

SECTION 4:

MANAGEMENT ISSUES

SECTION EDITOR: *Raymond W. Lam*

SECTION AUTHORS: *Raymond W. Lam, Anthony J. Levitt, Robert P. Kraus, Rudradeo C. Bowen, Rachel L. Morehouse, Gary Hasey, and Robert D. Levitan*

How do you choose between light therapy and medications?

The current evidence for efficacy of treatments does not conclusively indicate which treatment should be considered “first line” for every patient with SAD. Some experts have suggested that light therapy is the treatment of choice for SAD, given that the response is rapid, that side effects are minimal, and that the effect sizes of light therapy studies have been greater than those in antidepressant studies (Wirz-Justice, 1998). The methodological differences between light therapy and antidepressant studies, however, make it difficult to directly compare results. Different placebo conditions, for example, may engender different expectations by patients and therefore generate different placebo responses. There are more studies demonstrating efficacy of light therapy than of antidepressants, but the antidepressant studies have larger sample sizes. All of the light-box studies have been conducted at single centres, whereas the antidepressant studies were multicentre trials. Multicentre study designs usually show greater variability of results and, hence, smaller effect sizes. One advantage of multicentre studies is that results may be more generalizable to clinical practice.

Unfortunately, there is only one published study directly comparing light therapy and antidepressants. Ruhrmann and colleagues (1998) conducted a study comparing bright-light therapy (3,000 lux for two hours per day) plus pill placebo to fluoxetine at 20 mg per day plus dim-light therapy (100 lux for two hours per day). Twenty SAD patients in each condition were treated for five weeks. The response rates (defined as greater than 50% reduction in SIGH-SAD scores) were not significantly different between bright-light therapy (70%) and fluoxetine (65%). When defining strict remission rates (posttreatment SIGH-SAD scores in the normal range), there was a trend ($p > 0.10$) to superiority of the

light therapy (50%) over fluoxetine (25%). However, the small sample size in this study limited the ability to determine a true difference between treatments.

Without direct comparisons showing clear superiority in efficacy, tolerability, or safety of one treatment over another, the decision for first-line treatment must be based on an individual assessment of benefits and risks and on patient preference. Factors to consider when making this decision are summarized in Table 6 and discussed below. Note that none of these factors is absolute. For a given patient, the relative importance of each factor should be taken into account.

In patients with less severe depression, in whom compliance is reasonable, light therapy can be considered as the first choice for treatment. Patients with atypical symptoms of depression may have better responses to light therapy, whereas those with more melancholic features may

Table 6

Factors to consider in the choice between light therapy and antidepressant medications as first-line treatments

Light therapy	Medications
<ul style="list-style-type: none"> • Depression less severe • More atypical symptoms • Good compliance for light therapy 	<ul style="list-style-type: none"> • More severe depression • More melancholic symptoms • Low interest or motivation for light therapy • Light therapy too inconvenient
<ul style="list-style-type: none"> • Warrants nonpharmacological treatment (e.g., pregnancy, breast feeding) 	
<ul style="list-style-type: none"> • Able and willing to make time commitment for light therapy 	<ul style="list-style-type: none"> • Unable to make time commitment for light therapy
<ul style="list-style-type: none"> • Relative contraindications to drug therapy (e.g., hepatic disease, allergies) 	<ul style="list-style-type: none"> • Relative contraindications to light therapy (e.g., retinal disease, photosensitizing drug)
<ul style="list-style-type: none"> • Intolerant to medication side effects 	<ul style="list-style-type: none"> • Intolerant to light therapy side effects
<ul style="list-style-type: none"> • Assessing costs: greater initial cost but less expensive ongoing costs 	<ul style="list-style-type: none"> • Assessing costs: less initial cost but greater ongoing costs
<ul style="list-style-type: none"> • Assessing costs: light box covered by insurance? 	<ul style="list-style-type: none"> • Assessing costs: medications covered insurance?

Note: None of the factors is absolute.

not respond as well (Terman et al., 1996) and may do better with medications. For more severe depressions, medication alone, or a combination of antidepressants and light therapy, is recommended. A study of fluoxetine found greater separation between active drug and placebo in those patients who were more severely depressed (Lam et al., 1995). The advantage of combining treatments is that some patients may experience more rapid responses to the light therapy, but if not, then treatment with an antidepressant would not be delayed. Severely depressed patients, however, usually have greatly impaired energy and motivation, so they find it difficult to obtain and use a light box. Family support is usually required to include light therapy in the treatment regimen. The disadvantage of combining treatments, however, is that one cannot be sure which treatment is actually producing the clinical responses or side effects (see next subsection).

Patient preference and compliance are also very important factors. Many patients prefer a nonpharmacological treatment, and light therapy is an understandable treatment that “makes sense” to SAD patients. Women of child-bearing age are particularly interested in nondrug treatments, even though there are no data on effects of light therapy during pregnancy, or on the fetus, or with breastfeeding. On the other hand, light therapy involves a commitment to spend at least 30 minutes a day, even with the newer protocols, under a light box. Many patients find this commitment inconvenient, and medications are a better choice for them.

Side effects should also be considered when deciding on a treatment. Although the newer medications are well tolerated by most patients, the side effects of light therapy are generally more mild than those of antidepressants. Some patients have risk factors for using light therapy, such as retinal disease or use of photosensitizing medications, and others have risk factors for use of antidepressants, such as medication sensitivity, liver disease, or potential drug interactions.

Cost is another issue for many patients. Commercial light boxes cost between CDN\$300 and CDN\$500. Although this is the equivalent of the cost of one season’s treatment with the newer antidepressants, the light box is potentially more cost effective because it can be used over many seasons. However, light boxes may not be covered under health insurance plans, whereas most of the costs of some medications are reimbursed. Some patients may not be able to afford a light box if they are not covered by insurance. Others may not be covered for medications, so the light box is less expensive in the long run.

When should you combine medications and light therapy?

There are no studies of combined treatment with light therapy and antidepressants. For the vast majority of patients with SAD who are receiving treatment for the first time, it makes the most clinical sense to start one treatment – either light therapy or antidepressant medications. Commencing both simultaneously introduces clinical confusion in terms of determining which treatment has been beneficial and/or which treatment has produced side effects. Furthermore, if the treatment is only partially effective, it may not be clear which treatment to alter. Finally, as detailed in the “ocular effects” subsections, some antidepressants or psychotropic medications may increase the risk of ocular complications of light. However, there are circumstances when both light therapy and antidepressants may be given at the same time, and they are outlined below.

For patients who are already taking an antidepressant that is only partially effective, adding light therapy is an option. In this case, the usual dose of light therapy is used, and the antidepressant dose does not usually need to be reduced. When the combination is effective, some clinicians will recommend that patients remain on both treatments for the duration of the treatment. Alternatively, it may be possible to reduce and discontinue the antidepressant and to remain on the light therapy alone. However, the opportunity to treat winter depression is limited by the duration of episodes. By the time that a patient has sought treatment, failed to completely respond to an antidepressant, and undergone a trial of light therapy, the winter is usually over. In addition, if the patient relapses following cessation of the antidepressant, then there is usually little time left to reintroduce the antidepressant. Therefore, most patients will remain on the combination for the duration of the winter season. In contrast to discontinuing the antidepressant, there is no utility in discontinuing the light therapy and having the patient remain on the antidepressant alone, since the antidepressant alone was insufficient in the first place.

For patients who are already receiving light therapy that is only partially effective, it may also be reasonable, once every effort has been made to optimize the light therapy, to add an antidepressant (see “How do you manage patients who do not respond to light therapy?”). There does not need to be a dose reduction in light, and usual doses of antidepressant may be given. The issue of what to do when a patient responds is similar to that described in the previous paragraph: it is most reasonable to keep the patients on both treatments until the end of the

treatment period, but some clinicians may also suggest to patients that the light therapy be tapered or withdrawn. In this circumstance, since any effects of light therapy are quickly lost but also quickly regained, a trial discontinuation of light therapy may be a reasonable alternative.

For patients who have demonstrated a partial response to light therapy alone and a partial response to antidepressant alone in the past, using the combination may provide a more robust antidepressant effect, and the combination may allow lower doses of antidepressant to be used. The combination treatment is especially useful for patients who have been unable to take full doses of antidepressants due to side effects.

For some patients who have failed to respond to a variety of treatments for SAD and have a significant treatment-resistant form of the disorder, using a combined treatment may prove helpful. For highly treatment-resistant patients, it may also be reasonable to commence both treatments simultaneously, since these patients may be severely ill and have prolonged dysfunction. When commencing treatment simultaneously, it is usually wise to commence the antidepressant at a lower dose and increase it more cautiously.

Recommendations: Light Therapy, Antidepressants, or Both?

There are only preliminary studies comparing the efficacy of light therapy and antidepressants, no studies of combined treatment, and therefore few data to guide decisions about the first-choice treatment. Recommendations are therefore based on clinical experience and panel consensus. [Level 5 evidence]

- (1) Factors to consider when deciding on a first-line treatment include severity of depression, symptom profile, side effects, safety, patient preference, patient compliance, and cost.
 - (2) Generally, one treatment should be used at a time to minimize clinical confusion about the therapeutic effects and the side effects of treatment.
 - (3) Clinical situations in which combined light therapy and antidepressants would be considered include (a) partial response to light therapy alone, (b) partial response to antidepressants alone, (c) partial response to light therapy or antidepressants in past episodes, and (d) severe or treatment-refractory depression associated with prolonged dysfunction.
-

How long is an adequate trial of light therapy or medications?

The data are unclear about the optimal length of a trial of light treatment. Most studies have used a treatment length of one week, with fewer studies using two-week trials (Labbate et al., 1995) or longer (Bauer et al., 1994; Eastman et al., 1992; Eastman et al., 1998; Ruhrmann et al., 1998). One study (Labbate et al., 1995) showed that the response rates and remission rates were higher after two weeks (65% and 62% respectively) than after one week (62% and 27% respectively). After two weeks, but not after one week, 15% of the patients showed a response. The longer studies (four- and five-week studies) also suggest that a longer length of treatment results in a greater proportion of subjects responding (Bauer et al., 1994; Eastman et al., 1998; Ruhrmann et al., 1998). However, other studies show no advantage to light treatment beyond two weeks (Terman et al., 1998). There is a suggestion that recovery from atypical symptoms may be slower than recovery from more typical symptoms (Terman et al., 1994).

For those who do not respond optimally after one or two weeks of treatment, the recommendation is to continue acute treatment for up to four weeks. As is consistent with recommendations for nonseasonal depression, one would be more likely to pursue this course if there were at least a partial response in the first two weeks.

In a five-week, double-blind study of fluoxetine and placebo, fluoxetine was not statistically superior on the termination depression scores, but fluoxetine was superior on the rate of clinical responses (Lam et al., 1995). In this study, the placebo and fluoxetine groups started to separate by the fourth week of treatment, but differences were not significant by the fifth week. In an eight-week, placebo-controlled study, sertraline was found to be superior to placebo in both the depression scores and the clinical response rate (Moscovitch et al., 1995). An optimal trial of medication should therefore be at least six weeks long for the acute phase. Of interest for longer trials is that the response rates of both fluoxetine and placebo began to increase by March (Lam et al., 1995). Therefore, the rate of spontaneous remission can increase dramatically after the end of February, so one must be cautious when interpreting results of light or drug treatment in late winter.

How long should a patient with SAD be treated within a season?

The data are sparse for strategies on managing the patient once response occurs. North American reports suggest that rapid relapse is common,

usually within a week or two, after discontinuation of light therapy (Rosenthal et al., 1984a; Terman et al., 1994). In fact, that observation was critical to the successful use of crossover study designs using brief (one-week) treatment lengths in light therapy studies (Terman et al., 1989b). A few European studies, however, suggest that some patients show sustained remission after a brief course of light therapy (Partonen and Lonnqvist, 1995; Wirz-Justice et al., 1986). Others have suggested that a short course of treatment early in the season can have a preventative effect (Meesters et al., 1993a), though this finding has not been consistently replicated (Meesters et al., 1994).

Patients sometimes choose to continue treatment at a reduced schedule. Relapse following discontinuation of treatment is more common if treatment occurs early in the season (Terman et al., 1994), and response is more common if treatment occurs late in the season (Lam et al., 1995). It is possible that hypomania becomes more common the longer that patients are treated with light or medication. One study found that 4 of 12 patients developed hypomanic symptoms during a four-week trial of light therapy, but these symptoms remitted when the daily light exposure was reduced or temporarily discontinued (Bauer et al., 1994). There are also reports of hypomanic responses to antidepressant medications in SAD (Lam et al., 1995).

In the absence of clear data, the clinical opinion of the consensus panel is that treatment for SAD should continue for the duration of the season, until the time of usual spring remission, which should be determined individually. There are no data on discontinuation effects of light therapy or antidepressants in SAD. Light therapy can usually be discontinued abruptly, but clinical experience suggests that antidepressants should be tapered because of possible discontinuation effects, unless there are specific reasons for rapid discontinuation (e.g., allergy or toxicity).

Should treatment continue throughout the summer?

There are currently no published studies in SAD pertaining to either light or antidepressant therapy continuation or maintenance through the summer. The potential benefit, in accordance with maintenance therapy in recurrent unipolar depression (e.g., Kupfer et al., 1992), would be protection against an anticipated depressive episode in the next fall-winter season. Potential disadvantages include lack of need (during spring and summer), cost, inconvenience (light therapy), and risk of exacerbating spring-summer hypomania and/or accelerating cycle frequency.

One small study showed that patients felt slightly better in the summer when off treatment compared to when treated with light therapy during the winter (Postolache et al., 1998). In the absence of relevant data, the consensus panel recommendation is that most patients with a clear diagnosis of SAD can discontinue treatment during the summer and restart it in the autumn/winter.

In some situations, year-round treatment may be indicated. For example, patients may have difficulty recognizing early symptoms of depression and miss starting their treatment in the winter, leading to a depressive episode with impairment of function. For others, where compliance is difficult, it may be easier to keep them on an antidepressant medication throughout the year rather than starting and stopping it. Some patients require a longer period to taper medications on and off, and it may be easier simply to continue them throughout the summer. Other patients experience mild, transient symptoms during the summer (especially during extended periods of cloud cover) and find it helpful to use light therapy during those times or to continue their medications.

When should treatment be restarted in the year following successful treatment?

Restarting treatment in subsequent years should be based on individual assessment by the clinician and patient. Many patients are comfortable holding off treatment until first onset of symptoms. This is particularly true for light therapy because many patients experience rapid relief of symptoms. That way, they will not require treatment if they happen to skip a winter depressive episode. Some patients treated with medications, however, will have a two-week to four-week lag time before response. These patients, and those who find it difficult to gauge initial onset of symptoms (and thus are at risk of “sliding” into a depressive episode), may wish to start treatment prior to the usual onset of symptoms. For example, patients with predictable time of onset may restart light therapy two weeks prior to the expected onset of symptoms and restart antidepressants four weeks prior to onset. For SAD patients in whom timing of onset varies by several weeks from year to year, treatment can be reinitiated prior to the earliest date that a past episode began. Some may choose to remain on effective treatment year-round for an indefinite period and not bother trying to determine the usual onset of symptoms. Others may choose to “wait and see” if a new winter depressive episode occurs before restarting treatment.

Recommendations: Length of Treatment

- (1) A therapeutic trial of light therapy should be two to four weeks long. [Level 2 evidence]
 - (2) A therapeutic trial of antidepressants should be six to eight weeks long. [Level 2 evidence]
 - (3) Because of risk of relapse, patients should continue with treatment for the entire winter season, until the time of their natural spring or summer remission. Treatment is not generally recommended during the summer months. [Level 2 evidence]
 - (4) Light therapy can be discontinued abruptly. When possible, antidepressants should be tapered instead of abruptly discontinued. [Level 5 evidence]
 - (5) Following a season of successful treatment, the treatment should be restarted in subsequent years either with onset of mild symptoms or in advance of the usual onset of symptoms. [Level 5 evidence]
 - (6) Intermittent light therapy may be helpful during the summer for occasional transient symptoms. [Level 5 evidence]
 - (7) Preventative year-round antidepressant treatment (including the summer) should be considered when (a) patients are poorly compliant or motivated, (b) they take a long time to taper off and on medications, (c) they are unable to recognize early signs and symptoms of depression, (d) they have very early onset or very late offset of symptoms, and (e) they experience transient symptoms during the summer. [Level 5 evidence]
-

How do you manage comorbidity?

Psychiatric comorbidity has been reported in patients with SAD since the syndrome was first described by Rosenthal and colleagues in 1984. Unfortunately, comorbidity has not been well characterized in large studies, and the literature is mostly in the form of single-case reports or small case series. In considering the issue of comorbidity, it may be useful to review the different types of comorbidity:

Type I: A comorbid psychiatric disorder that may also have a seasonal pattern (e.g., seasonal bulimia nervosa or panic disorder).

Type II: A comorbid psychiatric disorder that has no apparent seasonal component (e.g., obsessive compulsive disorder, pain syndromes) worsened by winter depression.

A number of psychiatric disorders may have Type I comorbidity and may be responsive to the same treatments as SAD. The most extensively studied disorder is bulimia nervosa. Over a dozen studies have reported significant seasonal worsening of mood symptoms and eating behaviours (binge eating and purging) (as reviewed in Lam and Goldner, 1998). Comorbid SAD may occur in up to one-third of patients with bulimia nervosa. Two controlled studies of light therapy for bulimia nervosa have shown significant improvement in mood and bulimic symptoms (Blouin et al., 1996; Lam et al., 1994).

Other disorders that may have significant seasonal patterns include premenstrual dysphoric disorder (PMDD, previously known as late luteal phase dysphoric disorder) (Maskall et al., 1997) and panic disorder (Marriott et al., 1994). In a small-sample study of SAD patients, PMDD was the most common comorbid diagnosis, reported in 70% of patients (Partonen and Lonnqvist, 1995). The investigators noted that patients with comorbid PMDD preferred evening light treatment to morning sessions. Response to light therapy in patients with PMDD (not comorbid with SAD) remains controversial, with conflicting results found within the same research group (Parry et al., 1987, 1989, 1993). Comorbid panic disorder was found to occur in 24% of a small sample of 38 consecutive patients with SAD (Halle and Dilsaver, 1993). The panic attacks were present only in the context of depression and were thus restricted to the fall and winter months. A subset of these patients with panic disorder was treated and improved with open-label trials of light therapy or pharmacotherapy.

The specificity of the finding of seasonality in bulimia nervosa, PMDD, and panic disorder is bolstered by data that seasonality is not associated with obsessive-compulsive disorder (Yoney et al., 1991) or anorexia nervosa (Lam et al., 1996a). Of interest is that several of these disorders (e.g., bulimia nervosa, PMDD) share common symptoms (e.g., depressive mood, overeating behaviours, oversleeping) and common treatments (response to SSRI antidepressants and light therapy) with SAD. This commonality has led to speculation that there are common pathophysiological factors, such as serotonergic dysfunction or circadian dysregulation, in their etiologies (Lam and Goldner, 1998).

An example of Type II comorbidity is Axis II (personality) disorders. Personality disorders have been reported in SAD clinic samples, including avoidant personality disorder (Partonen and Lonnqvist, 1995) and other cluster C disorders (includes avoidant, dependent, obsessive-compulsive, and passive-aggressive personality disorders) (Reichborn-Kjennerud et al., 1994). However, the prevalence of personality disorders

was similar to that reported in nonseasonal depression. Follow-up of patients with comorbid avoidant personality disorder found that they often chose to continue light therapy until late spring, suggesting that light therapy may also be treating the mood/temperament component of personality disorder (Partonen and Lonnqvist, 1995). A small, but not statistically significant, decrease in personality disorder diagnoses was noted after light therapy, but the presence of a personality disorder was also associated with a poorer clinical response to light therapy (Reichborn-Kjennerud et al., 1994).

Other evidence for Type II comorbidity comes from scattered case reports of seasonal worsening in disorders such as trichotillomania ($n = 1$), obesity ($n = 4$), cocaine abuse ($n = 2$), and obsessive-compulsive disorder ($n = 1$). Some authors have suggested the possibility that SAD might represent a media-popularized somatoform-spectrum disorder (similar to somatization disorder, environmental hypersensitivity, or chronic fatigue syndrome) (Eastwood and Peter, 1988). There is little support for this view in the literature. Two small case series of SAD with chronic fatigue syndrome (Lam, 1991) and with environmental hypersensitivity and somatization (Hotopf, 1994) found that the patients improved with light therapy. In contrast, one report found that seasonality scores were significantly lower in patients with chronic fatigue compared to patients with SAD, or nonseasonal major depression, or atypical depression (Zubieta et al., 1994). However, a more extensive study showed that up to 37% of patients with chronic fatigue syndrome have a pattern of atypical symptoms that is indistinguishable from SAD (Terman et al., 1998b). Furthermore, the seasonal-pattern patients were more likely to have experienced a recent major depressive episode than the nonseasonal patients. Thus, chronic fatigue syndrome may be an example of Type I comorbidity.

In summary, comorbidity may be commonly found in SAD, especially with eating disorders (bulimia nervosa), anxiety disorders (panic disorder), and personality disorders. There are few data on management of comorbidity in SAD. Some studies have shown that light therapy may treat both the symptoms of SAD and the symptoms of the comorbid disorder. Some comorbid diagnoses (e.g., personality disorder) may be associated with poorer response to treatment, as found in studies of nonseasonal depression. There are no studies of medication treatment for SAD with comorbid conditions, although many of the comorbid conditions also respond to medications, especially SSRI antidepressants.

The clinical consensus is that comorbid conditions should be identified because these patients may require additional treatment to the primary treatment for SAD. For example, cognitive therapy may be indicated for comorbid panic disorder or bulimia nervosa.

Recommendations: Managing Comorbidity

- (1) Comorbid diagnoses are common with seasonal affective disorder (SAD), especially bulimia nervosa, premenstrual depressive disorder, panic disorder, and personality disorders, but there is insufficient research to determine prevalence rates. [Level 2 evidence]
 - (2) Comorbid diagnoses should be identified because there are treatment implications for these patients:
 - Comorbid diagnoses that also have a seasonal component or pattern may benefit from light therapy (e.g., seasonal bulimia nervosa, seasonal panic disorder). [Level 3 evidence]
 - Comorbid diagnoses may be associated with a poorer treatment response (e.g., personality disorders). [Level 3 evidence]
 - Comorbid diagnoses may require additional treatment specific to that disorder (e.g., cognitive therapy for panic disorder). [Level 5 evidence]
 - Comorbid diagnoses may require combination treatment with light therapy and antidepressants (e.g., bulimia nervosa). [Level 5 evidence]
-

Can psychotherapy serve as an adjunct to light therapy or medications for SAD?

Surprisingly, the use of psychotherapy for SAD has not been the subject of empirical study. Most clinicians agree that counselling and advice for issues such as physical exercise, maintaining a regular sleep-wake cycle (sleep hygiene), and attention to nutrition and stress reduction produce benefits for patients with SAD. Certainly, encouragement to adhere to a schedule for light treatment or to spend more time in bright ambient outdoor light (Wirz-Justice et al., 1996) may lead to disorder-specific improvement. However, there are no data on more formal, manualized psychotherapies such as cognitive-behavioural therapy (CBT) or interpersonal psychotherapy (IPT).

There is considerable evidence showing that nonseasonal depression may improve with brief psychotherapy such as CBT or IPT (for review, see Thase, 1997). These psychotherapies can also be used in conjunction with somatic therapies to enhance compliance or treat residual symptoms. The panel consensus was that psychotherapy might also benefit some patients with SAD. However, the specific type of psychotherapy that may be effective, the duration of treatment, or the relationship between the timing of therapy and the season of onset is not known.

How do you manage patients who do not respond to treatment?

Patients may have a full response, partial response, or nonresponse to treatment. To operationalize these definitions, scores on depression rating scales (e.g., the Hamilton Depression Rating Scale, 29-item SAD version, or the Beck Depression Inventory II) are often used. A clinically significant response to treatment is often defined as greater than 50% reduction in depression scores compared with baseline. Clinical remission is usually defined more strictly, such as greater than 50% improvement in depression scores and a posttreatment depression score that is within the normal range. A partial response can be defined as between 25% and 50% reduction in scores from baseline or as a posttreatment depression score that is still in the symptomatic range. Finally, nonresponse is usually considered to be less than 25% improvement in baseline depression scores.

There are few studies to guide clinical decisions for limited response to treatment, and, indeed, treatment studies use varied definitions for clinical response, making comparisons difficult. The consensus panel recommends a step-by-step approach similar to that described for “treatment resistant depression” (e.g., Thase and Rush, 1997). **Step 1** is to reverify the diagnosis of recurrent major depression with seasonal pattern. **Step 2** is to ensure that an adequate trial of treatment (i.e., an adequate dose and adequate length of time) has occurred and that the patient has adhered to the recommended treatment. **Step 3** is to consider factors that can contribute to treatment resistance. The numerous potential factors may be grouped in six subgroups:

- (1) unrecognized subtype of major depression (e.g., psychotic depression, subtle bipolar II disorder);

- (2) comorbid psychiatric disorders (e.g., undisclosed substance abuse, panic disorder, personality disorder);
- (3) unrecognized medical illness (e.g., subclinical hypothyroidism);
- (4) direct medication effects (e.g., glucocorticoids);
- (5) chronic psychosocial stresses (e.g., ongoing abuse);
- (6) pharmacokinetic or biological interactions with treatment (e.g., is patient a rapid metabolizer of antidepressants? are cataracts interfering with light therapy?)

Once these factors are assessed, specific interventions can be considered for patients who show limited response to either light therapy or antidepressant treatment.

(1) Limited response to light therapy?

The first therapeutic strategy for limited response is to optimize the antidepressant treatment. There are no studies that examine the effects of changing the treatment parameters to optimize light therapy in nonresponders, so recommendations are limited to the clinical opinions of the consensus panel. First, with partial or nonresponse, it is important that the clinician ensure that the patient has had an adequate trial of light therapy (see Section 2). If there is only a partial response after 14 days of adequate light therapy, then there are two treatment options to consider:

- (1) *Increase the "dose" of light.* Increase in dose can be achieved for 10,000 lux light exposure by either increasing the duration of exposure time to as much as 45 minutes or one hour daily by extending the morning session or by adding a second period of light exposure in the afternoon or evening. Alternatively, the dose can be raised by increasing the intensity of the light being received (e.g., if patients are receiving only 2,500 lux light). Some light units have different settings, but for others moving closer to the light source will increase the intensity. Unfortunately, moving closer is an imprecise way of increasing the dose, and often the increased brightness or glare makes this alternative impractical.
- (2) *Change the timing of light.* Although morning light appears to be superior to evening light for many patients, a small number of patients may respond better to evening light (Terman et al., 1990c; Terman et al., 1998). Therefore, if patients do not respond

fully to morning light, then it is reasonable to switch to evening light.

There are few data about managing nonresponders after optimizing light therapy. Only one study has examined the issue of partial responders to light therapy. Open-label l-tryptophan, 1 g t.i.d., was added to light therapy in 14 SAD patients showing no or limited response after two weeks of a standardized trial of light therapy (Lam et al., 1997a). Substantial improvement was found in 9 of the 14 patients with the combination treatment. Another option for partial responders, or patients who experience recurrence of symptoms after an initial response to light, is to add an antidepressant medication, as discussed in the subsection on combination treatment.

If there has been no response to treatment after two weeks of light therapy, then many clinicians recommend that light therapy be discontinued and an alternative treatment (e.g., antidepressant medications) commenced. This recommendation is based on the clinical observations that a majority of patients who eventually respond to light therapy show some response in the first week and that, among patients who fail to show even a partial response at two weeks, few will respond if treatment is extended. Furthermore, such an extension must be balanced against the risk of continued depression. Treatment with antidepressants and other agents is discussed in the section on medications.

(2) Limited response to antidepressants?

When the patient does not respond to an adequate trial of antidepressants, with appropriate increases in dose, the consensus panel recommends trying a combination of light therapy with the (previously ineffective) antidepressant as the first change in management. If this approach proves unsuccessful, then the light therapy should be discontinued and the usual stepwise approach for managing treatment-resistant depression (e.g., augmentation, switch to an antidepressant of a different class, combination with other antidepressants, electroconvulsive therapy, etc.) may need to be employed. Due to the (relatively) short seasonal length of the depression in such patients, the depressive symptoms should begin to lift before such alternative strategies can be systematically tried. In this case, the process may need to “start where last left off” during the next fall-winter depression, until an effective approach is reached.

Recommendations: Managing Limited Treatment Response

Because of lack of data, recommendations are based on clinical experience and panel consensus – that is, Level 5 evidence.

- (1) Patients showing limited response to treatment should first be evaluated to ensure that they have adequate dosing of treatment (light therapy or medications) and that they are compliant with treatment.
 - (2) If treatment is adequate, then patients should be evaluated for factors that may contribute to a poor response, including depression subtypes, psychiatric comorbidity, unrecognized medical illness, other medication effects, chronic psychosocial stresses, and specific factors that interfere with treatment.
 - (3) Strategies for dealing with partial responses to light therapy include increasing the dose, changing the timing, and trying alternative therapies, such as l-tryptophan augmentation or combining with antidepressants.
 - (4) Strategies for dealing with partial responses to antidepressant medications include combining with light therapy, switching to another antidepressant, augmenting with another agent, combining with other antidepressants, and electroconvulsive therapy.
 - (5) In dealing with patients with refractory illness, it is important to take a methodical, stepwise approach with clear documentation of treatments.
 - (6) Psychological treatments, such as cognitive-behaviour therapy or interpersonal therapy, may be of benefit in some patients with SAD. Until evidence is accrued, psychotherapy cannot be considered a first-line treatment for SAD.
-

References

- Bauer MS, Kurtz JW, Rubin LB, Marcus JG. Mood and behavioral effects of four-week light treatment in winter depressives and controls. *J Psychiatr Res* 1994; 28:135-45.
- Blouin AG, Blouin JH, Iversen H, Carter J, Goldstein C, Goldfield G, Perez E. Light therapy in bulimia nervosa: a double-blind, placebo-controlled study. *Psychiatry Res* 1996; 60:1-9.
- Eastman CI, Lahmeyer HW, Watell LG, Good GD, Young MA. A placebo-controlled trial of light treatment for winter depression. *J Affect Disord* 1992; 26:211-21.

- Eastman CI, Young MA, Fogg LF, Liu L, Meaden PM. Bright light treatment of winter depression: a placebo-controlled trial. *Arch Gen Psychiatry* 1998; 55:883-9.
- Eastwood MR, Peter AM. Epidemiology and seasonal affective disorder. *Psychol Med* 1988; 18:799-806.
- Halle MT, Dilsaver SC. Comorbid panic disorder in patients with winter depression. *Am J Psychiatry* 1993; 150:1108-10.
- Hotopf M. Seasonal affective disorder, environmental hypersensitivity and somatisation. *Br J Psychiatry* 1994; 164:246-8.
- Kupfer DJ, Frank E, Perel JM, Cornes C, Mallinger AG, Thase ME, et al. Five-year outcome for maintenance therapies in recurrent depression. *Arch Gen Psychiatry* 1992; 49:769-73.
- Labbate LA, Lafer B, Thibault A, Rosenbaum JF, Sachs GS. Influence of phototherapy treatment duration for seasonal affective disorder: outcome at one vs. two weeks. *Biol Psychiatry* 1995; 38:747-50.
- Lam RW. Seasonal affective disorder presenting as chronic fatigue syndrome. *Can J Psychiatry* 1991; 36:680-2.
- Lam RW, Goldner EM. Seasonality of bulimia nervosa and treatment with light therapy. In Lam RW (ed). *Seasonal Affective Disorder and Beyond: Light Treatment for SAD and Non-SAD Conditions*. Washington, DC: American Psychiatric Press, 1998. 193-220.
- Lam RW, Goldner EM, Grewal A. Seasonality of symptoms in anorexia and bulimia nervosa. *Int J Eat Disord* 1996a; 19:35-44.
- Lam RW, Goldner EM, Solyom L, Remick RA. A controlled study of light therapy for bulimia nervosa. *Am J Psychiatry* 1994; 151:744-50.
- Lam RW, Gorman CP, Michalon M, Steiner M, Levitt AJ, Corral MR, Watson GD, Morehouse RL, Tam W, Joffe RT. Multicenter, placebo-controlled study of fluoxetine in seasonal affective disorder. *Am J Psychiatry* 1995; 152:1765-70.
- Marriott PF, Greenwood KM, Armstrong SM. Seasonality in panic disorder. *J Affect Disord* 1994; 31:75-80.
- Maskall DD, Lam RW, Misri S, Carter D, Kuan AJ, Yatham LN, Zis AP. Seasonality of symptoms in women with late luteal phase dysphoric disorder. *Am J Psychiatry* 1997; 154:1436-41.
- Meesters Y, Jansen JH, Beersma DG, Bouhuys AL, Van den Hoofdakker RH. Early light treatment can prevent an emerging winter depression from developing into a full-blown depression. *J Affect Disord* 1993a; 29:41-7.
- Meesters Y, Jansen JH, Beersma DG, Bouhuys AL, Van den Hoofdakker RH. An attempt to prevent winter depression by light exposure at the end of September. *Biol Psychiatry* 1994; 35:284-6.
- Moscovitch A, Blashko C, Wiseman R, Eagels J, Darcourt G, Thompson C, Kasper S, Patten S. A double-blind, placebo-controlled study of sertraline in patients with seasonal affective disorder. *New Research Abstracts*, 151st meeting of the American Psychiatric Association, 1995.
- Parry BL, Berga SL, Mostofi N, Sependa PA, Kripke DF, Gillin JC. Morning versus evening bright light treatment of late luteal phase dysphoric disorder. *Am J Psychiatry* 1989; 146:1215-7.

- Parry BL, Mahan AM, Mostofi N, Klauber MR, Lew GS, Gillin JC. Light therapy of late luteal phase dysphoric disorder: an extended study. *Am J Psychiatry* 1993; 150:1417-9.
- Parry BL, Rosenthal NE, Tamarkin L, Wehr TA. Treatment of a patient with seasonal premenstrual syndrome. *Am J Psychiatry* 1987; 144:762-6.
- Partonen T, Lonnqvist J. The influence of comorbid disorders and of continuation of light treatment on remission and recurrence in winter depression. *Psychopathology* 1995; 28:256-62.
- Postolache TT, Hardin TA, Myers FS, Turner EH, Yi LY, Barnett RL, et al. Greater improvement in summer than with light treatment in winter in patients with seasonal affective disorder. *Am J Psychiatry* 1998; 155:1614-6.
- Reichborn-Kjennerud T, Lingjaerde O, Dahl AA. Personality disorders in patients with winter depression. *Acta Psychiatr Scand* 1994; 90:413-9.
- Rosenthal NE, Sack DA, Gillin JC, Lewy AJ, Goodwin FK, Davenport Y, Mueller PS, Newsome DA, Wehr TA. Seasonal affective disorder: a description of the syndrome and preliminary findings with light therapy. *Arch Gen Psychiatry* 1984a; 41:72-80.
- Ruhrmann S, Kasper S, Hawellek B, Martinez B, Hoefflich G, Nickelsen T, Moeller H-J. Effects of fluoxetine versus bright light in the treatment of seasonal affective disorder. *Psychol Med* 1998; 28:923-33.
- Terman M, Amira L, Terman JS, Ross DC. Predictors of response and nonresponse to light treatment for winter depression. *Am J Psychiatry* 1996; 153:1423-9.
- Terman M, Levine S, Terman JS, Doherty S. Chronic fatigue syndrome and seasonal affective disorder: comorbidity, diagnostic overlap, and implications for treatment. *Am J Med* 1998b; 105:115S-24S.
- Terman JS, Terman M, Amira L. One-week light treatment of winter depression near its onset: the time course of relapse. *Depression* 1994; 2:20-31.
- Terman M, Terman JS, Quitkin FM, McGrath PJ, Stewart JW, Rafferty B. Light therapy for seasonal affective disorder: a review of efficacy. *Neuropsychopharmacology* 1989b; 2:1-22.
- Terman M, Terman JS, Rafferty B. Experimental design and measures of success in the treatment of winter depression by bright light. *Psychopharmacol Bull* 1990c; 26:505-10.
- Terman M, Terman JS, Ross DC. A controlled trial of timed bright light and negative air ionization for treatment of winter depression. *Arch Gen Psychiatry* 1998; 55:875-82.
- Thase ME. Psychotherapy of refractory depressions. *Depression and Anxiety* 1997; 5:190-201.
- Thase ME, Rush AJ. When at first you don't succeed: sequential strategies for antidepressant nonresponders. *J Clin Psychiatry* 1997; 58 Suppl 13:23-9.
- Wirz-Justice A. Beginning to see the light. *Arch Gen Psychiatry* 1998; 55:861-2.
- Wirz-Justice A, Bucheli C, Graw P, Kielholz P, Fisch HU, Woggon B. How much light is antidepressant? *Psychiatry Res* 1986; 17:75-6.
- Wirz-Justice A, Graw P, Krauchi K, Sarrafzadeh A, English J, Arendt J, Sand L. "Natural" light treatment of seasonal affective disorder. *J Affect Disord* 1996; 37:109-20.

Yoney TH, Pigott TA, L'Heureux F, Rosenthal NE. Seasonal variation in obsessive-compulsive disorder: preliminary experience with light treatment. *Am J Psychiatry* 1991; 148:1727-9.

Zubieta JK, Engleberg NC, Yargic LI, Pande AC, Demitrack MA. Seasonal symptom variation in patients with chronic fatigue: comparison with major mood disorders. *J Psychiatr Res* 1994; 28:13-22.