Canadian Consensus Guidelines for the Treatment of Seasonal Affective Disorder

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Edited by
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Note: The authors have worked to ensure that all information in this book concerning drug dosages, schedules, and routes of administration is accurate as of the time of publication and that it is consistent with standards set by the Health Protection Branch of Health and Welfare Canada and the general medical community. As medical research and practice advance, however, therapeutic standards may change. For this reason and because human and mechanical errors sometimes occur, we recommend that readers follow the advice of a physician who is directly involved in their care or the care of a member of their family.

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Contents

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Abbreviations Used

5-HT	5 hydroxytryptamine (serotonin)
ACTH	adrenocorticotropic hormone
BDI	Beck Depression Inventory
BDI-II	Beck Depression Inventory, version II
CBT	cognitive behavioural therapy
CES-D	Centres for Epidemiological Studies – Depression
CIDI	Composite International Diagnostic Interview
CRH	corticotropin-releasing hormone
DSM-III-R	Diagnostic and Statistical Manual for Mental Disorders, 3rd edition, revised
DSM-IV	Diagnostic and Statistical Manual for Mental Disorders, 4th edition
EOG	electrooculography
GSS	Global Seasonality Score
HAM-D	Hamilton Depression Rating Scale
HDRS	Hamilton Depression Rating Scale
HMU	head mounted unit
HPA	hypothalamic-pituitary-adrenal
ICD-10	International Classification of Diseases, 10th edition
IOP	intraocular pressure
IPT	interpersonal psychotherapy
ISV	Inventory of Seasonal Variation
LED	light emitting diode
m-CPP	m-chlorophenylpiperazine
MDD	major depressive disorder
MDE	major depressive episode
MeSH	Medical Subject Headings
NIH	National Institutes of Health
NIMH	National Institute of Mental Health
PMDD	premenstrual dysphoric disorder

RCT	randomized controlled trial
RDC	Research Diagnostic Criteria
RMR	resting metabolic rate
SAD	seasonal affective disorder
SCN	suprachiasmatic nucleus
SIGH-SAD	Structured Interview Guide for the Hamilton Depression Rating Scale, SAD version
SP	seasonal pattern
SPAQ	Seasonal Pattern Assessment Questionnaire
S-SAD	subsyndromal seasonal affective disorder
SSRI	selective serotonin reuptake inhibitor
T3	triiodothyronine
T4	thyroxine
TRH	thyroid releasing hormone
TSH	thyroid stimulating hormone

Preface

Dan A. Oren, MD
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The Book of Ecclesiastes records that "there is nothing new under the sun" (1:9). The story of winter depression (seasonal affective disorder) is eloquent testimony to this ancient dictum. The struggle to treat the sometimes disabling symptoms of this disorder occupies the minds of some of today's best psychiatrists and psychologists, much as it caught the attention of physicians as ancient as Hippocrates almost two and a half millennia ago. A record of Greco-Roman physicians treating depression and lethargy with sunlight dates back to the second century (Adams, 1856; Aurelianus, 1950). Post-Enlightenment descriptions of seasonal depression appeared in the medical literature sporadically during the past two centuries (Oren and Rosenthal, 1992; Wehr, 1989b). But such reports failed to stimulate a coherent line of scientific investigation of the clinical phenomena or the novel treatment.

Beginning in the late 1970s, however, a number of investigators developed an insight that disorders of the biological clock and the processing of light thought important to regulate that clock might play etiological or at least pathophysiological roles in some psychiatric illnesses. In 1981, Daniel F. Kripke published the first modern paper demonstrating that some patients with depression had clinical responses to bright-light treatment. What had probably played the catalytic role in bringing an obscure field of science to the pages of *Science,* however, was a groundbreaking paper in 1980 by Alfred J. Lewy and his colleagues at the National Institute of Mental Health (NIMH) in Bethesda, Maryland, USA. Demonstrating that bright light has the capacity to suppress melatonin production in humans, these researchers crossed a paradigmatic barrier and established that humans, like virtually every other animal ever studied, possess a functional "switch" that is acutely sensitive to bright light. In short order, Herbert A. Kern became aware of this work and approached the NIMH researchers with his own record of

recurrent winter depressions and the hope that their work with light might successfully treat his depression. The results were dramatic (Lewy et al., 1982). NIMH researcher Norman E. Rosenthal and colleagues' landmark papers demonstrating that winter depression or "seasonal affective disorder" can be considered a distinct subtype of major depression and that light therapy is an effective treatment for the disorder quickly attracted the attention of the media, patients, and researchers across the globe (Rosenthal et al., 1984a; 1985).

In the subsequent decade and a half, the number of papers about the subject has steadily increased. As a crude measure of this growth, a survey by this author of Medline-cited papers on the topics of "seasons" or "seasonal affective disorder" and "depression" shows that nine were published in 1985 whereas 45 were published in 1997! It would be conservative to state that by 1998 more than 1,000 patients worldwide had participated in controlled clinical trials of light or antidepressant medication therapy for the disorder. The great interest in the field led to the formation of the Society for Light Treatment and Biological Rhythms, an international academic and clinical society devoted partly to the understanding and treatment of winter depression.

We are now at an exciting threshold in the study of the phenomenon. Controversies that have beset the field have achieved some resolution or at least been addressed to allow new formulations of investigative directions. Perhaps the primary controversy has been whether light therapy is an effective treatment or just a placebo treatment for the disorder. Landmark papers just published by Michael Terman et al. (1998), Alfred J. Lewy et al. (1998b), and Charmane I. Eastman et al. (1998) take major steps toward putting this critical question to rest. Although the question still remains whether winter depression is a disorder whose etiology and treatment rest in the domain of delayed biological rhythms that are advanced by light or other interventions, much of the literature supports the basic elements of the circadian "phase-shift" hypothesis (Lewy et al., 1987a).

The molecular basis of the syndrome remains a mystery. While the work of Raymond W. Lam et al. (1996b) and others clearly demonstrates that serotonin regulation plays a role in the syndrome, other neurotransmitters may also play critical roles. The failure by basic and clinical researchers to establish which photoreceptors or photoreceptor molecules mediate light's effects in the syndrome led this author to propose that humoral factors may act as photoreceptors and transduce the antidepressant and rhythm-shifting effects of light (Oren et al., 1996; Oren,

1997). Although such a theoretical model remains to be proved or disproved, publication of the work of Scott S. Campbell and Patricia J. Murphy (1998), demonstrating that light applied to the popliteal skin (behind the knees) has the capacity to reset circadian rhythms in humans, is consistent with this construct.

Similar to the pace in so many areas of medicine, what we have learned in the past 15 years about this disorder surely equals or exceeds what was learned in the 1,500 years before. In this context, these consensus guidelines assembled by Raymond W. Lam and Anthony J. Levitt and their Canadian colleagues mark a culmination and summation of an era. The documents that follow are based on careful assessment of the strengths and weaknesses of virtually every known study ever conducted for the treatment of winter depression. By summarizing a world literature demonstrating the efficacy of light therapy, and now a pharmacotherapy for winter depression, these guidelines will surely reach landmark status in their own right. Having had the privilege to attend the authors' first consensus-gathering meeting on the subject, I can bear witness to their thorough review and their tough-minded insistence on valuing sound scientific data, while being appropriately cautious about rubber-stamping clinical impressions gathered without controlled trials. These consensus guidelines will surely be of value to Canadian health care providers and to clinicians the world over, for there is simply nothing to match this accomplishment.

I expect that in another 15 years Lam and Levitt will wish to reconvene their panel to integrate the results of studies still to come. If scientific interest remains at its current level, by then we will know not just what time of day is best to treat winter depression with light but also why. We will know not just the value of antidepressants for the disorder but also the specific neurotransmitters that are regulated to have the antidepressant effect. More exotic treatments currently under study will also emerge as either dramatic successes or disappointing failures. In the interim, any clinician interested in offering a patient with winter depression the best that medical science has to offer will surely be well advised to turn to these guidelines.

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INTRODUCTION

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In 1994, we organized a Canadian Consensus Group on seasonal affective disorder (SAD) to attend a workshop that was funded by grants from the Medical Research Council of Canada and Health and Welfare Canada. Clinicians-researchers from the major academic centres in Canada were invited to the Clarke Institute of Psychiatry in Toronto to present their work, develop consensus on the diagnosis and treatment of SAD, and discuss directions for future research. Although a major review of the literature arose from this workshop (Tam et al., 1995), the consensus then was that there were too few controlled studies to formulate treatment guidelines for SAD.

By 1998, the situation had changed. Several randomized, large-sample, placebo-controlled studies of light therapy and antidepressant therapy have since been published, and there has been new research on the diagnosis, epidemiology, and pathophysiology of SAD. Much of this research has been conducted in Canada, where SAD carries a significant burden for the health care system. We decided that it was timely to reconvene the Canadian Consensus Group on SAD to develop expert consensus guidelines for the treatment of SAD. Dr. Dan Oren of Yale University was invited to participate as an external consultant.

The purpose of the consensus guidelines project was to systematically review all available evidence regarding the diagnosis, clinical features, epidemiology, pathophysiology, and treatment of SAD and to produce a series of recommendations that were clinically and scientifically meaningful. The target audience for the guidelines included family physicians, psychiatrists, psychologists, nurses, and other health professionals who treat depression and SAD.

A rigorous method to reach consensus was adopted. A Medline search (updated as of June 1, 1999) was conducted for all indexed articles using MeSH and text word searches for papers relating to SAD, seasonal

depression, and light therapy. Additionally, consensus panel members reviewed the bibliography for omissions, and researchers in the Society for Light Treatment and Biological Rhythms were canvassed for studies completed or in press. Eventually, over 650 articles were reviewed.

Two consensus panel members were assigned to independently review each topic using level of evidence criteria (Steering Committee, 1998) and to summarize their findings in evidence tables. These levels of evidence are defined as follows:

Level 1 = randomized, controlled trials (RCTs) with sufficient numbers or good-quality meta-analyses based on RCTs

Level 2 = RCTs with smaller numbers (therefore insufficient power or limited generalizability of results)

Level 3 = Non-randomized, controlled or cohort studies, case series, case-controlled studies or high-quality retrospective studies

Level 4 = evidence based on the published opinions of expert committees, such as consensus/guidelines committees

Level 5 = evidence that expresses the opinions of the committee members who have reviewed the literature and guidelines, following discussion with peers (note that, following the consensus process, level 5 evidence becomes level 4 evidence).

The reports from the reviewers were then presented during a consensus meeting held during a joint meeting of the Society for Light Treatment and Biological Rhythms and the Society for Research in Biological Rhythms, at Amelia Island, Florida, in June 1998. Consensus on controversial areas was obtained, and a draft guidelines document was completed. In September 1998, the draft guidelines were ratified and adopted at a consensus meeting held during the annual meeting of the Canadian Psychiatric Association in Halifax, Nova Scotia. The draft guidelines were then reviewed by Dr. Dan Oren, Dr. Michael Terman at Columbia University in New York, and Dr. Anna Wirz-Justice in Basel, Switzerland.

In summary, these guidelines were arrived at by consensus and have undergone both internal review by the 14 members of the Canadian Consensus Group and by international consultants. Recommendations are based on the scientific literature and on the clinical experience of the consensus panel. To make the guidelines more accessible to the practising clinician, we chose to present the findings in a question-and-answer format followed by conclusions or recommendations. The levels

of evidence on which the recommendations are based are listed after each recommendation, so that areas where data are limited are apparent. There are sections on diagnosis, epidemiology, pathophysiology, light treatment, medication treatment, and management issues. Finally, a resource list and a full bibliography are included in the appendices. Note that we have used the term "SAD" in this document to indicate winter depression, and "light therapy" is used as per consensus in the field, to distinguish light therapy for SAD from other types of phototherapy (e.g., for hyperbilirubinemia).

Dissemination of clinical guidelines is also an important issue. An executive summary of these guidelines was completed to provide a quick reference for the clinician. This summary was published as a supplement to the *Canadian Journal of Diagnosis* (Lam and Levitt, 1998) to ensure the widest distribution of this information to physicians across Canada. The summary is also available on the Internet (see Resources).

These guidelines would not have been possible without the hard work of many people. We want to thank all the members of the Canadian Consensus Group on SAD and our external consultants for their dedication to the tight deadlines that we imposed. Thanks, too, to Arvinder Grewal and Julie Thomson for their management and secretarial support. We also thank Pfizer Canada for providing an unrestricted educational grant in support of these guidelines and Steven Kost for his encouragement throughout the project.

We hope that the information presented in these guidelines will assist clinicians to better identify patients with SAD and to manage the disorder more effectively. We also hope that the guidelines will help physicians to answer some of the many questions that patients and family members ask about SAD.

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