

# Enfermedad de Lev y Lenegre

Existe una confusión en la literatura. Lenegre y Lev ocasionan ambos progresivo compromiso en la conducción intraventricular, no obstante ambas entidades son totalmente diferentes. Encuanto el Lenegre es causada principalmente por mutaciones en el gen SCN5A consecuentemente es un alelo del síndrome de Brugada y de la variante 3 del SQT. Por ese motivo esta entidad se observa en el adulto diferentemente del Lev que es patrimonio del viejo

Les mando las diferencias (en ingles)

## **Progressive dromotropic disorders of the His Purkinje system: "Lenègre disease"**

Both entities, called Progressive Cardiac Conduction Defects (PCCD), are grouped together as primary conduction diseases (Lev-Lenègre).

Both Lenègre disease—known as "primary" PCCD—as well as the secondary mechanic lesion—sclerosis of the left "cardiac skeleton" or Lev disease —usually cause LBBB or RBBB, frequently associated with fascicular blocks.

Occasionally, they develop into more advanced degrees of block with a potential to cause SCD due to total AV block, to the extent that they represent the most important cause of pacemaker implantation in the first world: 0.15 per 1,000 inhabitants a year.

The same mutation in novel single SCN5A missense mutation can lead either to Brugada syndrome or to an PCCD. Modifier gene(s) may influence the phenotypic consequences of a SCN5A mutation. A G-to-T mutation at position 4372 was identified by direct sequencing and was predicted to change a glycine for an arginine (G1406R) between the DIII-S5 and DIII-S6 domain of the Na<sup>+</sup> channel protein.

## Differences Between Lenègre and Lev Disease

- **Lenègre disease:** Age adults
  - **Lev disease:** Age Elderly
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- **Lenègre disease:** Progressive sclerosis of the intraventricular His-Purkinje conduction system.
  - **Lev disease:** Mechanical progressive fibrosis of the left “cardiac skeleton.” Calcification of the mitral valve ring, fibrous central body, membranous part of the aorta base, apex muscular septum, and direct Hisian system and antero-superior fasciculus of the left branch
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- **Lenègre disease:** progressive conduction disease consequence of genetic causes
  - **Lev disease** Mechanical progressive fibrosis of the left “cardiac skeleton.” Calcification of the mitral valve ring, fibrous central body, membranous part of the aorta base, apex muscular septum, and direct Hisian system and antero-superior fasciculus of the left branch.
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- **Lenègre disease:** Allelic heterozygotic mutation with Brugada syndrome located in the alpha subunit of the sodium channel in the SCN5A gene.
  - Substitution of asparagine by aspartic acid within the IV domain of S3 (D1595N)
  - Substitution of 514 cysteine by glycine (G514C)
  - Substitution of glycine by threonine in the 4372 position and glycine by arginine (G1405R) between the DIII-S5 domains of the sodium channel.
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- **Lev disease:** Idiopathic. Mechanical acceleration of the aging process.
  - **Lenègre disease:** Identification of genetic defect 1) Substitution of the serine amino acid by glycine (G298S) in the domain of the I S5-S6 loop.

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## Brugada syndrome and Lenègre disease relationship

Tan et al (Tan 2001) have identified a single mutation in five affected family members; this mutation results in the substitution of cysteine 514 for glycine (G514C) in the channel protein. Biophysical characterization of the mutant channel shows that there are abnormalities in voltage-dependent 'gating' behaviour that can be partially corrected by dexamethasone, consistent with the salutary effects of glucocorticoids on the clinical phenotype. Computational analysis predicts that the gating defects of G514C selectively slow myocardial conduction, but do not provoke the rapid cardiac arrhythmias associated previously with SCN5A mutations.

A two new allelic heterozygotic mutations with Brugada syndrome, located in the alpha subunit of the Na<sup>+</sup> channel in the SCN5A gene, what has been clinically translated into AV block. They are the result of the substitution of the serine amino acid by glycine (G298S) in the domain of the I S5-S6 loop, and asparagine by aspartic acid within the S3 of the IV domain (D1595N). Both mutations prevent fast inactivation, reduce sodium channel density, and accentuate the slow component of inactivation. This combination causes a decrease in conduction velocity and leads to AV block.

A mutation was identified, which causes intraventricular dromotropic disorder secondary to substitution of the cysteine amino acid by glycine (G514C) in the Na<sup>+</sup> proteic fast channel

In Brugada syndrome, the PR interval and the HV of the electrogram are prolonged in nearly 50% of cases. HV can reach a duration of approximately twice its maximal normal limit.

Lenègre disease should not continue to be classified as an idiopathic progressive disease of the His-Purkinje system. It should be called a Progressive Cardiac Conduction Defect or PCCD. It has been identified as a disease of the Na<sup>+</sup> fast channel or channelopathy by mutation in the SCN5A gene, and as allele of Brugada syndrome with a different phenotypic expression, in a similar fashion to the LQT3 variant of the hereditary-familial LQTS. The same missense mutation in the SCN5A gene can cause both phenotypes: Brugada disease and Lenègre disease.

References

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