**21BIO112  
INTELLIGENCE OF BIOLOGICAL SYSTEMS-2**

**PROJECT TITLE:  
  
 Brugada Syndrome**

**Batch: 04**



**Under the guidance of:**

**Dr. Amrita thakur**

**Team members:**

**M Ramya Sree – BL.EN.U4AIE21072  
 Poli Vamsi Vardhan Reddy – BL.EN.U4AIE21101  
 Mettu Siddhartha –BL.EN.U4AIE21080**

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**INTRODUCTION:**

Brugada (brew-GAH-dah) syndrome is a rare but potentially life-threatening heart rhythm condition (arrhythmia) that is sometimes inherited.

Brugada syndrome (BrS) is a [genetic disorder](https://en.wikipedia.org/wiki/Genetic_disorder) in which the electrical activity of the [heart](https://en.wikipedia.org/wiki/Heart) is abnormal due to [channelopathy](https://en.wikipedia.org/wiki/Channelopathy).

It increases the risk of [abnormal heart rhythms](https://en.wikipedia.org/wiki/Heart_arrhythmia) and [sudden cardiac death](https://en.wikipedia.org/wiki/Sudden_cardiac_death). Those affected may have episodes of [syncope](https://en.wikipedia.org/wiki/Syncope_(medicine)).

The abnormal heart rhythms seen in those with Brugada syndrome often occur at rest. They may be triggered by a [fever](https://en.wikipedia.org/wiki/Fever).

About a quarter of those with Brugada syndrome have a family member who also has the condition.

 Some cases may be due to a new genetic [mutation](https://en.wikipedia.org/wiki/Mutation) or certain medications. The most commonly involved [gene](https://en.wikipedia.org/wiki/Gene) is [SCN5A](https://en.wikipedia.org/wiki/Nav1.5) which encodes the cardiac [sodium channel](https://en.wikipedia.org/wiki/Sodium_channel).

 Diagnosis is typically by [electrocardiogram](https://en.wikipedia.org/wiki/Electrocardiogram) (ECG), however, the abnormalities may not be consistently present. Medications such as [ajmaline](https://en.wikipedia.org/wiki/Ajmaline) may be used to reveal the ECG changes.

Similar ECG patterns may be seen in certain [electrolyte disturbances](https://en.wikipedia.org/wiki/Electrolyte_imbalance) or when the [blood supply to the heart has been reduced](https://en.wikipedia.org/wiki/Ischemia).

People with Brugada syndrome have an increased risk of irregular heart rhythms beginning in the lower chambers of the heart (ventricles).

Treatment of Brugada syndrome includes preventive measures such as reducing fever and avoiding medications that might trigger the arrhythmia. Some people with Brugada syndrome need a medical device called an implantable cardioverter-defibrillator (ICD).

**Brugada Syndrome**

Those at higher risk of sudden cardiac death may be treated using an [implantable cardioverter defibrillator](https://en.wikipedia.org/wiki/Implantable_cardioverter_defibrillator) (ICD). In those without symptoms the risk of death is much lower, and how to treat this group is less clear. [Isoproterenol](https://en.wikipedia.org/wiki/Isoproterenol) may be used in the short term for those who have frequent life-threatening abnormal heart rhythms, while [quinidine](https://en.wikipedia.org/wiki/Quinidine) may be used longer term. Testing people's family members may be recommended.

The condition affects between 1 and 30 per 10,000 people. It is more common in males than females and in those of Asian descent. The onset of symptoms is usually in adulthood. It is named after the Spanish cardiologists Pedro and Josep Brugada who described the condition in 1992. Their brother Ramon Brugada was the first to describe one potential genetic cause in 1998.

**HISTORY**

Brugada syndrome is named after the Spanish cardiologists Josep and Pedro Brugada who described the condition in 1992,  although the association between the characteristic ECG pattern and sudden cardiac death had been reported in 1989. Brugada syndrome was described as a cause for the sudden unexplained cardiac death syndrome seen in Thai men in 1997. The first genetic mutations affecting the SCN5A gene associated with the syndrome were identified by their brother Ramon Brugada in 1998, with many more mutations affecting at least 19 genes subsequently identified by others. Studies in the 2000s led to competing theories surrounding the mechanisms by which abnormal heart rhythms were generated. Research into Brugada syndrome is ongoing, identifying new genetic variants, exploring mechanisms of arrhythmias, and searching for better treatments.

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*Symptoms*

While many of those with Brugada syndrome do not have any symptoms, Brugada syndrome may cause fainting or sudden cardiac death due to serious abnormal heart rhythms such as [ventricular fibrillation](https://en.wikipedia.org/wiki/Ventricular_fibrillation) or [polymorphic ventricular tachycardia](https://en.wikipedia.org/wiki/Ventricular_tachycardia).[[8]](https://en.wikipedia.org/wiki/Brugada_syndrome#cite_note-Pri2013-8) Blackouts may be caused by brief abnormal heart rhythms that revert to a normal rhythm spontaneously. If a dangerous heart rhythm does not stop by itself and is left untreated, the person may have a fatal cardiac arrest. However, blackouts can occur in those with Brugada syndrome despite a normal heart rhythm due to a sudden drop in blood pressure, known as [vasovagal syncope](https://en.wikipedia.org/wiki/Reflex_syncope).[[2]](https://en.wikipedia.org/wiki/Brugada_syndrome#cite_note-Pol2017-2)

The abnormal heart rhythms seen in Brugada syndrome often occur at rest, following a heavy meal, or even during sleep.[[5]](https://en.wikipedia.org/wiki/Brugada_syndrome#cite_note-Sar2016-5) These situations are linked to periods when the [vagus nerve](https://en.wikipedia.org/wiki/Vagus_nerve) is activated, referred to as periods of high [vagal tone](https://en.wikipedia.org/wiki/Vagal_tone). Abnormal heart rhythms may also occur during [fever](https://en.wikipedia.org/wiki/Fever) or following excessive alcohol. [Sodium channel blocking](https://en.wikipedia.org/wiki/Sodium_channel_blocker) medications, commonly used to treat cardiac arrhythmia, may also worsen the tendency to abnormal heart rhythms in patients with Brugada syndrome and should be avoided.[[12]](https://en.wikipedia.org/wiki/Brugada_syndrome#cite_note-Postema_2009-12)[[13]](https://en.wikipedia.org/wiki/Brugada_syndrome#cite_note-Brugada_Syndrome-13)

**CAUSES**

The individual [cells of the heart](https://en.wikipedia.org/wiki/Cardiac_muscle_cell) communicate with each other with electrical signals, and these electrical signals are disrupted in those with Brugada syndrome. As a [genetic condition](https://en.wikipedia.org/wiki/Genetic_disorder), the syndrome is ultimately caused by changes to a person's [DNA](https://en.wikipedia.org/wiki/DNA), known as [genetic mutations](https://en.wikipedia.org/wiki/Mutation). The first mutations described in association with Brugada syndrome were in a [gene](https://en.wikipedia.org/wiki/Gene) responsible for a protein or [ion channel](https://en.wikipedia.org/wiki/Ion_channel) that controls the flow of [sodium ions](https://en.wikipedia.org/wiki/Sodium) through the [cell membrane](https://en.wikipedia.org/wiki/Cell_membrane) of [heart muscle cells](https://en.wikipedia.org/wiki/Cardiac_muscle_cell) – the [cardiac sodium channel](https://en.wikipedia.org/wiki/Sodium_channel). Many of the genetic mutations that have subsequently been described in association with Brugada syndrome influence the sodium current in some way, or affect other ionic currents.[[7]](https://en.wikipedia.org/wiki/Brugada_syndrome#cite_note-Ant2013-7)

A long list of factors that can generate a Brugada ECG pattern have been described, including certain medications, electrolyte disturbances such as a [decrease in the levels of potassium in the blood](https://en.wikipedia.org/wiki/Hypokalemia), and a [reduction in blood supply](https://en.wikipedia.org/wiki/Ischemia) to key areas of the heart, specifically the [right ventricular outflow tract](https://en.wikipedia.org/wiki/Ventricular_outflow_tract).[[7]](https://en.wikipedia.org/wiki/Brugada_syndrome#cite_note-Ant2013-7) Drugs that have been implicated include [antiarrhythmic](https://en.wikipedia.org/wiki/Antiarrhythmic_agent) medications such as [flecainide](https://en.wikipedia.org/wiki/Flecainide), [verapamil](https://en.wikipedia.org/wiki/Verapamil) and [propranolol](https://en.wikipedia.org/wiki/Propranolol), antidepressants such as [amitryptiline](https://en.wikipedia.org/wiki/Amitriptyline" \o "Amitriptyline), and drugs that enhance vagal tone such as [acetylcholine](https://en.wikipedia.org/wiki/Acetylcholine). The ECG pattern can also be seen following excessive use of [alcohol](https://en.wikipedia.org/wiki/Alcohol_intoxication) or [cocaine](https://en.wikipedia.org/wiki/Cocaine).[[7]](https://en.wikipedia.org/wiki/Brugada_syndrome#cite_note-Ant2013-7)

Etiology

The first genetic association with Brugada syndrome discovered was a loss-of-function mutation in the cardiac voltage-gated sodium channel gene SCN5A. It is thought to be found in 15-30% of Brugada Syndrome cases. [[2]](https://www.ncbi.nlm.nih.gov/books/NBK519568/) Mutations in calcium and potassium channels, associated channel proteins, and desmosomal proteins have also been linked with the disease. Brugada syndrome is inherited in an autosomal dominant pattern; however, affected individuals may demonstrate variable expressivity and reduced penetrance. Additionally, many environmental and genetic factors may influence the phenotype, including temperature, medications, electrolyte abnormalities, and cocaine.[[3]](https://www.ncbi.nlm.nih.gov/books/NBK519568/)

Epidemiology

The prevalence of Brugada Syndrome is approximately 3 to 5 per 10,000 people. Brugada syndrome is approximately 8 to 10 times more common in males than females. This gender difference, however, is not found in pediatric patients. This has been hypothesized to be due to higher testosterone levels after puberty and different proportions of ionic currents based on sex. Brugada syndrome is also more prevalent in those who are of Southeast Asian descent. The mean affected age is 41 years old. Brugada syndrome accounts for 4% of all sudden cardiac deaths. [[3]](https://www.ncbi.nlm.nih.gov/books/NBK519568/)

**PREVENTION AND TREATMENT**

The main aim when treating people with Brugada syndrome is to reduce the risk of sudden death due to serious [abnormal heart rhythms](https://en.wikipedia.org/wiki/Heart_arrhythmia) such as ventricular fibrillation or polymorphic ventricular tachycardia.[[36]](https://en.wikipedia.org/wiki/Brugada_syndrome#cite_note-36) While some with this condition are at high risk of serious heart rhythm disturbances, others are at much lower risk, meaning that some may require more intensive treatment than others.[[8]](https://en.wikipedia.org/wiki/Brugada_syndrome#cite_note-Pri2013-8) In addition to treating the person who has Brugada syndrome, it is often important to investigate members of their immediate family to see if they too carry the condition.

**Diagnosis**

* Brugada syndrome usually is diagnosed in adults and sometimes in adolescents.
* It's rarely diagnosed in young children because the symptoms are often unnoticed.
* To diagnose Brugada syndrome, a health care provider should perform a physical exam and listen to the heart with a stethoscope.
* Once Tests are done to check the heartbeat and diagnose one can confirm Brugada syndrome or not.

**Medication**

* Quinidine is an antiarrhythmic drug that may reduce the chance of serious abnormal heart rhythms occurring in some people with Brugada syndrome.
* It is most frequently used in people with Brugada syndrome. who have experienced several episodes of life-threatening arrhythmias
* It can be also be used in people at high risk of arrhythmias.
* Isoprenaline, a drug that has similarities with adrenaline,
* It can be used in an emergency for people with Brugada syndrome who are having frequent repeated life-threatening arrhythmias, known as an "electrical storm".
* This drug must be given as a continuous infusion into a vein and therefore is not suitable for long-term use.

**References**

<https://en.wikipedia.org/wiki/Brugada_syndrome>

<https://www.ncbi.nlm.nih.gov/books/NBK519568/>

**THANK YOU**