

Epilepsy, Juvenile Myoclonic

Jose E Cavazos, MD, PhD, FAAN, Associate Professor with Tenure, Departments of Neurology, Pharmacology, and Physiology, University of Texas Health Science Center at San Antonio; Co-Director, South Texas Comprehensive Epilepsy Center; Director of the Epilepsy Center, Audie L Murphy Veterans Affairs Medical Center

Mark Spitz, MD, Professor, Department of Neurology, University of Colorado Health Sciences Center

Updated: Jan 7, 2010

Introduction

Background

Juvenile myoclonic epilepsy (JME) is an idiopathic generalized epileptic syndrome characterized by myoclonic jerks, generalized tonic-clonic seizures (GTCSs), and sometimes absence seizures. JME is relatively common and usually responds well to treatment with appropriate anticonvulsants. However, JME is frequently misdiagnosed until the patient is specifically asked about the leading symptom, jerky movements occurring primarily within the first couple of hours after awakening. Other keys to the diagnosis include normal intelligence, onset around adolescence, GTC seizures occurring shortly after awakening, family history of the condition, and seizures after precipitating factors such as sleep deprivation or psychological stress. Although patients usually require lifelong treatment with anticonvulsants, their overall prognosis is generally good.

Brief history of JME

In 1867, Herpin was the first to describe a probable case of JME.^[1] He described a bright boy aged 13 years who developed upper-body jerks that progressed to "full seizures" 3 months later. Later, Rabot^[2], Lundborg^[3], and other physicians reported patients who had similar seizures, and terms such as *impulsions* were used to describe the myoclonic jerks. Janz and Mathes published a monograph about patients with "propulsive petit mal epilepsy" in 1955.^[4] In 1957, Janz and Christian published observations of a group of patients with a syndrome now known as JME.^[5] Janz named this syndrome "impulsive petit mal epilepsy." Lund introduced the term *juvenile myoclonic epilepsy* in 1975^[6], and the International League Against Epilepsy has adopted this term.

Definition

Under the proposal for revised classification of epilepsies and epileptic syndromes, in 1989 the Commission on Classification and Terminology of the International League Against Epilepsy defined JME (impulsive petit mal) as follows: "Impulsive petit mal appears around puberty and is characterized by seizures with bilateral, single or repetitive, arrhythmic, irregular myoclonic jerks, predominantly in the arms. Jerks may cause some patients to fall suddenly. No disturbance of consciousness is noticeable. Often, there are GTCS and, less often infrequent absences. The seizures usually occur shortly after awakening and are often precipitated by sleep deprivation. Interictal and ictal EEG have rapid, generalized, often irregular spike-waves (SW) and polyspike-waves (PSW); there is no close phase correlation between EEG spikes and jerks. Frequently the patients are photosensitive. The disorder may be inherited and sex distribution is equal. Response to appropriate drugs is good."

In one case of identical twins in the first author's experience (JEC), one twin exclusively had absences and had been treated only with ethosuximide since childhood. She never had myoclonic or generalized tonic-clonic seizures, and her seizures were well controlled with a drug that was considered ineffective in the treatment of these other types of seizures. The other twin first presented with generalized tonic-clonic seizures at the age of 18 years; in retrospect, she had noticed morning myoclonic jerks for 2 years before her presentation. She had never had absences. Their EEGs showed typical polyspike and slow-wave discharges interictally in both cases with no obvious difference between the twins.

Pathophysiology

Etiology

JME is an idiopathic generalized epilepsy syndrome. It is not associated with conditions such as head trauma, brain tumor, or encephalitis. Neuropathologic studies involving specialized staining techniques in patients with primary generalized seizures (including a few with a diagnosis of JME) have revealed microscopic brain alterations. Changes include an increase in the number of partially dystopic neurons in the stratum moleculare, white matter, hippocampus, and cerebellar cortex; an indistinct boundary between the cortex and the subcortical white matter and between lamina 1 and 2; and a columnar arrangement of cortical neurons. These findings are termed microdysgenesis and have been interpreted as a manifestation of minimal developmental disturbances. However, results of routine pathologic analysis of brain specimens from patients with JME are typically normal.

The exact cause of this disorder remains unknown. However, considerable progress has been made in the understanding of some families with specific mutations that yield the clinical phenotype of JME. Some of the known mutations result in abnormalities in ion channel proteins such as the beta-4 subunit of calcium channels and the chloride channel 2 protein. A protein called myoclonin has been identified. Its function remains uncertain but has been implicated in apoptosis, cell division, and cell migration. These functions might explain the subtle abnormalities in cortical migration reported in the neuroimaging of some patients with JME.

A 2008 published study demonstrated increased GABA-A receptor subunit degradation in a mutation of the alpha1-subunit (A322D) of GABA-A receptor identified in a large Canadian family with juvenile myoclonic epilepsy.^[7] This results in a decreased lifespan of the functional GABA-A receptor on the plasma membrane. A review article by MacDonald and Kang describes additional mechanisms that might result in hyperexcitability.^[8]

In another study, there was a reduction in the regional binding potential to the dopamine transporter (DAT) in the substantia nigra and midbrain (but not in caudate or putamen) in a PET study of patients with JME as compared with healthy controls.^[9]

Genetics

JME is an inherited disorder, but the exact mode of inheritance is not clear. About a third of patients with JME have a positive family history of epilepsy. About 17-49% of patients with JME have relatives who have epileptic seizures, including parents (about 4%) and children (about 7%). The risk of expressing clinical JME might be slightly higher in female individuals than in male individuals and in relatives of people with JME. However, some studies have shown similar sex-related risks.

Progress in identifying genetic mutations in patients and families with JME has been considerable. Dr. Delgado-Escueta has written a comprehensive review about the genetics of JME.^[10] The syndrome of JME likely consists of many genetic diseases that result in a similar electroclinical syndrome. See Causes for a further discussion on specific mutations.

Although investigators in most studies have presumed that JME is an autosomal dominant condition (ie, 50% risk of inheritance), it has incomplete penetrance, which means that some individuals who inherit the JME gene or genes do not express clinical JME. However, their children may inherit the JME genes and express clinically obvious disease. To an untrained observer, the disease seems to skip generations. For relatives of a patient with JME, the risk of having clinically obvious JME is small: 3.4% in parents, 7% in siblings, and 6.6% in children.

Despite similar genetic burden, the phenotype of JME might vary among relatives just as exemplified above in the case of identical twins with the proband having JME (myoclonus and GTC seizures) and the identical twin only having childhood absence epilepsy. A French-Canadian study of probands with JME demonstrated only an absence syndrome in 27% of relatives with seizures.^[11]

Frequency

United States

The risk of JME in the general population is estimated to be 1 case per 1000-2000 people. JME is a relatively common idiopathic generalized epilepsy. It represents about 5-10% of all epilepsies; however, the exact figures may be higher, as the condition is often misdiagnosed.

International

The incidence and prevalence of JME appear to be the same in all the populations that have been studied.

Mortality/Morbidity

Sudden unexpected death in epilepsy (SUDEP) and accidental morbidity and mortality have been observed as in other epileptic syndromes with generalized tonic clonic seizures. Seizure precautions to minimize these risks are discussed later in this chapter.

Race

No systematic racial differences have been observed. However, it is likely that some specific genetic mutations among the different types described in families with JME might be more prevalent among different racial groups. For example, the myoclonin (EFHC1) mutation has been found in 9-20% of Mexican-American families with JME, but only in 3% of Japanese families with this disorder.^[10]

Sex

Findings from some studies suggest that JME is slightly more prevalent among females than males. The reason is unknown. However, data from other studies indicate similar prevalences in both sexes.

Age

- JME typically begins in adolescence. Although the age of onset varies from 6-36 years, symptoms typically begin in adolescents aged 12-18 years.
- Myoclonic jerks, GTCSs, and absence seizures all have an age-related onset in JME.
- If absence seizures are a feature, they usually begin between the ages of 5 years and 16 years. Myoclonic jerks may follow 1-9 years later, usually around the age of 15 years. GTCSs typically appear a few years later than myoclonic jerks.
- Why the onset of this genetic disorder is delayed until adolescence is unclear.

Clinical

History

JME is diagnosed based on clinical findings. Video EEG monitoring of typical seizures is the criterion standard, but in the great majority of patients, a working diagnosis of probable JME is made on clinical history. Although observers' descriptions of seizures are helpful, caution must be used regarding their validity. The most important element in the diagnosis of JME is the patient's history. Any patient who presents with generalized tonic clonic seizures (GTCSs) without an aura should be questioned about myoclonic jerks, the time of day when the seizures occurred, and any precipitating factors.

- Symptoms usually begin in adolescence.
- Leading symptom is jerky movements that occur in the morning but might occur throughout the day.
- Patients do not lose consciousness during myoclonic jerks.
- Typically, seizures occur shortly after awakening.
- Intelligence is normal.
- Precipitating factors include sleep deprivation and psychological stress.
- About 17-49% of patients have a family history of epilepsy.
- Myoclonic jerks or seizures
 - Myoclonic jerks or seizures without impairment of consciousness are the cardinal symptoms of JME. Although an occasional, strong myoclonic jerk may make patients momentarily seem to be "in a fog," a key feature is that consciousness is preserved during these jerks.
 - The jerks are usually brief, bilateral, arrhythmic contractions that mainly involve the shoulders and arms. However, some patients report jerking in the lower limbs, trunk, or head. Some jerks occur unilaterally. In a video-EEG study, Hirano et al characterized myoclonic jerks in patients with JME as being more likely to occur in clusters, with distal predominance, and involving extension muscles.^[12]
 - The frequency and intensity of these jerks may vary. For instance, they may be perceived only internally, as an electric shock-like sensation. If the jerks are violent, patients may throw objects they are holding or even fall to the floor.
 - Myoclonic jerks can occur in rapid succession and even progress to myoclonic status epilepticus. However, more often a rapid succession of myoclonic jerks evolves into a primary GTCS.

- Myoclonic jerks occur as the only seizure type in approximately 17% of patients with JME; the rest have GTCSs, or absence seizures, or both in addition to myoclonic jerks.
- Myoclonic seizures tend to subside by the fourth decade^[13], but other seizure types might continue.
- Generalized tonic-clonic seizures
 - GTCSs occur in approximately 80% of patients with JME.
 - GTCSs of JME are typically symmetric, with a prolonged tonic phase that may lead to cyanosis and tongue biting and no sensory aura.
 - GTCSs are sometimes preceded by a series of myoclonic jerks of increasing severity that evolve into an initial clonic phase of a GTCS. The GTCSs often cause a patient with JME to seek medical attention; in this setting, patients should be questioned specifically about myoclonic jerks because most patients do not mention them.
- Absence seizures
 - In JME, absence seizures occur somewhat less often than do GTCSs. Janz reported that 28% of his patients with JME also had absence seizures.
 - When these seizures are a feature of JME, they are often the first clinical manifestation of the syndrome, with myoclonic jerks typically following 1-9 years later. In JME, absence seizures are typically short, lasting a few seconds, and they usually are not accompanied by motor signs.
 - Severity of seizures is somewhat age dependent. When they appear in children younger than 10 years, absence seizures of JME are reported less often than those of childhood absence epilepsy. Some recollection of the ictal events is common, particularly in patients that have persistence of these seizures during adulthood. Automatism is rare. When the seizures begin in children aged 10 years or older, absence seizures of JME may be even less severe than they otherwise would be, with merely a brief interruption in the patient's ability to concentrate. In a video-EEG monitoring study of patients with absence seizures, Sadleir et al found that patients with JME tend to have shorter seizures than patients with other epileptic syndromes with absences.^[14]
 - Sometimes, the first manifestations of JME are childhood absence seizures. A clue to this diagnosis is the development of GTCSs or myoclonic seizures within a couple of years after starting treatment with ethosuximide.
 - Approximately 3-8% of children who present with absence seizures ultimately receive a diagnosis of JME.
- Seizure presentations
 - Patients may have myoclonic jerks plus a combination of other seizure types.
 - In about 60% of patients, JME begins with myoclonic jerks, which are followed by the onset of relatively uncommon GTCSs a few years later.
 - The finding of myoclonic jerks plus absence seizures and GTCSs is the next most common combination, occurring in approximately 30% of patients with JME.
 - The combination of myoclonic jerks and absence seizures without GTCSs is rare, occurring in only 2% of patients.
- Precipitating factors of seizures
 - Seizures of JME often are precipitated by lack of sleep, psychological stress, noncompliance of medication, and drinking alcohol. These factors can be a particular problem in adolescents; staying up late at night to study or party can easily lead to myoclonic seizures or GTCS the next morning. Patients with JME tend to be

sensitive to photic stimulation. Approximately 30% of patients with JME are photosensitive; females typically are more sensitive than males.

- The time of day is also important because JME has a characteristic circadian pattern of clinical activity. Myoclonic jerks, GTCSs, and absence seizures all tend to occur in the early morning after the patient awakens. To a lesser extent, these symptoms also occur in the evening when the patient is relaxing. When myoclonic jerks occur in the mornings, patients may have difficulty in eating breakfast or brushing their teeth. In some studies, nearly 90% of patients with JME had myoclonic jerks on awakening; the rest had either random jerks throughout the day or jerks at night.
- [TMS] In a study using transcranial magnetic stimulation (TMS) to examine the diurnal variability of cortical excitability, Badawy et al demonstrated that short and long intracortical inhibition was considerably more impaired in the mornings as compared with the afternoons in patients with JME.^[15] This might suggest a biological basis for the clinical observation of increased seizure frequency within the first hour upon awakening in patients with JME.
- Precipitating factors can be summarized as follows:
 - Sleep deprivation
 - Psychological stress
 - Alcohol use
 - Noncompliance of medication
 - Photic stimulation
 - Menses
 - Time of day - Usually mornings
- Comorbidities
 - Psychiatric comorbidities have been described often in patients with JME. In one study, 49% of patients with JME had a psychiatric comorbidity.^[16] Anxiety and mood disorders were reported in 23% and 19% of patients with JME, respectively.
 - Neuropsychological testing of patients with JME have shown selected frontal lobe dysfunction in tests such as the Wisconsin Card Sorting test and the Word Fluency test.^[17] This is despite having normal IQ testing through conventional Wechsler testing. Impairment in executive function has also been reported.^[18]

Physical

- Findings on physical examination are usually normal. No abnormalities are usually identified in patients with JME.
- Intelligence is normal. This observation is in contrast to findings with diseases such as progressive myoclonic epilepsies, in which progressive mental deterioration is the rule.

Causes

The exact cause of JME remains unknown. Several families have specific mutations in various genes and a complex mode of inheritance.

Mutations in genes encoding ion channels have been associated with JME, including those encoding for the beta-4 calcium channel subunit (*CACNB4*), the gamma-aminobutyric acid (GABA) receptor subunit (*GABRA1*), and the chloride channel (*CLCN2*). Each of these channelopathies have been described in a single family and are rare causes of JME.^[19]

One approach has been the use of linkage studies in several families with JME at the same time. This approach led to the identification of 3 additional loci: *EJM1* at chromosomal region 6p12-p11, *EJM2* at 15q14, and *EJM3* at 6p21.

Suzuki et al described a gene (*EFHC1*) in the *EJM1* site at 6p12–p11, which had 5 missense mutations that cosegregated with epilepsy or EEG PSW in affected members of 6 unrelated families with JME.^[20] Small, R-type calcium currents were observed with the mutations of *EFHC1*. Apoptosis, a form of programmed cell death, was also reduced with mutations of *EFHC1*.

A more recent study examined the expression profile and distribution of *EFHC1* messenger RNA in rats and mice during development.^[21] Expression is intense in ependymal cells. In both species, *EFHC1* expression appeared to be greater early in brain development with a progressive decrease in expression from birth to 14 days of life suggesting that some of the abnormalities described in cortical development might be due to inappropriate expression of *EFHC1*. Mice deficient in *EFHC1* develop spontaneous myoclonic seizures during adulthood and they have an increased susceptibility to pentylenetetrazol-induced convulsions.^[22]

A study by the Genomic group of Delgado-Escueta demonstrated that 4 of the polymorphisms of the coding region for *EFHC1* do not contribute as susceptibility alleles in a population of sporadic JME patients.^[23] However, in consecutive JME patients seen in tertiary clinics in Mexico and Honduras, 9% of them had mutations in Myoclonin1/*EFHC1*.^[24]

The causative gene at the *EJM2* locus has not been identified. The *EJM3* locus has been associated with 2 SNP variants of the promoter of the *BRD2 (RING3)* gene in patients with JME.^[25] *BRD2 (RING3)* is presumed to be a nuclear transcriptional regulator during development. However, a Dutch study failed to replicate the association between *BRD2 (RING3)* and JME.^[26] The mutations found in *EJM1* and *EJM3* pinpoint genetic factors that are important during development. Therefore, microdysgenetic abnormalities are likely to be found in patients with JME.

Differential Diagnoses

Absence Seizures

Benign Childhood Epilepsy

Frontal Lobe Epilepsy

Tonic-Clonic Seizures

Other Problems to Be Considered

Epilepsy with generalized tonic-clonic seizures on awakening

Nocturnal generalized tonic-clonic seizures

Myoclonic absence epilepsy

Myoclonus

Partial seizures with secondary generalization

Progressive myoclonic epilepsies

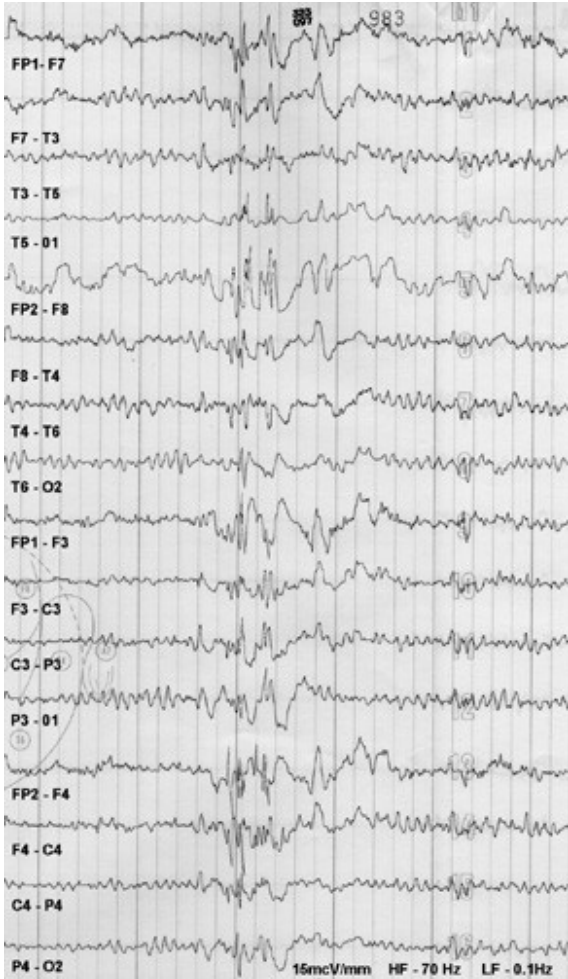
Workup

Imaging Studies

- Neuroimaging studies are typically normal in juvenile myoclonic epilepsy (JME). Many clinicians believe that, in the presence of an adequate supportive history, EEG abnormalities, normal intelligence, and normal neurologic findings, neuroimaging studies are unnecessary. However, the clinical scenario might not be as clear as the classical description.
- MRIs of the brain are usually unremarkable. This observation reflects the fact that JME is an idiopathic generalized epilepsy and not caused by conditions such as brain tumors or encephalitis. However, quantitative morphometric studies using a voxel-based technique have shown some differences among patients with JME. For example, decreased gray matter volume was found in thalami, insula cortices, and cerebellar hemispheres bilaterally in patients with JME. An increase in gray matter volume was observed in the right superior frontal, orbitofrontal, and medial frontal gyri of patients with JME as compared with age-matched controls. Patients with JME who are photosensitive have decreased gray matter volume in the visual cortex as compared with the control group; this was not found in patients with JME who were not photosensitive.^[27]
- Some patients with brain MRIs, particularly if the MRIs are high definition, or high Tesla studies, have shown minor abnormalities of cortical development. Tae et al reported reduction in the cortical thicknesses of frontal and temporal gyri in patients with JME.^[28] However, these observations were not confirmed in the study by Roebeling et al.^[29] Progressive thalamic atrophy was also reported in patients with JME by the same group.^[30] The decreased thalamic volume has been confirmed by several other groups and might be related to executive function impairment.^[31,32] Furthermore, studies using diffusion tensor imaging (DTI) have also confirmed that abnormalities in the degree of thalamocortical fiber orientation and tissue anisotropy correlate with the frequency of generalized tonic clonic seizures.^[33]
- Despite these minor quantitative differences, the guidelines of the International League Against Epilepsy (ILAE) do not recommend routine neuroimaging studies in patients with JME.^[34]
- Other neuroimaging studies
 - Magnetic resonance spectroscopy (MRS) has also confirmed abnormalities in the thalamus and thalamocortical system of patients with JME.^[35,36]
 - Studies using transcranial magnetic stimulation show abnormalities in cortical excitability in patients with JME.^[37]
 - Functional MRI (fMRI) studies have not shown significant abnormalities in patients with JME.^[29]

Other Tests

- Study of choice to confirm the clinical diagnosis is sleep-deprived EEG with activation procedures (ie, hyperventilation, photic stimulation). A normal study does not rule out epilepsy or JME. Typical EEG abnormalities are highly supportive of the clinical diagnosis (see Media file 1).



Findings in a man with a history of generalized tonic-clonic seizures (mostly nocturnal) and myoclonic jerks (mostly in the morning) since the age of 14 years. Carbamazepine exacerbated his myoclonic seizures. Sleep-deprived EEG was digitally recorded and then plotted by using an analog paper machine. The patient was getting drowsy when this burst of polyspike and slow wave was recorded.

- The typical interictal EEG abnormality consists of a generalized 4- to 6-Hz spike or polyspike and slow-wave discharges lasting 1-20 seconds (see Media file 1). Usually, 1-3 spikes precede each slow wave. When absence seizures are also present, 3-Hz spike-and-wave activity may be seen in addition to the polyspike-and-wave pattern.

- The ictal EEG associated with myoclonic jerks typically reveals 10- to 16-Hz polyspike discharges. These may be preceded by spike and wave activity and are often followed by 1- to 3-Hz slow waves. The number of spikes is typically 5-20 and tends to be proportionately correlated with the clinical intensity of the seizure. These epileptic discharges may briefly persist, even after clinical activity has ceased. Seizures in patients with JME tend to be associated with polyspikes and disorganization of the paroxysm.^[38]
- Absence seizures of JME may be associated with ictal EEG patterns consisting of 3-Hz spike-and-wave activity. Sometimes, these are preceded by 4- to 6-Hz polyspike-and-wave discharges, which slow to 3 Hz as the patient loses consciousness.
- Background activity of the EEG is normal in JME. Hyperventilation and photic stimulation often facilitate the appearance of epileptiform discharges. Photic stimulation frequently precipitates spike-and-wave patterns. This occurs in approximately 30% of patients with JME, compared with 18% of patients with childhood absence epilepsy, 13% of patients with epileptic seizures on awakening, and 7.5% of patients with juvenile absence epilepsy. Photosensitivity of the EEG in patients with JME has been reported to be as high as 50% of the cases.^[39] The EEG background has also been studied quantitatively in small groups of patients with JME.^[40]
- Treatment with medications clinically effective in JME might also reduce the frequency of interictal abnormalities. Levetiracetam adjunctive therapy in patients with JME increased the likelihood of a normal EEG from 8% to 53% after achieving maintenance therapy. There was a decrease in frequency of interictal discharges and suppression of the paroxysms induced by photic stimulation.^[41]
- Ictal and interictal polyspike-and-wave discharges are not pathognomonic of JME; they may be seen in other primary generalized epilepsies as well as in myoclonic epilepsies of early childhood.
- In addition to generalized epileptiform discharges, focal abnormalities may be found in 20-55% of patients with JME. These include focal slow waves, generalized discharges that evolve from a focal onset, and focal spikes or spike-and-wave discharges. Ignorance of these changes may lead to one's mistakenly ruling out the syndrome. The etiology of these focal abnormalities is unclear. A possible explanation is structural changes in the cerebral cortex secondary to recurrent seizures or head injury; another is fluctuation in the refractoriness of the cortex to the influence of a spike/wave generator.
- A morning EEG has been proposed as a superior strategy to detect generalized epileptiform discharges in patients with JME. In this particular study, a morning awake EEG detected interictal epileptiform discharges in 69% of patients while an afternoon awake EEG in the same patients demonstrated epileptiform discharges in fewer than 20% of patients.^[42]
- Video EEG monitoring in patients with atypical features of JME might be needed. In a one study, most people with JME only required no more than 2 days of stay to demonstrate diagnostic abnormalities in the EEG.^[43]
- A combined magnetoencephalography and EEG study demonstrated interictal spikes with localizations mainly in the central and premotor regions (Stefan et al., 2009) in patients with JME as compared with other absence syndromes.^[44]

Treatment

Medical Care

Medical therapy with anticonvulsants typically is needed (see Medication). Avoidance of precipitating events such as alcohol use and sleep deprivation may be useful but is not sufficient to control the seizures of juvenile myoclonic epilepsy (JME).

The selection of AEDs for the treatment of JME depends several factors, including patient's comorbidities, preferences, prior history of adverse events, and gender. Traditionally, divalproex sodium has been used as first-line therapy for JME despite not having an approved FDA indication for this condition. Several studies using lamotrigine, topiramate, levetiracetam, and zonisamide have shown similar efficacy, and in some cases better tolerability, than divalproex sodium. In 2006, levetiracetam became the first drug that received an FDA indication for use specifically in JME.

Surgical Care

Surgical treatment is not indicated, as JME is a primary generalized epilepsy. Some uncontrolled studies have suggested that vagal nerve stimulation might be helpful for patients with intractable seizures of primary generalized onset, such as JME.

Consultations

JME is rarely diagnosed in the primary care setting. Most often, an epileptologist diagnoses the condition after several years of inadequate treatment with medications such as carbamazepine or phenytoin.

Activity

Seizure precautions, including restrictions on driving, must be observed until seizures that impair consciousness are controlled (ie, seizure free) for the recommended period, typically 3-12 months, though the length varies from state to state in the United States. Other precautions include the avoidance of heights, swimming alone, and taking unsupervised baths. Patients with seizures cannot have a commercial driving license until they complete a seizure-free period of 5 years. In addition, patients with seizures are not permitted to fly aircraft.

Studies have shown that patients with JME experience similar decreases in quality of life as compared with other epileptic syndromes.^[45]

Medication

The goal of pharmacotherapy is to reduce morbidity and prevent complications.

The US Food and Drug Administration (FDA) has not approved any anticonvulsant solely for the treatment of JME. In 2006, the FDA approved the adjunctive use of levetiracetam for the treatment of JME. Divalproex sodium has been approved as adjunctive therapy for patients with multiple seizure types that include absence seizures. However, many patients with JME do not have absence seizures. In most patients with JME, seizures are well controlled with monotherapy. Valproic acid has been considered the treatment of choice for JME for many years, but epileptologists are increasingly using other choices as first-line therapies. Approximately 80% of patients with JME become seizure free with valproate monotherapy.

Levetiracetam is useful for the treatment of myoclonic seizures.^[46,47] It received FDA approval for adjunctive therapy for the treatment of JME in 2006. Noachtar et al demonstrated in a randomized, double-blinded, placebo-controlled trial that levetiracetam adjunctive therapy reduced all seizure types and myoclonic seizures in patients with juvenile myoclonic epilepsy.^[48]

Meta-analysis of 2 randomized controlled trials affirm that JME is highly responsive to treatment with levetiracetam.^[49] Small, uncontrolled studies of levetiracetam monotherapy in JME suggest efficacy and tolerability.^[50,51]

Lamotrigine may also be useful in the treatment of JME. This agent is ideal for patients who cannot tolerate the adverse effects of valproate, such as weight gain, tremor, stomach upset, and hair loss. In some patients, lamotrigine monotherapy has completely controlled their seizures. However, recent evidence indicates that lamotrigine may exacerbate myoclonic jerks. Data from a recent open-label study suggested that lamotrigine was better tolerated than valproate, with similar efficacy.^[52] A European expert opinion study showed that lamotrigine was first-line choice for JME in adolescent females while valproate was the first-line choice in adolescent males.^[53]

Topiramate has been useful in the treatment of primary generalized seizures; it may effectively prevent the seizures of JME.^[54]

Findings from an open-label study also suggested that zonisamide might be effective and well tolerated in patients with JME.^[55]

In general, low doses of appropriate anticonvulsants are needed to successfully treat JME. Although treatment with phenytoin, carbamazepine, or phenobarbital may control some seizure components of JME (typically at high doses), these drugs may increase seizure frequency (eg, myoclonic exacerbation with carbamazepine) and occasionally precipitate new seizure types, such as absence seizures. However, they may be used in combination if the patient's condition does not respond to other drugs.^[56]

Clonazepam is often used during seizure exacerbations in patients with JME; however, it is inadequate as long-term treatment.

A patient's medication should rarely be changed because he or she is not having seizures. In medical school, physicians are taught to treat patients and not serum concentrations. A low-dose requirement is not unusual; in fact, the great majority of patients with JME need relatively low levels of anticonvulsants to achieve adequate seizure control (as long as it is an appropriate medication for the syndrome). A valproic-acid serum concentration of

Pediatric

2-12 years: Used as add-on therapy

With divalproex sodium: 0.15 mg/kg/d PO qd or divided bid initial dose; round down to nearest 5 mg; double (0.3 mg/kg/d) 2 wk later (wk 3, 4); usual maintenance dose is 1-5 mg/kg/d; not to exceed 200 mg/d; bid typically best tolerated

With EIAEDs: 0.6 mg/kg/d divided bid initial dose; increase to 1.2 mg/kg/d 2 wk later

>12 years: Administer as in adults

Interactions

Acetaminophen increases renal clearance, decreasing effects; phenobarbital and phenytoin increase metabolism, decreasing levels; valproic acid increases half-life

Contraindications

Documented hypersensitivity, known drug-induced rash

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Serious rash that requires hospitalization (exceeding dosing recommendations during titration may increase risk of this problem); risk of serious rash similar to that of carbamazepine, phenytoin, phenobarbital, and other anticonvulsants

Topiramate (Topamax)

Indicated and FDA approved as adjunctive therapy for adults and children with partial-onset seizures and primary GTCSs. Approved for monotherapy in primary GTCSs. Some patients with JME have primary GTCSs but may also have myoclonic and absence seizures. Available as 25-, 100-, and 200-mg tab and as 15- and 25-mg sprinkle cap.

Dosing

Adult

Initial: 25-50 mg PO qhs; increased by 25-50 mg/d qwk bid until maximum tolerated dose or 400 mg/d

Authors' regimen: 25 mg/d initially; increased 25 mg/d bid qwk; this regimen may be best tolerated; target dose in JME is 200 mg/d; titration to higher doses might be needed.

Pediatric

2-16 years

Initial dose: 1-3 mg/kg/d PO; increase by 1-3 mg/kg/d q2wk until maintenance dose achieved

Maintenance dose: 5-9 mg/kg/d PO divided bid

Interactions

Phenytoin, carbamazepine, and valproic acid substantially reduce levels; reduces digoxin and norethindrone levels; may increase risk of renal-stone formation if given with carbonic anhydrase inhibitors (avoid combination); extreme caution with CNS depressants (may have additive effect in CNS depression as well as other cognitive or neuropsychiatric adverse events)

Contraindications

Documented hypersensitivity, concomitant carbonic anhydrase inhibitors

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Caution in renal or hepatic impairment; eliminated mostly through kidneys; metabolism not well understood; 1.5% risk of renal stones (drug is carbonic anhydrase inhibitor)

Zonisamide (Zonegran)

Indicated for adjunctive treatment of partial seizures with or without secondary generalization. Evidence suggests effectiveness in myoclonic and other generalized seizure types as well.

Dosing

Adult

100 mg/d PO qd or bid for 2 wk, then increase by 100 mg/d PO q2wk; not to exceed 400 mg/d

Pediatric

Not established

Interactions

May increase serum carbamazepine levels; carbamazepine may increase concentrations; phenobarbital may decrease levels

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

C - Safety for use during pregnancy has not been established.

Precautions

May cause drowsiness, weight loss, ataxia, nausea, and slowing of mental activity; increased risk of oligohidrosis and hyperthermia in children

Levetiracetam (Keppra)

Indicated as adjunctive therapy for myoclonic seizures in adults and adolescents and in primary generalized tonic clonic seizures. Mechanism of action is unknown, but it is presumed to involve binding to the SV2A site in synaptic terminals.

Dosing

Adult

1000-3000 mg/d PO divided in bid administration

Pediatric

10-30 mg/kg/d PO bid

Interactions

None reported

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Caution in renal impairment; major adverse effects include somnolence, asthenia, incoordination, mild leukopenia (3%) and behavioral changes (eg, anxiety, hostility, emotional lability, depression and psychosis [1-2%], depersonalization); may cause drowsiness, weight loss, ataxia, nausea, and slowing of mental activity; increased risk of oligohidrosis and hyperthermia in children

Follow-up

Prognosis

- Seizure control in juvenile myoclonic epilepsy (JME) tends to be excellent with relative low doses of the appropriate anticonvulsants (eg, valproic acid).
 - The severity of JME seizures appears to decrease in adulthood and senescence.

- Whether patients outgrow JME, as compared with other primary generalized epilepsies, at a late age (ie, >60 y) is unknown. However, in one author's experience, older relatives of people with JME who have a history of seizures are often untreated and rarely have seizures. An epidemiologic study is needed to settle this issue.
- Risk of recurrence is more than 80% if anticonvulsants are withdrawn during adolescence or adulthood, even after many years of complete seizure control with low doses of appropriate medications.
- Life-long treatment is usually necessary. However, treating a patient older than 60 years with this condition is rare. Whether JME spontaneously remits after a particular age is uncertain. Rare cases of late-onset JME have been reported as late as the eighth decade of life.^[57]
- Camfield and Camfield conducted a long-term population-based study of patients with juvenile myoclonic epilepsy. Between 1977 and 1985, the 24 patients in Nova Scotia who developed JME by age 16 years were contacted 25 years later. In 17%, all seizure types in JME had resolved; in 13%, only myoclonus persisted. Nevertheless, many patients' lives were complicated by depression, social isolation, unemployment, and social impulsiveness.^[58]

Patient Education

- The Epilepsy Foundation has a large selection of brochures and informational booklets for patients and their families. The American Epilepsy Society is the professional organization for people treating patients with epilepsy or for those doing research in this field.
- For excellent patient education resources, visit eMedicine's Brain and Nervous System Center. Also, see eMedicine's patient education article Epilepsy.

Miscellaneous

Medicolegal Pitfalls

- The medicolegal pitfalls comprise 2 categories: inappropriate diagnosis and liability of the patients having seizures.
 - One reason for inappropriate diagnosis is that patients often do not report myoclonic jerks. In most patients, JME is diagnosed after they have a generalized tonic-clonic seizure and are treated with one of the usual first-line anticonvulsants, such as phenytoin or carbamazepine. In some cases, carbamazepine increases the frequency of myoclonic seizures, often unmasking the diagnosis. Recognition of worsening with carbamazepine should lead to appropriate diagnosis and therapy. Myoclonic seizures are typically not harmful and rarely associated with any kind of injury.
 - Patients with suspected seizures manifesting as lapses of consciousness during wakefulness should be educated and warned about seizure precautions. Documenting on the patient's chart that driving and occupational hazards for people with seizures were discussed is helpful. Physicians should be aware of state regulations regarding driving, which considerably vary among states and nations.
- Seizure precautions include warnings about unpredictable lapses of consciousness due to seizures during a variety of activities, including the following:
 - Driving vehicles or flying aircraft
 - Immersing oneself in water, eg, for baths, swimming, and other purposes

- Being at heights, eg, on roofs, scaffolds, and ladders
- Using fire, eg, on stoves, in ovens, in open fires
- Using power tools, eg, drills and saws
- Warnings should be tailored to each specific patient, and they should include factors such as seizure control, time of the occurrence of seizures, medication compliance, and the patient's occupation, among other concerns.

Special Concerns

- Most of the time, when a neurologist examines a pregnant woman with epilepsy, it is after the first 6 weeks of gestation (ie, after the neural tube normally closes).
 - That is one of the reasons all women of childbearing age who are taking anticonvulsants should also take folic acid 1 mg/d.
 - In general, most epileptologists believe that the anticonvulsants that help that patient the most should be continued during pregnancy.
 - Frequent monitoring of drug levels is recommended, as pregnancy induces clinically significant changes in drug metabolism, clearance, and volume of distribution.
 - Women with JME are no different than other women who need to take anticonvulsants.
- A great majority of children born to women taking anticonvulsant monotherapy are healthy.
 - Valproic acid and divalproex sodium clearly pose a recognized risk of neural-tube defects (category D) that is higher than the risk associated with older anticonvulsants.
 - Evidence suggests that supplementation with folic acid may decrease this risk.
- Experience is limited with the newer anticonvulsants, including lamotrigine (category C), levetiracetam (category C), and topiramate (category C).
 - Laboratory data indicate some teratogenicity with topiramate, but the effect in humans is unknown.
 - Animal studies have revealed no evidence of teratogenicity related to lamotrigine.
 - Lamotrigine is a weak folic-acid antagonist in the gut; therefore, folic-acid supplementation is required in women of childbearing age taking this drug.

References

1. Herpin TH. Des ascès incomplets de l'épilepsie. *J Balliere et Fils*. 1867.
2. Rabot T. *De la myoclonia epileptique*. Paris, France: Medical thesis; 1899.
3. Lundborg H. *Die Progressive Myoklonusepilepsie (Unverricht's Myoklonie)*. Stockholm, Sweden: Almqvist & Wiksell; 1903.
4. Janz D, Mathes A. *Die Propulsiv Petit Mal Epilepsie*. New York, NY: Garger; 1955.
5. Janz D, Christian W. Impulsive petit mal. *Deutsche Leitschrift f Nervenheilkunde*. 1957;176:346-386.

6. Lund M, Reintoft H, Simonsen N. Ein kontrolleret social og psykologisk Undersgelse af Patienter med Juvenil Myoklon Epilepsi. *Ugeskr Laeg.* 1975;137:2415-18.
7. Bradley CA, Taghibiglou C, Collingridge GL, Wang YT. Mechanisms involved in the reduction of GABAA receptor alpha1-subunit expression caused by the epilepsy mutation A322D in the trafficking-competent receptor. *J Biol Chem.* Aug 8 2008;283(32):22043-50. [[Medline](#)].
8. Macdonald RL, Kang JQ. Molecular Pathology of Genetic Epilepsies Associated with GABA(A) Receptor Subunit Mutations. *Epilepsy Curr.* Jan-Feb 2009;9(1):18-23. [[Medline](#)].
9. Ciumas C, Wahlin TB, Jucaite A, Lindstrom P, Halldin C, Savic I. Reduced dopamine transporter binding in patients with juvenile myoclonic epilepsy. *Neurology.* Sep 9 2008;71(11):788-94. [[Medline](#)].
10. Delgado-Escueta AV. Advances in genetics of juvenile myoclonic epilepsies. *Epilepsy Curr.* May-Jun 2007;7(3):61-7. [[Medline](#)].
11. Kinirons P, Rabinowitz D, Gravel M, Long J, Winawer M, Sénéchal G, et al. Phenotypic concordance in 70 families with IGE-implications for genetic studies of epilepsy. *Epilepsy Res.* Nov 2008;82(1):21-28. [[Medline](#)].
12. Hirano Y, Oguni H, Funatsuka M, Imai K, Osawa M. Differentiation of myoclonic seizures in epileptic syndromes: a video-polygraphic study of 26 patients. *Epilepsia.* Jun 2009;50(6):1525-35. [[Medline](#)].
13. Baykan B, Altindag EA, Bebek N, Ozturk AY, Aslantas B, Gurses C, et al. Myoclonic seizures subside in the fourth decade in juvenile myoclonic epilepsy. *Neurology.* May 27 2008;70(22 Pt 2):2123-9. [[Medline](#)].
14. Sadleir LG, Scheffer IE, Smith S, Carstensen B, Carlin J, Connolly MB, et al. Factors influencing clinical features of absence seizures. *Epilepsia.* Dec 2008;49(12):2100-7. [[Medline](#)].
15. Badawy RA, Macdonell RA, Jackson GD, Berkovic SF. Why do seizures in generalized epilepsy often occur in the morning?. *Neurology.* Jul 21 2009;73(3):218-22. [[Medline](#)].
16. Filho GM, Rosa VP, Lin K, Caboclo LO, Sakamoto AC, Yacubian EM. Psychiatric comorbidity in epilepsy: a study comparing patients with mesial temporal sclerosis and juvenile myoclonic epilepsy. *Epilepsy Behav.* Jul 2008;13(1):196-201. [[Medline](#)].
17. Piazzini A, Turner K, Vignoli A, Canger R, Canevini MP. Frontal cognitive dysfunction in juvenile myoclonic epilepsy. *Epilepsia.* Apr 2008;49(4):657-62. [[Medline](#)].
18. Iqbal N, Caswell HL, Hare DJ, Pilkington O, Mercer S, Duncan S. Neuropsychological profiles of patients with juvenile myoclonic epilepsy and their siblings: a preliminary controlled experimental video-EEG case series. *Epilepsy Behav.* Mar 2009;14(3):516-21. [[Medline](#)].

19. Wallace R. Identification of a new JME gene implicates reduced apoptotic neuronal death as a mechanism of epileptogenesis. *Epilepsy Curr.* Jan-Feb 2005;5(1):11-3. [\[Medline\]](#).
20. Suzuki T, Delgado-Escueta AV, Aguan K, et al. Mutations in EFHC1 cause juvenile myoclonic epilepsy. *Nat Genet.* Aug 2004;36(8):842-9. [\[Medline\]](#).
21. Conte FF, Ribeiro PA, Marchesini RB, Pascoal VD, Silva JM, Oliveira AR, et al. Expression Profile and Distribution of Efhc1 Gene Transcript During Rodent Brain Development. *J Mol Neurosci.* Feb 4 2009;[\[Medline\]](#).
22. Suzuki T, Miyamoto H, Nakahari T, Inoue I, Suemoto T, Jiang B, et al. Efhc1 deficiency causes spontaneous myoclonus and increased seizure susceptibility. *Hum Mol Genet.* Mar 15 2009;18(6):1099-109. [\[Medline\]](#).
23. Bai D, Bailey JN, Durán RM, Alonso ME, Medina MT, Martínez-Juárez IE, et al. DNA variants in coding region of EFHC1: SNPs do not associate with juvenile myoclonic epilepsy. *Epilepsia.* May 2009;50(5):1184-90. [\[Medline\]](#).
24. Medina MT, Suzuki T, Alonso ME, Durán RM, Martínez-Juárez IE, Bailey JN, et al. Novel mutations in Myoclonin1/EFHC1 in sporadic and familial juvenile myoclonic epilepsy. *Neurology.* May 27 2008;70(22 Pt 2):2137-44. [\[Medline\]](#).
25. Pal DK, Evgrafov OV, Tabares P, et al. BRD2 (RING3) is a probable major susceptibility gene for common juvenile myoclonic epilepsy. *Am J Hum Genet.* Aug 2003;73(2):261-70. [\[Medline\]](#).
26. de Kovel CG, Pinto D, de Haan GJ, Kasteleijn-Nolst Trenité DG, Lindhout D, Koeleman BP. Association analysis of BRD2 (RING3) and epilepsy in a Dutch population. *Epilepsia.* Nov 2007;48(11):2191-2. [\[Medline\]](#).
27. Lin K, Jackowski AP, Carrete H Jr, de Araújo Filho GM, Silva HH, Guaranha MS, et al. Voxel-based morphometry evaluation of patients with photosensitive juvenile myoclonic epilepsy. *Epilepsy Res.* Oct 2009;86(2-3):138-45. [\[Medline\]](#).
28. Tae WS, Kim SH, Joo EY, Han SJ, Kim IY, Kim SI, et al. Cortical thickness abnormality in juvenile myoclonic epilepsy. *J Neurol.* Apr 2008;255(4):561-6. [\[Medline\]](#).
29. Roebeling R, Scheerer N, Uttner I, Gruber O, Kraft E, Lerche H. Evaluation of cognition, structural, and functional MRI in juvenile myoclonic epilepsy. *Epilepsia.* Jun 1 2009;[\[Medline\]](#).
30. Kim JH, Lee JK, Koh SB, Lee SA, Lee JM, Kim SI, et al. Regional grey matter abnormalities in juvenile myoclonic epilepsy: a voxel-based morphometry study. *Neuroimage.* Oct 1 2007;37(4):1132-7. [\[Medline\]](#).
31. Pulsipher DT, Seidenberg M, Guidotti L, Tuchscherer VN, Morton J, Sheth RD, et al. Thalamofrontal circuitry and executive dysfunction in recent-onset juvenile myoclonic epilepsy. *Epilepsia.* May 2009;50(5):1210-9. [\[Medline\]](#).

32. de Ara?jo Filho GM, Lin K, Lin J, Peruchi MM, Caboclo LO, Guaranha MS, et al. Are personality traits of juvenile myoclonic epilepsy related to frontal lobe dysfunctions? A proton MRS study. *Epilepsia*. May 2009;50(5):1201-9. [\[Medline\]](#).
33. Deppe M, Kellinghaus C, Duning T, M?ddel G, Mohammadi S, Deppe K, et al. Nerve fiber impairment of anterior thalamocortical circuitry in juvenile myoclonic epilepsy. *Neurology*. Dec 9 2008;71(24):1981-5. [\[Medline\]](#).
34. [Guideline] Gaillard WD, Chiron C, Cross JH, Harvey AS, Kuzniecky R, Hertz-Pannier L, et al. Guidelines for imaging infants and children with recent-onset epilepsy. *Epilepsia*. Sep 2009;50(9):2147-53. [\[Medline\]](#).
35. Lin K, Carrete H Jr, Lin J, Peruchi MM, de Ara?jo Filho GM, Guaranha MS, et al. Magnetic resonance spectroscopy reveals an epileptic network in juvenile myoclonic epilepsy. *Epilepsia*. May 2009;50(5):1191-200. [\[Medline\]](#).
36. de Ara?jo Filho GM, Jackowski AP, Lin K, Guaranha MS, Guilhoto LM, da Silva HH, et al. Personality traits related to juvenile myoclonic epilepsy: MRI reveals prefrontal abnormalities through a voxel-based morphometry study. *Epilepsy Behav*. Jun 2009;15(2):202-7. [\[Medline\]](#).
37. Akgun Y, Soysal A, Atakli D, Yuksel B, Dayan C, Arpaci B. Cortical excitability in juvenile myoclonic epileptic patients and their asymptomatic siblings: a transcranial magnetic stimulation study. *Seizure*. Jul 2009;18(6):387-91. [\[Medline\]](#).
38. Sadleir LG, Scheffer IE, Smith S, Carstensen B, Farrell K, Connolly MB. EEG features of absence seizures in idiopathic generalized epilepsy: impact of syndrome, age, and state. *Epilepsia*. Jun 2009;50(6):1572-8. [\[Medline\]](#).
39. Lu Y, Waltz S, Stenzel K, Muhle H, Stephani U. Photosensitivity in epileptic syndromes of childhood and adolescence. *Epileptic Disord*. Jun 2008;10(2):136-43. [\[Medline\]](#).
40. Santiago-Rodr?guez E, Harmony T, C?rdenas-Morales L, Hern?ndez A, Fern?ndez-Bouzas A. Analysis of background EEG activity in patients with juvenile myoclonic epilepsy. *Seizure*. Jul 2008;17(5):437-45. [\[Medline\]](#).
41. Specchio N, Boero G, Michelucci R, Gambardella A, Giallonardo AT, Fattouch J, et al. Effects of levetiracetam on EEG abnormalities in juvenile myoclonic epilepsy. *Epilepsia*. Apr 2008;49(4):663-9. [\[Medline\]](#).
42. Labate A, Ambrosio R, Gambardella A, Sturniolo M, Pucci F, Quattrone A. Usefulness of a morning routine EEG recording in patients with juvenile myoclonic epilepsy. *Epilepsy Res*. Oct 2007;77(1):17-21. [\[Medline\]](#).
43. Park KI, Lee SK, Chu K, Lee JJ, Kim DW, Nam H. The value of video-EEG monitoring to diagnose juvenile myoclonic epilepsy. *Seizure*. Mar 2009;18(2):94-9. [\[Medline\]](#).
44. Stefan H, Paulini-Ruf A, Hopfeng?rtner R, Rampf S. Network characteristics of idiopathic generalized epilepsies in combined MEG/EEG. *Epilepsy Res*. Aug 2009;85(2-3):187-98. [\[Medline\]](#).

45. Westphal-Guitti AC, Alonso NB, Migliorini RC, da Silva TI, Azevedo AM, Caboclo LO, et al. Quality of life and burden in caregivers of patients with epilepsy. *J Neurosci Nurs*. Dec 2007;39(6):354-60. [\[Medline\]](#).
46. Sullivan JE, Dlugos DJ. Idiopathic Generalized Epilepsy. *Curr Treat Options Neurol*. May 2004;6(3):231-242. [\[Medline\]](#).
47. Specchio LM, Gambardella A, Giallonardo AT, Michelucci R, Specchio N, Boero G, et al. Open label, long-term, pragmatic study on levetiracetam in the treatment of juvenile myoclonic epilepsy. *Epilepsy Res*. 2006;71(1):32-39. [\[Medline\]](#).
48. Noachtar S, Andermann E, Meyvisch P, Andermann F, Gough WB, Schieman-Delgado J. Levetiracetam for the treatment of idiopathic generalized epilepsy with myoclonic seizures. *Neurology*. Feb 19 2008;70(8):607-16. [\[Medline\]](#).
49. Rosenfeld WE, Benbadis S, Edrich P, Tassinari CA, Hirsch E. Levetiracetam as add-on therapy for idiopathic generalized epilepsy syndromes with onset during adolescence: analysis of two randomized, double-blind, placebo-controlled studies. *Epilepsy Res*. Jul 2009;85(1):72-80. [\[Medline\]](#).
50. Sharpe DV, Patel AD, Abou-Khalil B, Fenichel GM. Levetiracetam monotherapy in juvenile myoclonic epilepsy. *Seizure*. Jan 2008;17(1):64-8. [\[Medline\]](#).
51. Verrotti A, Cerminara C, Coppola G, Franzoni E, Parisi P, Iannetti P, et al. Levetiracetam in juvenile myoclonic epilepsy: long-term efficacy in newly diagnosed adolescents. *Dev Med Child Neurol*. Jan 2008;50(1):29-32. [\[Medline\]](#).
52. Morris GL, Hammer AE, Kustra RP, Messenheimer JA. Lamotrigine for patients with juvenile myoclonic epilepsy following prior treatment with valproate: results of an open-label study. *Epilepsy Behav*. Aug 2004;5(4):509-12. [\[Medline\]](#).
53. Wheless JW, Clarke DF, Arzimanoglou A, Carpenter D. Treatment of pediatric epilepsy: European expert opinion, 2007. *Epileptic Disord*. Dec 2007;9(4):353-412. [\[Medline\]](#).
54. Prasad A, Kuzniecky RI, Knowlton RC, et al. Evolving antiepileptic drug treatment in juvenile myoclonic epilepsy. *Arch Neurol*. Aug 2003;60(8):1100-5. [\[Medline\]](#).
55. Kothare SV, Valencia I, Khurana DS, et al. Efficacy and tolerability of zonisamide in juvenile myoclonic epilepsy. *Epileptic Disord*. Dec 2004;6(4):267-70. [\[Medline\]](#).
56. Nicolson A, Appleton RE, Chadwick DW, Smith DF. The relationship between treatment with valproate, lamotrigine, and topiramate and the prognosis of the idiopathic generalised epilepsies. *J Neurol Neurosurg Psychiatry*. Jan 2004;75(1):75-9. [\[Medline\]](#).
57. Tóth V, Rósonyi G, Fogarasi A, Kovács N, Auer T, Janszky J. Juvenile myoclonic epilepsy starting in the eighth decade. *Epileptic Disord*. Sep 2007;9(3):341-5. [\[Medline\]](#).

58. [Best Evidence] Camfield CS, Camfield PR. Juvenile myoclonic epilepsy 25 years after seizure onset: a population-based study. *Neurology*. Sep 29 2009;73(13):1041-5. [\[Medline\]](#).
59. Aliberti V, Grunewald RA, Panayiotopoulos CP, Chroni E. Focal electroencephalographic abnormalities in juvenile myoclonic epilepsy. *Epilepsia*. Mar-Apr 1994;35(2):297-301. [\[Medline\]](#).
60. Atakli D, Sozuer D, Atay T, et al. Misdiagnosis and treatment in juvenile myoclonic epilepsy. *Seizure*. Feb 1998;7(1):63-6. [\[Medline\]](#).
61. Biton V, Montouris GD, Ritter F, et al. A randomized, placebo-controlled study of topiramate in primary generalized tonic-clonic seizures. Topiramate YTC Study Group. *Neurology*. Apr 22 1999;52(7):1330-7. [\[Medline\]](#).
62. Buchanan N. The use of lamotrigine in juvenile myoclonic epilepsy. *Seizure*. Jun 1996;5(2):149-51. [\[Medline\]](#).
63. Canevini MP, Mai R, Di Marco C, et al. Juvenile myoclonic epilepsy of Janz: clinical observations in 60 patients. *Seizure*. Dec 1992;1(4):291-8. [\[Medline\]](#).
64. Delgado-Escueta AV, Enrile-Bacsal F. Juvenile myoclonic epilepsy of Janz. *Neurology*. Mar 1984;34(3):285-94. [\[Medline\]](#).
65. Delgado-Escueta AV, Greenberg DA, Treiman L, et al. Mapping the gene for juvenile myoclonic epilepsy. *Epilepsia*. 1989;30 Suppl 4:S8-18; discussion S24-7. [\[Medline\]](#).
66. Delgado-Escueta AV, Serratosa JM, Liu A, et al. Progress in mapping human epilepsy genes. *Epilepsia*. 1994;35 Suppl 1:S29-40. [\[Medline\]](#).
67. Dreifuss FE. Juvenile myoclonic epilepsy: characteristics of a primary generalized epilepsy. *Epilepsia*. 1989;30 Suppl 4:S1-7 discussion S24-7. [\[Medline\]](#).
68. Durner M, Janz D, Zingsem J, Greenberg DA. Possible association of juvenile myoclonic epilepsy with HLA-DRw6. *Epilepsia*. Sep-Oct 1992;33(5):814-6. [\[Medline\]](#).
69. Gram L, Alving J, Sagild JC, Dam M. Juvenile myoclonic epilepsy in unexpected age groups. *Epilepsy Res*. Mar-Apr 1988;2(2):137-40. [\[Medline\]](#).
70. Grunewald RA, Panayiotopoulos CP. Juvenile myoclonic epilepsy. A review. *Arch Neurol*. Jun 1993;50(6):594-8. [\[Medline\]](#).
71. International League Against Epilepsy. Proposal for classification of epilepsies and epileptic syndromes. Commission on Classification and Terminology of the International League Against Epilepsy. *Epilepsia*. May-Jun 1985;26(3):268-78. [\[Medline\]](#).

72. Janz D. Epilepsy with impulsive petit mal (juvenile myoclonic epilepsy). *Acta Neurol Scand*. Nov 1985;72(5):449-59. [\[Medline\]](#).
73. Janz D. Juvenile myoclonic epilepsy. Epilepsy with impulsive petit mal. *Cleve Clin J Med*. 1989;56 Suppl Pt 1:S23-33; discussion S40-2. [\[Medline\]](#).
74. Janz D. The grand mal epilepsies and the sleeping-waking cycle. *Epilepsia*. Mar 1962;3:69-109. [\[Medline\]](#).
75. Kleveland G, Engelsen BA. Juvenile myoclonic epilepsy: clinical characteristics, treatment and prognosis in a Norwegian population of patients. *Seizure*. Feb 1998;7(1):31-8. [\[Medline\]](#).
76. Knott C, Panayiotopoulos CP. Carbamazepine in the treatment of generalised tonic clonic seizures in juvenile myoclonic epilepsy [letter]. *J Neurol Neurosurg Psychiatry*. Apr 1994;57(4):503. [\[Medline\]](#).
77. Lancman ME, Asconape JJ, Penry JK. Clinical and EEG asymmetries in juvenile myoclonic epilepsy. *Epilepsia*. Mar-Apr 1994;35(2):302-6. [\[Medline\]](#).
78. Meencke HJ, Janz D. Neuropathological findings in primary generalized epilepsy: a study of eight cases. *Epilepsia*. Feb 1984;25(1):8-21. [\[Medline\]](#).
79. Meencke HJ, Janz D. The significance of microdysgenesis in primary generalized epilepsy: an answer to the considerations of Lyon and Gastaut. *Epilepsia*. Jul-Aug 1985;26(4):368-71. [\[Medline\]](#).
80. Obeid T, Panayiotopoulos CP. Juvenile myoclonic epilepsy: a study in Saudi Arabia. *Epilepsia*. May-Jun 1988;29(3):280-2. [\[Medline\]](#).
81. Oguni H, Mukahira K, Oguni M, et al. Video-polygraphic analysis of myoclonic seizures in juvenile myoclonic epilepsy. *Epilepsia*. Mar-Apr 1994;35(2):307-16. [\[Medline\]](#).
82. Panayiotopoulos CP, Obeid T, Tahan AR. Juvenile myoclonic epilepsy: a 5-year prospective study. *Epilepsia*. Mar-Apr 1994;35(2):285-96. [\[Medline\]](#).
83. Panayiotopoulos CP, Obeid T, Waheed G. Differentiation of typical absence seizures in epileptic syndromes. A video EEG study of 224 seizures in 20 patients. *Brain*. Aug 1989;112 (Pt 4):1039-56. [\[Medline\]](#).
84. Panayiotopoulos CP, Tahan R, Obeid T. Juvenile myoclonic epilepsy: factors of error involved in the diagnosis and treatment. *Epilepsia*. Sep-Oct 1991;32(5):672-6. [\[Medline\]](#).
85. Pedersen SB, Petersen KA. Juvenile myoclonic epilepsy: clinical and EEG features. *Acta Neurol Scand*. Mar 1998;97(3):160-3. [\[Medline\]](#).

86. Penry JK, Dean JC, Riela AR. Juvenile myoclonic epilepsy: long-term response to therapy. *Epilepsia*. 1989;30 Suppl 4:S19-23; discussion S24-7. [\[Medline\]](#).
87. Shinnar S, Berg AT, Moshe SL, et al. Discontinuing antiepileptic drugs in children with epilepsy: a prospective study. *Ann Neurol*. May 1994;35(5):534-45. [\[Medline\]](#).
88. Wirrell EC, Camfield CS, Camfield PR, et al. Long-term prognosis of typical childhood absence epilepsy: remission or progression to juvenile myoclonic epilepsy. *Neurology*. Oct 1996;47(4):912-8. [\[Medline\]](#).

Keywords

JME, idiopathic generalized epileptic syndrome, myoclonic jerks, generalized tonic-clonic seizures, GTCSs, absence seizures