Is it dumping and/or hypoglycemia how do I know and what to do?

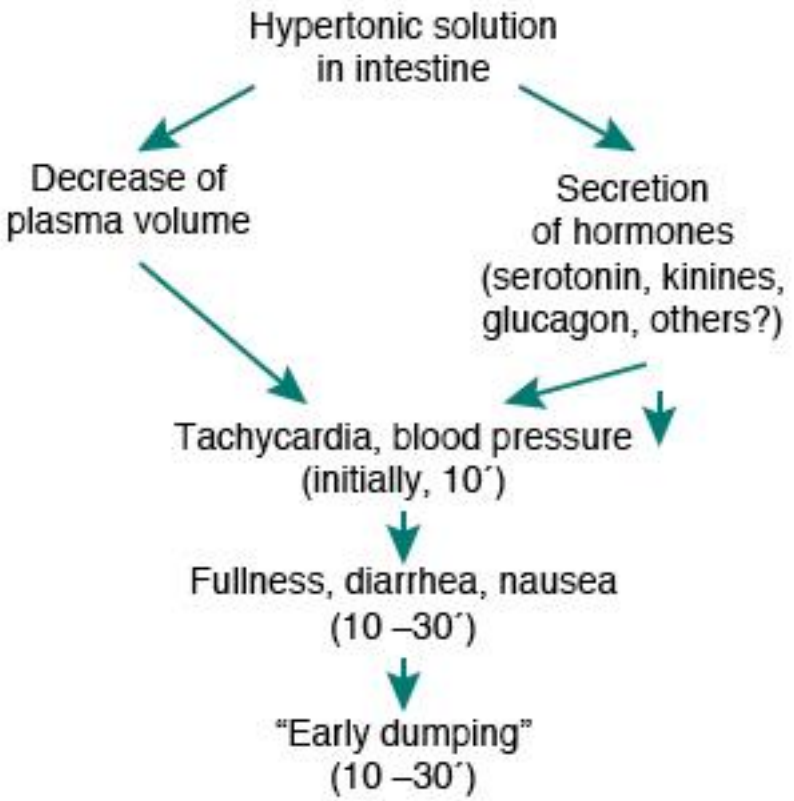
Prof Francois Pattou

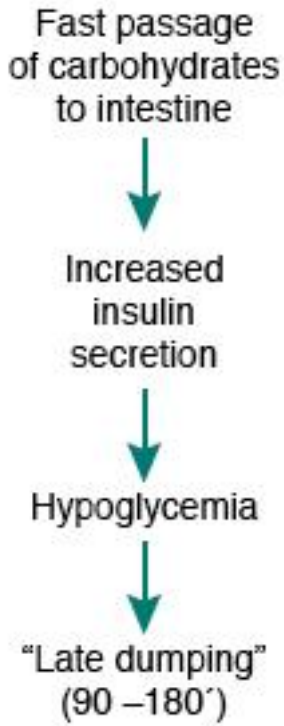
University Hospital of Lille, France

Post prandial syndrome

Dumping syndrome
30 minutes

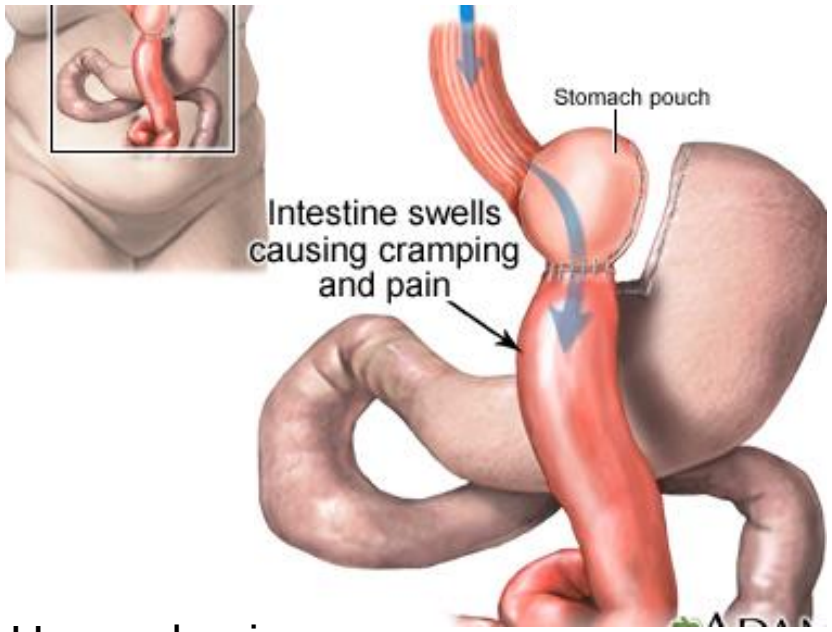
Hypoglycemia
90–180 minutes



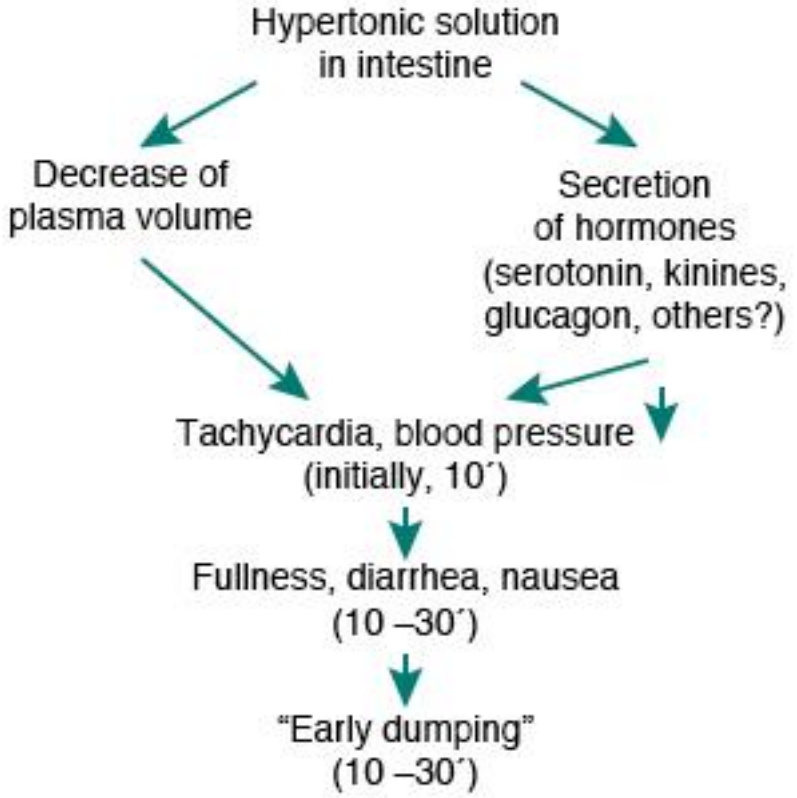


Dumping syndrome

Dumping syndrome
30 minutes



Hypovolemia
Instestinal distension



-> Sigstad / Arts questionnaires

Sigstad clinical diagnostic score

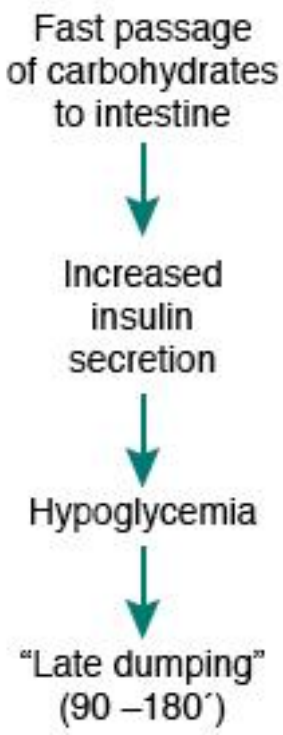
≤ 4
unlikely

Pre-shock or shock	+5
Loss of consciousness, fainting	+4
Will lie down or sit	+4
Dyspnea	+3
Physical fatigue, exhaustion	+3
Sleep, listlessness, blurred vision	+3
Palpitation	+3
Restlessness, agitation	+2
Dizziness, vertigo	+2
Headache	+1
Feeling hot, sweating, paleness, clammy skin	+1
Nausea	+1
Abdominal distension, meteorism	+1
Borborygm	+1
Eructation	-1
Vomiting	-4

> 7
dumping

Postprandial hyperinsulinic hypoglycemia (PHH)

90–180 minutes



Neuroglycopenia

Bizarre behaviour

Fatigue

Paralysis

Seizure

Coma

Neurogenic response

Palpitation

Tremor

Anxiety

Paresthesia

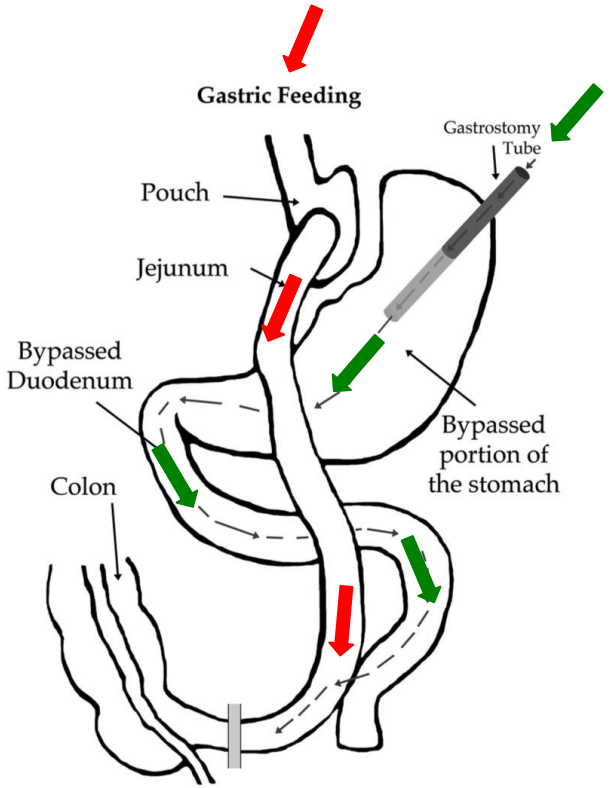
Sweating

Hunger

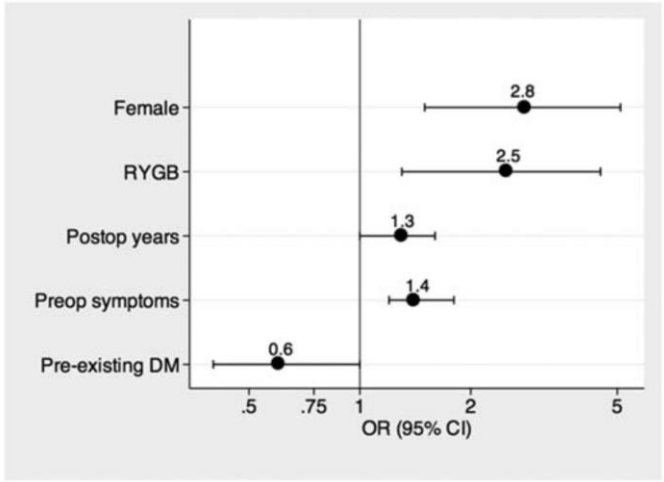
Causal relation between RYGP and PHH

McLaughlin et al.
J Clin Endocrinol Metal

Oral vs gastrostomy feeding

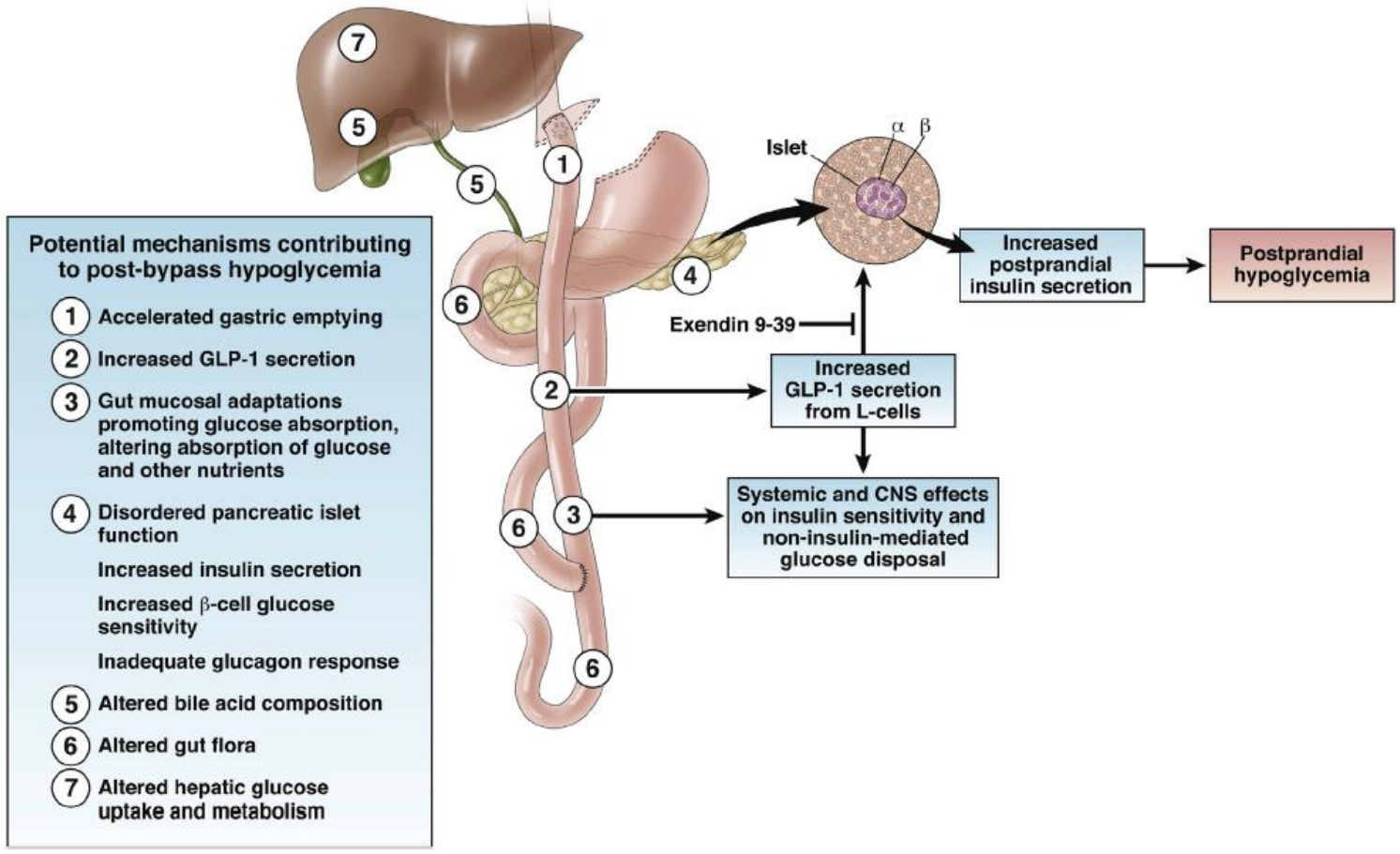


Determinants of PHH (30%)
in a cross sectional study
after RYGB or Sleeve (N=450)



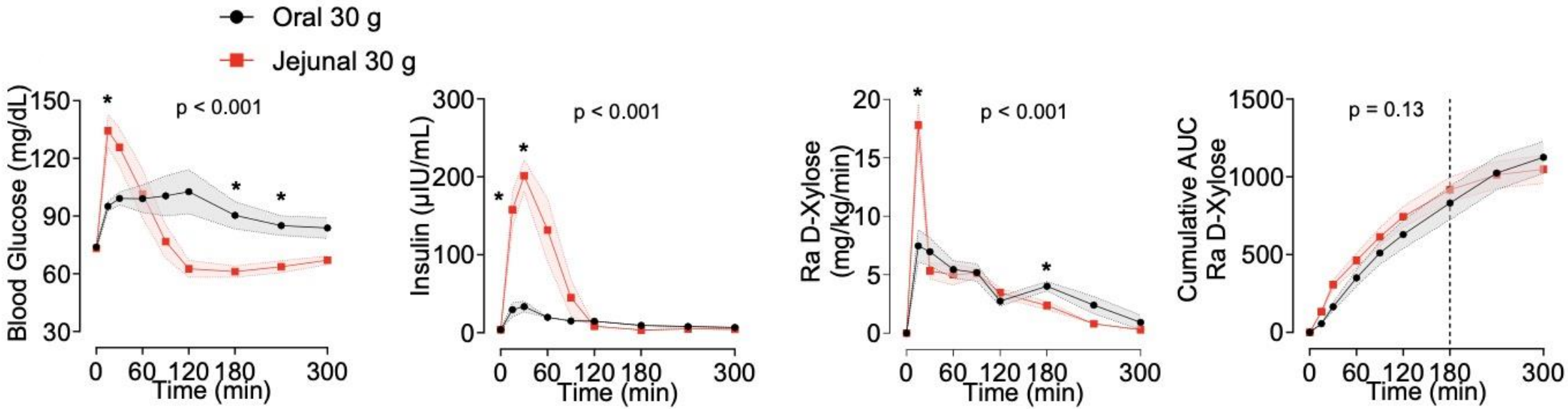
Lee et al.
Obesity 2015

Potential mechanisms



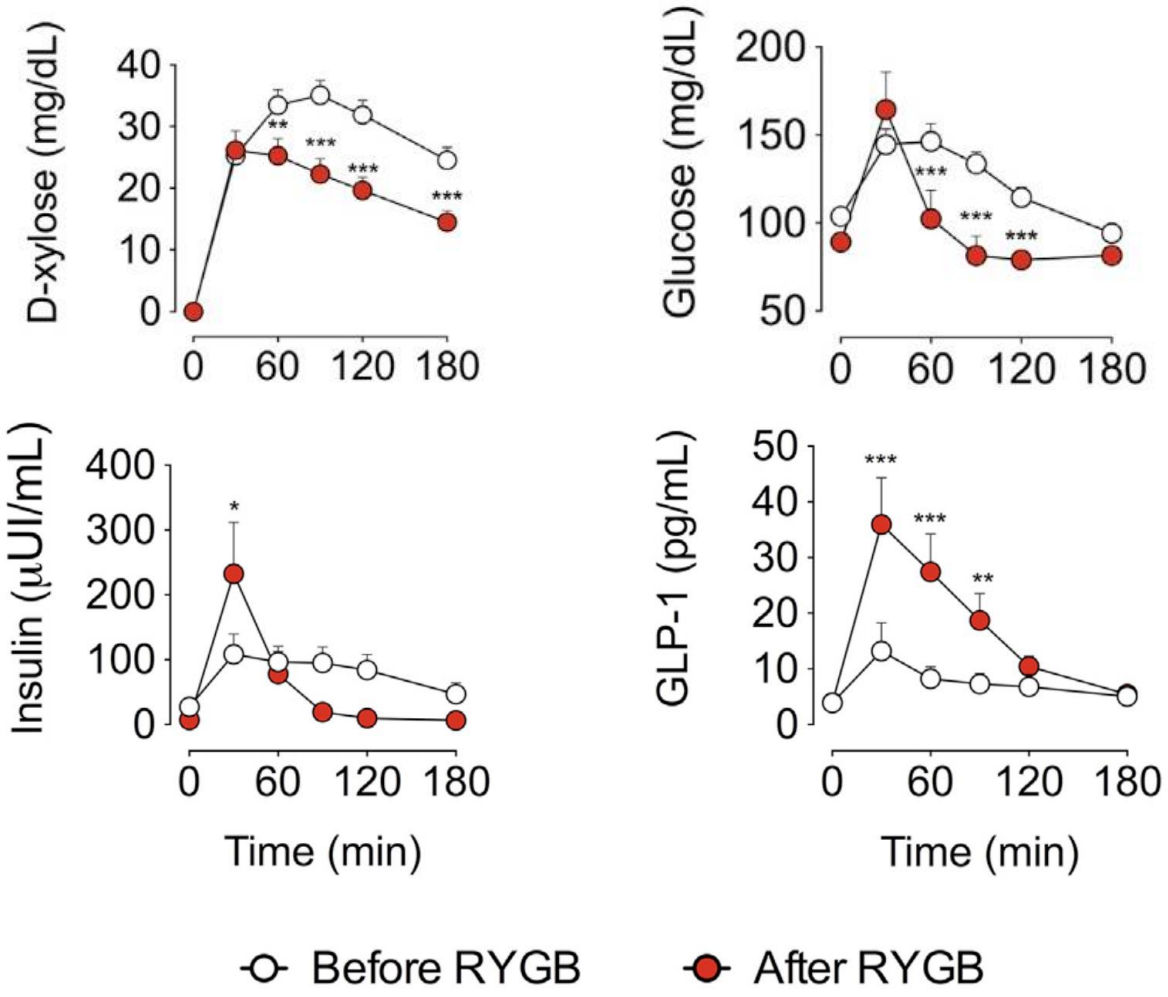
Accelerated gastric emptying / blood glucose

Mixed meal Xylose test (n=5)



Roux-en-Y gastric bypass / post prandial glucose

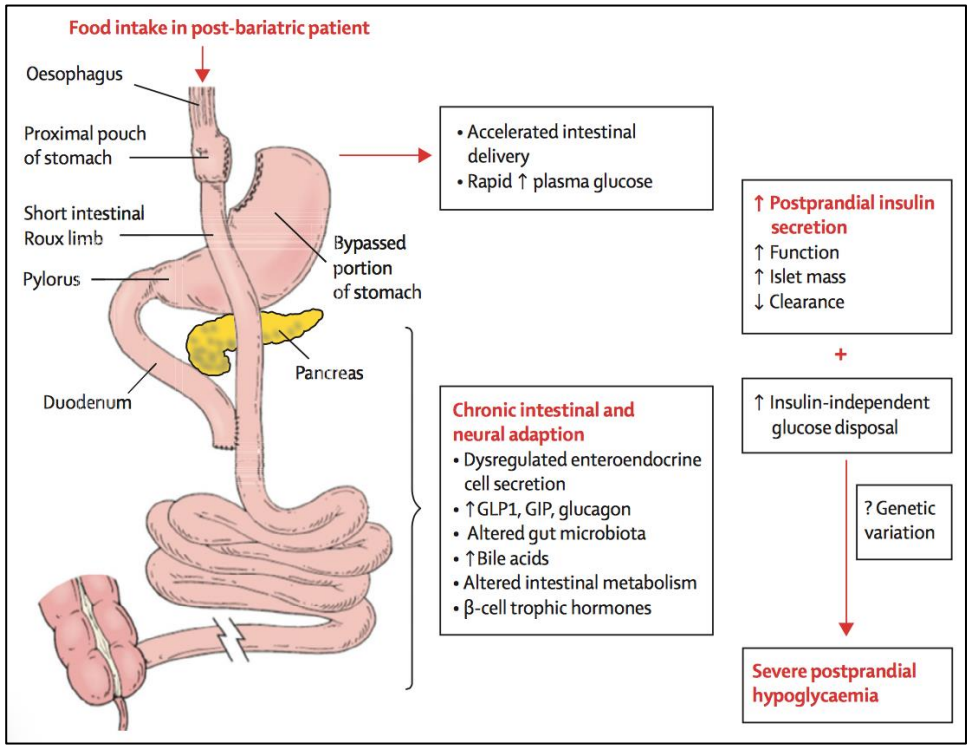
Mixed meal
Xylose test
(n=9)



Gregory Baud et al.
Cell Metabolism 2016

The rollercoaster of post-bariatric hypoglycaemia

Patti & Goldfine
Lancet Diabetes Endocrinol 2016



Several key questions remain

-

Prevalence is uncertain (0.1 to 30%) but likely underestimated

Biological determinants are unknown ?

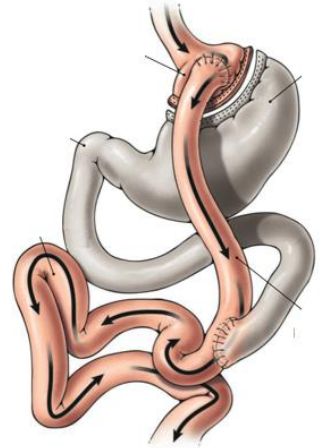
Is PHH associated with weight regain, long term cognitive function ?

Best treatment ?

Is there any preoperative predictive factors ?

-> Longitudinal studies are crucial to answer these questions

PHH study in ABOS prospective cohort



BMI >40 kg/m2
BMI >35 kg/m2 + comorbidities

Patients with OGTT (%)

957 (100%) N = 959 Baseline

RYGB

N= 758 (86%) N = 885 1 year

N=177 (53%) N = 335 5 years

Body composition
Glucose tolerance
Insulin secretion
Lipids
Renal function

Raverdy et al.
Ann Surg 2018

Metabolic assessment

Standard Oral glucose tolerance test (OGTT)
repeated at baseline / 1 year / 5 years
after laparoscopic Roux en Y gastric bypass (RYGB)

Post prandial hyperinsulinemic hypoglycemia (PHH)

= blood glucose < 50 mg/dl at 120 mn
AND plasma insulin > 3mU/l

Beta cell function

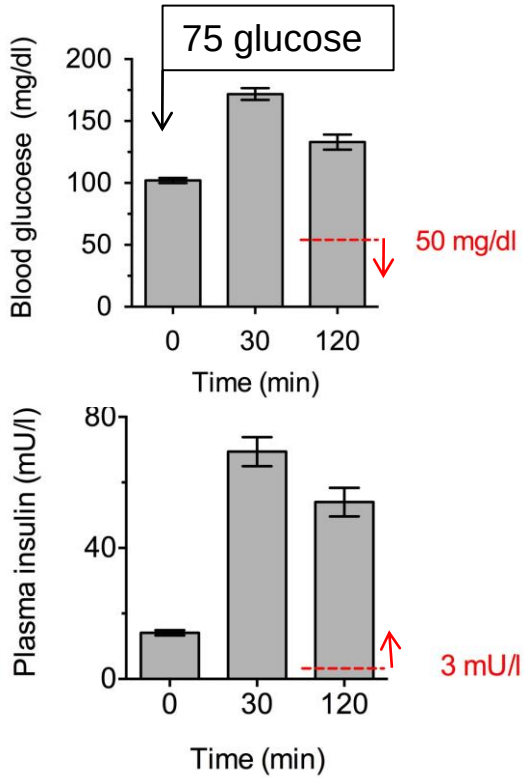
->Insulinogenic index : $(Ins_{30} - Ins_0) / (Glc_{30} - Glc_0)$
Phillips et al *Diabet Med* 1994

Insulin sensitivity

-> Matsuda index : $10{,}000 / \text{sqrt}((Glc_0 \times Ins_0) \times (Glc_{120} \times Ins_{120})$
Matsuda & de Fronzo, *Diabetes Care* 1999

Beta cell mass

-> Meier index : $\text{C-peptide}_0 / Glc_0$
Meier et al *Diabetes* 2009



PHH prevalence during 5 years after RYGB

	All patients at each visit			Patients who completed all 3 visits		
	Baseline (n=957)	12 months (n=758)	60 months (n=177)	Baseline (n=161)	12 months (n=161)	60 months (n=161)
Female gender; n (%)	711(74.3)	557 (73.5)	133 (75.1)	121 (75.2)		
Age (yr)	43.0±16.0	44.0±16.0***	50.0±16.0 ***	45.0±14.0	46.0±14.0***	50.0±14.0***
BMI (kg/m²)	46.3±10.3	32.4±7.9***	34.5±8.0***	47.2±11.3	33.2±7.7***	34.4±8.3***
Weight loss (%)	-	30.8±11.1	26.9±16.4	-	30.2±11.1	26.7±16.2
Type 2 diabetes; n (%)	355 (37.1)	139 (18.3)***	35 (19.8)***	69 (42.9)	31 (19.3)***	32 (19.9)***
Dyslipidemia; n (%)	580 (60.6)	241 (31.8)***	89 (50.3)***	101 (62.7)	65 (40.4)***	82 (50.9)***
Hypertension; n (%)	542 (56.6)	282 (37.2)***	77 (43.5)***	102 (63.4)	69 (42.9)***	69 (42.9)***
HBA1C; %	5.9±1.2	5.4±0.6***	5.5±0.8***	6.1±1.1	5.6±0.5***	5.5±0.7***
Fasting glucose; mg/dL	102.0±33.1	87.8±12.4***	92.9±19.3***	102.9±37.3	88.8±15.4***	92.9±19.3***
Fasting insulin; nmUIL	14.1±12.3	5.3±3.9***	5.6±5.1***	13.0±10.8	5.2±3.7***	5.6±4.7***
Fasting C peptide; ng/mL	3.9±1.9	2.1±0.9***	2.2±1.1***	4.1±1.9	2.1±1.1***	2.2±1.0***
HOMA2-B*	118.0±74.6	88.1±36.7***	82.0±41.7***	114.0±75.8	86.1±35.0***	81.5±42.9***
HOMA2-S*	48.7±38.3	117.6±71.8***	102.6±72.3***	50.1±37.8	118.4±75.0***	106.3±69.8***
Beta cell mass‡	0.4±0.2	0.2±0.1***	0.2±0.1***	0.3±0.2	0.2±0.1***	0.2±0.1***
Insulinogenic index¶	0.8±1.1	0.6±0.8	0.5±0.7	0.5±0.9	0.5±0.6	0.5±0.7
Matsuda index⌘	11.8±15.0	20.3±17.9***	17.5±20.2	12.3±14.1	21.0±16.9***	17.5±19.9*
PHH; %	5 (0.5)	69 (9.1)***	14 (7.9)***	1 (0.6)	10 (6.2)***	12 (7.5)***

Mean ± SEM; *** P<0.001 vs Baseline (Mixed model for repeated measures)

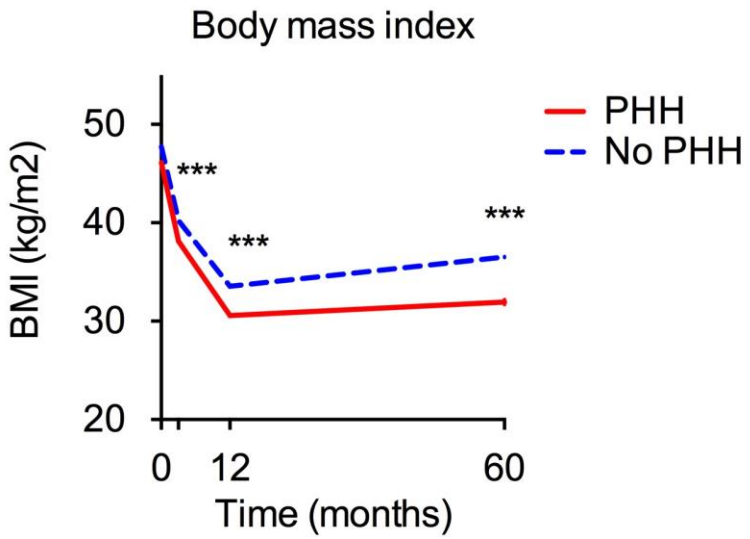
Clinical biological profile associated with PHH

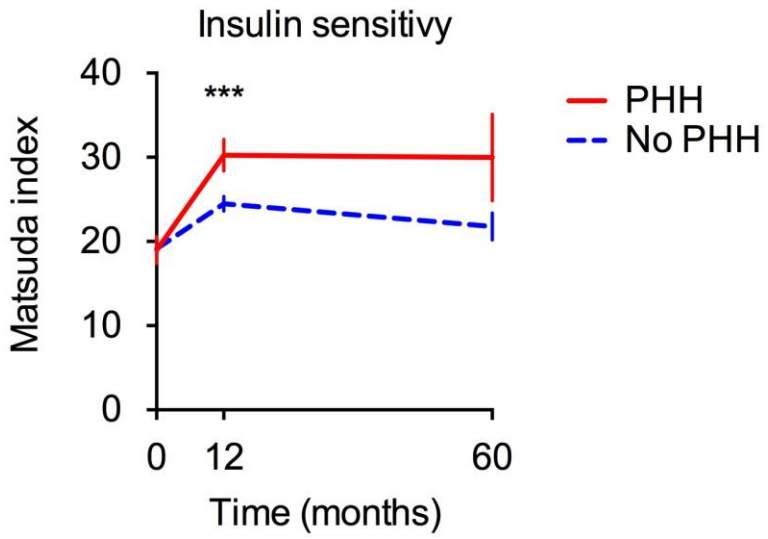
Table 2. Clinical and biological characteristics associated with PHH in patients submitted to RYGB at anytime during follow-up

	No PHH N =853	PHH N = 83	Univariate analysis P	Multivariate analysis P'
Female gender; n (%)	627 (73.5)	63 (75.9)	0.697	-
Type 2 diabetes; n (%)	173 (20.3)	2 (2.4)	**<0.001**	0.987
Age; year	50.0 ± 17.0	47.0 ± 15.5	0.109	**0.005**
Weight loss; kg	29.7 ± 11.7	35.0 ± 11.6	**<0.001**	**0.031**
Fasting blood glucose; mg/dL	88.9 ± 15.1	83.8 ± 6.5	**<0.001**	0.102
Fasting plasma insulin; nmUlL	5.3 ± 4.2	5.0 ± 3.3	0.114	0.158
Fasting plasma C peptide; ng/mL	2.2 ± 1.0	2.0 ± 0.8	**0.009**	0.061
HOMA2-B£	85.8 ± 37.0	98.6 ± 33.4	**0.002**	**0.006**
HOMA2-S£	116.0 ± 74.5	118.0 ± 64.2	0.417	-
Beta cell mass‡	0.2 ± 0.1	0.2 ± 0.1	0.381	-
Insulinogenic index¶	0.5 ± 0.8	1.0 ± 1.1	**<0.001**	**0.002**
Matsuda index⌘	18.5 ± 17.8	29.7 ± 15.8	**<0.001**	**<0.001**

Weight loss and insulin sensitivity

80 patients with PHH vs 877 patients with no PHH after RYGB

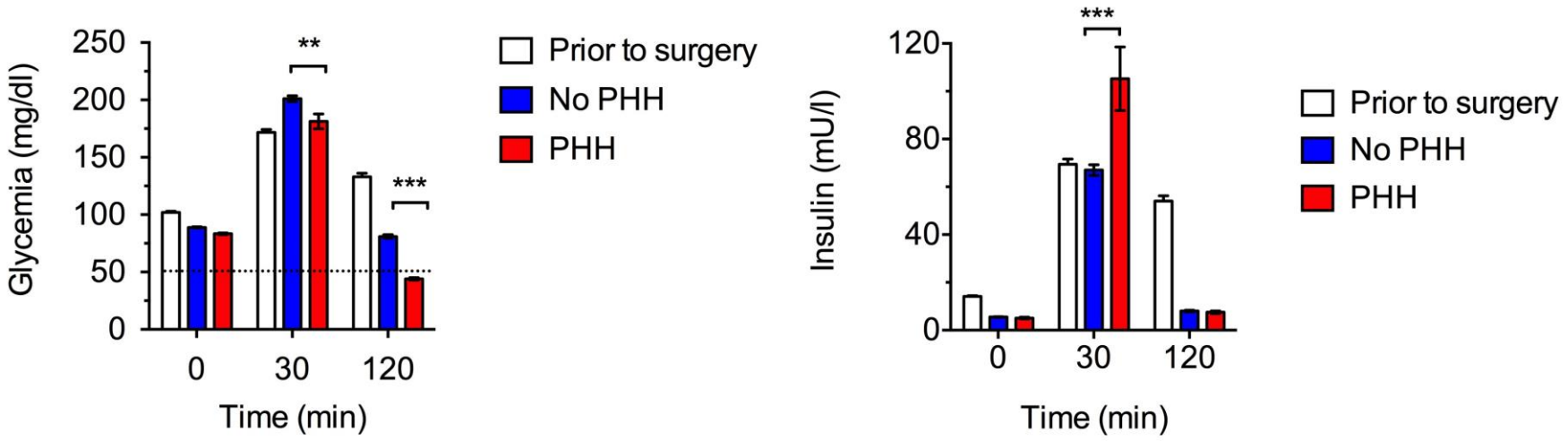




Raverdy et al. *Ann Surg* 2018

Post prandial glucose response after RYGB

936 postoperative OGTT -> 83 PHH (21-49 mg/dl) in 80 patients (M12 and/or M60)



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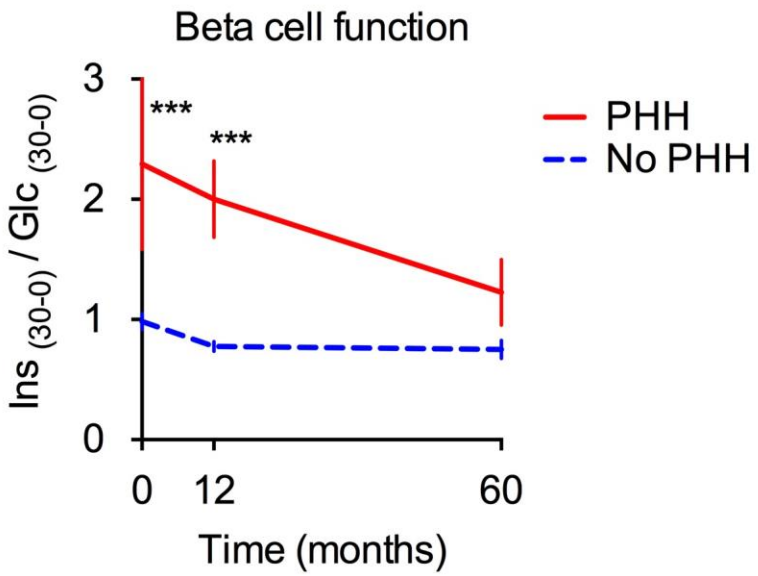
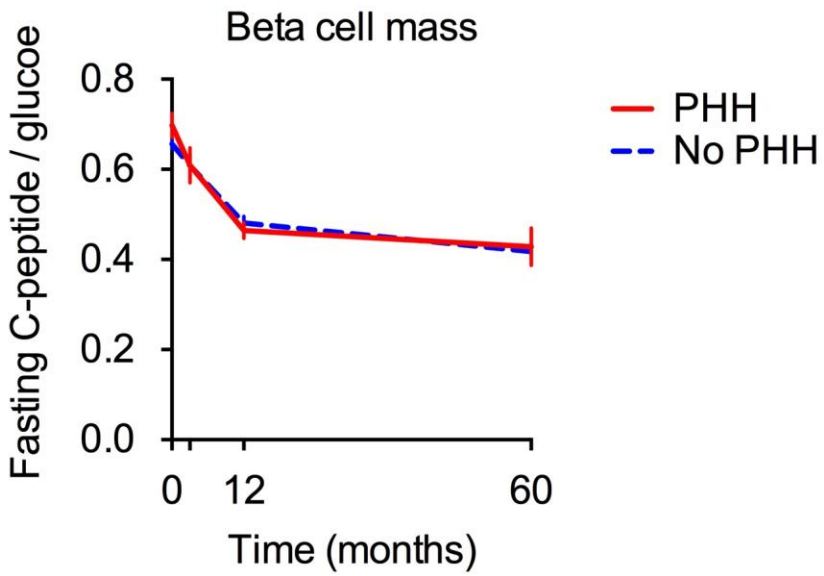
Beta cell function and mass

80 patients with PHH vs 877 patients with no PHH after RYGB





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Predictive factors of PHH

Table 3 : Baseline clinical and biological characteristics of PHH patients and those without PHH at any time after RYGB

Preoperative value	No PHH N =877	PHH N = 80	Univariate analysis P	Multivariate analysis P'
Female gender; n (%)	649 (74.0)	62 (77.5)	0.593	NA
Age; year	43.0 (34.0 ; 51.0)	42.0 (33.8 ; 49.0)	0.332	NA
Type 2 diabetes; n (%)	344 (39.2)	11 (13.8)	**<0.001**	0.162
Body mas index; kg/m2	46.4 (42.2 ; 52.7)	44.4 (41.0 ; 49.6)	0.051	0.056
Fasting blood glucose; mg/dL	103.1 (92.9 ; 129.3)	95.4 (89.8 ; 107.3)	**<0.001**	0.579
Fasting plasma insulin; nmUIL	14.2 (9.1 ; 21.7)	12.6 (8.9 ; 18.2)	0.076	0.800
Fasting plasma C peptide; ng/mL	3.9 (3.1 ; 5.0)	3.7 (3.0 ; 4.5)	0.158	0.403
HOMA2-B£	117.6 (83.5 ; 159.8)	127.5 (91.3 ; 158.2)	0.179	0.629
HOMA2-S£	48.0 (32.7 ; 71.1)	53.6 (37.3 ; 73.0)	0.170	0.911
Beta cell mass‡	0.35 (0.27 ; 0.45)	0.36 (0.29 ; 0.43)	0.424	NA
Insulinogenic index¶	0.72 (0.27 ; 1.35)	1.23 (0.68 ; 1.99)	**<0.001**	**0.040**
Matsuda index⌘	11.6 (6.8 ; 22.0)	13.3 (8.5 ; 24.9)	0.053	0.202

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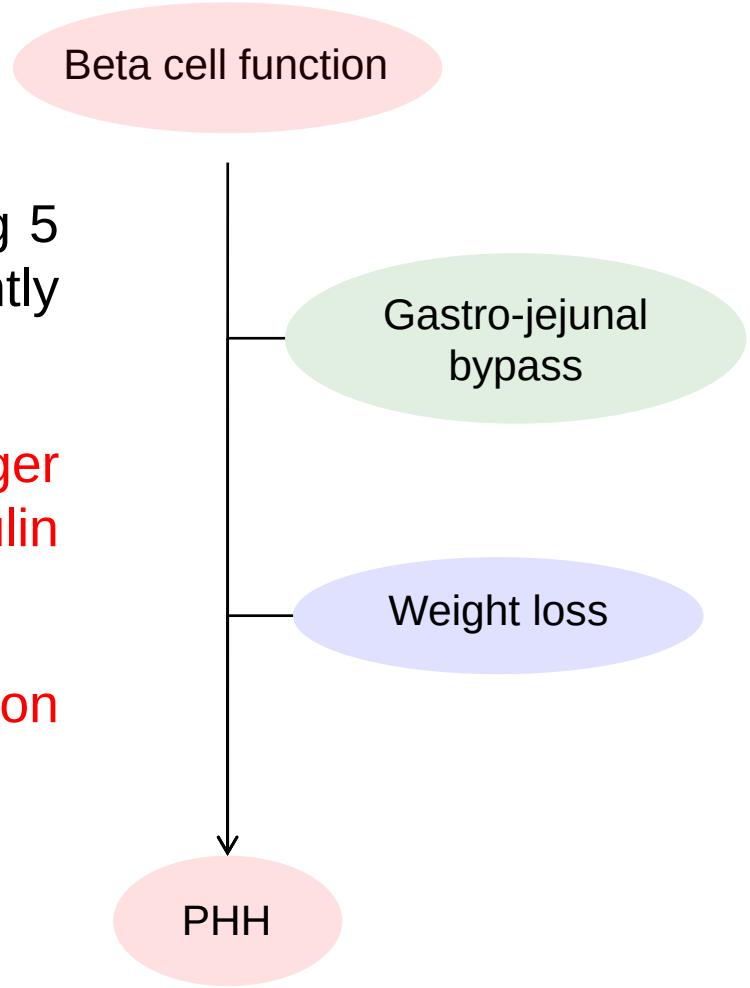
Summary

1. Prevalence of PHH between 5% and 10% during 5 years after RYGB, and does not significantly increase with time

2. PHH after RYGB was associated with a younger age, a higher beta cell function, more insulin sensitivity, and more weight loss

3. Patients with high preoperative beta cell function are at higher risk to develop PHH after RYGB



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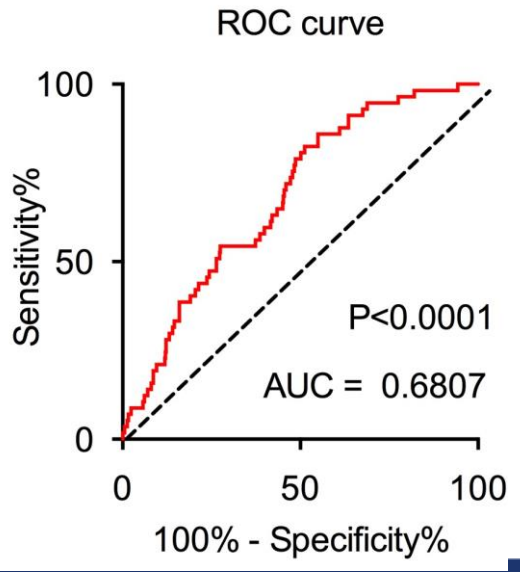
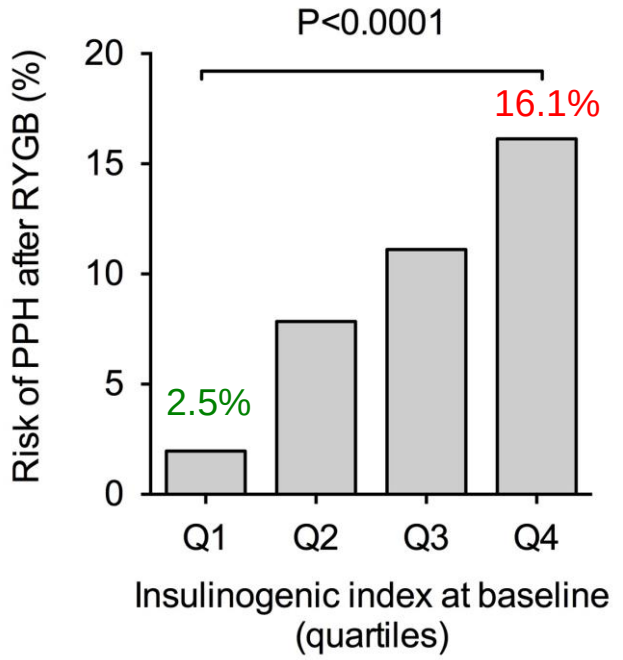
Preoperative prediction of PHH / OGTT ?

The value of insulinogenic index (Ins_{30} - Ins_0) / (Glc_{30} - Glc_0) during a 75 g oral glucose tolerance test prior to surgery can predict the risk of PHH after RYGB



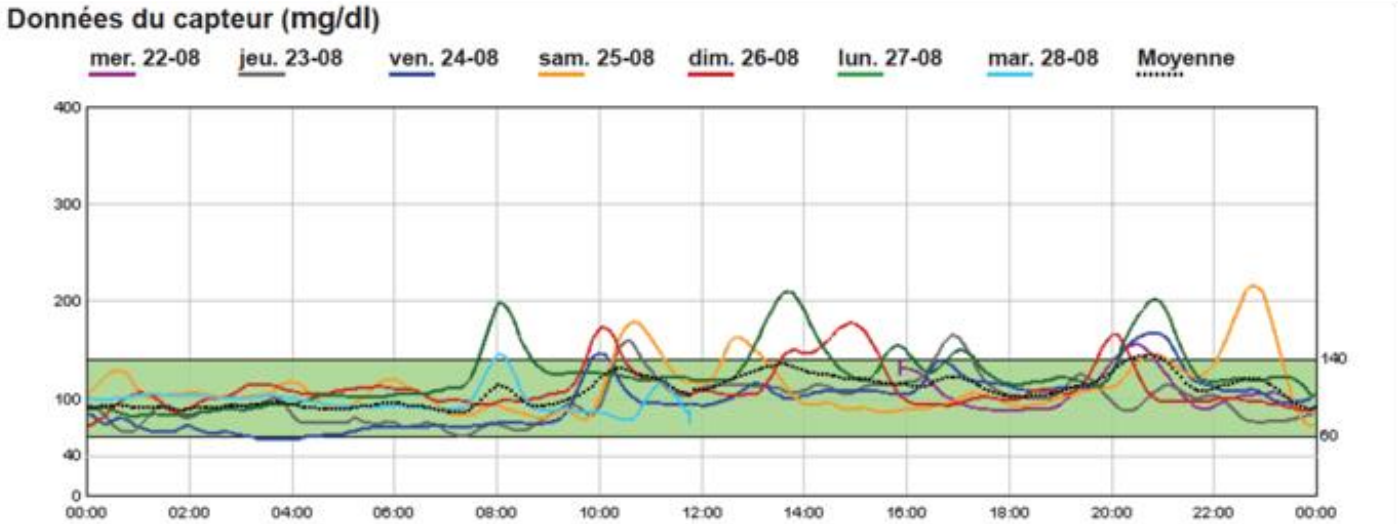


what to do?

Diet

- Split food intake in 6 meals
- Avoid high GI CHO, limit to 30g per meal
- Respect 30 min between food and fluid intake
- A « sieste » slows gastric emptying
- Increase viscosity with pec<n or guar gum
- Eat in peaceful condi<ons (avoid stress)

Therapeutic education / CGMS



	mer. 22-08	jeu. 23-08	ven. 24-08	sam. 25-08	dim. 26-08	lun. 27-08	mar. 28-08	Moyenne/Total
Nb valeurs du capteur	98	288	288	288	288	288	142	1 680
La plus élevée	155	165	167	217	177	210	145	217
La plus basse	87	61	57	71	72	81	78	57
Moyenne	107	97	96	112	111	124	98	107
Écart type	20	22	26	28	22	30	12	27
% d'Écart Moyen Absolu	8,9	7,1	1,3	11,4	6,9	26,7	2,0	11,3
Corrélation	N/A	N/A	N/A	0,96	N/A	N/A	N/A	0,82
Nb calibrations valides	2	4	3	5	4	5	1	24
Désignation	X					X	X	

Drugs

- Diazoxide (reduces insulin secretion)
- Acarbose (reduce glucose absorption)
- Verapamil (reduces insulin secretion)
- SMS analogs (reduces GLP1 secretion)
- SGLT2 (reeduce glucose absorption ?)

Surgery

Gatric banding
Reversal to normal anatomy

Is it dumping and/or hypoglycemia – how do I know and what to do?

Prof Francois Pattou

University Hospital of Lille, France