What is a rare melanocortin-4 receptor pathway disease?

Rare melanocortin-4 receptor (MC4R) pathway diseases can be caused by genetic variants within the MC4R pathway (part of the central melanocortin pathway).[1]

This can impair signalling in the pathway that controls hunger, leading to hyperphagia (pathological, insatiable hunger) and increased body weight.[1]

Characteristics and behaviours of hyperphagia[2]

Heightened and prolonged hunger

Severe preoccupation with food (hyperphagic drive)

Longer time to reach satiety

Food-seeking behaviours (sneaking or stealing food)

Shorter duration of satiety

Distress and functional impairment if denied food

Should your patient be evaluated for a rare MC4R pathway disease?

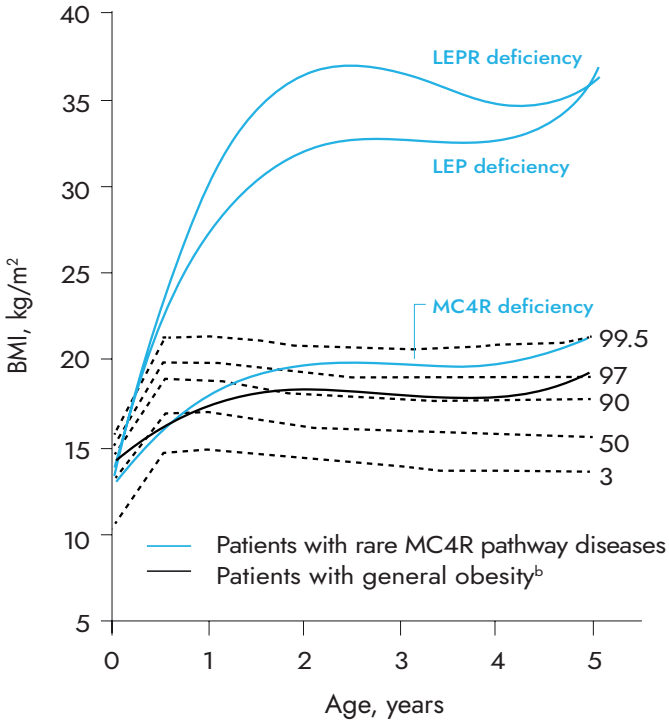
Look for the following signs[3-4]

Hyperphagia

Early-onset, severe obesity[a]

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

Growth curves in patients with early-onset, severe obesity[5]



b) Patients with general obesity have a BMI >30 kg/m^2 by age 14 to 16 years and do not have a variant in *LEP, LEPR,* or *MC4R*.

Reprinted with permission from Springer Nature from Kohlsdorf K, et al. *Int J Obes (Lond).* 2018;42(9):1602–1609.

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. Huvenne H, et al. *Obes Facts*. 2016;9(3):158–173. 4. Hampl SE, et al. *Pediatrics*. 2023;151(2):e2022060640. 5. Kohlsdorf K, et al. *Int J Obes (Lond)*. 2018;42(9):1602–16095.

This information is provided by Rhythm Pharmaceuticals B.V. (EU_Medinfo@rhythmtx.com). Last updated November 2023.

Rhythm® PHARMACEUTICALS