

# Assessment: Techniques associated with the diagnosis and management of sleep disorders

Report of the Therapeutics and Technology Assessment Subcommittee  
of the American Academy of Neurology

The objective study of sleep is a relatively recent phenomenon. While confined mostly to research laboratory studies in the early 1950s and 1960s, the recording of human sleep has now emerged as a major clinical tool for the diagnosis and management of specific illnesses related to sleep and wakefulness. The full evaluation of patients with complaints of sleep disorders is multifaceted, involving a detailed history/physical examination, extensive questionnaires, sleep diaries/logs, and, often, psychological testing. Many patients are referred for formal sleep studies, which include all-night polysomnography (PSG) and physiologic measures of daytime sleepiness (Multiple Sleep Latency Test [MSLT] or its variant, the Maintenance of Wakefulness Test [MWT]).

Neurologists, psychiatrists, pulmonologists, pediatricians, psychologists, surgeons, and various specialists collaborate within sleep centers to deliver multidisciplinary care to patients with sleep-related disturbances. This clinical effort is often coordinated by an individual specifically trained in sleep disorders medicine. In any given case, the decision for formal sleep studies should be made in conjunction with a sleep disorders specialist.

**Technology. Polysomnography.** The technology used in the diagnosis of sleep disorders is well founded in standard electrophysiologic recording systems.<sup>1</sup> The basic PSG format is standardized and includes, as a minimum, continuous monitoring of eye movements, at least one channel of EEG (usually C3/A2 or C4/A1), respiratory parameters (at minimum, airflow), ECG, submental EMG, and anterior tibialis EMG. Minimal monitored respiratory parameters for evaluation of sleep-disordered breathing (SDB) include airflow (thermistors, thermocouples, or expired CO<sub>2</sub> sensors), respiratory effort (strain gauges, inductance plethysmography, impedance pneumography, endoesophageal pressure, intercostal EMG), and a measure of gas exchange (oximetry). Other parameters may be

monitored as clinically indicated, such as extensive EEG for parasomnias, esophageal pH for gastroesophageal reflux, or penile tumescence for erectile function. Specific PSG recording techniques as accepted by the American Electroencephalographic Society have been outlined.<sup>2</sup> Sleep-stage scoring techniques are standardized and widely accepted.<sup>3</sup> Any study termed a "polysomnogram" must, by definition, include EEG monitoring of sleep.

In a single nighttime PSG, it is possible to accurately quantify and characterize the various stages of sleep, as well as determine the presence of (1) disruption of sleep architecture, (2) cardiopulmonary abnormalities, (3) sleep-related motor activity, and (4) other sleep-associated disorders.

The scoring of sleep stages and respiratory parameters of neonates and infants requires special experience and skill. For instance, clinically significant sleep-disordered breathing resulting in sleep fragmentation (particularly in children) may not be associated with either frank apnea or hemoglobin oxygen desaturation.

Visual interpretation of PSGs is the current standard. Currently available computer-aided systems to evaluate sleep disorders await objective, published verification of reliability.<sup>4</sup> Advances in technology and objective validation across age groups and clinical populations may allow clinical utility of computer-aided systems in the future. The difficulty in determining some forms of SDB with commonly employed transducers, the masquerading of other sleep disorders as SDB, the indeterminate nature of sleep stages in some patient populations, the problems recording normal and abnormal EEG features, difficulties caused by artifact, and the inability to maintain high-level signal quality explain some of the challenges.<sup>5,6</sup>

**Multiple Sleep Latency Test.** The MSLT is a standardized and well-validated measure of physiologic sleepiness. The same parameters as for basic PSG are monitored (usually two eye movements and two EEG channels [central and occipital], in

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addition to ECG, airflow, and submental EMG). The MSLT consists of four to five 20-minute nap opportunities offered at 2-hour intervals.<sup>7</sup> The MWT is a variation on this theme, and may be of value in certain circumstances such as determination of efficacy of stimulant therapy in narcolepsy.<sup>8</sup>

The MSLT is designed to (1) quantitate sleepiness to determine need for treatment,<sup>9,10</sup> and (2) to determine the premature occurrence of REM sleep. Studies in normal persons have demonstrated that the latency to sleep onset during these naps is correlated with the duration of sleep on one or several nights preceding the study,<sup>11-14</sup> maturation,<sup>15</sup> age,<sup>14</sup> continuity of sleep,<sup>10,16</sup> time of day,<sup>17</sup> and ingestion of drugs.<sup>18-20</sup> Pathologic ranges of sleep latency have been carefully defined. To insure validity, proper interpretation of the MSLT can only be made following a PSG performed on the preceding night.

For each nap, the latency between "lights out" and sleep onset is determined. A mean latency of 5 minutes or less indicates severe excessive sleepiness. The number of naps during which REM sleep appears is also noted.

Repeat MSLT testing is necessary only when (1) the initial test is believed to be an invalid representation of the patient's status, (2) the initial test is inconclusive, (3) response to treatment needs to be ascertained, or (4) more than one sleep disorder is suspected.

**Safety of sleep studies.** There are no serious safety issues posed by this technology and its common clinical use. The presence of a physician during the PSG or MSLT is not necessary.

**Efficacy of sleep studies.** *Sleep-disordered breathing.* Specific findings on PSG studies in cases of SDB (obstructive apnea, central apnea, mixed apnea, sleep-associated hypoventilation, and Cheyne-Stokes respiration), *define* the condition, which cannot be objectively evaluated in any other manner. The significance of obstructive sleep apnea is emphasized by its estimated incidence of 1 to 10% in the general population.<sup>21</sup>

The major issue is not whether a sleep study is necessary for the diagnosis of sleep apnea, but rather what criteria beyond history should be used for selecting patients for the overnight PSG. Ideally, some form of a screening sleep study could be an adjunct to routine PSG. However, at present, there are no adequate studies comparing existing screening technology with laboratory-based diagnosis to determine accurate sensitivity and specificity criteria for screening methods.<sup>22</sup> These "ambulatory" (home) or "screening" studies usually include oximetry, but often do not include sleep monitoring. Although intended to be less costly, such screening studies more often become add-ons. They are prone to technical difficulties (eg, keeping electrodes on), and may not indicate how much sleep was monitored or whether all

stages of sleep occurred. They usually do not allow monitoring or observation for patient body position, which is most important in SDB. If the complaint is excessive daytime sleepiness (EDS) and the study fails to reveal a cause, the patient needs formal sleep studies to determine the cause of EDS. If they are positive for SDB, again, formal sleep studies are usually necessary to determine the exact nature of the apnea and any response to treatment. One indication for home oximetry is a need to determine whether sleep period desaturation is sufficient to explain gross physiologic consequences of SDB (ie, polycythemia, unexplained pulmonary hypertension, or congestive heart failure). If such a recording is thought to adequately sample sleep and to be technically adequate, and is negative, the study has been valuable. If there is desaturation sufficient to result in such severe physiologic consequences, a formal sleep study is indicated.

Daytime nap studies performed for the purpose of determining the presence and/or severity of SDB are to be discouraged, as the duration of the evaluation is usually inadequate to allow the appearance of REM sleep. Furthermore, the severity of the SDB tends to increase somewhat as the night progresses<sup>23</sup>; therefore, the short daytime study may not detect apnea that is sleep duration- and/or circadian-dependent. A negative nap study does not rule out significant SDB.<sup>22,24</sup>

To promote the proper use of sleep diagnostic testing, the American Thoracic Society<sup>22</sup> has published specific cardiopulmonary criteria for overnight PSG to assess the presence and/or severity of SDB. These include (1) symptoms of excessive daytime sleepiness or sleep maintenance insomnia, (2) chronic obstructive pulmonary disease complicated by pulmonary hypertension, right heart failure, or polycythemia, (3) restrictive ventilatory disorders or disorders of respiratory control complicated by chronic hypoventilation, polycythemia, pulmonary hypertension, disturbed sleep, morning headaches, or daytime somnolence and fatigue, and (4) nocturnal cyclic bradytachyarrhythmias, nocturnal abnormalities of atrioventricular conduction, and ventricular ectopy during sleep that appears increased relative to wakefulness. PSG for the presence of snoring, obesity, systemic hypertension, or nocturnal nonspecific cardiac arrhythmias without other symptoms is not indicated.<sup>22</sup>

PSG is also beneficial in the selection and assessment of therapeutic options for sleep apnea. For example, it is possible to administer supplemental oxygen or apply nasal continuous positive airway pressure (CPAP) to determine whether abnormalities documented during PSG can be corrected.<sup>25</sup>

The use of the MSLT in evaluating the degree of EDS in patients with SDB is useful, as these patients often underestimate the degree of, or deny, hypersomnia. The presence of objective hypersomnia is an important consideration in the

therapeutic recommendation and in counseling regarding the need for caution in driving and in other potentially dangerous situations.

PSG has been proven as safe and effective in the diagnosis of sleep-disordered breathing (SDB). PSG monitoring is used in the evaluation of treatment efficacy (ie, during nasal continuous positive airway pressure titration or following other forms of treatment). The MSLT has been proven safe and effective in determining the degree of hypersomnia in patients with SDB.

*Narcolepsy and idiopathic CNS hypersomnia.* Narcolepsy occurs in 50 to 70 persons per 100,000 population.<sup>26</sup> As with SDB, formal sleep studies define the conditions of narcolepsy and idiopathic CNS hypersomnia. The consensus statement developed at the First International Symposium on Narcolepsy<sup>27</sup> in 1975 established a definition of narcolepsy based on REM abnormalities in the MSLT.<sup>28-30</sup>

The major symptomatic presentation suggesting a diagnosis of narcolepsy is severe daytime somnolence that may be associated with cataplexy, sleep paralysis, or hypnagogic hallucinations.<sup>28,31</sup> It should be remembered that, at presentation, 30% of patients with narcolepsy will not exhibit cataplexy—and only about one-half of this group will eventually develop cataplexy, but not for up to 20 years.<sup>32,33</sup> Only 20 to 25% of narcoleptics experience the full range of symptoms.<sup>34</sup>

Definitive diagnosis is established by PSG recording that reveals no other primary cause of hypersomnia, and an MSLT that documents severe daytime sleepiness and the abnormal occurrence of REM sleep.<sup>1,28,29</sup> Stringent criteria for the standardization of MSLT measurement and interpretation have been published.<sup>7</sup> A single nap test for the determination of narcolepsy is inadequate, as REM sleep in an isolated nap is not specific for narcolepsy and may occur in normal individuals (particularly in the morning)<sup>35</sup> or in patients with obstructive sleep apnea.<sup>36</sup> The diagnosis of idiopathic CNS hypersomnia is made following an unremarkable PSG with severe sleepiness by MSLT, without the appearance of REM sleep. Objective confirmation of narcolepsy or idiopathic CNS hypersomnia is highly desirable. Treatment involves the administration of stimulant medication. The effects of medications and/or withdrawal from medications commonly prescribed for these conditions (stimulants/tricyclic antidepressants) may interfere with the interpretation of formal sleep studies. Objective diagnosis once treatment has been instituted necessitates discontinuation of medication for at least 3 weeks prior to study.

The combination of PSG followed by MSLT has been proven *safe and effective* in establishing the diagnosis of *narcolepsy and idiopathic CNS hypersomnia*.

*Sleep-related violent or injurious behaviors.* Patients with a history of repetitive nocturnal

injuries frequently present to sleep disorders centers for evaluation. There is a risk of serious, even life-threatening injury for these patients.<sup>37,38</sup>

In many cases, it is not possible to accurately diagnose conditions leading to abnormal behavior or movement disorders during sleep by history alone. The differential diagnosis encompasses a wide variety of parasomnias (undesirable behaviors arising from sleep) including NREM parasomnias (ie, somnambulism, sleep terrors, confusional arousals), sleep-related seizures, REM behavior disorder, and psychogenic dissociative phenomena. These conditions notoriously masquerade as one another. A complete evaluation with meticulous PSG assessment and, when appropriate, psychiatric and neurologic consultation, is highly desirable.<sup>37</sup>

Sleep terrors, sleepwalking, and confusional arousals may be associated with complex, potentially injurious or violent behavior. Although most common in childhood, they may present in adulthood. Contrary to popular opinion, they are frequently not associated with significant psychiatric disorders.<sup>39</sup> PSG findings include precipitous arousals from all stages of NREM sleep with the simultaneous occurrence of wakeful and NREM sleep EEG patterns.

Seizures occur frequently during sleep but present little diagnostic difficulty in most patients, in whom routine daytime diagnostic testing confirms the diagnosis of a seizure disorder. However, in some cases, the diagnosis of nocturnal seizures may be difficult. Approximately 10% of seizure patients experience seizures exclusively or predominantly during sleep.<sup>40</sup> In some instances, waking, sleep-deprived, and sleep-induced EEGs may not confirm a diagnosis.<sup>41,42</sup>

Atypical nocturnal spells are often difficult to classify because of bizarre symptoms that may masquerade as other parasomnias or psychiatric conditions. These spells often represent unusual seizures and have been extensively reviewed.<sup>37,43-45</sup> Seizures have been mistakenly assumed to be recurrent dreams or nightmares, sleepwalking, sleep terrors, or normal arousals from sleep.

Recently, a chronic REM sleep behavior disorder (RBD) has been described in humans. RBD is characterized by the absence of the usual REM-related muscle atonia. Affected individuals often display dramatic and often violent and injurious behavior during sleep that is frequently misdiagnosed as either a seizure disorder or psychiatric disorder. PSG provides direct observation of alterations in REM sleep muscle atonia characteristic of these patients.<sup>45</sup>

Psychogenic dissociative states may arise exclusively from the sleep period, disguised as other parasomnias. Diagnosis is made by recording a typical clinical spell arising from a background of well-established EEG wakefulness.<sup>46</sup>

The indications for formal studies in parasomnias include (1) potentially injurious or violent

sleep-related behaviors, (2) severe disruption of the sleep of other household members, and (3) symptoms resulting in the complaint of excessive daytime sleepiness. As the differential diagnosis of parasomnias is complex and may involve very unusual conditions, comprehensive polygraphic monitoring (including extensive EEG with a paper speed of at least 15 mm/sec, continuous technician attendance, and audiovisual recording) is best conducted in an experienced center and the PSG interpreted by veteran personnel. Such extensive PSG evaluation is valuable in cases of violent or injurious nocturnal behavior and has led to or supported a definitive diagnosis in 91% of cases.<sup>39</sup> Multiple sequential PSGs may be necessary to capture a clinical or subclinical event. Ambulatory studies are usually inadequate for the evaluation of violent sleep-related behaviors.

*Comprehensive* PSG monitoring has been proven *safe and effective* in the diagnosis of conditions resulting in *sleep-related violent or injurious behaviors*.

*Persistent insomnia.* Insomnia is the most common sleep-related complaint.<sup>47-50</sup> Most authors have recommended that diagnostic sleep studies be used in a restricted sense for the diagnosis and management of chronic insomnia.<sup>47</sup> In general, the diagnosis of acute insomnia does not require PSG since most symptoms are related to intercurrent psychiatric, situational, or easily recognized medical conditions.<sup>48,49</sup> On the other hand, management of chronic insomnia may, in certain instances, require clinical PSG.

Formal studies may yield valuable information in difficult cases that do not respond to therapy aimed at the initial clinical diagnosis. For example, cryptic periodic movements of sleep (PMS) or central sleep apnea, or seizure-induced arousals, may result in the complaint of insomnia. Such sleep-related phenomena could not be detected without PSGs.

As has been recorded in three separate studies,<sup>50-52</sup> a large percentage of patients with the subjective perception of insomnia are either documented to have an unsuspected sleep disorder, such as sleep apnea, or determined to have no detectable abnormality of sleep quantity or quality. Thus, appropriate therapy may be initiated in the former, and the inappropriate and often problematic treatments spared in the latter.

In one study, approximately 30% of patients with serious, long-term insomnia benefited from PSG evaluation.<sup>53</sup> Although the specific reasons for patient or physician satisfaction were not characterized, the data do suggest that sleep center evaluations provide diagnostic and therapeutic services that are perceived useful by both patients and physicians. In another study of 123 consecutive chronic insomnia patients, PSG data were reported to provide valuable, clinically useful

information in 49% of all cases.<sup>52</sup>

The role of sleep diagnostic testing in insomnia in the absence of signs and symptoms of sleep apnea, narcolepsy, or movement disorders during sleep was discussed at the NIH Consensus Development Conference, The Treatment of Sleep Disorders of Older People.<sup>54</sup> It was thought that there are insufficient data to assess the value of PSG in the routine evaluation of insomnia. The summary statement from this conference asserts: "When necessary, referrals should be made to individuals, or a center with recognized skills, in the indications for an application of more specialized tools and recommendations for therapy."

In the absence of controlled clinical trials assessing the value of PSG in the diagnosis of insomnia patients or treatment outcome, and consistent with the NIH consensus conference statement, the Standards of Practice Committee of the American Sleep Disorders Association recently surveyed 12 psychiatrists and psychologists recognized as experts in the diagnosis and management of insomnia. These individuals reached consensus that patients meeting all of the following criteria would be appropriate for polysomnographic assessment of insomnia:

(1) The insomnia complaint has been present for a minimum of 6 months (at least 4 nights per week); (2) the insomnia has not responded to behavior/sleep hygiene intervention or withdrawal from sedative/hypnotic medication; (3) the insomnia has not responded to a therapeutic trial with sleep-promoting medication, or sleep-promoting medication is contraindicated, and (4) a medical or psychiatric cause has been excluded, or treatment of a presumed medical or psychiatric cause has been unsuccessful.

The combination of PSG followed by MSLT has been proven as *safe and effective* in the diagnosis and evaluation of *insomnia* in *selected cases*.

*Periodic movements of sleep (nocturnal myoclonus).* PMS is a PSG-defined condition characterized by periodic contraction of the anterior tibialis muscles, often associated with brief arousal. PMS may present with the complaint of insomnia or EDS, or may be an apparently incidental finding. It is present in many patients complaining of the restless legs syndrome. The extremity movements may be clinically subtle, escaping perception by the subject and/or bed partner.<sup>55</sup>

PSG has been proven as *safe and effective* in the diagnosis of periodic movements of sleep. The MSLT has been proven as safe and effective in determining the degree of hypersomnia in patients with suspected PMS presenting with the complaint of EDS.

*Circadian rhythm disorders/affective disorders.* Patients with disorders of the biologic clock such as

the delayed sleep phase syndrome may present to sleep disorders centers.<sup>56</sup> Similarly, there appear to be circadian rhythm irregularities in certain affective disorders, particularly seasonal affective disorder.<sup>57</sup> The diagnosis is usually made by examination of detailed sleep diaries. Information such as total sleep time, the timing of the sleep phase, and daytime sleepiness as determined by PSG and MSLT may be of value in refractory cases that do not respond to customary therapy for the assumed clinical diagnosis.

The combination of PSG followed by MSLT has been proven as *safe and effective* in the evaluation and diagnosis of circadian rhythm disorders in *selected cases*.

**Final PSG/MSLT report.** In addition to conventional demographic data, the following minimal information must be included in the sleep disorders evaluation report.<sup>22</sup>

1. Parameters monitored.
2. Start time and duration of day/night of study.
3. Sleep staging (time and percent time spent in each stage), total sleep time, sleep efficiency, number/duration of awakenings, latency to both NREM and REM sleep.
4. Respiratory patterns including type (central/obstructive/periodic), number, mean/range of duration, effect on oxygenation, sleep stage/body position relationship, and response to any diagnostic/therapeutic maneuvers.
5. Cardiac rate/rhythm and any effect of SDB upon ECG.
6. Detailed behavioral observations.
7. EEG or EMG abnormalities.
8. Individual subtest sleep latencies, mean sleep latency, and the number of REM occurrences on the MSLT.

**Therapy.** The treatment of sleep disorders is directed at reducing morbidity, reducing excess mortality, and improving quality of life for patient and family.<sup>54</sup> This is particularly true for the treatment of EDS, which has serious socioeconomic and public safety consequences if untreated. Effective treatment of hypersomnolent states has an immense social and economic impact upon the patient, family, and society as a whole.

The treatment of obstructive sleep apnea (OSA) includes surgery (tracheostomy, uvulopalatopharyngoplasty [UPP], and maxillofacial reconstruction), and nasal CPAP.<sup>58,59</sup> Weight loss may be effective in some but is difficult to achieve, especially in severely hypersomnolent individuals. Medications (progesterone, tricyclic antidepressants) are rarely useful in clinically significant SDB. The efficacy of mechanical (tongue-retaining, dental) devices awaits objective verification. Repeat sleep studies following UPP is indicated, due to the high discrepancy between subjective and objective response. Follow-up studies in patients treated

with tracheostomy or CPAP is not warranted unless hypersomnia persists. There is a 6% coincidence of OSA and narcolepsy, so the persistence of EDS following apparently effective treatment of OSA requires repeat PSG (with treatment during study) followed by a MSLT.

Treatment of narcolepsy usually includes stimulant medication and strategic napping for the hypersomnia and tricyclic antidepressants or monoamine oxidase inhibitors for the cataplexy.<sup>33</sup> Idiopathic CNS hypersomnia is treated with stimulants.

The treatment of PMS usually includes clonazepam, carbidopa-levodopa, or opiates.<sup>55</sup>

The treatment of violent sleep-related behavior depends upon the verified etiology: self-relaxation or benzodiazepines for sleep terrors/sleepwalking, clonazepam for RBD, anticonvulsants for nocturnal seizures, and psychotherapy for psychogenic dissociative states.<sup>44</sup>

The treatment of circadian rhythm disturbances and certain affective disorders may include chronotherapy or phototherapy.<sup>56,57</sup>

**Summary.** Polysomnography and measurements of physiologic sleepiness (MSLT/MWT) have been established as effective and safe in identifying many sleep/wake disorders, and have identified and defined a number of specific conditions such as SDB, narcolepsy, idiopathic CNS hypersomnia, periodic movements of sleep, and the REM sleep behavior disorder. The performance of these studies requires specialized equipment and accommodations. This technology, coupled with other clinical information and appropriate medical tests, particularly in experienced hands, is valuable in the diagnosis, classification, and treatment of patients with sleep disorders.

## Conclusion

1. **Safety:** PSG for the evaluation of nighttime sleep and for the determination of daytime sleepiness is a safe procedure.
2. **Effectiveness:** The suggested effectiveness of PSG according to the type of sleep disorder is as follows:
  - A. **Sleep-disordered breathing:** *Established.* Strong positive recommendation based upon well-designed clinical studies (class II).
  - B. **Narcolepsy/idiopathic CNS hypersomnia:** *Established.* Strong positive recommendation based upon well-designed clinical studies (class II).
  - C. **Sleep-related violent or injurious behaviors:** *Established.* Strong positive recommendation based upon well-designed clinical studies (class II).
  - D. **Insomnia (selected cases):** *Established.* Positive recommendation based upon strong

consensus of expert opinion and cohort studies (class II).

- E. **Periodic movements of sleep:** *Established.* Strong positive recommendation based upon well-designed clinical studies (class II).
- F. **Circadian rhythm disorders/affective disorders:** *Promising.* Positive recommendation based upon expert opinion and small series (class III).

#### Definitions

**A. Safety and effectiveness** (From Clifford Goodman's "Profiles of 20 Technology Assessment Programs," in the Institute of Medicine publication, *Assessing Medical Technologies*, Washington, DC: National Academy Press, 1985)

**Safety:** a judgment of the acceptability of risk in a specified situation, eg, for a given medical problem, by a provider with specified training, at a specified type of facility.

**Effectiveness:** producing a desired effect under conditions of actual use.

**B. Ratings** (From "Diagnostic and Therapeutic Technology Assessment [DATTA]" JAMA 1988; 260:997-1000. Copyright 1988, American Medical Association)

**Established:** accepted as appropriate by the practicing medical community for the given indication in the specified patient population.

**Promising:** given current knowledge, this technology appears to be appropriate for the given indication in the specified patient population. As more experience and long-term follow-up are accumulated, this interim rating will change.

**Investigational:** evidence insufficient to determine appropriateness, warrants further study. Use of this technology for given indication in the specified patient population should be confined largely to research protocols.

**Doubtful:** given current knowledge, this technology appears to be inappropriate for the given indication in the specified patient population. As more experience and long-term follow-up are accumulated, this interim rating will change.

**Unacceptable:** regarded by the practicing medical community as inappropriate for the given indication in the specified patient population.

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This statement is provided as an educational service of the American Academy of Neurology. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

#### Suggested reading

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