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Light Therapy

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ABSTRACT

The susceptibility of the circadian system to selective phase shifting by timed light exposure has broad implications for the treatment of sleep-phase and depressive disorders. Light therapies have been devised that can normalize the patterns of delayed sleep phase syndrome (through circadian phase advances) and advanced sleep phase syndrome (through circadian phase delays). Doctors and patients need to become cognizant of the daily intervals when light exposure—and darkness—can facilitate or hamper adjustment. The primary intervals lie at the edges of the "subjective night," which coincide with the tails of the nocturnal melatonin cycle, but they can be inferred clinically through a chronotype questionnaire. The lighting schedule may have to be continually adjusted as the subjective night shifts gradually in the desired direction.

The treatment strategy for seasonal and nonseasonal depressive disorders is similar. In winter depression, the magnitude of phase advances correlates with the degree of mood improvement, and the optimum timing of light therapy must be specified relative to circadian rather than solar time. Apart from its use as a monotherapy, light therapy in both outpatient and inpatient trials indicates that light therapy accelerates remission of nonseasonal depression in conjunction with medication.

Exploratory applications for treatment of antepartum and premenstrual depression, bulimia nervosa, sleep disruption of senile dementia, and shift work and jet lag disturbance are considered. The chapter provides the clinician with guidelines for selecting lighting apparatus based on safety, efficacy, and comfort factors; summarizes adverse effects of light overdose; and offers a straightforward protocol for selecting treatment time of day.

Exposure of the eyes to light of appropriate intensity and duration, at an appropriate time of day, can have marked effects on the timing and duration of sleep and on the affective and physical symptoms of depressive illness. The most extensive clinical trials have focused on winter depression, or *seasonal affective disorder* (SAD).

Here, we review and evaluate the application of light therapy for circadian rhythm sleep disorders including delayed sleep phase syndrome (DSPS), advanced sleep phase syndrome (ASPS), non–24-hour sleep phase syndrome, and the displaced sleep of shift work and jet lag. Beyond SAD, we also cover light therapy for nonseasonal depressions (recurrent, chronic, premenstrual, and antepartum), including combination treatment with wake therapy and medication; bulimia nervosa; and the sleep-wake problems of senile dementia. We describe the critical features of light delivery systems; safety factors and potential adverse effects; and timing and dose optimization for light administration, including a set of clinical case studies. (For a review of the underlying circadian physiology, see Terman.[1])

LIGHT DELIVERY

Apparatus

Light Boxes

Many of the early research studies used a standard 60-cm by 120-cm (2-foot by 4-foot) fluorescent ceiling unit, with a plastic prismatic diffusion screen, placed vertically on a table about 1 meter (3 feet) from the user. A bank of fluorescent lamps—full spectrum or cool white—provided approximately 2500-lux illuminance. Smaller, more lightweight units have become commercially available; however, specific design features of marketed light boxes have most often not been clinically tested.

Factors include lamp type (output and spectrum), filter, ballast frequency (for fluorescent lamps), size and positioning of radiating surface, heat emission, and so on. One clinically tested model (Fig. 121–1) illustrates second-generation apparatus modifications, including smaller size, portability, raised and downward-tilted placement of the radiating surface, a smooth polycarbonate diffusion screen with complete ultraviolet (UV) filtering (see Resources), and high-output fluorescent lamps (nonglaring 4000 K color temperature) driven by high-frequency solid-state ballasts. The combination of elements in this configuration yields a maximum illuminance of approximately 10,000 lux with the patient seated in a position with the eyes about 30 cm (1 foot) from the screen.

With the direction of gaze downward toward the work surface, such a configuration provides pleasant illumination suitable for reading and, despite illuminance far higher than in normal home lighting, is generally well tolerated (see Side Effects of Exposure to Bright Light). The presentation of light from above eye level is supported by a study showing enhancement of melatonin suppression with directional illumination of the lower retina.[2] As the apparatus becomes miniaturized, however, the field of illumination narrows, and even small changes in head position can substantially reduce the intensity of light that reaches the eyes.

Although light boxes are simple in design, home construction of such an apparatus is discouraged because of the danger of excessive irradiation; some amateur assemblers have experienced corneal and eyelid burns. Because the critical design features have not been specified or regulated by the government or the profession, clinicians should seek documentation by the manufacturer of the safety and effectiveness of any apparatus under consideration.

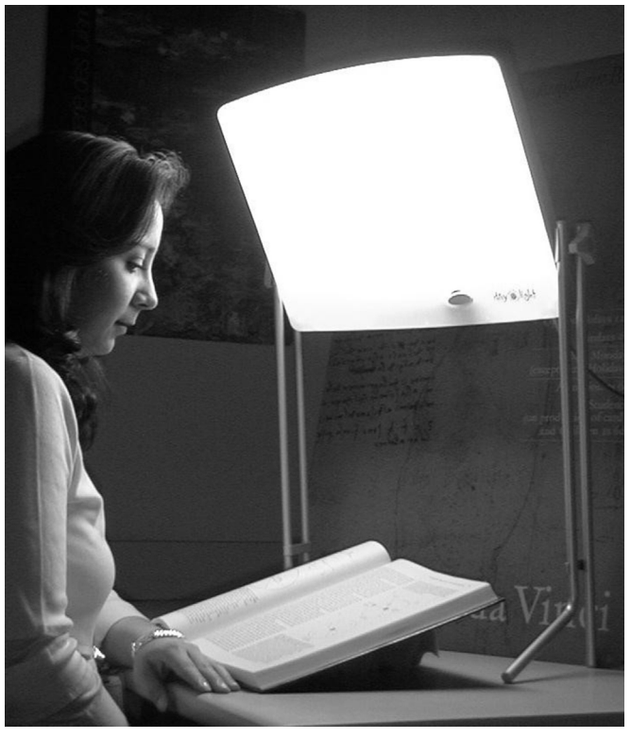


Figure 121–1. Table-mounted, tilted, 10,000-lux, UV-filtered 4000 Kelvin fluorescent light system. (Photograph courtesy of the Center for Environmental Therapeutics, www.cet.org.)

Claims for the specific efficacy of any particular lamp type or spectral distribution, although commonly given, are unsubstantiated. Unfortunately, systems are marketed that provide excessive visual glare, exposure of naked bulbs, direct intense illumination from below the eyes ("ski slope" effect), and intentionally augmented UV radiation. Claims that UV radiation is important for the therapeutic effect are unsubstantiated, and the risk of ocular and facial exposure must be avoided. Both the clinician and the consumer must be vigilant in the selection of an apparatus. Criteria are reviewed on the Suppliers website page of the nonprofit Center for Environmental Therapeutics, www.cet.org.

Light Visors

In an alternate configuration, head-mounted portable lighting units (in a visor configuration), which are intended to increase flexibility and convenience of use, have been marketed and are suited for novel applications such as in-flight treatment. However, despite a set of multicenter trials for SAD,[3-5] bright light exposure with this device has shown no advantage over dim light exposure (a putative placebo control), and there has been no convincing demonstration of clinical efficacy.[6] One visor study has demonstrated circadian phase shifting,[7] however, and pending design enhancements may yet show utility.

Dawn Simulators

Dawn simulation methodology provides a major contrast to bright light therapy. A computer-controlled lighting device delivers a mimic of gradual twilight transitions found outdoors in the spring or summer. The relatively dim, dynamically changing signals are presented to the patient while asleep, when eyes are adapted to the dark and the circadian system is most susceptible to phase advances (see Timing of Morning Light Exposure). As with bright light therapy, there is an antidepressant response and normalization of hypersomnic, phase-shifted, and fractionated sleep patterns.[8-10]

A laboratory study of healthy young adult subjects demonstrated that the addition of simulated, naturalistic dawn exposures blocks the delay drift of circadian rhythms under dim light-dark cycles.[11] A large, 6-week controlled clinical trial of log-linear light onset ramps (which differ from the curvilinear acceleration of naturalistic dawns) found signals rising to 250 lux between 4:30 and 6:00 AM significantly more antidepressant than dim red control signals rising to 0.5 lux.[12] Furthermore, the treatment was superior to postawakening bright light therapy administered between 6:00 and 6:30 AM.

The effectiveness of dawn simulation may depend on the presentation of diffuse, broad-field illumination that reaches the sleeper in varying postures. Such efficacy has not been demonstrated for inexpensive, commercial light "alarm clocks," which have small, directional fields.

Safety of Bright Light for the Eyes

Ophthalmologic evaluations of unmedicated patients with normal oculoretinal status have thus far shown no obvious acute light-induced pathology or long-term sequelae.[13] Although the intensity of bright light treatment falls well within the low outdoor daylight range, the exposure conditions differ from those outdoors, and prolonged use entails far greater cumulative light exposure than is normally experienced by urban dwellers and workers.[14,15]

Potentially damaging wavelengths above the UV range extend into the visible range up to 500 nm (blue light),[16-18] and one conservative proposal advocates screening out such low-wavelength light altogether.[19] On the other hand, recent data show that the blue wavelength range above 450 nm preferentially serves to suppress nocturnal melatonin production[20] and enhance circadian phase shifting.[21] Although selective therapeutic benefit of such light has yet to be ascertained, one already sees manufacturers rushing in with blue-light devices. A compromise solution may be assiduous filtering of wavelengths less than 450 nm—the blue-light hazard is magnified in that range.

At the opposite end of the light spectrum, ocular exposure to infrared illumination, which makes up about 90% of the output of incandescent lamps, poses risk of damage to the lens and cornea (as does UV) as well as the retina and pigment epithelium.[22] Thus, despite being marketed for light therapy, incandescent lamps are contraindicated.

Light box diffusion filters vary widely in short-wavelength transmission (for examples, see Remé et al.[19]). Transmission curves should be demanded of manufacturers and compared with published standards. Normal clouding of the lens and ocular media that begins in middle age, as well as cataract formation, serves to exacerbate perceptual glare, which can make high-intensity light exposure quite uncomfortable.[19]

Furthermore, both UV and short-wavelength blue light can interact with photosensitizing medications—including many standard antidepressant, antipsychotic, and antiarrhythmic agents, as well as common medications such as tetracycline—to promote or accelerate retinal pathology, whether acute or

slow and cumulative.[22] In one reported case, a patient received combination treatment with clomipramine (an anticholinergic tricyclic antidepressant) and full-spectrum fluorescent light. After 5 days, the patient had reduced contrast sensitivity, foveal sensitivity and visual acuity, and central scotomas and lesions, fortunately with only minor residual aftereffects in contrast sensitivity and scotoma 1 year after discontinuation.[23]

Filtered wrap-around goggles are available (see Resources) that eliminate transmission of short-wavelength blue light while maximizing exposure above 500 nm, reducing glare, enhancing visual acuity and subjective brightness, and minimizing the risk of drug photosensitization.[24]

Although there are no definite contraindications for bright light treatment other than for the retinopathies, research studies have routinely excluded patients with glaucoma or cataract. Some of these patients have used light therapy effectively in open treatment; this should be done, however, only with ophthalmologic monitoring. A simple eye checkup is advised for all new patients, for which a structured examination chart has been designed (see Resources).[25] The examination has occasionally revealed preexisting ocular conditions that should be distinguished from potential consequences of bright light treatment.

Side Effects of Exposure to Bright Light

If evening light is timed too late, the patient may initially have insomnia and hyperactivity. If morning light is timed too early, the patient may awaken prematurely and be unable to resume sleep. These problems are responsive to timing and dose (duration and intensity) adjustments during treatment of both circadian sleep phase and mood disorders.

The emergence of side effects relates in part to the parameters of light exposure, including intensity, duration, spectral content, and method of exposure (diffuse, focused, direct, indirect, and angle of incidence relative to the eyes). Thus far, side effects have been assessed primarily in patients with seasonal and nonseasonal mood disorders, and information is lacking for sleep disorders without mood disturbance.

The earliest clinical trials of 2500-lux full-spectrum fluorescent light therapy for SAD noted infrequent side effects of hypomania, irritability, headache, and nausea.[26,27] Such symptoms often subside after several days of treatment. If persistent, they can be reduced or eliminated with dose decreases. Rarely have patients discontinued treatment due to side effects. Studies with portable head-mounted units containing incandescent bulbs near the eyes and providing illuminance of 60 to 3500 lux have also noted side effects of headache, eyestrain, and feeling "wired," but symptoms were not dose dependent.[28]

Two cases of induced manic episodes have been reported in drug-refractory nonseasonal unipolar depressives beginning after 4 to 5 days of light treatment.[29] A few cases of light-induced agitation and hypomania have been noted, also in nonseasonal depressives.[30] A patient with seasonally recurrent brief depressions developed rapid mood swings after light overexposure (far exceeding 30 minutes per day at 10,000 lux),[31] and a unipolar SAD patient with similar exposure showed his first manic episode[32]; both patients required discontinuation and medication. We had one bipolar patient with SAD who became manic after the use of light and was administered lithium as an effective countermeasure; others who have used mood stabilizers have responded to light therapy without mania. Three cases of suicide attempt or ideation, also occurring in patients with SAD, were reported within 1 week of standard early-evening bright light treatment, and the patients required hospitalization.[33]

A 42-item side-effect inventory was administered to 30 patients with SAD after treatment with unfiltered full-spectrum fluorescent light at 2500 lux for 2 hours daily.[34] Other than for one case of hypomania, there were no clinically significant side effects. Patients given evening light (the timing relative to bedtime was unspecified) reported initial insomnia. Mild visual complaints included blurred vision, eyestrain, and photophobia.

Of specific interest is the side-effect profile for patients using a downward-tilted fluorescent light box protected by a smooth diffusion screen (see Fig. 121–1), with 30-minute daily exposures at 10,000 lux, because this method has had widespread application. A study of 83 patients with SAD who were evaluated for 88 potential side effects[35] identified a small number of emergent symptoms at a frequency of 6% to 16%, including nausea, headache, jumpiness or jitteriness, and eye irritation.[36] These results must be weighed against the improvement of other patients who showed similar symptoms at baseline but became asymptomatic after light treatment: All symptoms, except nausea, showed greater improvement than exacerbation, which forces attention to the risk-to-benefit ratio. Indeed, symptom emergence might reflect the natural course of depressive illness in nonresponders to light rather than a specific response to light exposure.

CASE MANAGEMENT, TIMING, AND DOSING

Patient Monitoring

Light treatment is typically self-administered at home on a schedule recommended by the clinician. To the extent that the timing of light exposure is important for obtaining a therapeutic effect, compliance is a sine qua non. When commencing treatment, therefore, it is helpful to ask the patient to call every few days or to fax log records of sleep, treatment times, and mood ratings; this will assist the clinician in managing timing and dose adjustments.

In contrast with structured research studies, the motivation and compliance of patients in open treatment can be problematic. Despite an agreement to awaken for light treatment at a specific hour, patients may ignore the alarm, considering additional sleep to be the priority of the moment, and may delay or skip treatment. Patients frequently attempt to test whether improvement can be achieved without rigid compliance, and they may quit if treatment is managed too rigidly. Indeed, the behavioral investment in a maintenance regimen of light treatment is considerable, far exceeding that of pharmacotherapy.

For hypersomnic patients who are unable to awaken when instructed, light exposure initially can be scheduled at the time of habitual awakening and then edged earlier across days toward the target interval. Some depressed patients compensate for earlier wake-up times with earlier bedtimes or napping (as do patients with DSPS), but others are comfortable with less sleep as the antidepressant effect sets in. Clinical experience suggests that most such patients could not sustain earlier awakening without the use of light.

Variability in the sleep pattern, if it occurs, may yield important information for determining the course of treatment. Online adjustments in scheduling, although labor intensive for the clinician, often succeed. Our strategy has been to encourage the adherence to a recommended light exposure schedule but to consider the obtained sleep pattern as a dependent measure that often reflects changes in mood state, sleep need, and circadian rhythm phase.

Timing of Morning Light Exposure

The thrust of recent clinical trials (see Seasonal Affective Disorder) leads to the recommendation that patients with SAD initially be given morning light shortly after awakening. A similar strategy applies to patients with DSPS. (In contrast, evening light is indicated for ASPS; see Case Example 6.) The dose of 10,000 lux for 30 minutes[37,38] appears to be most efficient. Although lower intensities also may be effective, they require exposure durations up to 2 hours,[39,40] and to accommodate such morning treatment, most patients would have to awaken far earlier than at baseline, with risk of a counterproductive circadian phase delay.

The advantage of morning light appears to lie in circadian rhythm phase advances, which can be measured as shifts in the time of nocturnal melatonin onset.[41] The magnitude of the antidepressant response varies with the magnitude of phase advances. In a protocol with 10,000-lux treatment for 30 minutes on habitual awakening, the magnitude of antidepressant response was negatively correlated with the interval between melatonin onset and treatment time ($r = -0.53$, a large effect size).[42] Indeed, light therapy given 7.5 to 9.5 hours after melatonin onset yields twice the remission rate (80% versus 38%) of light given 9.5 to 11.0 hours after melatonin onset.[43] The clock time of morning light administration is irrelevant, since baseline melatonin onset spans a 4-hour range or more. To maximize the likelihood of a treatment response, the clinician might therefore initiate morning light no later than 8.5 hours after a patient's melatonin onset.

Unfortunately, such diagnostic information is not readily available. A future solution may lie in the use of a salivary melatonin assay,[44] with home sampling and rapid turnaround by a commercial laboratory. An approximate solution, however, lies in the relation between melatonin onset and the Horne-Östberg Morningness-Eveningness Questionnaire (MEQ)[45] score, which for SAD patients are strongly correlated ($r = 0.80$, $N = 71$, $P < .001$).[46] One thus can schedule morning light exposure at individually specified circadian times by inferring the time of melatonin onset, a strategy that facilitates circadian rhythm phase advances as well as the antidepressant response.

A list of recommended light exposure times, derived from the regression of the MEQ score on melatonin onset, is shown in Table 121–1.

Sessions should begin within 10 minutes of scheduled wake-up time. In most cases, treatment will begin earlier than the baseline wake-up time—which is also highly correlated with melatonin onset and the MEQ score—depending on the patient's habitual sleep duration. For example, a short sleeper, whose bedtime is at midnight and who awakens at 6 AM, would start treatment on habitual awakening. In contrast, a long sleeper, with onset at 11:30 PM and awakening at 7:30 AM, would have to wake up 1 hour earlier, at 6:30 AM. For every half hour of sleep beyond 6 hours, awakening for light treatment is 15 minutes earlier than habitual awakening at baseline—a maximum of 1.5 hours earlier if sleep duration extends to 9 hours. The algorithm should be considered a "best guess" strategy to determine the initial timing of light exposure, with a potential need for adjustment depending on early results. An online version of the MEQ,[47] at www.cet.org, automatically returns the recommended light exposure interval to the user. Although the algorithm is based on SAD data, it has been applied successfully to patients with nonseasonal depression[48] and delayed sleep phase.

Table 121–1. Timing of Morning Light Therapy* Based on Morningness-Eveningness Score

MEQ Score	Start Time
16-18	0845
19-22	0830
23-26	0815
27-30	0800
31-34	0745
35-38	0730
39-41	0715
42-45	0700
46-49	0645
50-53	0630
54-57	0615
58-61	0600
62-65	0545
66-68	0530
69-72	0515
73-76	0500
77-80	0445
81-84	0430
85-86	0415

*Start of 10,000-lux, 30-minute session, approximately 8.5 hours after estimated melatonin onset.

LIGHT TREATMENT OF SPECIFIC DISORDERS

Circadian Sleep Phase Disorders

Delayed Sleep Phase Syndrome

Patients with DSPS have difficulty initiating sleep before 1 to 3 AM, and sometimes later, with commensurate difficulty awakening at an early hour (for a review and discussion of circadian rhythm correlates, see Terman et al.[49]). Once awake, most patients exhibit normal alertness and energy as long as they can maintain their displaced sleep schedule, but others report difficulties for several hours after awakening and spurts of energy after midnight. Not infrequently, patients with DSPS show comorbid mood and personality disorders.

Under delay chronotherapy,[50] the sleep episode is scheduled at successively later hours each night for about 1 week. Once the desired sleep phase is attained, the patient attempts to keep sleep-wake timing consistent. The original description of chronotherapy specified that sleep episodes occur in darkness. It follows that the timing of light exposure changes during and after the phase adjustment. An implication is that by the end of the procedure, the patient begins to receive a

normalized pattern of daily light exposure that serves to maintain the target phase. Early morning artificial bright light exposure can forestall further drifting toward the original delayed sleep phase, which is always a risk.

Indeed, morning light treatment can often directly normalize the timing of the sleep episode without the need for progressive delays with chronotherapy. In one study, patients with DSPS were given 2 hours of early-morning light treatment at 2500 lux, along with light restriction after 4:00 pm.[51] The body temperature rhythm and daily cycle of sleep-onset latencies showed phase advances, and there was an increase in morning alertness within 1 week. These effects were not obtained with the use of a dim light control.

In open treatment, if morning light exposure fails to induce and maintain the desired phase advance, chronotherapy may be used to successively delay the sleep episode until the desired target phase is achieved. Light treatment can be used to facilitate chronotherapy with presleep exposures during the delay period, followed by postsleep exposures during maintenance.

These approaches require the clinician's active supervision, with continual adjustment in sleep and light exposure schedules in response to patient feedback and ability to comply. Bright light treatment is administered in the context of complex daily patterns of indoor and outdoor light exposure, including dark periods, all of which may influence treatment outcome. In fact, a procedure may require ensured dark exposure at certain times of day in coordination with light treatment at other times. The patient can accomplish this by using highly filtered goggles when going outdoors during daylight hours.[52]

An interesting novel therapeutic approach uses a sleep mask embedded with light emitting diodes that turn on gradually 4 hours before the end of sleep,[53] in the manner of dawn simulation.[8] A subgroup of delayed sleep phase subjects with relatively late melatonin cycles responded with earlier sleep onset accompanied by melatonin phase advances.

Mild Sleep Phase Delay (Subsyndromal Delayed Sleep Phase Syndrome)

The common problem of chronic but mild initial insomnia that falls short of DSPS, accompanied by difficulty arising and low morning alertness, is often readily treatable with postsleep light, leading to rapid adjustment. Many such insomniacs do not respond to hypnotic medication and are not depressed.

CASE EXAMPLE 1: Phase Advance with Postsleep Light

Patient T.W. (Fig. 121–2A) reported a lifelong history of DSPS with variable sleep onset averaging 5:00 AM and occasional hypersomnic episodes lasting 11 to 12 hours. Although not depressed while seeking help, he also reported experiencing subsyndromal symptoms of winter depression. The treatment consisted of gradually shifting light exposure earlier across days, beginning at 10:30 AM, a time of typical spontaneous awakening.

The patient monitored his level of sleepiness and time of awakening to determine the rate of shift. He was able to achieve successively earlier wake-up times over a period of 2 weeks while light-treatment sessions were advanced from 10:30 to 7:30 AM, but even at that point he could not fall asleep before 2:30 AM. However, when the treatment session was further advanced to 7 AM—an unprecedented time of awakening for this patient—sleep onset abruptly jumped approximately 2 hours earlier. The sleep episode stabilized at about 1:15 to 6:30 AM with light treatment on awakening.

After several months, the patient reported having increased light duration from 30 minutes (at 10,000 lux) to 45 or 60 minutes to enhance daytime energy. He also reported a relapse when he discontinued treatment twice within the next year. He managed his readjustments and reported the remission of depressed mood in the winter.

CASE EXAMPLE 2: Phase Delay with Chronotherapy Followed by Stabilization with Morning Light

Patient M.L. (see Fig. 121–2B) had chronic major depression and was referred for light therapy because of refractory response to drugs. She reported a long history of DSPS and daytime fatigue, often staying in bed all day. In addition, she reported occasionally sleeping at successively later hours until her delayed sleep phase was reestablished. She would not comply with most sleep scheduling requests, but when a free-run appeared to start spontaneously, she agreed to attempt to schedule successive delays of bedtime—in a loose application of chronotherapy—and aim to restabilize with midnight sleep onset and regular outdoor daylight exposure.

Sleep was often fragmented during the week of chronotherapy, and several days after reaching the target phase, sleep became restless throughout the night. The appearance of initial insomnia at that time suggested that there would be further delays over the next days, overshooting the target phase. At this point, the patient began 30-minute light sessions at 10,000 lux on awakening at 7:30 AM, with a second session in midafternoon. She became highly energized after the first day's exposure sessions and was unable to sleep at all the next night. Sleep onset continued to drift later, and she complained of sleep deprivation.

On one occasion when she skipped afternoon light, sleep onset occurred hours earlier than expected. Morning light treatment was then rescheduled about 1 hour later, and despite a few episodes of middle-to-late insomnia, she was able to fall asleep by 2 AM or earlier and to awaken by 8 AM. When monitored several months later, the pattern had stabilized, with sleep onsets occurring around 12:30 to 1:00 AM accompanied by uninterrupted sleep for 8 hours. Despite slightly improved daytime energy, however, her depression did not lift, and she remained dysfunctional.

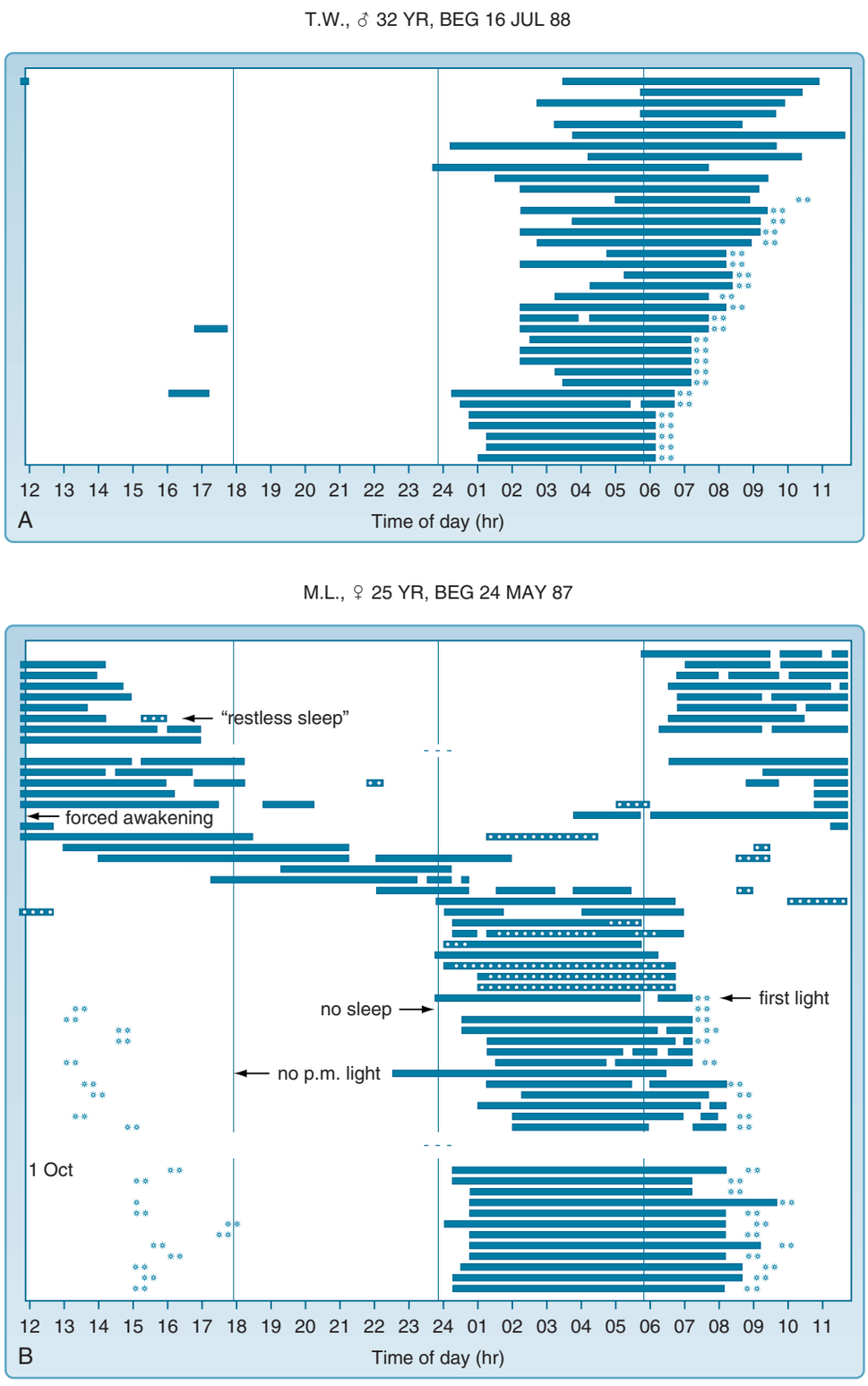


Figure 121–2. Self-report sleep records for five light-therapy patients with various sleep phase disturbances: **A**-**C**, delayed sleep phase syndrome (T.W., M.L., S.P.); **D**, mild sleep-phase delay (J.B.); **E**, non–24-h sleep-wake disorder (B.C.). Successive days are lined up, *top to bottom*, on the ordinate. *Bars* indicate intervals of sleep (including naps); *sun symbols* indicate 15-minute segments of bright light exposure; *ellipsis* indicates a gap in record. For patient M.L., *open circles* indicate "restless sleep." For patient S.P. (**C**), *B*, benzodiazepine hypnotic; *N*, waking due to noise. For patient B.C. (**E**), the duration of light exposure is indicated as the recommended average of 2.5 hours per day. In addition to morning light treatment, patients M.L. (**B**) and S.P. (**C**) used variations of chronotherapy to establish the desired sleep phase by successive delays of their sleep schedules.

Continued

CASE EXAMPLE 3: Phase Delay with Chronotherapy Followed by Stabilization with Morning Light

Patient S.P. (see Fig. 121–2C) showed a delayed sleep pattern similar to that of M.L. (Case Example 2), which was present since childhood. Although he was groggy on awakening, afternoon and evening energy levels were high, and he could work productively at those times. On nights when he used a benzodiazepine hypnotic, he could sometimes advance sleep onset by a few hours, which he considered trivial.

An attempt was then made to phase advance the sleep episode with the use of 10,000-lux, 30- to 45-minute light exposures on awakening. Despite intense effort over a 1-week trial, the patient could not be awakened before 12:30 PM, making successively earlier treatment sessions impossible. An alternative course of chronotherapy was then attempted.

The patient was instructed to delay successive sleep episodes by 2 hours, in conjunction with 1-hour light treatment sessions ending 2 hours before bedtime (a procedure intended to facilitate chronotherapy). However, he refused to enter bed until ready to fall asleep, resulting in successive daily delays that varied between 1 and 5 hours. After 6 days, the presleep light was discontinued, with instruction to substitute light exposure for 2 hours at 6 AM in an attempt to halt the delay drift. In the next weeks, the patient was able to maintain sleep onset between 11 PM and midnight and to awaken by 7:30 AM or earlier.

The resilience of the adjustment was tested on the occasion of two late-night parties after which the desired sleep pattern was easily recaptured. Subsequently, however, the patient discontinued treatment and resumed his former schedule, citing family stresses that he preferred to escape by sleeping during the day.

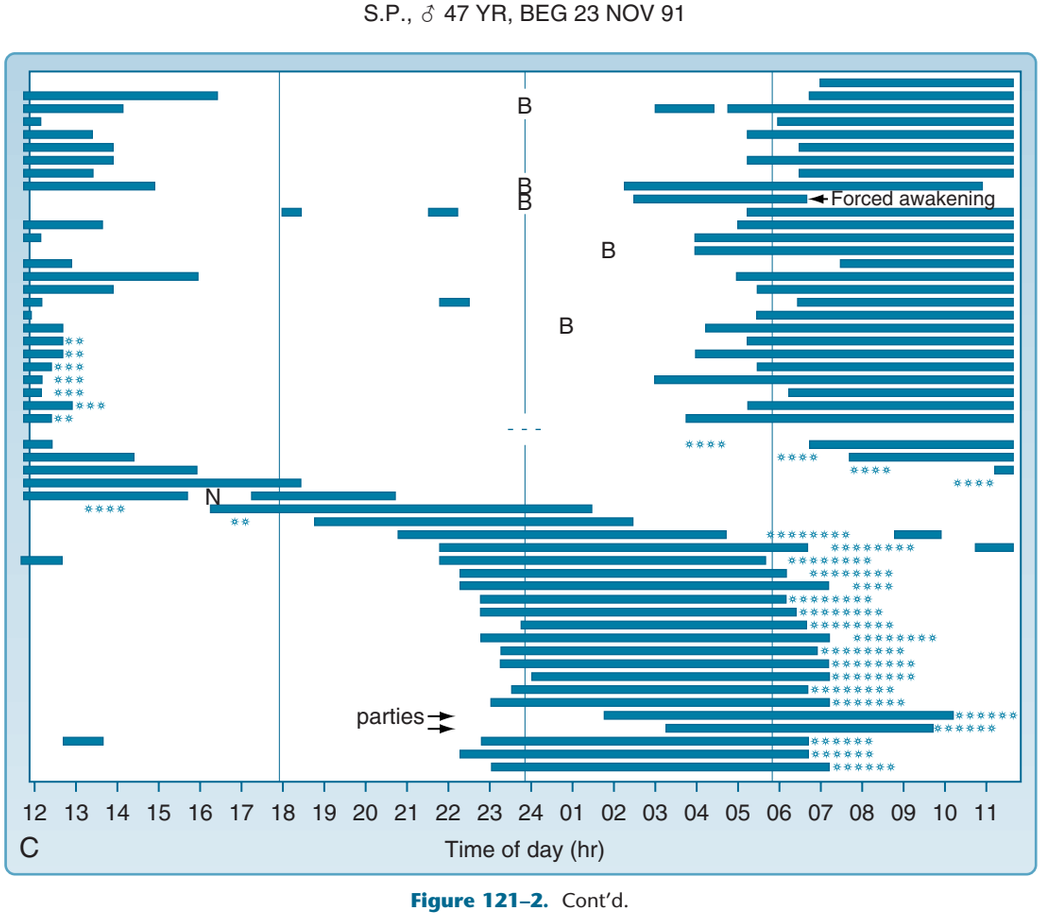
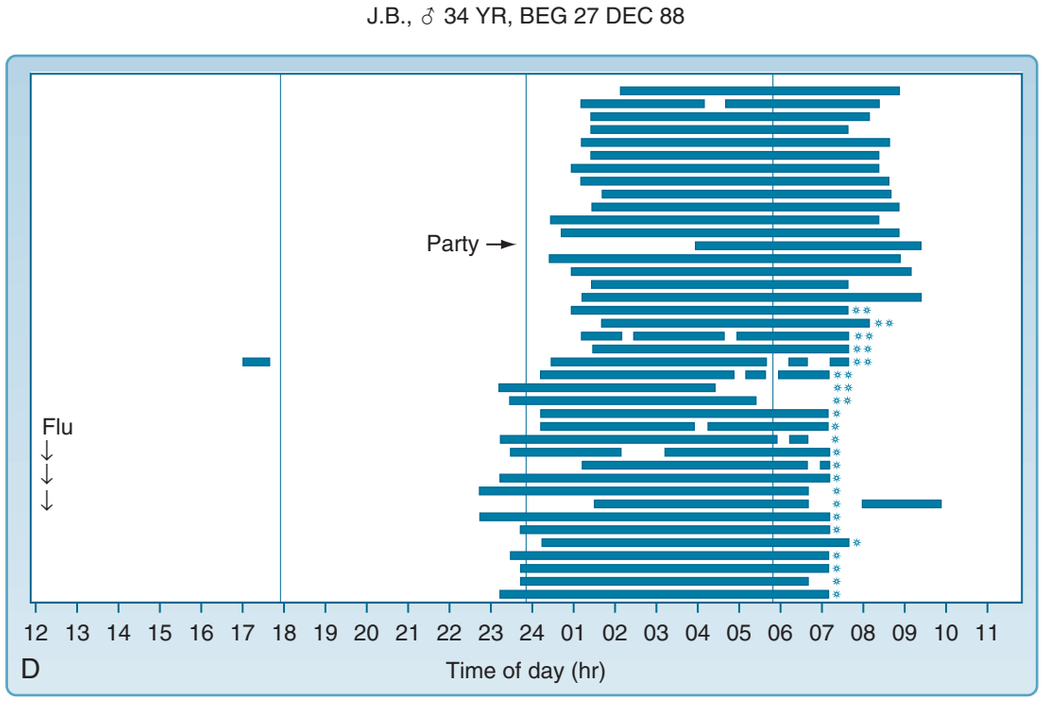


Figure 121–2. Cont'd.

CASE EXAMPLE 4: Mild Phase Delay Advanced with Postsleep Light

Patient J.B. (see Fig. 121–2D) could rarely fall asleep before 1:30 AM or wake up in time for a normal work day. Although he was allowed to work from midmorning into the evening, he was handicapped by low alertness till midafternoon and headaches at a computer terminal during the late afternoon.

Light treatment began with 10,000-lux exposures at 8 AM for 30 minutes, with no effect for several days. When the session was advanced to 7:30 AM, sleep onset spontaneously advanced by about 1 hour. However, several days of late insomnia followed, with awakenings before 6 AM, signaling an overdose. Reducing the treatment duration to 15 minutes at 7:30 AM alleviated this problem, with sleep onset maintained around midnight. This regimen was continued, with effortless awakening accompanied by improved morning alertness and complete remission of the headache.



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Non–24-hour Sleep-Wake Syndrome

When sleep phase does not stabilize but continually shifts later relative to clock time, the pattern resembles the free-run seen in normal subjects under conditions of temporal isolation without day-night cues. However, in non–24-hour sleep-wake syndrome, despite the presence of such cues, a failure of entrainment is evidenced by a hypernychthemeral[54] sleep pattern. Some patients with DSPS break into transient hypernychthemeral patterns (e.g., patient M.L. in Fig. 121-2*B* and Case Example 2), which suggests that non–24-hour sleep-wake syndrome and DSPS are associated disorders of varying severity.[55] Light therapy aims to halt the delay drift by timing postsleep exposure to start when the subjective and objective nights coincide.

CASE EXAMPLE 5: Phase Stabilization of Non–24-hour Sleep-Wake Syndrome with Morning Light

Patient B.C. (see Fig. 121–2E) showed a sleep-wake cycle length averaging 25 hours over approximately 13 years preceding treatment.[56] He was unemployed and socially withdrawn and refused to attempt to sleep when alert. Treatment began when sleep onset had drifted to midnight. The patient was exposed to light of 4000 to 8000 lux for 2 to 3 hours on awakening. The free-run immediately decelerated, and the sleep interval was maintained at approximately 1:30 to 8:15 AM for several weeks. In the long run, however, the sleep pattern continued to drift at a period of about 24.08 hours, a problem that might have been corrected with increased light dose.

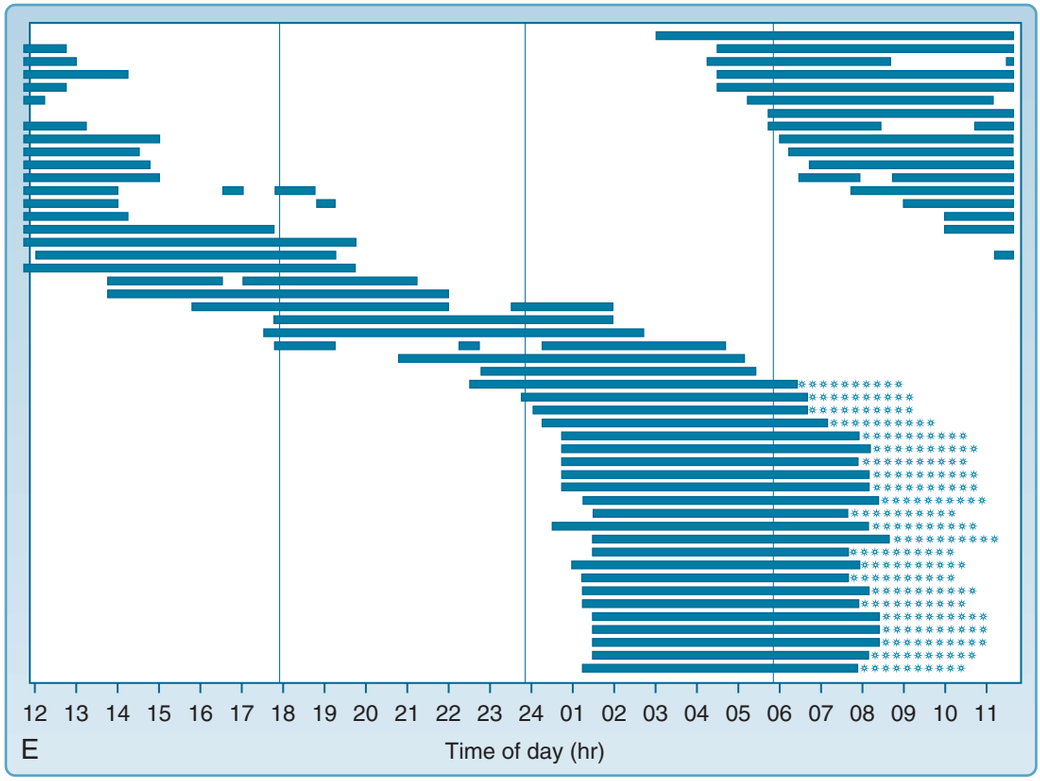

Figure 121–2. Cont'd.

Advanced Sleep Phase Syndrome

ASPS, in which sleep onset occurs in the evening with awakening well before dawn, would seem to provide a counterpart to DSPS, treatable with late evening light,[57] but such treatment has not been extensively investigated. Light presented in the first part of the subjective night is known to elicit phase delays in the onset of nocturnal melatonin secretion[58] and the decline of body temperature,[59] which might induce later sleep onset. Although ASPS is not strictly age related, it is more prevalent among the elderly, whose early rise times are a common cause of concern.

CASE EXAMPLE 6: Phase Advance with Presleep Light

The experience of a 38-year-old woman with lifetime history of ASPS[57] illustrates the potential use—and limitations—of evening light treatment. Patient K.W. was a mildly hypomanic high achiever, without seasonal pattern, who typically fell asleep at about 9:00 PM, and woke up between 2 and 4 AM, a pattern that led to marital stress. She could remain awake for occasional late-evening engagements, compensating with delayed time of arising at 5 to 6 AM. At baseline, she showed an early melatonin onset, at about 7:45 PM (Fig.121–3). Light exposure for up to 2 hours beginning at 8 PM hardly affected sleep phase or melatonin onset, whereas light exposure beginning at 9 PM succeeded in maintaining sleep onset at about 11 PM and wake-up between 4 and 5 AM, accompanied by a 1-hour delay in melatonin onset.

Campbell et al.[60] compared the effects of evening bright light exposure (more than 4000 lux for 2 hours) with a dim red light control in elderly subjects with histories of sleep maintenance insomnia. The bright light group showed improved sleep efficiency; after 12 days of treatment, nighttime wakefulness decreased by about 1 hour. Despite this benefit, most subjects were reluctant to continue treatment given the long exposure sessions and glare discomfort.

These drawbacks might be corrected with shorter exposures to higher intensity light with the use of an apparatus that minimizes short-wavelength blue glare (see Apparatus), which is exacerbated in elderly people due to normal clouding of the lens and ocular media.

Seasonal Affective Disorder

Patients with SAD experience annually recurrent mood disturbance often accompanied by an increased appetite for carbohydrates, weight gain, daytime fatigue and loss of concentration, anxiety, and increased sleep duration. The appetitive and sleep symptoms are considered atypical, in contrast with the poor appetite, weight loss, and late insomnia seen in melancholic depression. For a set of diagnostic and clinical assessment instruments, see Resources and the discussion in Terman et al.[61]

Most light therapy studies have focused on parameters that influence treatment response, such as time of day, duration of exposure, intensity, and wavelength. The original regimen tested at the National Institute of Mental Health used 2500-lux

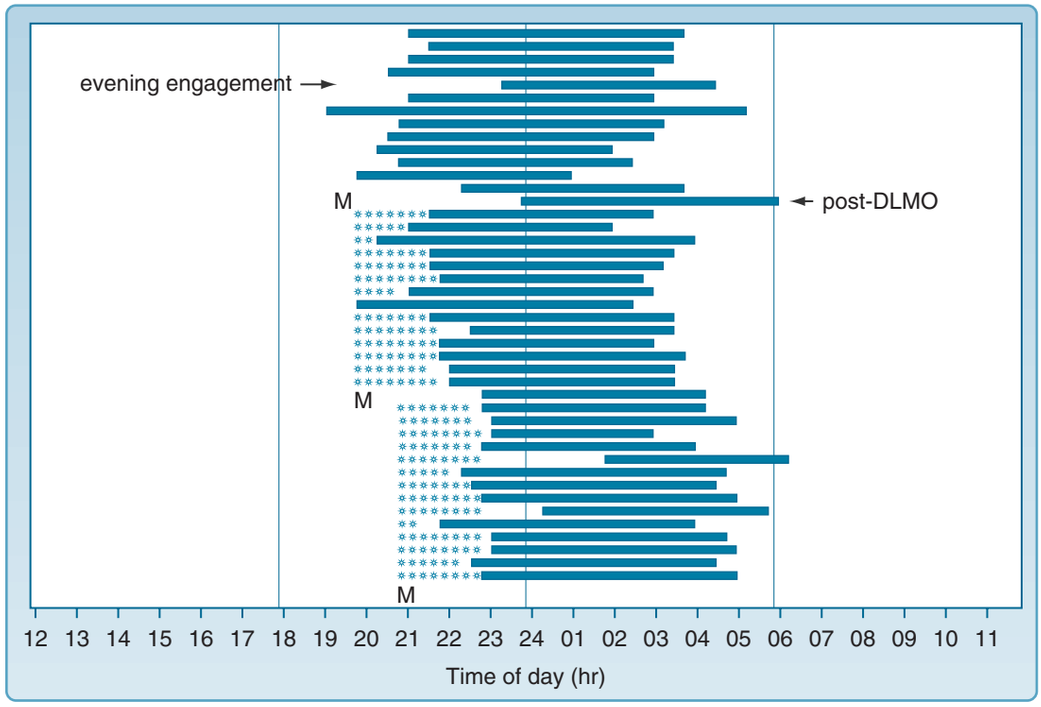

Figure 121–3. Self-report sleep record for a patient with advanced sleep phase disorder. *Bars* indicate intervals of sleep (including naps); *Sun symbols* indicate 15-minute segments of bright light exposure; M indicates the phase of dim light melatonin onset (DLMO), as determined on nights when treatment was omitted.

fluorescent illumination in 3-hour sessions in the morning and the evening.[26] A cross-center analysis of more than 25 studies that included 332 patients[62] summarized the results for dual daily sessions at 2500 lux for 2 hours; single morning, midday, and evening sessions; brief sessions (30 minutes); and lower light intensity (less than 500 lux). One week of morning bright light treatment produced a significantly higher remission rate (53%) than did evening (38%) or midday (32%) treatment. Dual daily sessions provided no benefit over morning light alone. All three bright light regimens were more effective than the dim light control; only morning (or morning plus evening) light was superior to the brief light control.

Two subsequent studies increased light intensity to 10,000 lux in 30- to 40-minute exposure sessions, with remission rates of approximately 75%, matching the most successful 2500-lux, 2-hour studies.[37,63] At these short durations, both dim light (400 lux) and lower-level bright light (3000 lux) were significantly less effective.

Until recently, individual studies of light therapy with standard fluorescent light boxes were limited by small sample sizes and did not consistently demonstrate time-of-day effects. The lack of convincing placebo controls led to controversy about whether improvement reflected the specific action of light. These problems have been successfully addressed in a set of three large clinical trials (for a summary, see Table 121–2).[38-40]

Eastman's group[39] administered light in the morning or evening, and an inert placebo (inactive negative ion generator), to parallel groups. Although all groups showed progressive

Table 121–2. Summary of Remission Rates in Controlled Clinical Trials of Bright Light Therapy for Seasonal Affective Disorder

	Remission Rate* (%/No. of Patients)		
Negative Ion Generator	**Morning Light**	**Evening Light**	**Placebo**
Terman et al.[38†]			
First treatment	54 (25/46)	33 (13/39)	11 (2/19)
Crossover	60 (28/47)	30 (14/47)	ND
Eastman et al.[39‡]			
First treatment	55 (18/33)	28 (9/32)	16 (5/31)
Lewy et al.[40§]			
First treatment	22 (6/27)	4 (1/24)	ND
Crossover	27 (14/51)	4 (2/51)	ND

From Wirz-Justice A. Beginning to see the light. Arch Gen Psychiatry 1998;55:861–862. Copyright 1998, American Medical Association.

*Baseline-to-posttreatment score reduction of ≥50%, with final score ≤8, on the Structured Interview for the Hamilton Depression Scale–Seasonal Affective Disorder Version (SIGH-SAD).

†6-year study; 10,000 lux for 0.5 h, 2 weeks.

‡6-year study; 6000 lux for 1.5 h, 4 weeks.

§4-year study; 2500 lux for 2 h, 2 weeks.

ND, not done

improvement over 4 weeks, patients administered morning light were most likely to show remissions, exceeding the placebo rate. Lewy's group[40] conducted a crossover study of morning and evening light. Although there was no placebo control, morning light proved to be more effective than evening light. Terman's group[38] performed both crossover and balanced parallel-group comparisons, which included nonphotic control groups that received negative air ions at a low or high concentration. Morning light produced a higher remission rate than evening light and the putative placebo, low-density ions. However, the response to evening light also exceeded that for placebo. Indeed, in the trials of both Lewy's group[40] and Terman's group,[38] a minority of patients responded preferentially to evening light.

Figure 121–4 presents sleep and light exposure logs for three patients who received 10,000-lux light treatment in 30-minute sessions. Treatment schedules were determined according to reported sleep habits and daytime commitments. The patients were urged to maintain consistent sleep times whether on or off treatment, waking up shortly before the time planned for morning treatment and keeping free a block of time for evening treatment at least 2 hours before bedtime. However, the patients often showed variations in sleep pattern that depended on the time of treatment (morning or evening), treatment response, and washout periods.

CASE EXAMPLE 7: Selective Antidepressant Response to Morning Light

Patient S.H. (see Fig. 121–4A) was depressed at baseline, showed middle insomnia, and overslept on weekends. During the course of evening light treatment, sleep onset was gradually delayed, with reduced insomnia, but she remained depressed. In contrast, under morning light treatment, sleep onset returned to the baseline pattern and sleep interruptions were largely eliminated, but sleep onset became earlier and duration became longer. Nevertheless, the depression remitted.

CASE EXAMPLE 8: Selective Antidepressant Response to Morning Light

Patient A.R. (see Fig. 121–4B), although depressed at baseline, showed fragmented sleep including napping, with highly variable total sleep duration. Under morning light, napping was eliminated, and although there was some late insomnia, the depression remitted. Under evening light—which failed clinically—sleep duration increased without a marked delay in sleep onset, and there were interruptions during the second half of sleep.

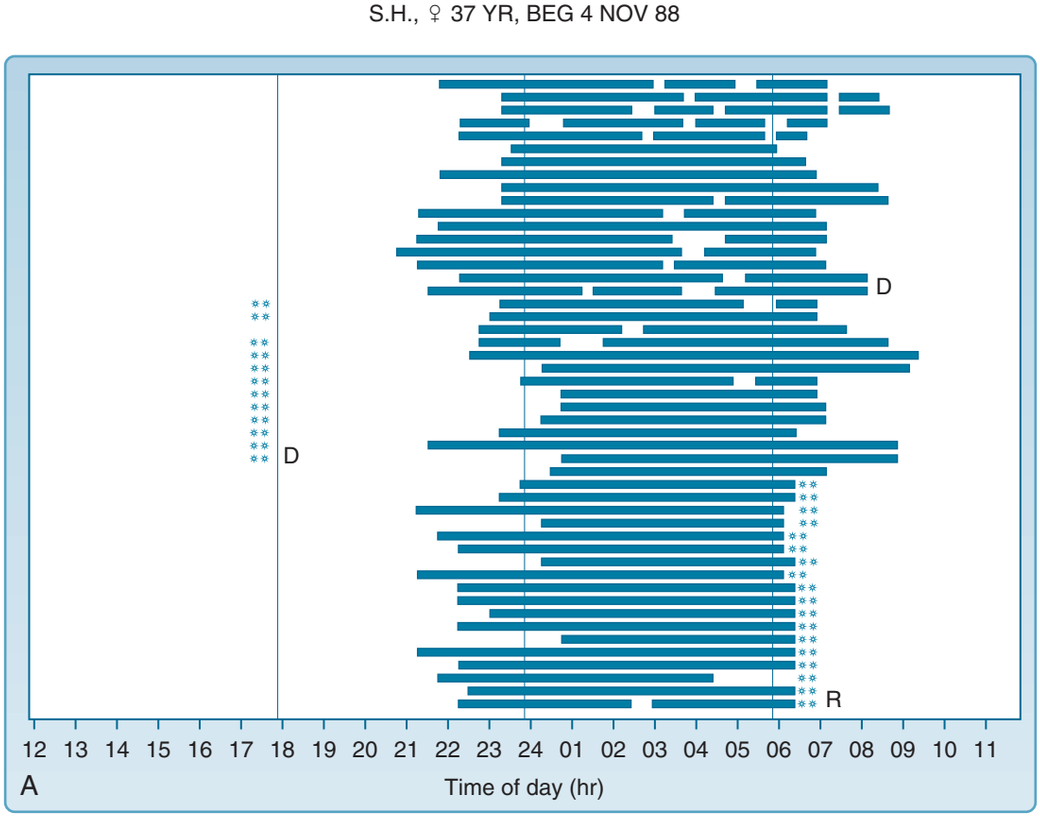

Figure 121–4. Self-report sleep records for three patients with winter depression, during baseline, light treatment, and withdrawal periods, for patients S.H. (**A**), A.R. (**B**), and D.F. (**C**). *Bars* indicate intervals of sleep (including naps); *sun symbols* indicate 15-min segments of bright light exposure. Clinical state is noted at the end of each period. *D*, depressed; *R*, responded (for quantitative criteria, see Terman et al.[58]). *Continued*

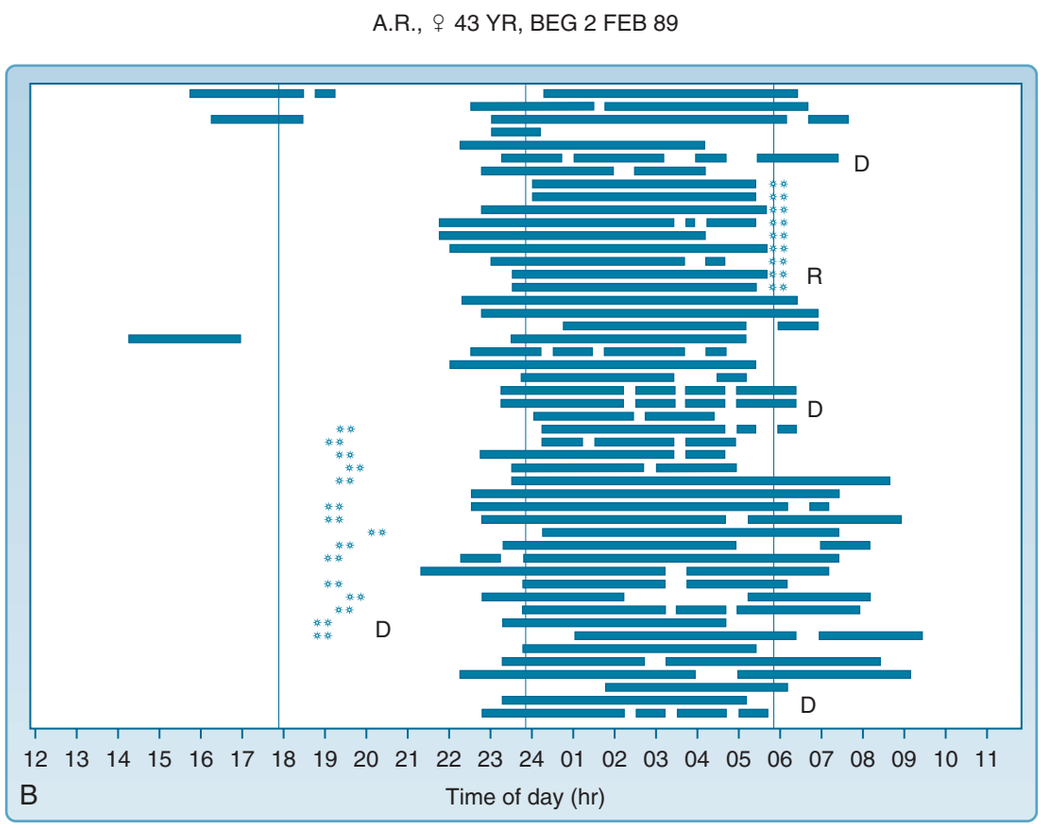

Figure 121–4. Cont'd.

CASE EXAMPLE 9: Nondifferential Antidepressant Response to Morning and Evening Light

Patient D.F. (see Fig. 121–4C) was monitored only briefly at baseline but reported consistent hypersomnia (subsequently also observed during washout phases) and agreed to attempt a 10:30 PM to 7:30 AM sleep schedule. Under evening light, tested twice, both sleep onset and time of arising were delayed relative to target, but sleep did not overshoot 9:30 AM. On both trials of evening light, the depression remitted. Over two washouts, sleep duration gradually increased, with relapse of depressive symptoms. Under morning light—which also was successful—the patient succeeded in advancing his wake-up time by several hours and was able to fall asleep, on target, at 10:30 PM, for modestly reduced sleep duration of 9 hours. Even though treatment was effective at both times of day, the patient preferred morning because of increased opportunity for activities given the earlier time of arising.

In summary, a lack of clinical response to evening light (patients S.H. and A.R.) appears to be correlated with delayed sleep onset, time of arising relative to baseline, or both. Morning light, which was uniformly effective, served to truncate morning sleep; in some cases, sleep onset also advanced, conserving sleep duration, whereas in others, duration decreased only modestly. Although baseline patterns of interrupted sleep often disappeared under effective treatment, initial, middle, or late insomnia sometimes emerged during treatment. These symptoms may be signs of light overdose that can be eliminated by reducing light intensity or duration (see Side Effects of Exposure to Bright Light) or by scheduling evening sessions earlier or morning sessions later.

Subsyndromal Seasonal Affective Disorder

The phenomenology of subsyndromal SAD, or winter doldrums, is similar to that of SAD, although major depression is absent. However, the presence and severity of atypical neurovegetative symptoms (including food cravings and difficulty awakening) can be similar to those in SAD, as can fatigability (leading to characterization as a seasonal anergic syndrome).[64] Clinical trials have demonstrated significant improvement with bright light therapy,[65] as well as dawn simulation therapy,[66] for subsyndromal SAD. For bright light, optimum light scheduling and dose appear to be similar for subsyndromal SAD and SAD; in other words, the lower severity of depressed mood does not imply that a lower light dose will be sufficient to relieve symptoms.

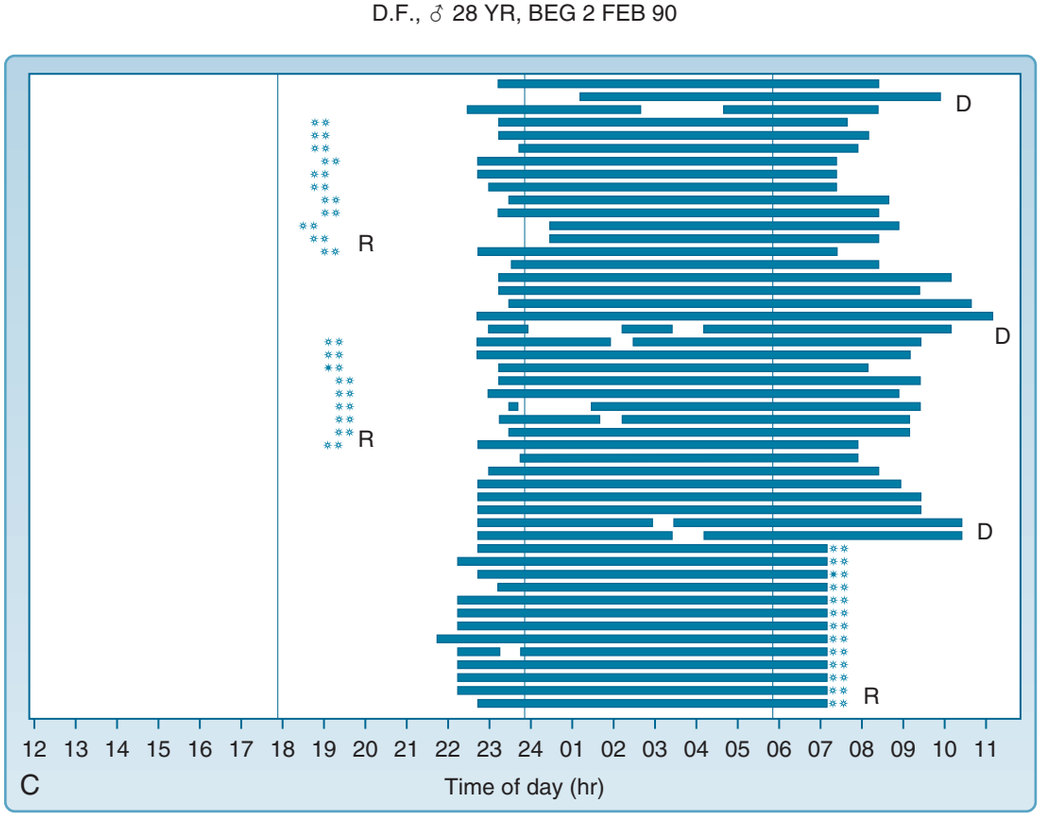

Figure 121–4. Cont'd.

FURTHER APPLICATIONS OF LIGHT THERAPY

Nonseasonal Depression

Beyond its established application for SAD, light therapy for nonseasonal depression appears both safe and effective. Kripke[67] compared several controlled trials in terms of the relative benefit of light versus placebo, and with light for as little as 1 week the results fell within the range of classic antidepressant drug studies of 4-16 weeks.

For example, a Japanese study of nonseasonal major depression gave 7 days of light therapy to 27 subjects, admitted as inpatients for the study, and obtained a benefit of 24% over a dim light placebo.[68] However, morning or evening exposure times showed no difference, nor did phase shifts of body temperature relate to clinical improvement. Goel and colleagues[69] gave 5 weeks of morning bright light therapy (10,000 lux, 60 minutes) to outpatients with chronic major depression lasting 2 years or longer. The study subjects experienced a remission rate of 50%; a control group given low-density negative air ionization showed only minor improvement. Using a ceiling-light installation at 3000-4000 lux, a 10-day open-label trial with 28 nonmedicated hospitalized patients in Switzerland resulted in depression rating scale improvement greater than 50% in 17 cases.[70]

Several investigators have combined light with drugs and found accelerated improvement relative to drugs alone (for an early review, see Kasper et al.[71]) and the method already has seen widespread use with European hospital patients.[71a] One such study demonstrated benefit among hospitalized patients with either unipolar or bipolar depression who were given 10,000-lux illumination in 30-minute morning sessions, with less improvement at 2500 lux.[72] In Denmark, a large-scale outpatient trial has combined 10,000-lux or 50-lux light therapy with standard sertraline medication.[73] Both remission rate and speed of improvement were greater under the active light condition.

Another study combined light with drugs and a single session of late-night sleep deprivation[74] ("wake therapy") at the start of treatment and achieved marked improvement in 1 day and benefit over a dim light control within 1 week.[75] In Italy, this model has been extended for general inpatient use, following treatment studies of nonseasonal major depression (in conjunction with citalopram medication)[48] and bipolar disorder (in conjunction with lithium)[76] that showed large benefits attributable to morning light exposure. Combined light and wake therapy can be feasibly self-administered at home. One controlled study yielded a remission rate of 43% in a group for whom standard antidepressants and psychotherapy had been deemed inadequate.[77] The recent successful completion of large-scale trials in Europe strongly supports the implementation of adjuvant light and wake therapy for treatment of major depression, with the prospect of reduced duration of hospitalization (F. Benedetti, personal communication).

Antepartum and Premenstrual Depression

Both open-label[78] and controlled[79] studies have successfully employed light therapy for major depression during pregnancy, which offers a safe somatic treatment alternative to antidepressant drugs whether or not the woman has a history of seasonality. Both efficacy and side effects have been shown to be dose-dependent.[79] For example, a nonresponder to 60 minutes of 7000-lux light administered upon awakening for 5 weeks showed full remission when session duration was increased to 75 minutes. A responder who developed irritable hypomania under the same initial treatment conditions became depressed when duration was reduced to 45 minutes but responded without hypomania when duration was increased to 50 minutes.

Although larger-scale, definitive trials are needed, morning light therapy is a viable option for open treatment of antepartum depression. Patients with both seasonal and nonseasonal premenstrual dysphoric disorder (PMDD) or milder premenstrual syndrome (PMS) have responded favorably to 1 week of bright light therapy (2500 lux for 2 hours) during the luteal phase, in a series of clinical trials by Parry and colleagues.[80] A placebo-controlled crossover study showed no difference between morning and evening exposures in 1-month trials, however.[81] Furthermore, bright and dim light had similar effects. By contrast, a 2-month study by Lam and coworkers[82] using 10,000-lux, 30-minute evening light during the luteal phase found significant improvement relative to a dim light control, with alleviation of both depressed mood and physical symptoms. Although larger controlled trials are needed and the relative advantage of morning light awaits investigation, Lam's method is a viable option for the open treatment of PMDD and PMS, especially for women who have not responded to medication.

Bulimia Nervosa

Lam and coworkers[83] became interested in this potential application of light therapy when a seasonal mood pattern was noted in many patients with bulimia; beyond the spectrum of SAD symptoms, this included binge eating and purging. In a 2-week crossover study, they showed a marked superiority of morning bright light therapy (30 minutes, 10,000 lux) over dim light, for both mood and bulimic symptoms. Furthermore, a 4-week open-treatment study yielded average reductions of 46% in binge eating and 36% in purging, along with 56% reduction in depression scale scores.[84]

In a placebo-controlled, parallel group study of morning light therapy during the winter months, Braun and colleagues[85] also obtained greater reductions in bingeing and purging under bright light than under a dim-light placebo. Interestingly, their patients did not have comorbid SAD, and mood improvement was unrelated to light intensity. The data thus augur well for the use of light therapy in seasonal bulimia with or without SAD.

Senile Dementia

Numerous small studies have found that symptoms of night wandering, sundowning, and daytime sleep are responsive to bright light therapy. Hospital trials in Japan indicated benefits of morning treatment over 1 month or longer,[86] and evening light exposure also succeeded in reducing disruptive nighttime activity.[87] A further trial of 27 patients ascertained significant increases in actigraphic sleep efficiency, with decreased number of awakenings and daytime napping; there was also a small improvement in cognitive state, although dementia ratings did not change.[88]

In another study, Dutch investigators installed diffuse indirect bright light tested for 2-week intervals in the hospital living quarters of demented patients.[89] Those without severe visual deficit showed significant reductions in day-to-day variability of the rest-activity rhythm (measured by actigraphy), whereas visually impaired patients showed no effect. For long-term management, such whole-room illumination may be more feasible than light boxes for patients with dementia, since light boxes require a stationary posture and direction of gaze. A further possibility is dusk-to-dawn simulation: When administered for 3 weeks at the bedside, it yielded trend improvements in sleep-onset latency, sleep duration, and nocturnal activity.[90]

In a crossover study of bright versus dim morning light therapy given for 4 weeks to patients with agitation, the active treatment selectively increased total nighttime sleep by nearly 2 hours, although agitation failed to improve.[91] Mishima et al.[92] distinguished patients with Alzheimer's-type from those with vascular dementia. After 2 weeks of morning bright light therapy, significant reduction in nocturnal activity was limited to the latter group, while neither group responded to dim light. A recent Norwegian 2-week open-label trial of 2-hour morning bright light exposure achieved the most dramatic improvement thus far.[93] Eleven patients with baseline actigraphic sleep efficiency averaging 73% improved to 86% within 2 weeks and nocturnal wake time reduced by 2 hours. Remarkably, post-treatment benefits lasted one month or longer.

All these very promising leads must be tempered by the results of the largest controlled trials to date, by Ancoli-Israel's group in San Diego. In one trial of 72 demented nursing home patients, separate groups received morning or evening bright light (2 hours, 2500 lux) or evening dim red light (<50 lux) for 10 days.[94] Actigraphic analyses found no improvement in nighttime sleep or daytime activity, even though morning light affected circadian rhythm parameters. A second trial of 92 patients with agitated behavior compared morning or evening bright light or morning dim red light (<300 lux).[95] Raters could not detect improvement in agitation under any condition, even though morning light phase-shifted the daily cycle of agitated behavior.

In summary, although we are impressed by the research activity in this very difficult area, the key to effective treatment has been elusive. Factors of diagnostic heterogeneity, stage and severity of disease, circadian system status, ocular status, optimal timing of light treatment, and exposure parameters and duration of treatment still need to be sorted out.[95a]

Shift Work Adjustment

Most research has focused on laboratory simulation studies in which sleep patterns and circadian measures can be closely monitored, work assignments can be kept simple and constant, and the interferences of family obligations and distractions can be minimized.[96] There have been few field tests, although bright light exposure regimens have been developed to phase shift circadian rhythms into synchrony with shift

work schedules, either as a preparatory measure,[97] during the shift itself,[98] or both.[98a]

Eastman's group has pioneered simulation protocols that accelerate circadian phase delays by carefully timed light exposure in combination with light restriction, using filtered lenses during the morning commute home and when outdoors and fully darkened bedrooms during daytime sleep.[99] This combination of interventions, they have shown, specifically benefits subjects with relatively early baseline circadian phase, for whom the phase delay presents the greatest challenage.[100] The model has been successfully applied to night-shift nurses, who have shown increased alertness,[100a] and achieved virtually complete reentrainment given bright nighttime light exposure timed for phase delays.[101] However, performance benefits have not yet been demonstrated.

The feasibility of these approaches for industrial shift workers has been questioned. The attempted reentrainment can be incompatible with standard rapid rotation schedules, further exacerbating worker distress. Additionally, most shift workers choose to revert to a normal schedule on days off, which jeopardizes their workweek adjustment with incompatible patterns of light exposure. Potential adverse long-term consequences of repeated shifts under lighting protocols have not been evaluated.

Even with complete reentrainment, it has not been demonstrated that night-shift performance is significantly enhanced. After one early field test in which the lighting regimen succeeded in suppressing nocturnal melatonin, shifting rhythms, and increasing subjective alertness, most workers recommended against continuing the protocol.[102] A major complaint was difficulty readapting to their daytime routine. A North Sea oil platform trial successfully addressed this problem by using light to reentrain workers after they returned home; however, the treatment did not benefit initial adaptation to the night shift.[103]

A priority is to demonstrate that light-guided phase shifting does in fact enhance night shift performance. If it does, the procedure might be acceptably imposed on workers in critical occupations (hospital, military, power station), whether or not it is subjectively favored. An alternative approach would be to increase nighttime illumination only moderately, without imposing large circadian phase shifts.[96,104]

Jet Lag Adjustment

Although laboratory simulation paradigms for jet lag and shift work adjustment correspond closely, in the field, geographic relocation has the advantage of establishing a new, consistent light-dark cycle without competing day-night cues.[96] However, jet lag is also compounded by travel stresses (e.g., in-flight sleep disruption) beyond circadian phase displacement. Timing recommendations for natural and artificial bright light exposure (and light avoidance), which vary with direction and distance of travel, have been generated to accelerate circadian rhythm reentrainment based on properties of the phase response curve.[105,106] Although there have been anecdotal successes with such strategies, both laboratory and field trials have had equivocal success (for a review, see Samel and Wegmann[107]).

One positive lead comes from a polysomnographic study of four subjects before and after a Tokyo-to-San Francisco flight.[108] Two of them, who received 3 hours of bright light at 11 AM (3 AM Tokyo time) for 3 days after arrival, showed enhanced sleep efficiency compared with the other two, who received dim light.

In a Zurich-to-New York trial, Boulos and coworkers[7] provided 20 subjects with a bright or dim head-mounted unit on the first two evenings after arrival. The bright-light group showed significantly larger phase delays in melatonin onset, but behavioral indices of jet leg, including actigraphic sleep efficiency, showed little benefit. At this writing, Boulos's group is proceeding with a bidirectional trial, New York-to-Zurich-to-New York, using an enhanced head-mounted device for within-subject ascertainment of both eastward and westward jet lag adjustment.

OFFICIAL RECOMMENDATIONS AND GUIDELINES

Society for Light Treatment and Biological Rhythms

The Society for Light Treatment and Biological Rhythms (SLTBR) was the first organization to conduct a consensus-building process for clinical applications of light therapy and safety issues, with recommendations published in 1991.[109] Clinical trials completed by that time had already demonstrated efficacy for SAD and probable efficacy for subsyndromal SAD. Furthermore, the report cited "ample evidence that light can advance, delay, and entrain human circadian rhythms" (p. 47)[109] based on timing of exposure according to human phase-response curves. Basic safety standards for light-therapy devices were outlined, including control of thermal and short wavelength radiation (ultraviolet and blue) through appropriate choice of lamp and filtering and evaluation of patients' oculoretinal status.

U.S. Public Health Service Agency for Health Care Policy and Research

In 1990, the Depression Guidelines Panel of the U.S. Public Health Service Agency for Health Care Policy and Research (now, Agency for Health Care Research and Quality) commissioned a critical review of clinical trials of light therapy,[110] and in 1993 the panel issued guidelines for the treatment of SAD in primary care practice. The guidelines include the treatment for subsyndromal SAD: "Light therapy is a treatment consideration only for well-documented mild to moderate seasonal, nonpsychotic, winter depressive episodes in patients with recurrent depressive or bipolar II disorders or milder seasonal episodes" (p. 102).[111] The panel cautioned against unsupervised treatment: "It should be administered by a professional with experience and training in its use who deems it suitable for the particular patient" (p. 103).[111] The panel further noted that "light therapy can be useful to augment the response (if partial) to antidepressant medication and vice versa" (p. 103).[111]

American Psychiatric Association

In its 1993 clinical practice guidelines for major depressive disorder,[112] the American Psychiatric Association (APA) noted that "in some patients with [SAD], depressive manifestations respond to supplementation of environmental light by means of exposure to bright white artificial light" (p. 10). Possible side effects were listed, and the APA noted that "no adverse interactions between light therapy and pharmacotherapy have

been identified" (but see Safety of Bright Light for the Eyes). In a 2003 meta-analysis of light therapy studies, the APA Committee on Research in Psychiatric Treatments concluded that "bright light treatment for SAD … and non-seasonal depression [appears] efficacious, with effect sizes equivalent to those found in most antidepressant trials."[113]

American Academy of Sleep Medicine

In 1993, the American Academy of Sleep Medicine (AASM; at that time, the American Sleep Disorders Association) and SLTBR jointly commissioned the Task Force on Light Treatment for Sleep Disorders. The task force published an extensive literature review and critique of the field in the Journal of Biological Rhythms[1] preparatory to review by the AASM Standards of Practice Committee. This committee conducted an evidence-based review of clinical trials of light therapy for the circadian sleep phase disorders, shift work and jet lag disturbances, dementia, and sleep complaints in the healthy elderly. (Guidelines for treatment of depression were deferred to the APA.) In 1999, the committee issued syndrome-specific guidelines, which concluded that "light therapy can be useful in treatment of DSPS and ASPS" (p. 641),[114] but they expressed less confidence in other applications. These guidelines have been incorporated by the National Guidelines Clearinghouse (www.guideline.gov), a collaboration of professional organizations, government agencies, and industry that includes the American Association of Health Plans.

Canadian Consensus Guidelines for the Understanding and Management of Seasonal Depression

Canadian specialists in SAD have published a thorough multicenter critical review (including evidence tables) of SAD diagnosis, epidemiology, pathophysiology, light treatment, medication management, and combination treatment.[115] Level 1 evidence from large, controlled trials was presented to justify recommending that the starting dose for light therapy with a fluorescent light box is 10,000 lux for 30 minutes a day; light boxes should use white, fluorescent light with the UV wavelengths filtered out; and light therapy should be started in the early morning, on awakening, to maximize treatment response.

Cochrane Collaboration

In a 2004 review of 49 randomized, controlled trials of light therapy for nonseasonal depression—most of which applied light as an adjuvant to drug treatment, wake therapy, or both—the reviewers concluded that light therapy "offers modest though promising antidepressive efficacy, especially when administered during the first week of treatment, in the morning, and as an adjunctive treatment to sleep deprivation responders. Hypomania as a potential adverse effect needs to be considered. Due to limited data and heterogeneity of studies these results need to be interpreted with caution" (p. 1).[116]

U.S. Food and Drug Administration

Despite the emerging professional consensus, the U.S. Food and Drug Administration (FDA) has not yet approved (or disapproved) light therapy for SAD or for other conditions, in part because the commercial community has yet to file applications for premarket approval. However, the agency intermittently continues to require that individual manufacturers of light therapy apparatuses cease sales and modify advertising copy that contains explicit or implicit medical claims.

The lack of FDA approval has discouraged third-party reimbursement, which, in turn, has limited the number of prospective patients and served to encourage self-treatment by consumers who obtain apparatuses on the open market. (In 1997, the Swiss Federal Department of the Interior mandated insurance reimbursement for light boxes used to treat SAD, although not for other therapeutic applications.[117])

Because regulatory standards have not been issued in the United States, there has been a proliferation of untested commercial products on the market. Some of these products explicitly violate consensus recommendations of the SLTBR, such as lack of lamp protection and UV shielding. There have been several unofficial attempts to promulgate safety standards and advise consumers and physicians (Consumer Reports on Health,[118] SLTBR,[109] and the Center for Environmental Therapeutics; see Resources), but these have had far less impact than marketing initiatives, some of which even have appeared under the guise of "medical education." The development of federal standards remains a priority.

RESOURCES

Tilted, 10,000-lux light boxes with polycarbonate UV filter diffusers are distributed by the nonprofit Center for Environmental Therapeutics (www.cet.org). Short-wavelength protective fit-over wrap-around lenses (product L-58, U-58, or S-58) are distributed by NoIR Medical Technologies, Inc. (www.noir-medical.com).

The *Columbia Eye Examination for Users of Light Treatment* (a structured chart for optometrists and ophthalmologists) and a set of questionnaires and structured interview guides for depressive disorders, written and tested by the Columbia group, is included in the Clinical Assessment Tools Packet distributed by the Center for Environmental Therapeutics. The website also includes an Ask the Doctor forum and on-line assessments of morningness-eveningness chronotype, depression, and seasonality, with individualized feedback.

The Society for Light Treatment and Biological Rhythms (www.sltbr.org) offers a continuing medical education course associated with its annual scientific meeting and hosts a lively listserv for members.

Clinical Pearl

Appropriately timed artificial light exposure can correct sleep-phase maladjustment and counteract seasonal and nonseasonal depression. The clinician's tasks are to determine the interval of the individual patient's "subjective night" and to schedule light at its end for phase advances or at its beginning for phase delays.

Acknowledgments

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