REPORT 4 OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH (A-12)
Light Pollution: Adverse Health Effects of Nighttime Lighting
Authors: David Blask, PhD, MD (Tulane University School of Medicine); George Brainard, PhD
(Jefferson Medical College); Ronald Gibbons, PhD (Virginia Tech); Steven Lockley, PhD
(Brigham and Women's Hospital, Harvard Medical School); Richard Stevens, PhD (University
Connecticut Health Center); and Mario Motta, MD (CSAPH, Tufts Medical School).

EXECUTIVE SUMMARY

Objective. To evaluate the impact of artificial lighting on human health, primarily through
disruption of circadian biological rhythms or sleep, as well as the impact of headlamps, nighttime
lighting schemes, and glare on driving safety. Concerns related to energy cost, effects on wildlife
and vegetation, and esthetics also are briefly noted.

Methods. English-language reports in humans were selected from a PubMed search of the
literature from 1995 to March 2012 using the MeSH terms "circadian/biological clocks/rhythm,"
"chronobiology/disorders," "photoperiod," "light/lighting" "sleep," "work schedule," or
"adaptation," combined with the terms "physiology," "melatonin," "adverse effects/toxicity,"
"pathophysiology," "neoplasm," "epidemiology/etiology," "mental disorders," "energy
metabolism," and "gene expression." Additional articles were identified by manual review of the
references cited in these publications; others were supplied by experts in the field who contributed
to this report (see Acknowledgement).

Results. Biological adaptation to the sun has evolved over billions of years. The power to
artificially override the natural cycle of light and dark is a recent event and represents a man-made
self-experiment on the effects of exposure to increasingly bright light during the night as human
societies acquire technology and expand industry. In addition to resetting the circadian
pacemaker, light also stimulates additional neuroendocrine and neurobehavioral responses
including suppression of melatonin release from the pineal gland improving alertness and
performance. Low levels of illuminance in the blue or white fluorescent spectrum disrupt
melatonin secretion. The primary human concerns with nighttime lighting include disability glare
(which affects driving and pedestrian safety) and various health effects. Among the latter are
potential carcinogenic effects related to melatonin suppression, especially breast cancer. Other
diseases that may be exacerbated by circadian disruption include obesity, diabetes, depression and
mood disorders, and reproductive problems.

Conclusion.   The natural 24-hour cycle of light and dark helps maintain precise alignment of
circadian biological rhythms, the general activation of the central nervous system and various
biological and cellular processes, and entrainment of melatonin release from the pineal gland.
Pervasive use of nighttime lighting disrupts these endogenous processes and creates potentially
harmful health effects and/or hazardous situations with varying degrees of harm. The latter
includes the generation of glare from roadway, property, and other artificial lighting sources that
can create unsafe driving conditions, especially for older drivers. More direct health effects of
nighttime lighting may be attributable to disruption of the sleep-wake cycle and suppression of
melatonin release. Even low intensity nighttime light has the capability of suppressing melatonin
release. In various laboratory models of cancer, melatonin serves as a circulating anticancer signal
and suppresses tumor growth. Limited epidemiological studies support the hypothesis that
nighttime lighting and/or repetitive disruption of circadian rhythms increases cancer risk; most
attention in this arena has been devoted to breast cancer. Further information is required to

evaluate the relative role of sleep versus the period of darkness in certain diseases or on mediators of certain chronic diseases or conditions including obesity. Due to the nearly ubiquitous exposure to light at inappropriate times relative to endogenous circadian rhythms, a need exists for further multidisciplinary research on occupational and environmental exposure to light-at-night, the risk of cancer, and effects on various chronic diseases

REPORT OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH

1 INTRODUCTION
2
3 Current AMA Policy H-135.937 (AMA Policy Database) advocates for light pollution control and
4 reduced glare from (electric) artifical light sources to both protect public safety and conserve
5 energy. Lighting the night has become a necessity in many areas of the world to enhance
6 commerce, promote social activity, and enhance public safety. However, an emerging consensus
7 has come to acknowledge the effects of widespread nighttime artificial lighting, including the: 1)
8 impact of artificial lighting on human health, primarily through disruption of circadian biological
9 rhythms or sleep; 2) intersection of ocular physiology, vehicle headlamps, nighttime lighting
10 schemes, and harmful glare; 3) energy cost of wasted and unnecessary electric light; and 4) impact
11 of novel light at night on wildlife and vegetation. In addition to these health and environmental
12 effects, an esthetic deficit is apparent with the progressive loss of the starry night sky and
13 interference with astronomical observations. With the assistance of experts in the field, this report
14 evaluates the effects of pervasive nighttime lighting on human health and performance. Concerns
15 related to energy cost, effects on wildlife and vegetation, and esthetics are also briefly noted.
16
17 METHODS
18
19 English-language reports in humans were selected from a PubMed search of the literature from
20 1995 to March 2012 using the MeSH terms "circadian/biological clocks/rhythm,"
21 "chronobiology/disorders," "photoperiod," "light/lighting" "sleep," "work schedule," or
22 "adaptation," combined with the terms "physiology," "melatonin," "adverse effects/toxicity,"
23 "pathophysiology," "neoplasm," "epidemiology/etiology," "mental disorders," "energy
24 metabolism," and "gene expression." Additional articles were identified by manual review of the
25 references cited in these publications; others were supplied by experts in the field who contributed
26 to this report (see Acknowledgement).
27
28 LIGHT AND HUMAN PHYSIOLOGY
29
30 The solar cycle of light and dark provides the essential basis for life on Earth. Adaptation to the
31 solar cycle has resulted in fundamental molecular and genetic endogenous processes in virtually all
32 life forms that are aligned with an approximately 24-hour period (circadian biological rhythm).
33 The circadian genetic clock mechanism is intimately involved in many, if not most, facets of
34 cellular and organismal function.[1] Although the circadian system spontaneously generates near-24-
35 hour rhythms, this master clock must be reset daily by the light-dark cycle to maintain proper
36 temporal alignment with the environment. In humans and other mammals, this daily entrainment is
37 achieved primarily by novel photoreceptors that project directly to the site of the circadian clock
38 (suprachiasmatic nuclei (SCN) of the hypothalamus).[2-5] The tandem development of an endogenous
39 rhythm sensitive to light presumably evolved to allow for precise 24-hour regulation of rest and
40 activity, and for adapting to seasonal changes in night-length, while maintaining the advantages of
41 an underlying physiology that anticipates day and night. Understanding the molecular and

1 physiological basis of endogenous rhythms, how light information is communicated, and the health
2 implications of disruptions to this system are topics of intensive study.
3
4 ELECTRIC LIGHTING AND HUMAN HEALTH
5
6 Biological adaptation to the sun has evolved over billions of years. The power to artificially
7 override the natural cycle of light and dark is a recent event and represents a man-made self-
8 experiment on the effects of exposure to increasingly bright light during the night as human
9 societies acquire technology and expand industry. At the same time, increasing numbers of people
10 work inside buildings under electric lighting both night and day. Artificial lighting is substantially
11 dimmer than sunlight and provides a very different spectral irradiance. Sunlight is strong at all
12 visible wavelengths, peaking in the yellow region, whereas electric lighting has either extreme
13 characteristic wavelength peaks (fluorescent) or exhibits a monotonic increase in irradiance as
14 wavelength lengthens (incandescent). In contrast to outdoor lighting conditions, much of the
15 modern world now lives and works in relatively dim light throughout the day in isolation from the
16 sun, with often poor contrast between night and day, even for those who live and work in sunny
17 environments.[6]
18
19 Extensive nighttime lighting is required for contemporary society and commerce. Therefore, it is
20 imperative to evaluate the unintended adverse health consequences of electric lighting practices in
21 the human environment, and determine their physiological bases so that effective interventions can
22 be developed to mitigate harmful effects of suboptimal light exposure. For example, engineers
23 have already developed less disruptive night lighting technologies, and continued progress in this
24 area is anticipated. That such technologies exist, however, does not guarantee that they will be
25 purchased, installed and properly implemented. The medical community and public can take the
26 lead on advocating a healthier environment, as illustrated by recent changes in public smoking
27 policies worldwide. As the research on the biology of circadian rhythms has advanced, the range
28 of potential disease connections due to disrupted circadian rhythms and sleep has expanded.
29
30 *Biological Impact of Light on Human Physiology*
31
32 Light is the most powerful stimulus for regulating human circadian rhythms and is the major
33 environmental time cue for synchronizing the circadian clock. In addition to resetting the circadian
34 pacemaker, light also stimulates additional neuroendocrine and neurobehavioral responses,
35 including suppression of melatonin release from the pineal gland, directly alerting the brain, and
36 improving alertness and performance.[7-9] Melatonin is one of the most studied biomarkers of the
37 human physiological response to light.[10] This substance is the biochemical correlate of darkness
38 and is only produced at night, regardless of whether an organism is day-active (diurnal) or night-
39 active (nocturnal). Conceptually, melatonin provides an internal representation of the
40 environmental photoperiod, specifically night-length. The synthesis and timing of melatonin
41 production requires an afferent signal from the SCN. Ablation of this pathway, which occurs in
42 some patients from upper cervical spinal damage, completely abolishes melatonin production.
43 Certain other circadian rhythms (e.g., cortisol, body temperature, sleep-wake cycles) do not depend
44 on this pathway and persist if the SCN pathway is damaged.
45
46 Light is not required to generate circadian rhythms or pineal melatonin production. In the absence
46 of a light-dark cycle (e.g., totally blind individuals), the circadian pacemaker generates rhythms
47 close to, but not exactly a 24-hour periodicity, reflecting the timing of processes under SCN
48 control.[2] However, as previously noted, the timing of SCN rhythms and consequently the rhythms
49 controlled by the circadian clock are affected by light, and require daily exposure to the light-dark
50 cycle to be synchronized with the 24-hour day.

When light information fails to reach the SCN to synchronize the clock and its outputs, the pacemaker reverts to its endogenous non-24-hour period (range 23.7-25.0 h). Consequently, the timing of physiology and behavior that is controlled by the circadian system, for example the sleep-wake cycle, alertness and performance patterns, the core body temperature rhythm, and melatonin and cortisol production, becomes desynchronized from the 24-hour day.[2] The resultant clinical disorder is termed "non-24-hour sleep-wake disorder" and is characterized by alternating episodes of restful sleep, followed by poor night-time sleep and excessive day-time napping, as the non-24-hour circadian pacemaker cycles in and out of phase with the 24-hour social day.[11] Another effect of light exposure at night is the immediate suppression of melatonin production. Under natural conditions, organisms would never be exposed to light during the night in substantial amounts and would not experience melatonin suppression. Electric light, however, efficiently suppresses melatonin at intensities commonly experienced in the home at night.[12]

Measures of Illumination

Luminous flux is the measure of the perceived power of light. The lumen is the standard international unit of luminous flux, a measure of the total "amount" of visible light emitted by a source, while illumination is a measure of how much luminous flux is spread over a given area (intensity of illumination). One lux is equal to one lumen/m^2. Luminous flux measurements take into account the fact that the human eye and visual system is more sensitive to some wavelengths than others. The peak luminosity function is in the green spectral region; white light sources produce far fewer lumens. To provide some perspective, the illuminance associated with a full moon is less than 1 lux, versus 50 lux for a typically incandescent lit family room, 80 lux in a narrower hallway, 325-500 lux for office lighting, 1,000 lux for an overcast day, and 32,000-130,000 lux for direct sunlight.

Initially it was thought that bright light of at least 2,500-20,000 lux was needed to suppress nighttime melatonin secretion or phase shift the melatonin rhythm (as in jet lag) in humans.[13-15] It is now established that when exposure of the human eye is carefully controlled, illuminance as low as 5−17 lux of monochromatic green light or 100 lux of broadband white light can significantly suppress melatonin in normal human volunteers.[12,16-18] Similarly, circadian phase shifts of the melatonin rhythm can be evoked with an illuminance of 5 lux of monochromatic blue light or <100 lux of white fluorescent light, however, exposure to red light is not disruptive.[18,19] Typical lighting in bedrooms in the evening after dusk (but before bedtime) can also suppress melatonin and delay its nocturnal surge.[12] Acute enhancement of both subjective and objective measures of alertness can be evoked with as little as 5 lux of monochromatic blue light.[20] Dose-response curves for melatonin suppression by night-time light exposure to fluorescent light show that ~100 lux of light induces 50% of the maximal response observed with 1,000-10,000 lux of light.[18,21]

Ocular Physiology Mediating Photic Effects

Factors that alter the amount and spectral quality of light reaching the retina include gaze behavior relative to a light source, age (of the ocular lens), and pupillary dilation. Once a light stimulus reaches the retina, physiology within the retina and within the nervous system determines the capacity of the stimulus to evoke circadian, neuroendocrine or neurobehavioral responses. This physiology includes: 1) the sensitivity of the operative photopigments and photoreceptors; 2) location of these photoreceptors within the retina; 3) the ability of the nervous system to integrate photic stimuli spatially and temporally; and, 4) the state of photoreceptor adaptation. In particular, both short and long-term photoreceptor adaptation can significantly modify the biological and behavioral responses to light and acutely suppress melatonin in humans.[22] For

1   example, a full week of daytime exposure to bright light (by daylight and/or indoor light boxes at ~
2   5,000 lux) or a three-day period of exposure to moderate indoor lighting (200 lux) reduces an
3   individual's sensitivity to light suppression of nighttime melatonin compared with exposure to dim
4   indoor lighting (0.5 lux); similar dim light conditions also enhance circadian phase shifting.[23-25]
5   Two hours of exposure to 18 lux of white incandescent light versus full dark exposure in a single
6   evening modifies the sensitivity of an individual for light-induced melatonin suppression later that
7   same night.[26] Hence, photoreceptor adaptation, like the other ocular and neural elements noted
8   above, can significantly modify the biological and behavioral responses to light.[16]
9
10   In general, photobiological responses to light are not all-or-none phenomena. In the case of acutely
11   suppressing high nighttime levels of melatonin or phase-shifting the entire melatonin rhythm, light
12   works in a dose-response fashion. Once threshold is exceeded, increasing irradiances of light elicit
13   increasing acute plasma melatonin suppression or longer-term phase-shifts of the melatonin rhythm
14   in healthy individuals.[16,18,27] All humans, however, are not equally sensitive to light; significant
15   individual differences exist in sensitivity to light for both neuroendocrine and circadian
16   regulation.[16,18] For a detailed description of the molecular and cellular basis for how
17   photoreceptive input regulates circadian and neuroendocrine system function, see the Addendum.
18
19   HUMAN CONCERNS-DISABILITY AND DISCOMFORT GLARE
20
21   Glare from nighttime lighting can create hazards ranging from discomfort to frank visual disability.
22   Disability glare has been fairly well-defined based on the physiology of the human eye and
23   behavior of light as it enters the ocular media. Discomfort glare is less well-defined and more
24   subjective as it is not based on a physical response per se but rather a psychological response.
25   Accordingly, the respective bases of (and research into) these two responses are fundamentally
26   different.
27
28   *Disability Glare*
29
30   Disability glare is unwanted and poorly directed light that temporarily blinds, causes poor vision by
31   decreasing contrast, and creates an unsafe viewing condition, especially at night, by limiting the
32   ability of the person to see. There are natural causes of disability glare, such as solar glare at sunset
33   on a dirty windshield which can be lessened by cleaning the windshield. Unfortunately, nighttime
34   glare while driving is not easily remedied. It is caused by the misapplication of luminaires that
35   comprise the lighting design which are generally overly bright and unshielded, and/or sources of
36   poorly directed light that enters the eye and scatters among ocular structures resulting in
37   diminished contrast and impeded vision. Such effects dramatically worsen as the human eye ages,
38   contributing to poor night vision and difficulty in driving at night for older drivers.
39
40   Disability glare is caused by light scatter from ocular media.[28] As light enters the eye, it collides
41   with cornea, lens, and vitreous humor, scattering photons and casting a veil of light across the
42   retina[29-31] (see Figure 1). The veil of light reduces the contrast of the object that the driver is trying
43   to see, having the same effect as increasing the background luminance of the object. This veiling
44   light is represented by the term veiling luminance. Veiling luminance is directly related to the
45   illuminance of the light source and inversely related to the square of the angle of eccentricity of the
46   light source with an age dependent multiplier across the entire equation.[28] This means that the
47   disability from a light source is lessened the farther the source is from the line of sight.[α]

[α] As an example, high mast lighting systems where the roadway lighting is over 100 feet in the air have
significantly less glare than traditional systems, which are typically located 30−50 feet in the air. Because of

1
2 Accordingly, proper design techniques and consideration for the glare caused by lighting systems
3 need to be considered. One of the primary difficulties, especially for roadways, is that the lighting
4 is not governed by a single jurisdiction. Roadway lighting may be designed properly and provide a
5 low level of glare; however lighting can emanate from adjacent properties, spilling out into the
6 roadway thus affecting the driver and overall performance and suitability of a lighting system.
7 Control over all environmental sources of nighttime lighting is therefore critical for the overall
8 control of disability glare.
9
10 *Discomfort Glare*
11
12 Discomfort glare is less well defined but emanates from a glare source that causes the observer to
13 feel uncomfortable. The definition of discomfort is not precise, and some research has shown that
14 a person's response to a glare source is based more on his/her emotional state than on the light
15 source itself. Discomfort glare may be based primarily on the observer's light adaptation level, the
16 size, number, luminance and location of the light sources in the scene.[32]
17
18 Both overhead roadway lighting and opposing headlamps are involved with discomfort glare in the
19 driver. A numerical rating scale based on the dynamic nature of glare in simulations is available to
20 measure the discomfort level experienced by drivers (Appendix).[33] The overall impact of
21 discomfort glare on fatigue and driver safety remains an issue.
22
23 Lighting and Glare. Both discomfort and disability glare have specific impacts on the user in the
24 nighttime environment. Research has shown that both of these glare effects occur simultaneously.
25 Research also shows that the effects of the glare are cumulative, meaning that the glare from two
26 light sources is the sum of the glare from the individual light sources. As a result, every light
27 source within the field of view has an impact on the comfort and visual capability of the driver.
28
29 *Overhead lighting*
30
31 For overhead roadway lighting, design standards include a methodology for controlling the
32 disability glare through a ratio of the eye adaptation luminance to the veiling luminance caused by
33 the light source. As the veiling luminance is related to the illuminance the light source produces at
34 the eye, a roadway luminaire that directs light horizontally has a much greater effect on the driver
35 than a light source that cuts off the horizontal light. A trend towards flat glass luminaires, which
36 provide a cut off of light at horizontal angles, provides a lower level of both disability and
37 discomfort glare.
38
39 Decorative luminaires (e.g., acorn or drop lens) have a high level of horizontal light and typically
40 are used in areas where pedestrians are the primary roadway users. The horizontal light in this
41 situation is useful for facial recognition of a pedestrian, but it limits the driver's ability to perceive
42 other objects in the roadway. As a result, many cities are designing and installing two lighting
43 systems, one for the pedestrian and one for the roadway.

44 Luminaires employing solid state technologies and light-emitting diodes (LED) provide light from
45 an array of small sources rather than a single large source. These designs either rely on each small
46 source to provide a component of the light distribution, or the components of the lighting array
47 provide individual luminating fields of the light distribution. In the first instance, the arrays are

---

the inverse squared relationship, a high mast system reduces glare by 75% compared with a traditional
system.

1   typically flat and have an optic to provide the light distribution; if a single LED fails, the others still
2   provide the light distribution. In the second method, the components of the array are aimed to
3   different areas of the beam distribution. This approach typically results in light aimed at the driver
4   and pedestrians causing a higher glare impact. The other issue with the multiple sources used in
5   LED luminaires is that each of the sources typically has a very high luminance itself as the source
6   is very small and very bright; in the absence of sufficient diffusion, they cause significant glare.
7   Accordingly, solid state lighting systems typically have a higher glare impact than traditional
8   sources.
9
10 The final issue with glare from overhead lighting is the cyclic nature of the impact. As drivers
11 course along a roadway, they pass from one luminaire to another. The glare experience increases
12 as they approach the luminaire and then diminishes as they pass beyond. While typically not an
13 issue for disability glare, this repetitive process can cause discomfort and fatigue.[34]
14
15 <u>Opposing vehicle headlamps</u>
16
17 Vehicle headlamps are aimed at the opposing driver eye level resulting in very high ocular
18 illuminance and significant disability glare. The impact of opposing headlamps on the ability of
19 the oncoming driver to observe beyond the headlamps is significant. For example, the visibility of
20 a pedestrian standing behind a vehicle can be reduced by as much as 50%.[35]
21
22 In order to minimize the glare impact, headlamps are designed with lower left side light intensity
23 than the right side. This reduces the glare to an opposing vehicle but does not eliminate it. New
24 technologies such as turning headlamps and headlamps that hide part of the headlamp beam when a
25 vehicle passes are possible solutions for this issue. With the advent of high intensity discharge
26 Xenon headlamps and LED-based technologies, the glare issue has become more serious. While
27 the intensity towards a driver is limited, the small but brighter source generates a much higher
28 impression of glare than traditional technologies. These "blue" headlamp sources have a higher
29 complaint rate for glare than for any other light source.
30
31 *Effects of Lighting Design on Traffic Accidents*
32
33 Adult, and especially elderly drivers, experience increased glare sensitivity, and elderly drivers
34 may not be able to sufficiently fulfill the criteria for night driving ability because of contrast and
35 glare sensitivity.[36] Prospective studies indicate that reduction in the useful field of view, visual
36 field loss, and glare sensitivity increase crash risk in older drivers.[37,38] Crash risk begins to increase
37 around age 50 years of age and continues to increase with aging.[39]   No studies have explicitly
38 compared traffic accident rates under different highway lighting conditions.
39
40 HEALTH EFFECTS OF DISRUPTED CIRCADIAN RHYTHMS
41
42 Epidemiological studies are a critical component of the evidence base required to assess whether or
43 not light exposure at night affects disease risk, including cancer. These studies, however, are
44 necessarily observational and can rarely provide mechanistic understanding of the associations
45 observed. Carefully designed and controlled basic laboratory studies in experimental animal
46 models have the potential to provide the empiric support for a causal nexus between light exposure
47 at night and biological/health effects and to help establish plausible mechanisms. One area of
48 considerable study on the possible effects of nighttime light exposure involves cancer.
49
50 CANCER
51

1 *Light at Night, Melatonin and Circadian Influences on Carcinogenesis*
2
3 Experimental Evidence. The majority of earlier studies in experimental models of either
4 spontaneous or chemically-induced mammary carcinogenesis in mice and rats demonstrated an
5 accelerated onset of mammary tumor development accompanied by increased tumor incidence and
6 number in animals exposed to constant bright fluorescent light during the night as compared with
7 control animals maintained on a strict 12 hours light/12 hours dark cycle.[40-51]
8
9 More recent work has focused on the ability of light at night to promote the growth progression and
10 metabolism in human breast cancer xenografts. Nocturnal melatonin suppresses the growth of both
11 estrogen receptor negative (ER-) and estrogen receptor positive (ER+) human breast cancer
12 xenografts; the essential polyunsaturated fatty acid, linoleic acid is necessary for the growth of such
13 (ER-) tumors, and its metabolism can be used as a biomarker of cellular growth.[52-55] Exposure of
14 rats with such cancer xenografts to increasing intensities of white, fluorescent polychromatic light
15 during the 12 hour dark phase of each daily cycle results in a dose-dependent suppression of peak
16 nocturnal serum melatonin levels and a corresponding marked increase in tumor metabolism of
17 linoleic acid and the rate of tumor growth. Exposure to even the very dimmest intensity of light
18 during the night (0.2 lux) suppressed the nocturnal peak of circulating melatonin by 65% and was
19 associated with marked stimulation in the rates of tumor growth and linoleic acid metabolic
20 activity. In this model, measurable effects on xenograft growth and linoleic acid metabolism were
21 apparent with 15% suppression in nocturnal melatonin levels.
22
23 The ability of light exposure at night to stimulate tumor growth (including dim exposures) has been
24 replicated in rat hepatoma models.[54,56-58] The reverse also is true; gradually restoring circulating
25 melatonin by reducing initial exposure to light at night (24.5 lux) is accompanied by a marked
26 reduction in tumor growth and linoleic acid metabolic activity to baseline rates in the breast cancer
27 and hepatoma models.[59]
28
29 The important role of melatonin as a nocturnal anticancer signal is further supported by the growth
30 responses of human breast cancer xenografts perfused with human whole blood collected from
31 young, healthy premenopausal female subjects exposed to complete darkness at night (e.g., high
32 melatonin), compared with xenografts that were perfused with blood collected from the same
33 subjects during the daytime (e.g., low melatonin).[54] The growth of xenografts perfused with blood
34 collected during the dark was markedly reduced. Addition of a physiological nocturnal
35 concentration of melatonin to blood collected from light-treated subjects restored the tumor
36 inhibitory activity to a level comparable to that observed in the melatonin-rich blood collected at
37 night during total darkness. Moreover, the addition of a melatonin receptor antagonist to the blood
38 collected during darkness (i.e., high melatonin) eliminated the ability of the blood to inhibit the
39 growth and metabolic activity of perfused tumors. Some evidence also exists that circadian
40 disruption by chronic phase advancement (e.g., simulating jet lag) may increase cancer growth in
41 laboratory animals.[60,61]
42

Potential Anticancer Mechanisms of Melatonin

The preponderance of experimental evidence supports the hypothesis that under the conditions of complete darkness, high circulating levels of melatonin during the night not only provide a potent circadian anticancer signal to established cancer cells but help protect normal cells from the initiation of the carcinogenic process in the first place.[62,63] It has been postulated that disruption in the phasing/timing of the central circadian pacemaker in the SCN, in general, and the suppression of circadian nocturnal production of melatonin, in particular, by light at night, may be an important biological explanation for the observed epidemiological associations of cancer risk and surrogates for nocturnal light exposure (such as night shift work, blindness, reported hours of sleep, etc.) (see below).[64]

Melatonin exerts several cellular effects that may be relevant in this regard. It exhibits antiproliferative and antioxidant properties, modulates both cellular and humoral responses, and regulates epigenetic responses.[65-67] Melatonin also may play a role in cancer cell apoptosis and in inhibiting tumor angiogenesis.[68,69]

Human Studies

While the experimental evidence from rodent cancer models links disruption of circadian rhythms and circulating melatonin concentrations (inversely) with progression of disease, the human evidence is indirect and based on epidemiological studies. Breast cancer has received the most study.

The hypothesis that the increasing use of electricity to light the night might be related to the high breast cancer risk in the industrialized world, and the increasing incidence and mortality in the developing world was first articulated in 1987.[70] Potential pathways include suppression of the normal nocturnal rise in circulating melatonin and circadian gene function.[54,71,72] Conceptually, this theory would predict that non-day shift work would raise risk, blind women would be at lower risk, reported sleep duration (as a surrogate for hours of dark) would be inversely associated with risk, and population nighttime light level would co-distribute with breast cancer incidence worldwide.[72,73] Only the first hypothesis has been systematically evaluated. Based on studies of non-day shift occupation and cancer (mostly breast cancer) published through 2007, the International Agency for Research on Cancer (IARC) concluded "shift-work that involves circadian disruption is *probably carcinogenic* to humans" (Recommendation Level 2A).[74] A detailed review of the individual studies supporting this conclusion is available.[75]

Since the IARC evaluation was conducted, several new studies of breast cancer and nighttime light have been published with mixed results.[76-79] Two found no significant association between shift work and risk of breast cancer.[76,77] A large case-control study of nurses in Norway[78] found a significantly elevated risk in subjects with a history of regularly working five or more consecutive nights between days off, and another found that as the type of shift (e.g., evening, night, rotating) became more disruptive, the risk increased.[79,80] In the Nurses Health Study cohort, increased urinary excretion of melatonin metabolites also was associated with a lower risk of breast cancer.[81] Each of these studies has strengths and limitations common to epidemiology, particularly in exposure assessment and appropriate comparison groups (e.g., no woman in the modern world is unexposed to light-at-night, but quantifying that exposure is difficult).

Although shiftwork represents the most extreme example of exposure to light at night and circadian disruption, perturbation of circadian rhythms and the melatonin signal is also experienced by non-shift workers with a normal sleep/wake-cycle.[12] Anyone exposing themselves to light after dusk or

before dawn is overriding the natural light-dark exposure pattern as noted in the earlier discussion on measures of illumination.

After lights out for bedtime, it is not yet clear whether the ambient background light from weak sources in the bedroom or outside light coming through the window could influence the circadian system; a brief exposure at these levels may not have a detectable impact in a laboratory setting, although long-term chronic exposure might. Four case-control studies have now reported an association of some aspect of nighttime light level in the bedroom with breast cancer risk.[82-85] The elevated risk estimate was statistically significant in two of them.[83,85] As case-control designs, in addition to the limitation of recall error, there is also the potentially significant limitation of recall bias.

Despite the difficulty of gathering reliable information on bedroom light level at night, the possibility that even a very low luminance over a long period of time might have an impact is important. The lower limit of light intensity that could, over a long time period, affect the circadian system is not established. In the modern world few people sleep in total darkness. When eyelids are shut during sleep, only very bright light can penetrate to lower melatonin and only in some individuals.[86] Frequent awakenings with low level light exposure in the bedroom and certain nighttime activities (e.g., bathroom visits) may disrupt the circadian system, but any related health effects are unknown.[87]

Other Cancers

Light-at-night and circadian disruptions have been suggested to play a role in other cancers including endometrial, ovarian, prostate, colorectal, and non-Hodgkins lymphoma but evidence comparable to that obtained for breast cancer has not yet been developed.[88] On the other hand, engaging in night shift work may protect against skin cancer and cutaneous melanoma.[89]

Other Diseases

Obesity, Diabetes, and Metabolic Syndrome. The modern world has an epidemic of obesity and diabetes that may be influenced by lack of sleep, lack of dark, and/or circadian disruption.[90] Non-day shift workers have a higher incidence of diabetes and obesity.[91] Epidemiological studies also show associations of reported sleep duration and risk of obesity and diabetes.[92] Circadian disruption may be a common mechanism for these outcomes and potential links between the circadian rhythm and metabolism.[93-95]

Other Disorders. Although in the early stage of development, emerging evidence suggests that other chronic conditions also may be exacerbated by light at night exposure and ongoing disruption of circadian rhythms, including depression and mood disorders, gastrointestinal and digestive problems, and reproductive functions.[88]

DARK VERSUS SLEEP

The circadian rhythm and sleep are intimately related but not the same thing. Adequate daily sleep is required for maintenance of cognitive function and for a vast array of other capabilities that are only partially understood. Sleep is not required to synchronize the endogenous circadian rhythm, whereas a stable 24-hour light-dark cycle is required. The epidemiological and laboratory research on sleep and health cannot entirely separate effects of sleep duration from duration of exposure to dark, because the sleep-wake cycle partitions light-dark exposure to the SCN and pineal gland.[96] The distinction is important because a requirement for a daily and lengthy period of dark to

maintain optimal circadian health has different implications than a requirement that one must be asleep during this entire period of dark; many individuals normally experience a wakeful episode in the middle of a dark night.[87]

Light during the night will disrupt circadian function as well as sleep, and the health consequences of short sleep and of chronic circadian disruption are being intensively investigated.[97] A growing number of observational and clinical studies on sleep and metabolism suggest short sleep periods have substantial harmful effects on health; however, it is not yet clear that sleep and dark have been entirely disentangled in these studies.[97,98] For example, in one study, sleep duration (verified by polysomnography) was associated with morning blood levels of leptin, a hormone that plays a key role in energy expenditure and appetite.[99] However, the duration of typical sleep reported by each subject was more strongly associated with leptin concentrations. Mean verified sleep was 6.2 hours, whereas mean reported sleep was 7.2 hours. Reported "sleep duration" probably reflects the time from when a person turns out their light for bed and falls asleep and when they get up in the morning (i.e., actual hours of dark exposure). An important question is to determine what portion of the health effects of dark disruption is due to sleep disruption and what portion is due directly to circadian impact of electric light intrusion on the dark of night.

Media use at night (i.e., televisions, computer monitors, cell phone screens) negatively affects the sleep patterns of children and adolescents and suppresses melatonin concentrations.[100-102] The American Academy of Pediatrics recommends removing televisions and computers from bedrooms to assist in limiting total "screen time" on a daily basis.[101] This action also may help in improving sleep patterns.

ENERGY COST

Electric lighting accounts for about 19% of electricity consumption worldwide and costs about $360 billion.[103] Much of the light that is produced is wasted, for example, by radiating light into space away from the task or environment intended to be illuminated. Estimates of how much is wasted vary; one estimate from the International Dark-Sky Association is 30% in the United States.[104] Such a percentage worldwide would account for an annual cost of about $100 billion.

ENVIRONMENTAL ISSUES

Although not directly under the purview of human health and disease, the following considerations are indirectly related to human well-being.

Esthetics

The Milky Way is no longer visible to the majority of people in the modern world. As societies have increasingly used electricity to light the night, it has become difficult to see more than a few of the innumerable stars from Earth's surface.[105] This has been carefully documented in a cover story by National Geographic Magazine in November 2008, which includes extensive visual documentation on its website.[106] Though the major impact of electric light at night is in major metropolitan areas, even the once pristine nights of the U.S. National Parks are beginning to be degraded, more rapidly in the East but also in parks in the West as well.[107]

Impact on Wildlife

Life on the planet has evolved to accommodate the 24-hour solar cycle of light and dark. Human imposition of light at night and disruption of the natural dark-light cycle represents a dramatic

1 change to the environment.[108] Study of the effects of light at night on animal and plant life is in the
2 early stages, but the entire spectrum of life, including animal, plant, insect, and aquatic species,
3 may be affected.
4
5 About 30% of all vertebrate species and 60% of invertebrate species on Earth are nocturnal and
6 depend on dark for foraging and mating.[108] Documented wildlife destruction by light at night has
7 been evident in bird species, which fly into lit buildings at night in enormous numbers when
8 migrating, and in the disruption of migration and breeding cycles in amphibians.[108-111] The most
9 studied case in reptiles involves sea turtle hatchlings on the coast of Florida, which historically
10 have scurried from their nest directly to the ocean. With increased development along the coast,
11 and attendant increased electric lighting at night, these hatchlings become confused and often
12 migrate away from shore to the lights. Hundreds of thousands of hatchlings are believed to have
13 been lost as a result of this stray electric lighting at night in Florida.[109] Furthermore, many billions
14 of insects are lost to electric light annually, which reduces food availability for other species in
15 addition to unnecessarily reducing living biomass. It is concerning that light at night also may be
16 vector attractant for diseases such as malaria.[112]
17
18 The circadian biology of plants is as robust as animals, and the impact of light at night on plant life
19 may also be considerable due to the role of light in photosynthesis and the fact that many plants are
20 pollinated at night.[113,114]
21
22 POLICY AND PUBLIC HEALTH IMPLICATIONS OF LIGHT AT NIGHT
23
24 Some responses to public health concerns associated with light-at-night exposures are readily
25 apparent, such as developing and implementing technologies to reduce glare from vehicle
26 headlamps and roadway lighting schemes, and developing lighting technologies at home and at
27 work that minimize circadian disruption, while maintaining visual efficiency and aesthetics.
28 Additionally, clinical studies support efforts to reduce child and adolescent night-time exposure
29 from exogenous light derived from various media sources, especially in the bedroom environment.
30 Recommendations to use dim lighting in residences at night raise issues for elderly patients. The
31 American Geriatrics Society recommends ensuring well lit pathways within households to reduce
32 the incidence of falls in elderly patients.[115]
33
34 Individuals who are subject to shift work experience disrupted circadian rhythms, fatigue, and
35 cognitive dysfunction. Many industries, including hospitals, require a 24-hour workforce. The
36 American College of Occupational and Environmental Medicine has established guidelines to
37 address fatigue risk management in the workplace.[116] In healthcare workers, such as nurses who
38 experience rapidly rotating shifts, brief morning light exposure improves subjective symptoms and
39 performance.[117] The judicious use of bright light and/or melatonin supplements can improve
40 adaptation to permanent, long-term night work.[118]
41
42 SUMMARY AND CONCLUSIONS
43
44 The natural 24-hour cycle of light and dark helps maintain precise alignment of circadian
45 biological rhythms, the general activation of the central nervous system and various biological and
46 cellular processes, and entrainment of melatonin release from the pineal gland. Pervasive use of
47 nighttime lighting disrupts these endogenous processes and creates potentially harmful health
48 effects and/or hazardous situations with varying degrees of harm. The latter includes the
49 generation of glare from roadway, property, and other artificial lighting sources that can create
50 unsafe driving conditions, especially for older drivers. Current AMA policy advocates that all
51 future outdoor lighting be of energy efficient designs to reduce energy use and waste. Future

streetlights should incorporate fully shielded or similar non-glare design to improve the safety of our roadways for all, but especially vision impaired and older drivers.

More direct health effects of nighttime lighting may be attributable to disruption of the sleep-wake cycle and suppression of melatonin release. Even low intensity nighttime light has the capability of suppressing melatonin release. In various laboratory models of cancer, melatonin serves as a circulating anticancer signal and suppresses tumor growth. Limited epidemiological studies support the hypothesis that nighttime lighting and/or repetitive disruption of circadian rhythms increases cancer risk; most attention in this arena has been devoted to breast cancer. The quality and duration of sleep and/or period of darkness affect many biological processes that are currently under investigation. Further information is required to evaluate the relative role of sleep versus the period of darkness in certain diseases or on mediators of certain chronic diseases or conditions including obesity. Due to the nearly ubiquitous exposure to light at inappropriate times relative to endogenous circadian rhythms, a need exists for further multidisciplinary research on occupational and environmental exposure to light-at-night, the risk of cancer, and exacerbation of chronic diseases.

RECOMMENDATIONS

The Council on Science and Public Health recommends that the following statements be adopted and the remainder of the report be filed:

That our American Medical Association:

1. Supports the need for developing and implementing technologies to reduce glare from vehicle headlamps and roadway lighting schemes, and developing lighting technologies at home and at work that minimize circadian disruption, while maintaining visual efficiency. (New HOD Policy)

2. Recognizes that exposure to excessive light at night, including extended use of various electronic media, can disrupt sleep or exacerbate sleep disorders, especially in children and adolescents. This effect can be minimized by using dim red lighting in the nighttime bedroom environment. (New HOD Policy)

3. Supports the need for further multidisciplinary research on the risks and benefits of occupational and environmental exposure to light-at-night. (New HOD Policy)

4. That work environments operating in a 24/7 hour fashion have an employee fatigue risk management plan in place. (New HOD Policy)

5. That Policy H-135.937 be reaffirmed. (Reaffirm HOD Policy)

Fiscal Note: Less than $500

Stevens, PhD (University Connecticut Health Center); and Mario Motta, MD (CSAPH, Tufts Medical School).

REFERENCES

1. Takahashi JS, Hong HK, Ko CH, McDearmon EL. The genetics of mammalian circadian order and disorder: implications for physiology and disease. *Nat Rev Genet*. 2008;9:764-775.

2. Lockley SW, Arendt J, Skene DJ. Visual impairment and circadian rhythm disorders. *Dialogues Clin Neurosci*. 2007;9:301-314.

3. Brainard GC, Hanifin JP, Greeson JM, et al. Action spectrum for melatonin regulation in humans: evidence for a novel circadian photoreceptor. *J Neurosci*. 2001;21:6405-6412.

4. Thapan, K, Arendt J, Skene DJ. An action spectrum for melatonin suppression: evidence for a novel non-rod, non-cone photoreceptor system in humans. *J.Physiol*. 2001;535:261-267.

5. Gooley JJ, Rajaratnam SM, Brainard GC, Kronauer RE, Czeisler CA, Lockley SW. Spectral responses of the human circadian system depend on the irradiance and duration of exposure to light. *Sci Transl Med*. 2010;2:31-33.

6. Cole RJ, Kripke DF, Wisbey J, et al. Seasonal variation in human illumination exposure at two different latitudes. *J Biol Rhythms*. 1995;10:324-334.

7. IESNA (Illuminating Engineering Society of North America). *Light and Human Health: An Overview of the Impact of Optical Radiation on Visual, Circadian, Neuroendocrine, and Neurobehavioral Responses*. IES TM-18-08, Illuminating Engineering Society of North America, New York, 2008.

8. Commission Internationale de l'Eclairage. *Ocular Lighting Effects on Human Physiology and Behaviour*. Commission Internationale de l'Eclairage, Technical Report #158, Vienna, 1-54, 2004.

9. Special Issue: Human circadian rhythms: regulation and impact. *J Biol Rhythms*. 2005;20:279-386.

10. Arendt J. *Melatonin and the Mammalian Pineal Gland*. Chapman and Hall, London 1995.

11. Uchiyama M, Lockley SW. Non-24-hour sleep–wake syndrome in sighted and blind patients. *Sleep Medicine Clinics of North America*. 2009;4: 195-211.

12. Gooley JJ, Chamberlain K, Smith KA, et al. Exposure to Room Light before Bedtime Suppresses Melatonin Onset and Shortens Melatonin Duration in Humans. *Endocrinology*. 2011;152:742.

13. Lewy AJ, Wehr TA, Goodwin FK, Newsome DA, Markey SP. Light suppresses melatonin secretion in humans. *Science*. 1980;210:1267-1269.

14. Lewy AJ, Sack RL, Miller LS, Hoban TM. Antidepressant and circadian phase-shifting effects of light. *Science*. 1987;235:352-354.

15. Czeisler CA, Allan JS, Strogatz SH, et al. Bright light resets the human circadian pacemaker independent of the timing of the sleep-wake cycle. *Science*. 1986;233:667-671.

16. Brainard GC, Lewy AJ, Menaker M, et al. Dose-response relationship between light irradiance and the suppression of melatonin in human volunteers. *Brain Research*. 1988;454:212-218.

17. Gaddy JR, Rollag MD, Brainard GC. Pupil size regulation of threshold of light-induced melatonin suppression. *Journal of Clinical Endocrinology and Metabolism*. 1993;77:1398-1401.

18. Zeitzer JM, Dijk D-J, Kronauer RE, Brown EN, Czeisler CA. Sensitivity of the human circadian pacemaker to nocturnal light: melatonin phase resetting and suppression. *J Physiology*. 2000;526:695-702.

19. Lockley SW, Brainard GC, Czeisler CA. High sensitivity of the human circadian melatonin rhythm to resetting by short wavelength light. *J Clin Endocrinol Metab*. 2003;88:4502-4505.

20. Lockley SW, Evans EE, Scheer FA, Brainard GC, Czeisler CA, and Aeschbach D. Short-wavelength sensitivity for the direct effects of light on alertness, vigilance, and the waking electroencephalogram in humans. *Sleep*. 2006;29:161-168.

21. Cajochen C, Munch M, Kobialka S, Krauchi K, et al. High sensitivity of human melatonin, alertness, thermoregulation, and heart rate to short wavelength light. *J Clin Endocrinol Metab*. 2005;90:1311-1316.

22. Brainard GC, Rollag MD, Hanifin JP. Photic regulation of melatonin in humans: ocular and neural signal transduction. *J Biological Rhythms*. 1997;12:537-546.

23. Hébert M, Martin SK, Lee C, Eastman CI. The effects of prior light history on the suppression of melatonin by light in humans. *J Pineal Res*. 2002;33:198-203.

24. Smith KA, Schoen MW, Czeisler CA. Adaptation of human pineal melatonin suppression by recent photic history. *JCEM*. 2004;89:3610-3614.

25. Chang AM, Scheer FA, Czeisler CA. The human circadian system adapts to prior photic history. *J Physiol*. 2011 Mar 1;589(Pt 5):1095-1102.

26. Jasser SA, Hanifin JP, Rollag MD, Brainard GC. Dim light adaptation attenuates acute melatonin suppression in humans. *J Biol Rhythms*. 2006;21:394-404.

27. McIntyre IM, Norman TR, Burrows GD, Armstrong SM. Human melatonin suppression by light is intensity dependent. *J Pineal Res*. 1989;6:149-156.

28. Holladay SA. Light scatter in ocular media. *Am J Opthalmol* 1927;4:122-129.

29. Vos JJ, Bouman MA. Contribution of the retina to entropic scatter. *J Opt Soc Am*. 1964;54:95-100.

30. Boyton RM, Clark JJ. Sources for entropic scatter in the human eye. *J Opt Soc Am*. 1962; 54:1326.

31. Adrian W, Bhanji A. Fundamentals of disability glare: A formula to describe straylight in the eye as a function of glare angle and age. In W. Adrian (Ed.), *Proceedings of the First International Symposium on Glare*. New York: Lighting Research Institute. 1992;185-193.

32. Van Bommel WJM, JB deBoer. *Road Lighting.* Kluwer Technische Boeken. B.V. Philips Technical Library, Antwerpen, 1980.

33. deBoer J B, Schreuder DA. Glare as a criterion for quality in street lighting. *Trans Illumin Engineer Soc.* 1967;32:117-135.

34. Bennett DW. Repetitive lighting and ocular fatigue. *Opthalmic Res*. 1995;27:34-41.

35. Gibbons RB, Hankey JM. Influence of vertical illuminance on pedestrian visibility in crosswalks. *Trans Res Record.* 2006;No. 1973.

36. Bbizhayev MA. Glare disability and driving safety. *Opthalmic Res*. 2003;35:19-25

37. Owsley C, Ball KB, McGwin G, et al. Visual processing impairment and risk of motor vehicle crash among older adults. *JAMA*. 1998;279:1083-1088.

38. Rubin GS, Ng ES, Bandeen-Roche K, et al. A prospective, population-based study of the role of visual impairment in motor vehicle crashes among older drivers: The SEE study. *Invest Opthalmol Visual Sci.* 2007;48:1483-1491.

39. Straus H, Gu X. The roads ahead: collision risks, trends, and safety of drivers. *Risk Analysis*. 2009;29:900-911.

40. Jöchle W. Trends in photophysiologic concepts. *Ann N Y Acad Sci.* 1964;117: 88-104.

41. Khaetski IK. Effect of hypothalamo-pituitary lesions induced by constant illumination on development of induced mammary tumors in rats. *Vopr Exp Oncol (Kiev)*. 1965;1:87-93.

42. Hamilton T. Influence of environmental light and melatonin upon mammary tumour induction. *Br J Surg*. 1969;56:764-766.

43. Aubert C, Janiaud P, Lecalvez J. Effect of pinealectomy and melatonin on mammary tumor growth in Sprague-Dawley rats under different conditions of lighting. *J Neural Transm*. 1980;47:121-130.

44. Kothari LS, Shah PN, Mhatre MC. Effect of continuous light on the incidence of 9,10-dimethyl-1,2-benzanthracene induced mammary tumors in female Holtzman rats. *Cancer Lett*. 1982;16:313-317.

45. Kothari LS, Shah PN, Mhatre MC. Pineal ablation in varying photoperiods and the incidence of 9,10-dimethyl-1,2-benzanthrace induced mammary cancer in rats. *Cancer Lett*. 1984;22:99-102.

46. Mhatre MC, Shah PN, Juneja HS. Effect of varying photoperiods on mammary morphology, DNA synthesis, and hormone profile in female rats. *J Natl Cancer Inst*. 1984;72:1411-1416.

47. Shah PN, Mhatre MC, Kothari LS.   Effect of melatonin on mammary carcinogenesis in intact and pinealectomized rats in varying photoperiods. *Cancer Res.* 1984;44:3403-3407.

48. Van den Heiligenberg S, Deprés-Brummer P, Barbason H, et al. The tumor promoting effect of constant light exposure on diethylnitrosamine-induced hepatocarcinogenesis in rats. *Life Sci*. 1999;64:2523-2534.

49. Travlos GS, Wilson RE, Murrell JA, et al.   The effect of short intermittent light exposures on the melatonin circadian rhythm and NMU-induced breast cancer in female F344/N rats. *Toxicol Pathol* . 2001;29: 126-136.

50. Beniashvili DS, Benjamin S, Baturin DA, et al.   Effect of light/dark regimen on N-nitrosoethylurea-induced transplacental carcinogenesis in rats. *Cancer Lett.* 2001;163:51-57

51. Anisimov VN, Baturin DA, Popovich IG, et al. Effect of exposure to light-at-night on life span and spontaneous carcinogenesis in female CBA mice. *Int J Cancer*. 2004;111:475-479.

52. Blask DE, Sauer LA, Dauchy RT, et al.   Melatonin inhibition of cancer growth in vivo involves suppression of tumor fatty acid metabolism via melatonin receptor-mediated signal transduction events. *Cancer Res.* 1999;59:4693-4701.

53. Blask DE, Dauchy RT, Sauer LA, et al.   Growth and fatty acid metabolism of human breast cancer (MCF-7) xenografts in nude rats: impact of constant light-induced nocturnal melatonin suppression. *Breast Cancer Res Treat* . 2003;79:313-320.

54. Blask DE, Brainard GC, Dauchy RT, et al. Melatonin-depleted blood from premenopausal women exposed to light at night stimulates growth of human breast cancer xenografts in nude rats. *Cancer Res*. 2005;65:11174-11184.

55. Wu J, Dauchy RT, Tirrell PC, et al. Light at night activates IGF-1R/PDK1 signaling and accelerates tumor growth in human breast cancer xenografts. *Cancer Res*. 2011;71:2622-2631.

56. Dauchy RT, Sauer LA, Blask DE, et al.   Light contamination during the dark phase in "photoperiodically controlled" animal rooms: effect on tumor growth and metabolism in rats. *Lab Anim Sci.* 1997;47:511-518.

57. Dauchy RT, Blask DE, Sauer LA, Brainard GC, Krause, JA. Dim light during darkness stimulates tumor progression by enhancing tumor fatty acid uptake. *Cancer Lett*. 1999;144:131-136.

58. Cos S, Mediavilla D, Martinez-Campa C, et al. Exposure to light-at-night increases the growth of DMBA-induced mammary adenocarcinomas in rats. *Cancer Lett*. 2006;235:266-271.

59. Dauchy RT, Dupepe LM, Ooms TG, et al. Eliminating animal facility light-at-night contamination and its effect on circadian regulation of rodent physiology, tumor growth and metabolism: a challenge in the relocation of a cancer research laboratory. *J Am Assoc Lab Anim Sci*. 2011;50:326-336.

60. Filipski E, Delaunay F, King VM, et al. Effects of chronic jet lag on tumor progression in mice. *Cancer Res.* 2004;64:7879-7885.

61. Filipski E, Innominato PF, Wu M, et al. Effects of light and food schedules on liver and tumor molecular clocks in mice. *J Natl Cancer Inst.* 2005;97:507-517.

62. Blask DE. Melatonin, sleep disturbance and cancer risk. *Sleep Med Rev*. 2009;13:257-264.

63. Blask DE, Hill SM, Dauchy RT, et al. Circadian regulation of molecular, dietary, and metabolic signaling mechanisms of human breast cancer growth by the nocturnal melatonin signal and the consequences of its disruption by light at night. *J Pineal Res*. 2011;51:259-269.

64. Stevens RG, Blask DE, Brainard GC, et al. Meeting Report: The role of environmental lighting and circadian disruption in cancer and other diseases. *Environ Health Perspec*. 2007;115:1357-1362.

65. Brzezinski A. Melatonin in humans. *N Engl J Med* 1997; 336:186-95.

66. Korkmaz A, Topal T, Tan DX, Reiter RJ. Role of melatonin in metabolic regulation. *Rev Endocr Metab Disord.* 2009;10:261-70.

67. Reiter RJ, Tan DX, Fuentes-Broto L. Melatonin: a multitasking molecule. *Prog Brain Res.* 2010;181:127-51.

68. Sainz RM, Mayo JC, Rodriguez C, et al. Melatonin and cell death: differential actions on apoptosis in normal and cancer cells. *Cell Mol Life Sci*. 2003;60:1407-1426.

69. Lissoni P, Rovelli F, Malugani F, Bucovec R, Conti A, Maestroni GJ. Antiangiogenic activity of melatonin in advanced cancer patients. *Neuro Endocrinol Lett*. 2001;22:45-47.

70. Stevens, RG. Review and Commentary: Electric power use and breast cancer: a hypothesis. *Am J Epidemiol*. 1987;125:556-561.

71. Hoffman AE, Yi CH, Zheng T, et al. CLOCK in breast tumorigenesis: genetic, epigenetic, and transcriptional profiling analyses. *Cancer Res*. 2010;70:1459-1468.

72. Stevens RG. Light at night, circadian disruption, and breast cancer: assessment of existing evidence. *Int J Epidemiol*. 2009;38:963-970.

73. Kloog I, Stevens RG, Haim A, Portnov BA. Nighttime light level co-distributes with breast cancer incidence worldwide. *Cancer Causes Control.* 2010;21:2059-2068.

74. Straif K, Baan R, Grosse Y, et al. Carcinogenicity of shift-work, painting, and fire-fighting. *Lancet Oncol*. 2007;8:1065-1066.

75. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*. Painting, Firefighting, and Shiftwork. Volume 98, 2010. http://monographs.iarc.fr/ENG/Monographs/vol98/index.php

76. Pronk A, Ji BT, Shu XO, et al. Night-shift work and breast cancer risk in a cohort of Chinese women. *Am J Epidemiol.* 2010;171:953-959.

77. Pesch B, Harth V, Rabstein S, et al. Night work and breast cancer - results from the German GENICA study. *Scand J Work Environ Health*. 2010;36:134-141.

78. Lie JAS, Kjuus H, Haugen A, Zienolddiny S, Stevens RG, Kjærheim K. Night work and breast cancer risk among Norwegian nurses: Assessment by different exposure metrics. *Am J Epidemiol*. 2011;173:1272-1279.

79. Hansen J, Stevens RG. Case–control study of shift-work and breast cancer risk in Danish nurses: Impact of shift systems. *Eur J Cancer*. 2011. Aug 16. [Epub ahead of print]

80. Stevens RG, Hansen J, Costa G, et al. Considerations of circadian impact for defining 'shift work' in cancer studies: IARC Working Group Report. *Occup Environ Med*. 2011;68:154-162.

81. Schernhammer ES, Hankinson SE. Urinary melatonin levels and postmenopausal breast cancer risk in the nurses' health study cohort. *Cancer Epidemiol Biomarkers Prev*. 2009;18:74-79.

82. Davis S, Mirick DK, Stevens RG. Night shift work, light at night, and risk of breast cancer. *J Natl Cancer Inst*. 2001;93:1557-1562.

83. O'Leary ES, Schoenfeld ER, Stevens RG, et al. Electromagnetic Fields and Breast Cancer on Long Island Study Group. Shift work, light at night, and breast cancer on Long Island, New York. *Am J Epidemiol*. 2006;164:358-366.

84. Li Q, Zheng T, Holford TR, Boyle P, Zhang Y, Dai M. Light at night and breast cancer: results from a population-based case-control study in Connecticut, USA. *Cancer Causes Control*. 2010;21:2281-2285.

85. Kloog I, Portnov BA, Rennert HS, Haim A. Does the modern urbanized sleeping habitat pose a breast cancer risk? *Chronobiol Int*. 2011;28:76-80.

86. Hatonen T, Alila-Johansson A, Mustanoja S, Laakso ML. Suppression of melatonin by 2000-lux light in humans with closed eyelids. *Biol Psychiatry*. 1999;46:827-831.

87. Wehr TA. In short photoperiods, human sleep is biphasic. *J Sleep Res*. 1992;1:103-107.

88. European Union. Scientific Committee on Emerging and Newly Identified Health Risks. *Health Effects of Artificial Light*. http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_033.pdf. Accessed March 4, 2012.

89. Schernhammer ES, Razavi P, Li TY, Qureshi AA, Han J. Rotating night shifts and risk of skin cancer in the nurses health study. *J Natl Cancer Inst*. 2011;103:602-606.

90. Cappuccio FP, Miller MA, Lockley SW, Eds. *Sleep, health and society: From Aetiology to Public Health*, Oxford, UK: Oxford University Press; 2010.

91. Pietroiusti A, Neri A, Somma G, et al. Incidence of metabolic syndrome among night-shift healthcare workers. *Occup Environ Med.* 2010;67:54-57.

92. Gangwisch JE. Epidemiological evidence for the links between sleep, circadian rhythms and metabolism. *Obes Rev.* 2009;10 Suppl 2:37-45.

93. Bass J, Takahashi JS. Circadian integration of metabolism and energetics. *Science.* 2010;330:1349-1354.

94. Schibler U. The daily timing of gene expression and physiology in mammals. *Dialogues Clin Neurosci.* 2007;9:257-272.

95. Bellet MM, Sassone-Corsi P. Mammalian circadian clock and metabolism - the epigenetic link. *J Cell Sci.* 2010;123(Pt 22):3837-3848.

96. Djjk D-J, Lockley SW. Integrations of human sleep-wake regulation and circadian rhythmicity. *Journal of Applied Physiology.* 2002;92(Pt 2):852-862.

97. Van Cauter E, Spiegel K, Tasali E, Leproult R. Metabolic consequences of sleep and sleep loss. *Sleep Med.* 2008;9 Suppl 1:S23-28.

98. Spiegel K, Tasali E, Leproult R, Van Cauter E. Effects of poor and short sleep on glucose metabolism and obesity risk. *Nat Rev Endocrinol.* 2009;5:253-261.

99. Taheri S, Lin L, Austin D, Young T, Mignot E. Short sleep duration is associated with reduced leptin, elevated ghrelin, and increased body mass index. *PLoS Med.* 2004:1(3):e62.

100. Garrison MM, Leikweg K, Christakis DA. Media use and child sleep: the impact of content, timing, and environment. *Pediatrics.* 2011;128:29-35.

101. Owens J, Maxim R, McGuinn M, Nobile C, Msall M, Alario A. Television-viewing habits and sleep disturbances in school children. *Pediatrics.* 1999;104;e27

102. Higuchi S, Motohashi Y, Liu Y, Ahara M, Kaneko Y. Effects of VDT tasks with a bright display at night on melatonin, core temperature, heart rate, and sleepiness. *J Appl Physiol.* 2003;94:1773-1776.

103. Organization for Economic Co-operation and Development (OECD)/International Energy Agency (IEA). Light's labour's lost policies for energy-efficient lighting. *OECD/IEA.* Paris, France, 2006.

104. International Dark-Sky Association (IDA). *Economic Issues in Wasted and Inefficient Outdoor Lighting.* Information Sheet #26.

105. Cinzano P, Falchi F, Elvidge CD. The first world atlas of the artificial night sky brightness. *Monthly Notices of the Royal Astronomical Society.* 2001;328:689-707.

106. Klinkenborg V, Richardson J. Our Vanishing Night. *National Geographic,*. November, 2008. (http://ngm.nationalgeographic.com/geopedia/Light_Pollution)

107. Albers A, Duriscoe D. Modeling light pollution from population data and implications for national park service lands. *The George Wright Forum*. 2001;18:56-68.

108. Hölker F, Moss T, Griefahn B, et al. The dark side of light: A transdisciplinary research agenda for light pollution policy. *Ecology and Society* 2010;15(4): article 13.

109. International Dark-Sky Association (IDA). Effects of artificial light at night on wildlife. *Practical Guide 2*. 2008.

110. Longcore T, Rich C. Ecological light pollution. *Frontiers Ecology Environ.* 2004;2:191-198.

111. Rich and Longcore 2006

112. Barghini A, de Medeiros BA. Artificial Lighting as a Vector Attractant and Cause of Disease Diffusion. *Environ Health Perspect*. 2010;118:1503-1506.

113. McClung, CR. Plant Circadian Rhythms. *Plant Cell.* 2006;18:792–803.

114. Sedbrook J. *The Night Shift*. 2010.
http://www.coopext.colostate.edu/4dmg/Flowers/night.htm

115. Panel on Prevention of Falls in Older Persons, American Geriatrics Society and British Geriatrics Society. Summary of the Updated American Geriatrics Society/British Geriatrics Society Clinical Practice Guideline for Prevention of Falls in Older Persons. *J Am Ger Soc.* 2010.

116. American College of Occupational and Environmental Medicine. Guidance Statement. Fatigue risk management in the workplace. *JOEM*. 2012; 54:231-258.

117. Tanaka K, Takahashi M, Tanaka M, et al. Brief morning exposure to bright light improves subjective symptoms and performance in nurses with rapidly rotating shifts. *J Occup Health.* 2011;53:258-266.

118. Palleson S, Bjorvatn B, Mageroy N, Saksvik IB, Waage S, Moen BE. Measures to counteract the negative effects of night work. *Scand J Work Environ Health*. 2010;36:109-121.

119. Brainard GC, Hanifin JP, Rollag MD, et al. Human melatonin regulation is not mediated by the three cone photopic visual system. *J Clin Endocrinol Metab*. 2001;86:433-436.

120. Brainard GC, Hanifin JP. Photons, clocks and consciousness. *J Biol Rhythms.* 2005;20: 314-325.

121. Gamlin PDR, McDougal DH, Pokorny J, et al. Human and macaque pupil responses driven by melanopsin-containing retinal ganglion cells. *Vision Res.* 2007;47:946-954.

122. Zaidi FH, Hull JT, Peirson SN, et al. Short-wavelength light sensitivity of circadian, pupillary, and visual awareness in humans lacking an outer retina. *Curr Biol.* 2007;17:2122-2128.

123. Warman VL, Dijk DJ, Warman GR, Arendt J, Skene DJ. Phase advancing human circadian rhythms with short wavelength light. *Neurosci Lett.* 2003;342:37-40.

124. Cajochen C, Jud C, Munch M, Kobialka S, Wirz-Justice A, Albrecht U. Evening exposure to blue light stimulates the expression of the clock gene PER2 in humans. *Eur J Neurosci.* 2006;23:1082-1086.

125. Revell VL, Arendt J, Terman M, Skene DJ. Short-wavelength sensitivity of the human circadian system to phase-advancing light. *J Biol Rhythms*. 2005;20:270-272.

126. Revell VL, Arendt J, Fogg LF, Skene DJ. Alerting effects of light are sensitive to very short wavelengths. *Neurosci Lett.* 2006;399:96-100.

127. Provencio I, Rodriguez IR, Jiang G, Hayes WP, Moreira EF, Rollag MD. A novel human opsin in the inner retina. *J Neurosci.* 2000;20:600-605.

128. Berson DM, Dunn FA, Takao M. Phototransduction by retinal ganglion cells that set the circadian clock. *Science*. 2002;295:1070-1073.

129. Hattar S, Liao H-W, Takao M, Berson DM, Yau K-W. Melanopsin-containing retinal ganglion cells: Architecture, projections, and intrinsic photosensitivity. *Science.* 2002;295:1065-1070.

130. Gooley JJ, Lu J, Chou TC, Scammell TE, Saper CB. Melanopsin in cell of origin of the retinohypothalamic tract. *Nature Neurosci.* 2001;4:1165.

131. Hattar S, Kumar M, Park A, et al. Central projections of melanopsin-expressing retinal ganglion cells in the mouse. *J Comparative Neurology.* 2006;497:326-349.

132. Altimus CM, Guler AD, Alam NM, et al. Rod photoreceptors drive circadian photoentrainment across a wide range of light intensities. *Nature Neuroscience.* 2010;13:1107-1113.

133. Lall GS, Revell VL, Momiji H, et al. Distinct contributions of rod, cone, and melanopsin photoreceptors to encoding irradiance. *Neuron.* 2010;66:417–428

134. Dacey DM, Liao H-W, Peterson BB, et al. Melanopsin expressing ganglion cells in primate retina signal colour and irradiance and project to the LGN. *Nature.* 2005;433:749-754.

Figure 1. Stray light in the ocular media
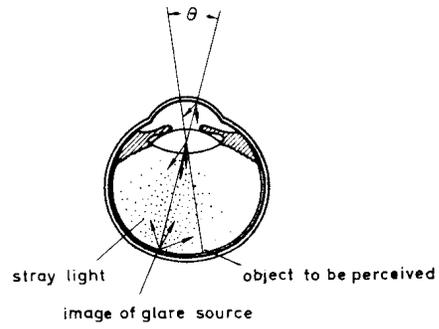
Appendix

DeBoer Scale

DeBoer Numerical Rating	Glare Intensity
1	Unbearable
3	Disturbing
5	Just Admissible
7	Satisfactory
9	Unnoticeable

<u>Addendum</u>

Molecular and Cellular Basis for Photoreceptive Regulation of Circadian and Neuroendocrine System Function

In the past decade, there has been an upheaval in the understanding of photoreceptive input to the human circadian and neuroendocrine systems. A study on healthy human subjects confirmed that the three-cone system that mediates human vision during the daytime is not the primary photoreceptor system that transduces light stimuli for acute melatonin suppression.[119] That discovery was rapidly followed by the elucidation of two action spectra in healthy human subjects that identified 446-477 nm as the most potent wavelength region for melatonin suppression.[3,4] To date, ten published action spectra have examined neuroendocrine, circadian, and neurobehavioral responses in humans, monkeys, and rodents. The action spectra demonstrate peak sensitivities in the blue region of the visible spectrum, with calculated peak photosensitivities ranging from 459 nm to 484 nm.[120-122] Further, a set of studies has confirmed that shorter wavelength, monochromatic light is more potent than equal photon densities of longer wavelength light for evoking circadian phase shifts, suppressing melatonin, enhancing subjective and objective correlates of alertness, increasing heart rate, increasing body temperature, and inducing expression of the circadian clock gene Per2 in humans.[19,20,123-126]

Studies using both animal and human models are clarifying the neuroanatomy and neurophysiology of the photosensory system that provides input for circadian, neuroendocrine, and neurobehavioral regulation. A recently discovered photopigment, named melanopsin, has been localized both in the retinas of rodents and humans.[127] More specifically, melanopsin is found in a subtype of intrinsically photoreceptive retinal ganglion cells (ipRGCs).[128,129] These light sensitive ganglion cells project to nuclei and regions of the central nervous system that mediate the biological and behavioral effects of light.[130,131] Although ipRGCs provide the strongest input for regulation of biology and behavior, studies on genetically manipulated rodents, normal monkeys, and humans demonstrate that the visual rod and cone photoreceptors integrate into this physiology.[5,132-134] Continued advances in understanding the physiology of this phototransduction will undoubtedly yield further insights into potential health impacts of electric lighting.