

# Daniella Di Benedetto, APD

## Bariatric Specialist & Clinical Dietitian

### PhD Candidate

PhD topic: The prevalence and implications for the management of Postprandial Hyperinsulinemic Hypoglycemia (PHH) in the Metabolic Bariatric Surgery population

Supervisors: Prof Gary Wittert, Dr Emily Meyer, Dr Pennie Taylor



**No conflict of interest to report**

IT'S NOT LATE DUMPING SYNDROME IT'S PHH!

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XXVII Ifso World Congress



Melbourne 2024

## Postprandial Hyperinsulinemic Hypoglycemia (PHH)

A spike in postprandial insulin (ie:  $>3\text{mU/L}$ ) leading to clinically significant hypoglycemia (ie:  $<2.8\text{-}3.0\text{mmol/L}$ )

May emerge as a late complication from 1-3+ yrs after MBS (esp RYGB)

Otherwise known as:

- Reactive Hypoglycemia
- Pancreatogenous Hyperinsulinemic Hypoglycemia
- Post-Bariatric Hypoglycemia

## Postprandial Hyperinsulinemic Hypoglycemia (PHH)

**Different from fasting hypoglycemia** - mostly **occurs after a meal** with high glycemic impact

Typically **occurs 1–3 hrs postprandially** with associated autonomic and **neuroglycopenic symptoms** which are **resolved after glucose ingestion**.

Patients show a **distinct postprandial glycemic pattern**

- **Sharp glycemic rise** reaching **peak levels after 30 min**, followed by a **rapid decline** leading to hypoglycemia

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## Concerning Symptoms Associated with PHH

Adrenergic Symptoms	Cholinergic Symptoms	Neuroglycopenic Symptoms	Hypoglycemic Unawareness
Tremor	Sweating	Weakness	Frequent hypoglycemia
Palpitations	Hunger	Altered Mental Status / Loss of consciousness	Drowsiness
Anxiety	Paraesthesia	Seizure	Nightmares / bizarre dreams
		Coma	Morning headaches
		Visual Disturbances	

## ASMBS Guide 2017 - Systematic review



ELSEVIER



CrossMark

*Surgery for Obesity and Related Diseases* 13 (2017) 371–378



SURGERY FOR OBESITY  
AND RELATED DISEASES



ASBMBS Guidelines/Statements

### ASMBS Position Statement on Postprandial Hyperinsulinemic Hypoglycemia after Bariatric Surgery

Dan Eisenberg, M.D., M.S.<sup>a,b,\*</sup>, Dan E. Azagury, M.D.<sup>c</sup>, Saber Ghiassi, M.D.<sup>d,e</sup>,  
Brandon T. Grover, D.O.<sup>f</sup>, Julie J. Kim, M.D.<sup>g</sup>

<sup>a</sup>Department of Surgery, Stanford School of Medicine, Stanford, California

<sup>b</sup>Department of Surgery, Palo Alto VA Health Care System, Palo Alto, California

<sup>c</sup>Section of Bariatric and Minimally Invasive Surgery, Stanford University School of Medicine, Stanford, California

<sup>d</sup>Yale School of Medicine, New Haven, Connecticut

<sup>e</sup>Department of Surgery, Bridgeport Hospital, Fairfield, Connecticut

<sup>f</sup>Department of Surgery, Gundersen Health System, La Crosse, Wisconsin

<sup>g</sup>Department of General Surgery, Tufts University School of Medicine,  
Boston, Massachusetts

Received December 7, 2016; accepted December 7, 2016

PHH should be  
suspected when  
postprandial  
neuroglycopenic  
symptoms occur  
after MBS.

## Pathophysiology of PHH

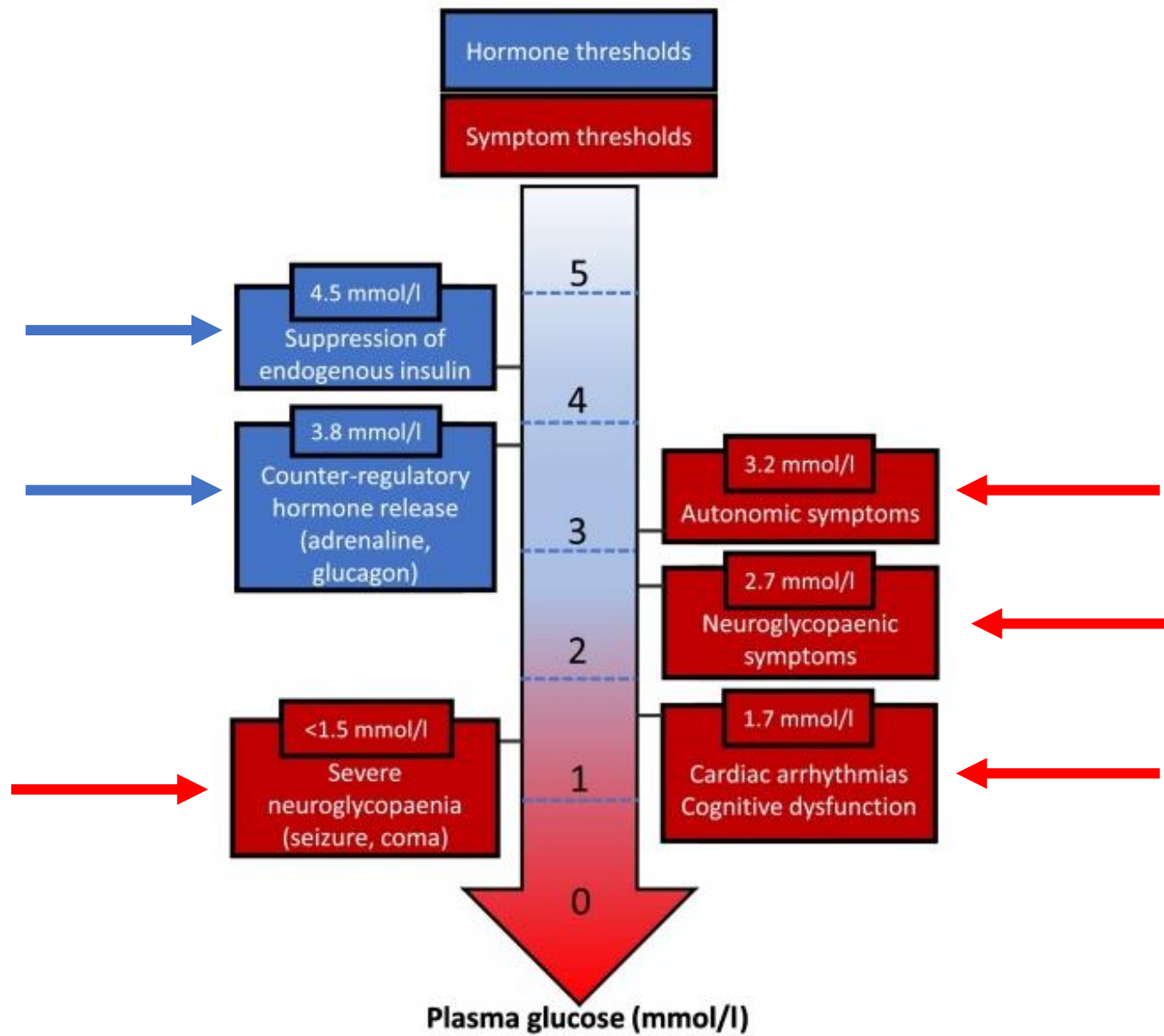
Patience et al., 2022

- **Physical alterations** to the digestive system
- **Changes in intestinal hormones**
- **Excessive postprandial insulin** response
- **Reduced insulin clearance**
- **Impaired counterregulatory hormone response** to low blood glucose

Soeby et al., 2020

- **Increased incretin levels** (GLP-1 and GIP) cause an excessive insulin secretion
- **Restoration of the  $\beta$ -cell sensitivity to GLP-1**
- **Persistence of the obesity-driven  $\beta$ -cell hyperfunction** despite weight loss
- **Increased tissues' insulin sensitivity** consequent to weight loss
- **Abnormal response of counterregulatory hormones**





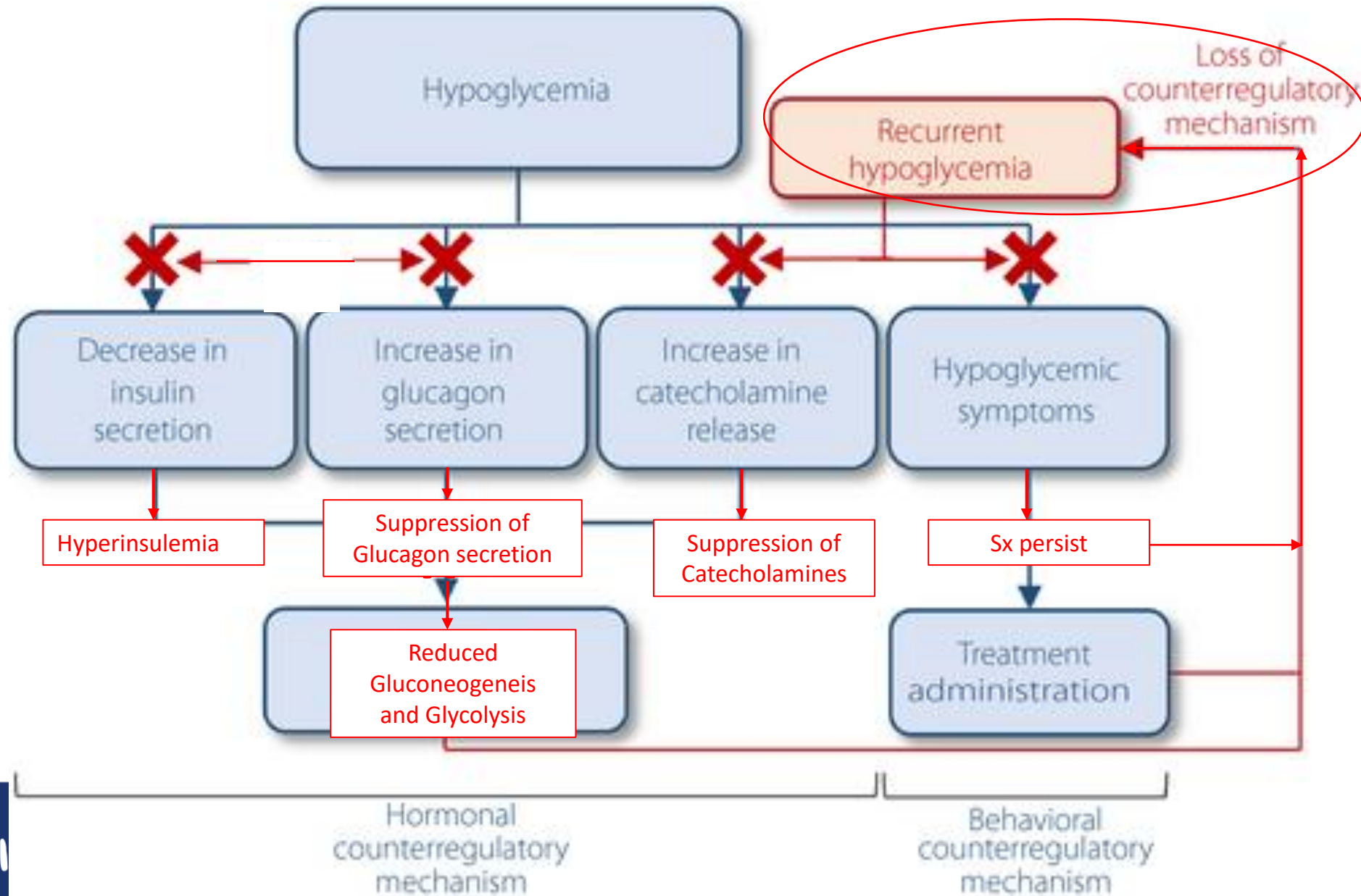
## Hypoglycemia Unawareness

**Frequent hypoglycaemic** events :

- Interfere with daily living
- Can **lead to defective glucose counter regulation**
- Can **lead to hypoglycaemia unawareness**

Hypoglycemia unawareness can lead to a **fear of eating, or a fear eating too much**

# Hypoglycemia Unawareness associated with PHH



Sankar et al 2020)

# IT'S NOT LATE DUMPING SYNDROME IT'S PHH!

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Similarities	Differences	
<ul style="list-style-type: none"> <li>- Palpitations</li> <li>- Light headedness</li> <li>- Weakness</li> <li>- Dizziness</li> <li>- Clammy</li> <li>- Diaphoresis</li> <li>- Severe Fatigue</li> <li>- Post-prandial</li> </ul>	Dumping Syndrome	PHH
	<p style="text-align: center;"><b>Early</b></p> <ul style="list-style-type: none"> <li>- 20-30mins Post-prandial</li> <li>- Blood glucose values not typically low</li> </ul> <p style="text-align: center;"><b>Late</b></p> <ul style="list-style-type: none"> <li>- Blood glucose values drop but not to a point of neuroglycopenia</li> <li>- Unlikely to develop Hypoglycemia Unawareness</li> <li>- Always post-prandial</li> </ul>	<ul style="list-style-type: none"> <li>→ 1-3hr post-prandial</li> <li>→ High risk of neuroglycopenia</li> <li>→ Likely to develop Hypoglycemia Unawareness</li> <li>→ Can occur during the night</li> </ul>

## Risk Factors for PHH

1. Female Gender
2. Younger Age at time of MBS
3. Non-diabetic pre-MBS
4. Lower HbA1c pre-MBS
5. History of Hypoglycemia or IR pre-MBS
6. Greater weight loss post-MBS

## Assessment of PHH

- **No** validated questionnaire
- **No** recent Best Practice Guidelines
- **No** practice pathway to predict risk of developing PHH
- **No** classification of severity and treatment pathway

PHH after MBS requires:

1. **Symptoms** occurring **at least a year after** surgery
2. **Normal fasting glucose and insulin levels**
3. Correlation of hypoglycemic symptoms, followed by spontaneous resolution of hypoglycemia
4. A **positive provocative test**

## Diagnosis of PHH – Provocative Testing

Firstly determine whether symptoms are truly linked to hypoglycemia

### Mixed Meal Tolerance Test (MMTT)

- Meal size, nutrient composition and duration of consumption could all play a role in the severity of PHH
- Glucose and insulin levels are determined during the fasting state and at 30m intervals after the mixed meal
- A positive MMTT found normal fasting glucose levels, hyperinsulinemia, before hypoglycemia

### Continuous Glucose Monitoring (CGM)

Assesses glucose levels during meal consumption and at the time of symptoms

- Can determine a patient's glucose response to food immediately and precisely
- Records interstitial fluid glucose levels every five minutes
- Useful for detecting hypoglycemia overnight

## Diagnosis of PHH – Provocative Testing

### Continuous Glucose Monitoring

- Valuable for **highlighting glycemic patterns** and linking these to symptoms
- Helps **identify triggers before neuroglycopenia develops**
- **Less accurate in the hypoglycemic ranges** therefore should **not be used for dx**
  - Interstitial glucose is not equal to a blood/capillary glucose
  - Blood / Capillary glucose level  $< 3.5$  mmol/L  
or  
Interstitial glucose  $< 3.8$  mmol/L



# Treatment

- (1) **Medical Nutritional Therapy**
- (2) Pharmacotherapy
- (3) **Continuous Enteral Feeding (Remnant stomach)**
- (4) Surgical Intervention

## Diabetes Treatment Vs PHH Treatment

Similarities in treatment of hypoglycemia however there are also key differences

- When symptomatic hypoglycemia develops, 10–15g oral CHO recommended to relieve symptoms and rapidly increase glucose to safe levels.
  - However, if acarbose is prescribed, treat with glucose exclusively as absorption of sucrose and fruit juice will be delayed.
- Severe neuroglycopenia – Glucagon can be administered
- Initial treatment should be followed by a low GI CHO snack mixed with fat/protein to reduce rebound
- Short-term - achieving safety is paramount
- Long-term - nutritional guidance should include optimising overall caloric balance to reduce weight gain.

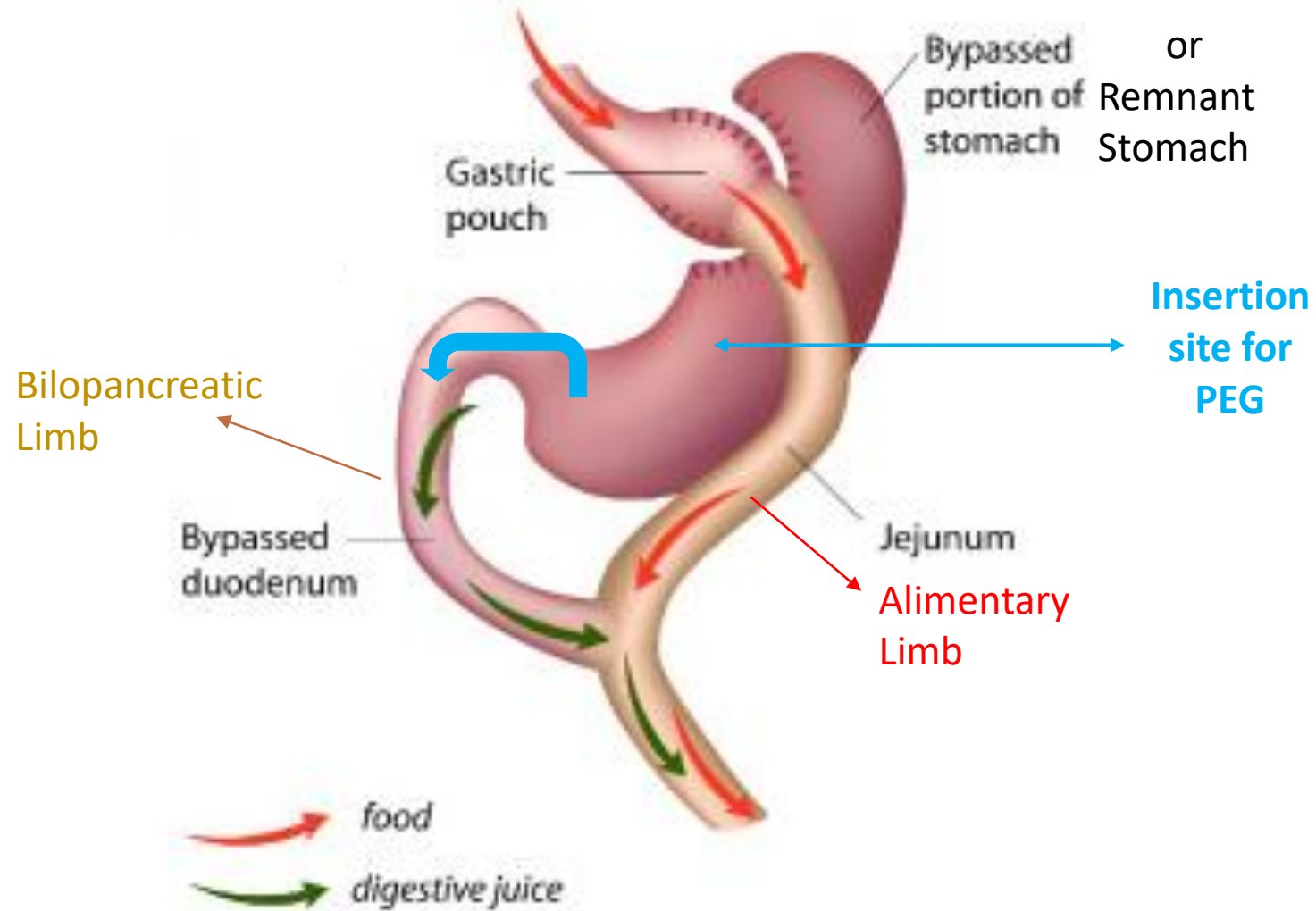
## Medical Nutritional Therapy

### **10-Point Nutrition Plan** (Suhl et al 2017)

1. Controlled portions of low GI carbohydrates, ie: 20-30g at meal times and 10-15g from snacks
2. Choose Low Glycemic Index (GI) carbohydrate
3. Avoid high GI carbohydrates
4. Include heart healthy fats, ie: 15g per meal and 5g per snack
5. Emphasise optimal protein intake at each meal and snack
6. Space meal and snacks 3-4hrs apart
7. Avoid liquids with meals and for 30mins after meals
8. Avoid caffeine
9. Avoid alcohol
10. Maintain post-bariatric vitamin and mineral intake

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Pintar T, Salobir J (2022)

## Conclusion

Frequent hypoglycemic events interfere with daily living and lead to defective glucose counter-regulation and hypoglycemia unawareness adversely affecting QOL

Since patients with PHH seem to have both recurrent hypoglycemia and hypoglycemic unawareness, early diagnosis and treatment are important

Accurate assessment tools and diagnostic criteria is imperative for clinical management

Medical Nutritional Therapy should always be the first approach to treatment

## THANK YOU!

### Any questions?

You can contact me on:

DDdietetics@outlook.com

0415 688 964

