could affect the development of breast cancer. Consistent with this idea is experimental evidence from a study of 10 healthy young women (aged 21–29 years) that partial sleep deprivation during the time of peak melatonin levels at night (1:30 AM) can result in increased circulating estradiol concentrations in the blood *(20)*. There is also limited experimental evidence that light exposure during the night can shorten menstrual cycle length *(21)* and that shorter cycles are associated with increased risk and longer cycles with reduced breast cancer risk *(22)*. It is also conceivable that the associations observed in this study with graveyard shiftwork and nonpeak sleep reflect, at least in part, exposures other than light at night that could be responsible for hormonal changes relevant to the development of breast cancer (e.g., stress). Thus, a confirmation of the present findings and a more controlled study of circadian disruption from altered lighting and/or sleep may be useful in further elucidating the effects of such exposures in the etiology of hormone-related diseases, including breast cancer.

REFERENCES

(1) Stevens RG, Davis S, Thomas DB, Anderson LE, Wilson BW. Electric power, pineal function, and the risk of breast cancer. FASEB J 1992;6:853–60.

(2) Stevens RG, Rea MS. Light in the built environment: potential role of circadian disruption in endocrine disruption and breast cancer. Cancer Causes Control 2001;12:279–87.

(3) Caplan LS, Schoenfeld ER, O'Leary ES, Leske MC. Breast cancer and electromagnetic fields—a review. Ann Epidemiol 2000;10: 31–44.

(4) Hansen J. Increased breast cancer risk among women who work predominantly at night. Epidemiology 2001;12:74–7.

(5) Pukkala E, Auvinen H, Wahlberg G. Incidence of cancer among Finnish airline cabin attendants, 1967–92. BMJ 1995;311:649–52.

(6) Tynes T, Hannevik M, Andersen A, Vistnes AI, Haldorsen T. Incidence of breast cancer in Norwegian female radio and telegraph operators. Cancer Causes Control 1996;7:197–204.

(7) Rafnsson V, Tulinius H, Jonasson J, Hrafnkelsson J. Risk of breast cancer in female flight attendants: a population-based study (Iceland). Cancer Causes Control 2001;12:95–101.

(8) Davis S, Mirick DK, Stevens RG. Residential magnetic fields and the risk of breast cancer. Am J Epidemiol. In press 2001.

(9) International Classification of Diseases for Oncology, First Edition. Geneva (Switzerland): World Health Organization; 1976. p. 12–3.

(10) Waksberg J. Sampling methods for random digit dialing. J Am Stat Assoc 1978;73:40–6.

(11) Yen SSC. Chronic anovulation due to CNS-hypothalamic-pituitary dysfunction. In: Yen SS, Jaffe RB, editors. Reproductive endocrinology. 3rd ed. Philadelphia (PA): W. B. Saunders; 1991. p. 631–89.

(12) Breslow NE, Day NE. Statistical methods in cancer research. Vol 1. The analysis of case–control studies. Lyon (France): International Agency for Research on Cancer; 1980. IARC Sci Publ No. 32.

(13) Hahn RA. Profound bilateral blindness and the incidence of breast cancer. Epidemiology 1991;2:208–10.

(14) Davis R. Light exposure and breast cancer [letter]. Epidemiology 1991;2:458–9.

(15) Feychting M, Osterlund B, Ahlbom A. Reduced cancer incidence among the blind. Epidemiology 1998;9:490–4.

(16) Pukkala E, Verkasalo PK, Ojamo M, Rudanko SL. Visual impairment and cancer: a population-based cohort study in Finland. Cancer Causes Control 1999;10:13–20.

(17) Verkasalo PK, Pukkala E, Stevens RG, Ojamo M, Rudanko SL. Inverse association between breast cancer incidence and degree of visual impairment in Finland. Br J Cancer 1999;80: 1459–60.

(18) Kliukiene J, Tynes T, Andersen A. Risk of breast cancer among Norwegian women with visual impairment. Br J Cancer 2001;84:397–9.

(19) Brainard GC, Kavet R, Kheifets LI. The relationship between electromagnetic field and light exposures to melatonin and breast cancer risk: a review of the relevant literature. J Pineal Res 1999;26:65–100.

(20) Baumgartner A, Dietzel M, Saletu B, Wolf R, Campos-Barros A, Graf KJ, et al. Influence of partial sleep deprivation on the secretion of thyrotropin, thyroid hormones, growth hormone, prolactin, luteinizing hormone, follicle stimulating hormone, and estradiol in healthy young women. Psychiatry Res 1993;48: 153–78.

(21) Lin MC, Kripke DF, Parry BL, Berga SL. Night light alters menstrual cycles. Psychiatry Res 1990;33:135–8.

(22) Harlow SD, Ephross SA. Epidemiology of menstruation and its relevance to women's health. Epidemiol Rev 1995;17:265–86.

NOTES

[1]*Editor's note:* SEER is a set of geographically defined, population-based, central cancer registries in the United States, operated by local nonprofit organizations under contract to the National Cancer Institute (NCI). Registry data are submitted electronically without personal identifiers to the NCI on a biannual basis, and the NCI makes the data available to the public for scientific research.

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