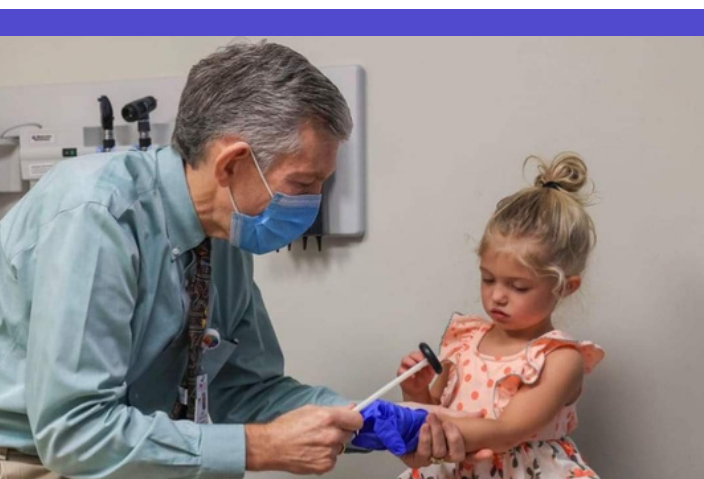


## What is Dravet Syndrome?

Dravet syndrome is a distinctive epilepsy syndrome that presents in the first year of life with a reported incidence of 1:15,700 [1]. Early clinical presentation of Dravet syndrome is unique, with onset of recurrent, convulsive seizures, which are often prolonged and triggered by fever, in a developmentally normal infant with normal MRI and nonspecific EEG findings [2-4]. In addition to refractory seizures, the few studies that assess long-term outcomes also show emergence of other comorbidities including, but not limited to: intellectual disability and behavioral issues, motor defects and gait issues, language impairment, sleep disorders, and dependence in adulthood [2-7]

Furthermore, persons with Dravet syndrome have significantly higher premature mortality due to status epilepticus, accidents, and Sudden Unexplained Death in Epilepsy (SUDEP), estimated at 15-20% [2,5-9]. Elimination or significant reduction of prolonged convulsive seizures and status epilepticus should represent the highest priority in treatment, as both the frequency and duration of convulsive seizures over 5 minutes as well as obtundation status are believed to have a significant impact on developmental outcome [2,6].



## After Diagnosis, Patients should receive info about:

- Genetic counseling
- Risk & management of prolonged seizures
- Expected seizure control
- Risk of SUDEP & seizure-related accidents
- Developmental outcomes & expectations
- Seizure detection devices & seizure diaries
- Social workers & resources
- Dravet support groups
- Home care & family support
- Seizure Action Plans
- Reproductive implications
- Reducing seizure triggers

## Effective Multidisciplinary Teams Include:

- Neurologist or epileptologist with expertise in DS
- Epilepsy nurse and a social worker with expertise in neurological disabilities
- Geneticist or genetic counselor
- Dietitian with ketogenic diet expertise
- Physiotherapist
- Occupational and Speech Therapist
- Sleep Medicine Specialist

## Best practices:

- Let patient get adequate sleep
- Avoid high ambient temperatures; use cooling vest
- Avoid high temperature baths
- Use prophylactic antipyretics and/or benzodiazepines with vaccination and illness
- Use sunglasses and/or avoid flashing lights



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# Could it be Dravet syndrome?



[www.dravetfoundation.org](http://www.dravetfoundation.org)

## Genetics in Dravet Syndrome

Mutations in the SCN1A gene are found in as many as 85% or more of patients clinically diagnosed with Dravet syndrome [3,9]. SCN1A mutations may also be found in less severe epilepsy types, such as generalized epilepsy with febrile seizures plus (GEFS+), and more severe forms of epilepsy such as migrating focal seizures [9,10], therefore careful clinical correlations are needed [4,11].

Genetic testing should be considered for all patients with a clinical picture suggestive of DS, including in teen and adult patients [2,4,11]. While simple SCN1A sequencing is appropriate when all clinical criteria are met, an epilepsy gene panel may be preferable for infants, when clinical history is less distinct, or when atypical features are present.

## Benefits of Early Diagnosis

Specialists experienced with Dravet syndrome believe that earlier diagnosis has the potential to improve long-term outcomes for patients with improved seizure control and possible improved cognition. At the very least, earlier genetic testing and diagnosis helps avoid the negative consequences of treatment with contraindicated medications such as sodium channel blockers that exacerbate seizures, as well as unnecessary, costly and, at times, invasive testing.

A diagnosis at any age can greatly benefit the patient, aiding in selection of treatment, preventative measures, and leading the family to patient support organizations.

Common misdiagnoses include Myoclonic Atonic Epilepsy (Doose syndrome), Lennox-Gastaut syndrome, Myoclonic Epilepsy in Infancy, PCDH19-clustering epilepsy, and generalized epilepsy with febrile seizures plus (GEFS+) [4,9,10].

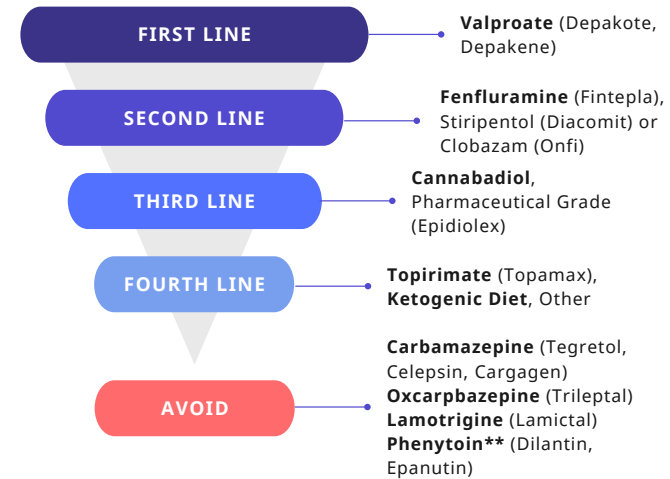
## Initial Presentation Includes: [2,4]

- Typical seizure onset is between 1-20 months.
- Recurrent generalized clonic, focal to bilateral tonic-clonic, or hemiclonic seizures, which are mandatory for diagnosis. These are often prolonged (>10 min), but may be shorter.
- Between 1.5 to 5 years of age, additional seizure types may occur, including myoclonic, focal impaired awareness, atypical absence, and atonic seizures, as well as nonconvulsive status epilepticus (obtundation status). Typical absences and epileptic spasms are atypical.
- Hyperthermia, which may be associated with vaccination or illness, triggers seizures in the majority of patients; other triggers may include flashing lights, visual patterns, bathing, changes in temperature, and overexertion.
- Normal development and neurological examination at onset.
- Normal MRI and nonspecific EEG findings at onset. Background slowing common after age 2.

## Presentation in Older Children and Adults: [5]

- Persisting seizures, which include focal and/or generalized convulsive seizures, and, in many cases, myoclonic, focal, atypical absence, and tonic seizures. Recurrent status epilepticus becomes less frequent with time, and may not be seen in adolescence and young adulthood.
- Hyperthermia as a seizure trigger may become less problematic in adolescence and adulthood.
- Seizure exacerbation with the use of sodium channel agents.
- Intellectual disability which is typically evident by 18-60 months of age.
- Abnormalities on neurological examination which are typically evident by age 3-4 years and include crouched gait, hypotonia, incoordination, and impaired dexterity.
- An MRI which is typically normal, but may show mild cerebral and cerebellar atrophy and/or hippocampal sclerosis.

## Maintenance Antiepileptic Medications [2]



\*\*Phenytoin and Fosphenytoin, while not recommended for daily use, are often used in emergency treatment of prolonged seizures with varying success in patients with Dravet syndrome. Caution is advised.

Vagus nerve stimulation may be considered after failure of front line therapies; efficacy is limited. Epilepsy surgery is not indicated. [2,4]

## Emergency Medications [2,4]

- At Home: Rectal/nasal diazepam or buccal/nasal midazolam for young patients; buccal/nasal midazolam for older patients. To be administered within 3-5 minutes of seizure onset unless there is a recent history of prolonged convulsive seizures. In this case, medication should be given at seizure onset, with a second full dose 5-10 minutes after the initial dose.
- In Hospital: Benzodiazepines as a first line therapy for a patient presenting at the hospital with an ongoing seizure. A second dose of benzodiazepine should be given if the seizure persists, particularly if the patient did not receive a dose of rescue medication at home. Either IV valproate or levetiracetam is a reasonable second line therapy, but specialists are not in agreement about subsequent treatment. IV phenytoin and fosphenytoin are of debated usefulness due to their action on sodium channels.