

General information on gastrointestinal issues in Phelan – McDermid syndrome

According to: Matuleviciene A, Siauryte K, Kuiper E, Grabrucker AM; European Phelan-McDermid syndrome guideline consortium. Consensus recommendations on chewing, swallowing and gastrointestinal problems in Phelan-McDermid syndrome. *Eur J Med Genet.* 2023 Jun;66(6):104763. doi: 10.1016/j.ejmg.2023.104763. Epub 2023 Apr 11. PMID: 37054968.



GI issue:

- Chewing and swallowing problems
- Gastroesophageal reflux disease (GERD)
- Cyclic vomiting
- Constipation

Taken together, all these GI problems are frequent across all age groups, in part due to limited cognitive development, hypotonia, abnormal chewing patterns, dental problems, and a functional role of *SHANK3* in the gastrointestinal system.

Matuleviciene A, Siauryte K, Kuiper E, Grabrucker AM; European Phelan-McDermid syndrome guideline consortium. Consensus recommendations on chewing, swallowing and gastrointestinal problems in Phelan-McDermid syndrome. Eur J Med Genet. 2023 Jun;66(6):104763. doi: 10.1016/j.ejmg.2023.104763. Epub 2023 Apr 11. PMID: 37054968.



Chewing and swallowing problems (occur in more than half of the people with PMS).

several reasons:

hypotonia (57–85%), making chewing and swallowing more difficult.

dental and palate problems (↑ 25%) (including malocclusion, widely spaced teeth, and a high palate; teeth grinding (25%); craving or eating inedible objects (60–88%).

The anatomical abnormalities, combined with the hypotonia and the typical chewing and mouthing behaviour, can lead to chewing and swallowing problems and saliva loss.

IMPORTANT: a pre-verbal speech therapist at an early stage.

NOTE: Proton pump inhibitors may affect nutrient uptake, as reported for the trace mineral zinc, and thereby potentially contribute to other clinical features, such as chronic pro-inflammatory signalling in the body.

Gastroesophageal reflux disease (GERD)

Reflux disease develops when stomach acid flows to the oesophagus, damaging the mucous membrane and causing an inflammatory reaction.

Reflux disease is more common in people with ID when there is obesity, drug use (anti-epileptics, benzodiazepines), spasticity, scoliosis, and an IQ under 35. Feeding tubes - increases the risk of reflux disease.

Complications: anaemia, strictures, or a Barret oesophagus.

DIAGNOSTICS: can be difficult due to limited communication.

ALARM SIGNALS: lack of appetite, food refusal, dental complaints, teeth grinding, regurgitation and vomiting.

ATYPICAL COMPLAINTS: as sleep disorders due to night-time reflux, restlessness, behavioural problems, and self-injuring behaviour.

ADDITIONAL INVESTIGATIONS: radiological GI tract examination with contrast (barium X-rays), gastroscopy including biopsies, screening for drug toxicity, and pH/impedance testing.

Cyclic vomiting

Cyclic vomiting syndrome (CVS) is characterised by recurring, acute episodes of severe nausea and vomiting for weeks.

AETIOLOGY: unknown;

PATHOPHYSIOLOGY: involves aberrant brain-gut and cellular pathways, including migraine, autonomic and hypothalamic-pituitary-adrenal axis hyperreactivity, and mitochondrial dysfunction (Romano et al., 2018).

IMPORTANT to exclude: cyclic vomiting Infections, increased intracranial pressure, migraine, epilepsy, intestinal obstruction, and a reaction to medication or food.

TREATMENT: cyproheptadine the first choice for prophylaxis (interemetic 5 phase).

Emetic phase - **alert for dehydration.**

The literature advises treating cyclic vomiting in children, such as infusions for dehydration.

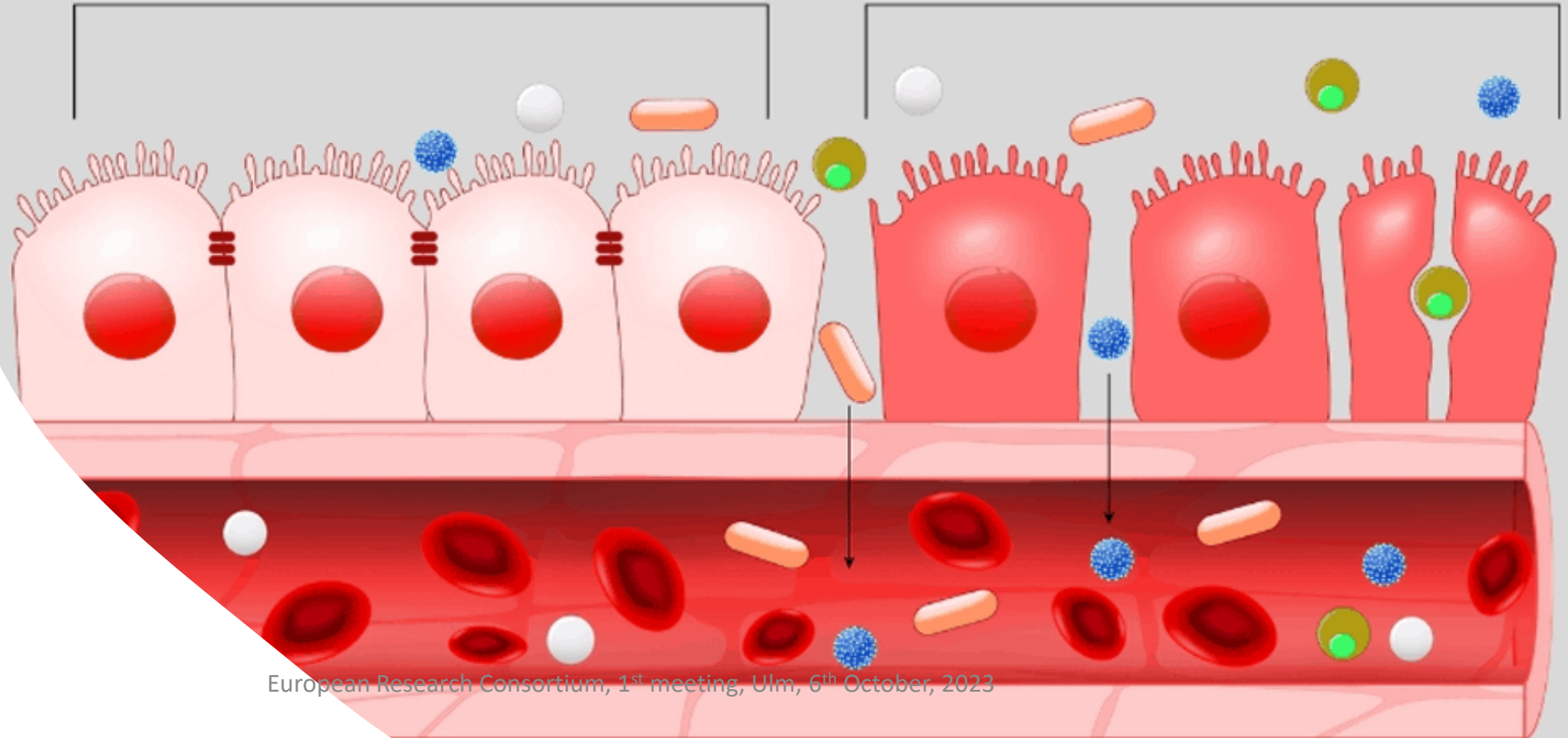


Leaky Gut

<https://balancetcm.co.nz/what-is-leaky-gut-acupuncture-hamilton-cambridge-raglan/>

NORMAL TIGHT JUNCTIONS

LEAKY & INFLAMED



GETTY IMAGES/ISTOCKPHOTO

European Research Consortium, 1st meeting, Ulm, 6th October, 2023



Constipation

Influenced by the following factors: pain, fever, dehydration, dietary and fluid intake, psychological issues, toilet training, medicines and impaired gastrointestinal motility. Hypothyroidism (~ 6%).

RISK FACTORS contributing constipation:

Impaired gastrointestinal motility: the gut's neuronal network has many connections to the central nervous system. The intestine's motility of the individuals with neurological problems may be impaired. This manifests as delayed gastric emptying, delayed colonic passage time, and constipation or diarrhoea.

Insufficient control over defecation: children with ID, including PMS, may have difficulty achieving normal toilet training. Insufficient conscious coordination of the pelvic floor musculature and the inability to integrate sensations of urgency into an adequate response.

Nutrition and moisture: easy-smash food (low in fibre). Fluid disbalance (including swallowing problems, vomiting, diarrhoea, and excessive loss of saliva), which increases the risk of constipation.

Reduced mobility: frequent hypotonia, fatigue, and sleep problems increases the risk of constipation

Side effects of medication: such as anti-epileptics (including valproic acid), anticholinergics, phenothiazines (including promethazine), and opiates negatively influence colonic transit time.

Furthermore, zinc deficiency may contribute to **diarrhoea**.

Recognizing non-retentive stool incontinence and functional constipation - appropriate personalised therapies.

Constipation diagnosis can be made based on the frequency, quantity, consistency of defecation, and a careful physical examination (at least two of the following criteria):

- straining on >25% of defecations;
- lumpy or hard stools on >25% of defecations;
- sensation of incomplete evacuation on >25% of defecations;
- sensation of anorectal obstruction/blockage on >25% of defecations;
- manual manoeuvres on >25% of defecations;
- less than 3 defecations per week;

IMPORTANT POINTS for the treatment: to determine the defecation problem phase: constipation with or without distension of the rectum ('megarectum') and with or without faecal incontinence.

DIAGNOSTICS: barium X-rays, exclusion somatic causes

A STOOL DIARY

TREATMENT with oral laxatives (osmotic, volume-increasing, or contact laxatives).



Recommendations (by the European Phelan-McDermid syndrome guideline consortium)

- Both gastroesophageal reflux and constipation should be considered if behavioural changes are observed in individuals with PMS.
- In individuals with PMS, evaluation of faecal incontinence is advised. Somatic causes should be excluded, and behavioural modifications should be considered (if needed, a behavioural specialist should be consulted).
- For treatment of gastroesophageal reflux, diarrhoea and constipation in individuals with PMS, refer to general national or international guidelines.
- A referral to a pre-verbal speech therapist for chewing and swallowing disorders should be considered.
- If zinc deficiency is present in an individual with PMS, dietary zinc supplementation should be considered.

Matuleviciene A, Siauryte K, Kuiper E, Grabrucker AM; European Phelan-McDermid syndrome guideline consortium. Consensus recommendations on chewing, swallowing and gastrointestinal problems in Phelan-McDermid syndrome. *Eur J Med Genet.* 2023 Jun;66(6):104763. doi: 10.1016/j.ejmg.2023.104763. Epub 2023 Apr 11. PMID: 37054968.