Rare melanocortin-4 receptor pathway diseases: Clinical features and genetic confirmation

Rare melanocortin-4 receptor (MC4R) pathway diseases can be caused by genetic variants within the pathway, which impair signalling that controls hunger.[1]

Hyperphagia (pathological, insatiable hunger) and **early-onset, severe obesity** are clinical features of a rare MC4R pathway disease.[1] If you see these features in your patients, **they may be living with a rare MC4R pathway disease**.[1]

Hyperphagia[2]

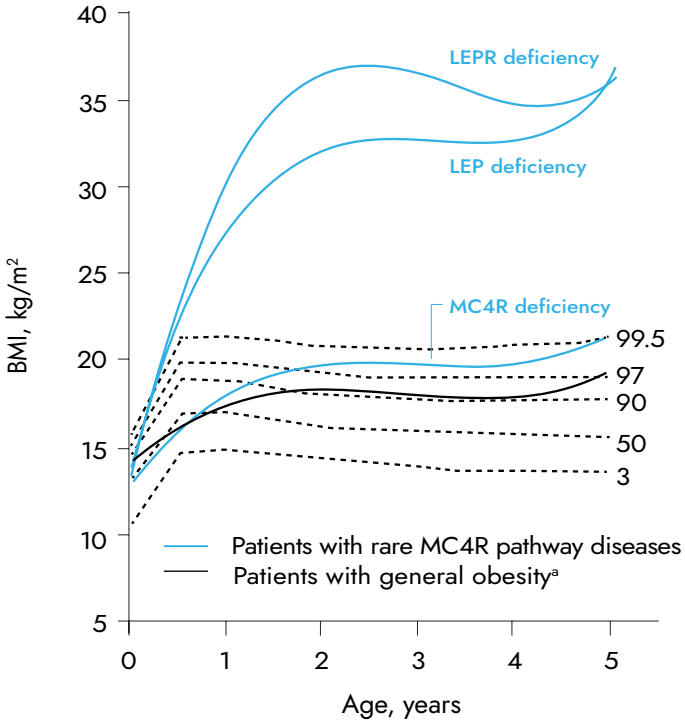
Also known as an abnormally strong sensation of hunger or desire to eat.

Characteristics and behaviours include:

- **Heightened and prolonged hunger**
- **Longer time to reach satiety**
- **Shorter duration of satiety**
- **Severe preoccupation with food** (hyperphagic drive)
- **Food-seeking behaviours** (sneaking or stealing food)
- **Distress and functional impairment if denied food**

Early-onset, severe obesity[3]

Defined as having a BMI ≥120% of the 95th percentile and onset before the age of 5.[4]



a) Patients with general obesity have a BMI >30 kg/m² by age 14 to 16 years and do not have a variant in *LEP*, *LEPR*, or *MC4R*.

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UK-DSE-2500001 I Date of preparation February 2025

Proactive identification of clinical features, and appropriate referral for genetic confirmation using correct gene panels can help move children living with a rare MC4R pathway disease onto their most appropriate care path.[5]

Access to appropriate tools means genetic variants that cause rare MC4R pathway diseases can be diagnosed early.[5]

The diagnosis pathway[5]

- Patient visits HCP to discuss symptoms
- HCP identifies clinical features
- HCP refers patient for genetic testing
- Genetic testing results confirm if the patient has a rare MC4R pathway disease

Through a correct referral, children with genetic variants that cause rare MC4R pathway diseases can be screened, and appropriately cared for

Current genetic screening allows many more rare diseases to be identified – rare MC4R pathway diseases can now be part of this

If you need more information on genetic confirmation or locating expert centres in your country, please contact us: EU_Medinfo@rhythmtx.com

References:
1. Loos, RJF and Yeo, GSH. Nat Rev Gens. 2022;23:120–133. **2.** Heymsfield SB, et al. Obesity (Silver Spring). 2014;22(suppl 1):S1–S17 **3.** Kohlsdorf K, et al. Int J Obes (Lond). 2018;42(9):1602–1609 **4.** Hampl SE, et al. Pediatrics. 2023;151(2):e2022060640 **5.** Styne DM, et al. J Clin Endocrinol Metab. 2017;102(3):709–757

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Reporting forms and information can be found at:
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Adverse events should also be reported to Rhythm Pharmaceuticals Netherlands B.V., Radarweg 29, 1043NX Amsterdam, Netherlands.
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