PERSPECTIVES

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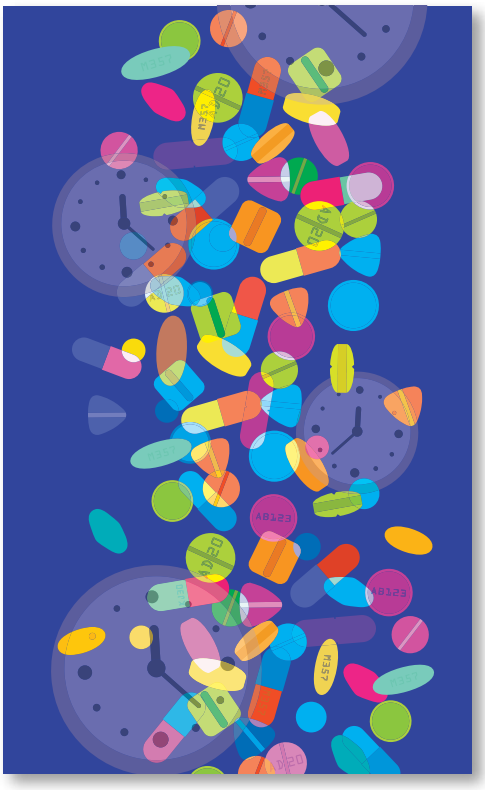
IN THIS ISSUE

A NOVEL APPROACH TO PRESCRIBING ANTIBIOTICS

Must you complete the course of prescribed antibiotics?

Doctors have always advised their patients to complete the course of prescribed antibiotics or run the risk of developing antibiotic resistance. In a recent article, Llewelyn et al. (2017) present their thoughts on the validity of this advice that, they state, is based on little research evidence. The authors argue that recommendations for antibiotic therapy were based on fear of undertreatment without regard to concerns about overuse. Moreover, individual patient differences and their specific responses to treatment are not taken into consideration when planning an antibiotic therapy regimen.



According to Llewelyn et al., "the idea that stopping antibiotic treatment early encourages antibiotic resistance is not supported by evidence, while taking antibiotics for longer than necessary increases the risk of resistance. Without explicitly contradicting previous advice, current public information materials from the U.S. Centers for Disease Control and Prevention (CDC) and Public Health England have replaced 'complete the course' with messages advocating taking antibiotics 'exactly as prescribed.'"

Mutants (new genetic characters) that can confer resistance may be selected during treatment with antibiotics, and these can reoccur after treatment failure or they can be transmitted before the disease is cured. Examples of this target selection are tuberculosis, malaria, gonorrhea and HIV. The authors state that resistance may be reduced by combination therapy rather than monotherapy (one antibiotic). Collateral selection, which occurs with resistance selection of bacteria that inhabit the gastrointestinal system or the skin during treatment of other infections, is more common than target selection.

"When a patient takes antibiotics for any reason, antibiotic-sensitive species and strains present among commensal flora (normal bacteria) on their skin or gut or in the environment are replaced by resistant species and strains ready to cause infection in the future. This collateral selection is the predominant driver of the important forms of antibiotic resistance affecting patients today. The longer the antibiotic exposure these opportunist bacteria are

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subjected to, the greater the pressure to select for antibiotic resistance." Opportunistic microorganisms take advantage of certain opportunities, such as a compromised immune system, to cause disease.

"Importantly for these opportunistic pathogens, resistant strains are transmitted between asymptomatic carriers rather than people with disease. Furthermore, many resistance-conferring genes can pass easily between bacterial strains or species. Thus, antibiotic selection may drive outbreaks of resistant infections independently of transmission of a specific strain or species."

ALTHOUGH THE AUTHORS HAVE PRESENTED SOME STUDIES TO SUPPORT THEIR CLAIM FOR SHORTER TIME FOR ANTIBIOTIC THERAPY, MORE CLINICAL STUDIES ARE REQUIRED TO DOCUMENT OPTIMAL DURATION OF ANTIBIOTIC THERAPY.

Barriers to reducing overuse of antibiotic therapy are diagnostic uncertainty and concerns about the negative consequences of ceasing the therapy when symptoms subside.

Although the authors have presented some studies to support their claim for shorter time for antibiotic therapy, more clinical studies are required to document optimal duration of antibiotic therapy. Patients must be informed that using antibiotics longer than necessary puts them at risk for antibiotic resistance. (Note: Antibiotics are not the right therapy for viral infections.)

Reference

Llewelyn MJ, Fitzpatrick JM, Darwin E, et al. The antibiotic course has had its day. *BMJ* 2017;358. doi: https://doi.org/10.1136/bmj.j3418.

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SAFETY AND EFFICACY OF SODIUM OXYBATE ADMINISTRATION IN NARCOLEPSY

A retrospective study was conducted in the United Kingdom (Drakatos 2017) to determine the efficacy and safety of sodium oxybate in the treatment of severe narcolepsy and cataplexy in 90 patients who were resistant to other treatments. Patients in the study continued their intake of stimulants or anti-cataplectic medications during the study period. Thus, we know neither the additive effect of these medications nor the interaction between the medications. Results indicated that the Epworth Sleepiness Score (ESS) and the cataplexy events were significantly reduced for all study subjects by administration of sodium oxybate. Sixty percent of the subjects either reduced or terminated the use of other medications for narcolepsy, 50 percent of the subjects experienced at least one side reaction, and 26.6 percent discontinued sodium oxybate due to the side reactions. Common side reactions noted were nausea, mood swings and enuresis. Older subjects were more likely than younger ones to discontinue treatment with sodium oxybate due to more severe side reactions, such as psychosis, experienced early in the treatment. Overall, the safety and efficacy of sodium oxybate were determined to be good.

Reference

Drakatos P, Lykouras D, D'Ancona G, Higgins S, et al. Safety and efficacy of long-term use of sodium oxybate for narcolepsy with cataplexy in routine clinical practice. *Sleep Med.* 2017;35:80-84. doi:10.1016/j.sleep.2017.03.028.

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DO PATIENTS' ASSESSMENTS OF THE QUALITY OF THEIR LIVES COINCIDE WITH PHYSICIANS' ASSESSMENTS OF GLOBAL IMPRESSION OF CHANGE?

A lower quality of life (QOL) in people with narcolepsy compared with the general population has been well established in several surveys in the United States and Europe. The results have been reported in past issues of our newsletter. The negative effects of narcolepsy have a wide range of effects on the person's physical, mental and social well-being, with further consequences on education and occupational life and on family members who may be ill-equipped to assist their loved one.

The most commonly used questionnaire to measure QOL in sleep disorders is the Medical Outcomes Study—Short Form (MOS-Short Form) or SF-36. Its shorter versions are SF-12 and SF-8, and SF-36, version 2, contains improved wording and instructions. The instrument does not measure quality of sleep but does measure eight dimensions of health/illness: physical functioning, role functioning–physical, role functioning–emotional, mental health, social functioning, vitality, bodily pain and general health. Information obtained from QOL studies can be applied to improve the quality of care provided to our patients.

How Do We Define QOL?

Perceptions of physical, emotional, intellectual, social and general well-being or life satisfaction are generally considered in evaluating QOL in our patients. Subjective feelings of well-being, including social performance and social well-being, the role of social support, and implications of social adjustment, are important considerations in evaluating QOL in patients.

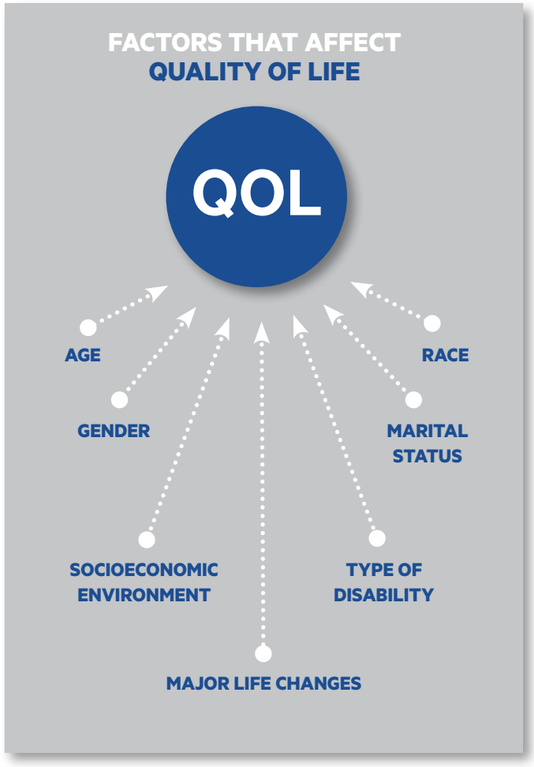
Several instruments that measure QOL incorporate individuals' choices of domains and aspirations that are meaningful to them. Perceptions of well-being could vary over the life cycle of individuals. Factors such as age, gender, ethnicity, race, socioeconomic environment, marital status, type of disability, and major life changes (e.g., job loss, divorce or death of a companion) are likely to affect perceptions of health and disability. Health and social behaviors, such as engaging in physical activity, following a nutritious diet, and participation in accessible recreational activities, will affect health objectively as well as a patient's subjective perceptions of health (Goswami 2010).

Recently, a study on 209 people with narcolepsy (Bogan et al. 2017) assessed the correlation between patients' perceptions of their conditions by responses to the SF-36 versus physicians' responses to the Clinical Global Impression of Change (CGI-C) that is based on physicians' assessments. Results showed that lower CGI-C scores (lower indicates improvement) were correlated with higher SF-36 subscale scores that also indicate improvement. The domains of vitality and role functioning–physical showed significant correlations. However, weak correlations were noted in the summary scores and in the domains of physical functioning, role functioning–emotional, mental health, social functioning, bodily pain and general health. This indicates that patients and doctors differ in their perspectives of the disorder and its effects. (Higher doses of sodium oxybate yielded stronger correlations for most SF-36 subscales.)

Whereas clinicians tend to focus on symptoms as indicators of the severity or absence of disease, patients may be more concerned about the symptoms as they affect their social functioning. They may learn to live with their disorder if reasonable functioning is possible. Biomedical effectiveness of treatment may not be acceptable to patients if the side reactions or long-term effects of medications impinge on their social roles, thereby reducing adherence to the prescribed treatment plan (Goswami 2010). This difference in perspective may partially explain the low association between the patients' assessments of their health status and that of the doctors.

MOST PATIENTS WOULD LIKE THEIR PROFESSIONALS TO GO BEYOND THE PHYSIOPATHOLOGICAL LEVEL OF HEALTH SERVICES AND CARE FOR THEM FROM A TOTAL PATIENT PERSPECTIVE.

Most patients would like their professionals to go beyond the physiopathological level of health services and care for them from a total patient perspective. Education and sensitivity training for professionals will narrow the gap in patients' and professionals' evaluations of the impact of a disorder on the lives of affected individuals.



In our clinical experience, a patient-centered and family-centered management regimen yields good results in improving management techniques and enhancing the QOL of our patients. Preventive measures and follow-up plans can be instituted to avert serious consequences of the disorder/condition or health behavior by incorporating results from QOL studies. Also, family members can be informed regarding the patient's condition to better understand the patient's unique needs and, therefore, provide an effective support system.

References

Goswami M. Quality of life and psychosocial issues in narcolepsy. In: Goswami M, Pandi-Perumal SR, Thorpy MJ, eds. *Narcolepsy: A Clinical Guide.* New York: Springer; 2010;189-204.

Bogan RK, Black J, Swick T, Mamelak M, et al. Correlation of changes in patient-reported quality of life with physician-rated global impression of change in patients with narcolepsy participating in a clinical trial of sodium oxybate: a post hoc analysis. *Neurol Ther.* 2017 Jul 13. doi:10.1007/s40120-017-0076-6. [Epub ahead of print]

RESEARCH NOTES

Narcolepsy, Breast-feeding and Sodium Oxybate

Women with narcolepsy type 1 (with cataplexy) or narcolepsy type 2 (without cataplexy) are generally advised to cease their intake of medications for narcolepsy during conception, pregnancy and breast-feeding. However, in severe cases of sleepiness and or cataplexy, the risks of the consequences of the symptoms may take precedence over the risks of the medications.

The only medication for narcolepsy (type 1 and type 2) approved by the U.S. Food and Drug Administration (FDA) is y-hydroxybuterate (GHB), the active agent in sodium oxybate (SXB). Narcolepsy patients have expressed concerns over the intake of GHB during pregnancy and breast-feeding. To address these concerns, a recent study was conducted at Brown University (Garker et al. 2017) on two patients with type 1 narcolepsy who chose to continue taking SXB during pregnancy and during breast-feeding. The results indicated that GHB levels in breast milk before SXB administration were similar to those levels of SXB measured more than six hours after drug administration, suggesting the safety of taking SXB during breastfeeding.

Reference

Barker EC, Puchowicz M, Letterio J, Higgins K, Sharkey KM. GHB levels in breast milk of women with narcolepsy with cataplexy treated with sodium oxybate. *Sleep Med.* 2017;36:172-177. doi:10.1016/j.sleep.2017.05.008.■

Narcolepsy and Multiple Sclerosis

A study in Brazil compared six patients with multiple sclerosis (MS) who were HLA-DQB1*06:02 positive with 12 MS patients who were HLA-DQB1*06:02 negative and found two patients with HLA-DQB1*06:02 with an Epworth Sleepiness Scale Score higher than 10. Further test results, including polysomnography and the multiple sleep latency test, showed negative results for narcolepsy in the study group. In this study, with its small sample size, the presence of HLA-DQB1*06:02 alone in MS patients was not sufficient to develop narcolepsy.

Reference

Lorenzoni PJ, Werneck LC, Crippa ACS, Zanatta A, et al. Is there a relationship between narcolepsy, multiple sclerosis and HLA-DQB1*06:02? *Arq Neuropsiquiatr.* 2017;75(6):345-348. doi:10.1590/0004-282X20170063.■

Co-occurrence of Narcolepsy and Sjögren's Syndrome

Bae et al. (2017) report a case of narcolepsy with Sjögren's syndrome (SS). The patient was a 61-year-old woman who presented symptoms of excessive daytime sleepiness and fatigue for six months. Other symptoms of narcolepsy, such as cataplexy, sleep paralysis and hypnagogic hallucinations, were not present. Cerebrospinal fluid analysis was normal. Polysomnography showed short sleep latency (0.2 minutes), and the multiple sleep latency test showed two occurrences of rapid eye movement sleep in a five-nap trial, indicating the presence of narcolepsy following the diagnostic criteria for narcolepsy.

The patient also presented symptoms of chronic dry eye and dry mouth, and the Schirmer test for SS was positive. Serum anti-SS-A/Ro and anti-aquaporin-4 antibodies were positive for neuromyelitis optica spectrum syndrome disorder (NMOSD). NMOSD is inflammation of the optic (eye) nerve and the spinal cord.

Sjögren's syndrome is an autoimmune disease in which the system mistakenly attacks the body's own cells and tissues. Commonly reported initial symptoms are dry mouth and dry eyes. Other symptoms may include swollen salivary glands (parotid, submandibular and sublingual glands); joint stiffness, pain or swelling; dry cough; or dry skin or rashes.

The concurrent presence of narcolepsy along with autoimmune disorders warrants astute clinical acumen and referral to appropriate specialists for the diagnosis and treatment of comorbid conditions.

Reference

Bae EK, Oh DA, Yoon BN. Symptomatic narcolepsy in Sjögren syndrome. J Rheumatol. 2017;44(6) 852-853; doi:0.3899/jrheum.160940.

A CASE REPORT: NARCOLEPSY AND COMORBID PSYCHOSIS IN A YOUNG GIRL

The Sleep and Epilepsy Unit in a hospital in Spain reports a case of a 14-year-old female who was referred to the clinic for complaints of daytime sleepiness, disturbed nighttime sleep, binge eating and weight gain for a period of one year. She was diagnosed with narcolepsy with cataplexy (type 1) and treated with modafinil and sodium oxybate. After initiating this treatment, she was hospitalized for psychotic symptoms—delusions, hallucinations and dysphoria (state of uneasiness or dissatisfaction). It is not clear if the psychotic symptoms were precipitated by the intake of medications for narcolepsy. The patient was treated with haloperidol (1 mg/day), which improved her psychotic symptoms but exacerbated the symptoms of narcolepsy. While she was on haloperidol, the treatment for narcolepsy was discontinued.

A polysomnogram showed fragmented nocturnal sleep, and five rapid eye movement (SOREM) periods were found in the multiple sleep latency test (MSLT). Examination of the cerebrospinal fluid (CSF) was positive for HLA-QB1*06:02, and undetectable levels of hypocretin were found in the CSF. Magnetic resonance imaging (MRI) and computed tomography (CT) scans were reportedly normal. The authors confirmed the diagnosis of narcolepsy type 1 and concurrent psychosis by utilizing the Diagnostic Interview for Genetic Studies Adapted for Narcolepsy (DIGSAN). The patient was treated with psychopharmacological medications, and her mood was reported to be normal after treatment. However, she continued to have severe daytime sleepiness, partial cataplexy and obesity. Academic difficulties and social isolation were also reported. Dual diagnoses pose additional challenges for practitioners in the management of narcolepsy.

Reference

Canellas-Dols F, Delgado C, Arango-Lopez C, Peraita-Adrados R. Narcolepsy-cataplexy and psychosis: a case study. *Rev Neurol.* 2017;65(2):70-74.

■

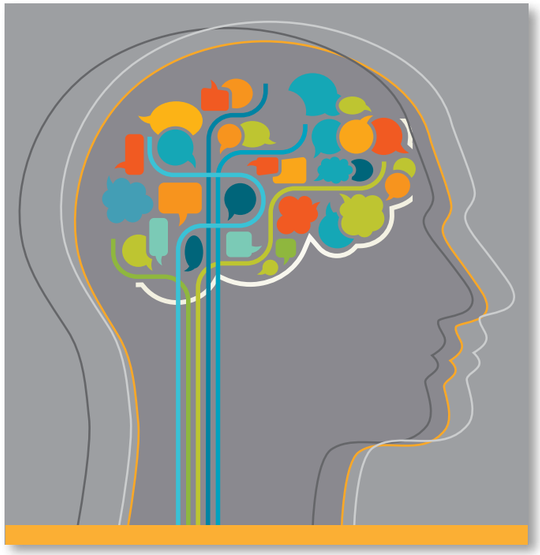
PATIENTS' CORNER

A Case of Cylert Psychosis

One of our patients with narcolepsy diagnosed by polysomnogram, a 23-year-old male, was treated with Cylert by his internist for several years. As Cylert is no longer recommended for narcolepsy because of its potential side effects, we recommended that he ask his doctor to discontinue the medication and replace it with Provigil. However, the patient ignored our recommendation and continued the treatment with Cylert. One year after our last contact with the patient, a call from a psychiatric clinic informed us that this patient was admitted for severe psychosis. He ultimately recovered after withdrawal from Cylert and several months of treatment with antipsychotic medications.

IT IS IMPORTANT FOR PATIENTS, AND FAMILY MEMBERS, IN THE CASE OF YOUNG PATIENTS, TO BE ATTENTIVE TO THE SYMPTOMS OF PSYCHOSIS AND NOT CONFUSE THE HALLUCINATIONS OF PSYCHOSES WITH THE HYPNAGOGIC HALLUCINATIONS OF NARCOLEPSY

It is important for patients, and family members, in the case of young patients, to be attentive to the symptoms of psychosis, not confuse the hallucinations of psychoses with the hypnagogic hallucinations of narcolepsy and make timely follow-up visits to the doctor. Early intervention will prevent further progression of symptoms.



DID YOU KNOW?

1. Sleep debt may evoke mood instability. A study on 18 healthy adult men subjected to three hours of nighttime sleep for two nights found mood deterioration by reducing the suppression of the amygdala (the part of the brain that processes emotions) by the medial prefrontal cortex (the front portion of the brain). The study also found that reduction in rapid eye movement (REM) sleep was involved in functional changes in the brain. Adequate REM sleep could be important for positive mental health.

Reference

Motomura Y, Michitaka Yoshimura R, Mishima K. Two days' sleep debt causes mood decline during resting state via diminished amygdala-prefrontal connectivity. *Sleep* 2017;40(10). doi:10.1093/sleep/zsx133.

2. Short sleep duration is likely to have a negative impact on metabolic health. A population-based cohort survey of 162,121 healthy adults aged 20–80 (men 47.4 percent) revealed that compared with regular sleep duration (six to eight hours per night), short sleep (less than six hours per night) significantly increased the risk for central obesity (abdominal obesity), elevated fasting glucose, high blood pressure, low high-density lipoprotein (HDL), hypertriglyceridemia (elevated triglyceride levels) and metabolic syndrome (a collection of symptoms that lead to diabetes and heart disease). Potential confounding variables were controlled in the analysis, which found that insomnia did not modify the effects of sleep duration. Long sleep duration (more than eight hours) lowered the risk for metabolic syndrome and hypertriglyceridemia.

Reference

Deng HB, Tam T, Zee BCY, Chung RYN, et al. Short sleep duration increases metabolic impact in healthy adults: a population-based cohort study. *Sleep* 2017;40:10. doi:https://doi.org/10.1093/sleep/zsx130.

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THE ROLE OF COMPASSION IN HEALTHCARE

Compassionate care may improve healthcare outcomes

"Compassion is based on a clear acceptance or recognition that others, like oneself, want happiness and have the right to overcome suffering. On that basis one develops some kind of concern for the welfare of others, irrespective of one's attitude to oneself. That is compassion."—Dalai Lama, *The Art of Living*

We define compassion as a recognition of and feeling for the needs, discomfort and suffering of others accompanied by a wish, followed by appropriate action, to fulfill the needs and alleviate the discomfort and suffering. A compassionate act gives personal satisfaction to the giver and joy to the receiver.

Providing compassionate care in healthcare settings has attained significant importance in evaluating quality of care, and many studies have emerged to evaluate the quality of care. The indicators for measuring quality of care are generally developed from the professional perspective. What is the patient's perspective on the role of compassion in the healthcare delivery system? To find answers to this question, researchers in Canada conducted a study on 53 advanced cancer inpatients in a hospital setting. Semi-structured questionnaires were utilized in personal interviews to measure a patient's concept of compassion and experience in receiving professional care.

THE SEVEN DISTINCTIVE COMPONENTS OF THE CLINICAL MODEL OF COMPASSION

Analysis of data yielded seven categories that comprise distinctive components of the clinical model of compassion as described by patients. These categories are:

VIRTUES

1 Virtues are reported by participants as drivers of compassionate care. Virtues are described as noble qualities in the character of the provider, such as love, authenticity, openness, understanding, kindness, tolerance and acceptance.

RELATIONAL SPACE

2 Relational space comprises patient awareness—that is, the patient's awareness of compassion on the part of the provider and engaged caregiving, which is the extent that the provider is involved in caregiving over time.

VIRTUOUS RESPONSE

3 Virtuous response includes knowing the person (patient), prioritizing the patient's needs and showing beneficence (wanting to do the best for the patient).

SEEKING TO UNDERSTAND

4 Seeking to understand is defined as "the extent to which health care providers attempt to understand the patient as a person and to understand the person's unique needs to optimize the effect of compassion." Seeking to understand was identified as a basic component of compassionate care.

RELATIONAL COMMUNICATION

5 Relational communication consists of verbal and nonverbal communication expressed by the provider's demeanor, behavior, affect (showing feelings) and engagement in the provider/patient relationship. Does the provider acknowledge the patient's suffering?

ATTENDING TO NEEDS

6 Attending to needs is an essential feature of compassionate care. Does the provider take appropriate action to address the patient's expressed needs in a timely and supportive manner? Expressed needs may be physical, mental, social and spiritual. If the provider does not have the expertise in a specific field, does he or she refer the patient to the appropriate source?

PATIENT-REPORTED OUTCOMES

7 Patients reported that compassionate care had an "ameliorating effect on suffering" and also enhanced their well-being. Some patients reported a better provider/patient relationship, and others felt compassion improved their health outcome. Negative effects of lack of compassion were frustration and low spirits.

The role of communication, both verbal and nonverbal, is an essential feature of providing compassionate care. Active listening, engagement, acknowledging the patient's discomfort or suffering, and providing feedback are skills that can be taught to providers. Proper communication requires spending a few extra minutes with the patient; the benefits will go a long way in developing improved and rewarding provider/patient relationships.

Reference

Sinclair S, McClement S, Raffin-Bouchal S, Hack T, et al. Compassion in health care: an empirical model. *J Pain Symptom Manage*. 2016;5(2):193-203.

"Compassion is the basis of morality."—**Arthur Schopenhaur**

"For it is in giving that we receive."—**Saint Francis of Assisi**

"Silence. All human unhappiness comes from not knowing how to stay quietly in a room."—**Blaise Pascal, 17th century**

Eight degrees of charity

"There are eight degrees of charity, each one higher than the other.

"The highest degree is to aid a man in want by offering him a gift or a loan, by entering into partnership with him, or by providing work for him, so that he may become self-supporting.

"The next highest degree is when he who gives and he who receives are not aware of each other.

"The third, lesser degree is when the giver knows the recipient, but the recipient does not know the giver.

"The fourth, still lower, degree is when the recipient knows the giver, but the giver does not know the recipient.

"The fifth degree is when the giver puts the alms into the hands of the poor without being asked.

"The sixth degree is when he puts the money into the hands of the poor after being asked.

"The seventh degree is when he gives less than he should, but does so cheerfully.

"The eighth degree is when he gives grudgingly."—**Maimonides**

PERSPECTIVES FROM THE NARCOLEPSY INSTITUTE

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About the Institute

Narcolepsy is a chronic sleep disorder of neurological origin. Its main symptoms are (1) excessive daytime drowsiness with a tendency to sleep at inappropriate times; (2) cataplexy (sudden loss of strength in the muscles generally provoked by strong emotions, especially laughter or stress); (3) sleep paralysis (inability to move upon awakening); and (4) hypnagogic hallucinations (extremely vivid dreams or images upon sleep onset or upon awakening). Disturbed nighttime sleep, problems with memory, and fatigue are common complaints of people with narcolepsy. Narcolepsy type 1 is narcolepsy with cataplexy, and type 2 is narcolepsy without cataplexy.

The Narcolepsy Institute, initiated in 1985, is committed to providing comprehensive care to people with narcolepsy by integrating the medical, social, psychological and spiritual dimensions of health, in a spirit of kindness and respect toward all, irrespective of race, creed, ethnicity or social class; that the recipients of care may realize their potential and live productively in joy, peace, harmony and dignity, and thus improve the quality of their lives.

Activities of the Narcolepsy Institute include: conducting professionally led support groups, advocacy, and public and professional education. Counseling in a group setup entails comprehensive management of the symptoms of narcolepsy and strategically applying behavioral and nonpharmacological approaches to ally the devastating impact of narcolepsy on the personal, social, educational and occupational lives of affected individuals and their families. Our patients benefit most by a family-centered and person-centered approach to improve the quality of their lives.

The contents of this publication are not intended to provide advice for individual problems nor to replace medical advice. Readers are urged to consult with their professionals before initiating self-therapy. We welcome comments and suggestions about the contents of the newsletter.

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