# 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?

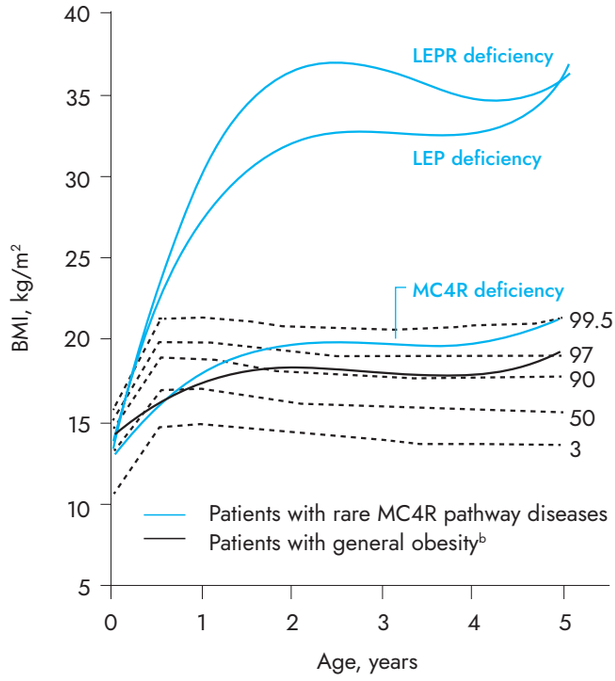
## Look for the following signs[3-4]

**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/m² by age 14 to 16 years and do not have a variant in *LEP, LEPR,* or *MC4R*.

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**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.

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