CREUF 2023

30 & 31 Mars 2023
MULHOUSE ● ALSACE

Insuffisance intestinale

Pr Gaël Piton
CHU de Besançon

Plan

Plan

1- Introduction

- Définir l'insuffisance intestinale
- Epidémiologie
- Pronostic

2- Physiopathologie

3- Biomarqueurs entérocytaires

4- Conclusion

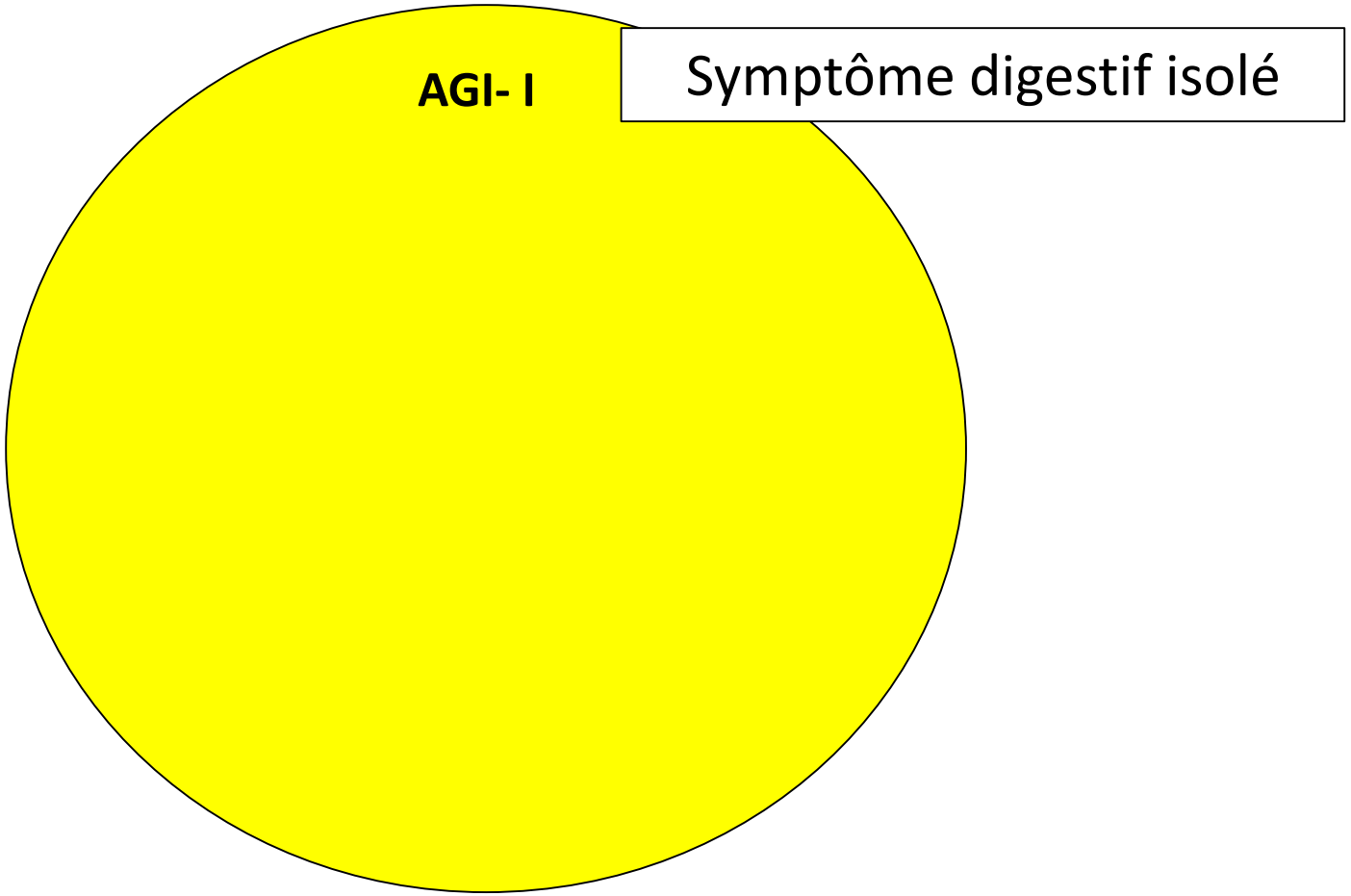
Partie 1

1

Introduction

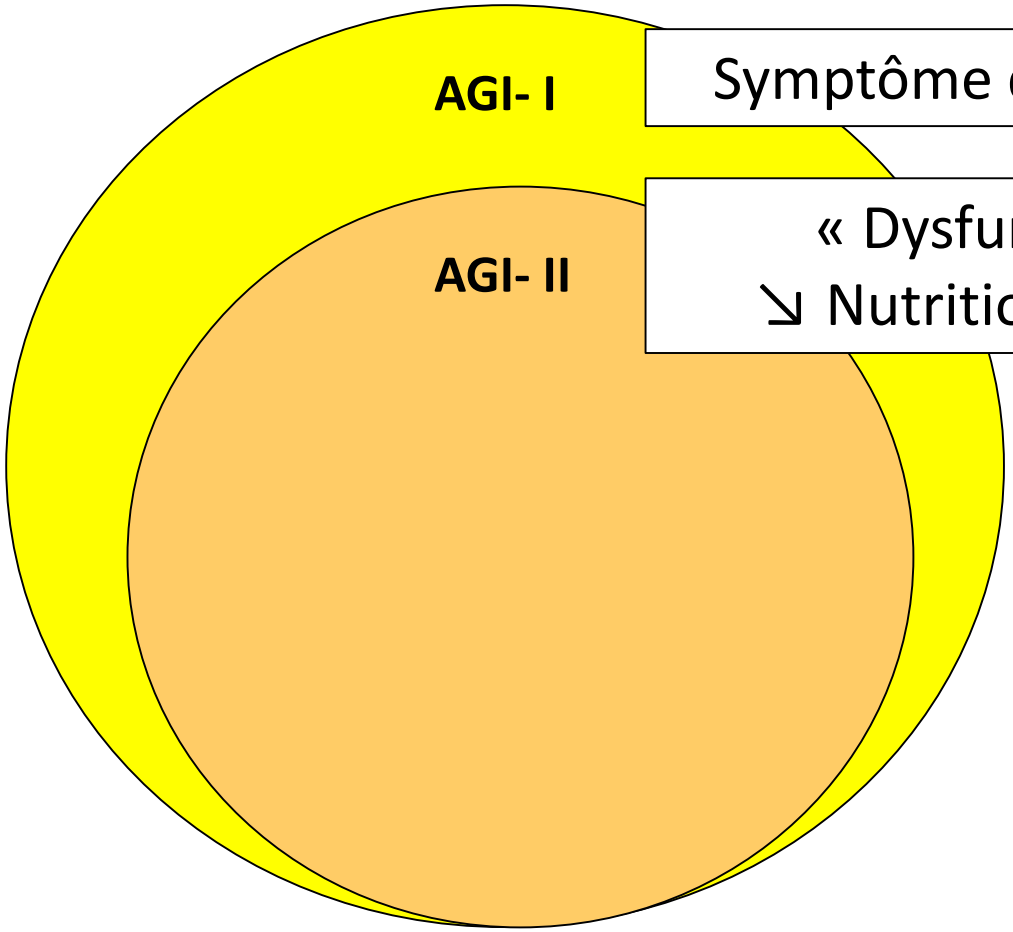
a) Définir l’insuffisance intestinale ?

Acute Gastrointestinal Injury



Reintam et al, ICM 2012

Acute Gastrointestinal Injury

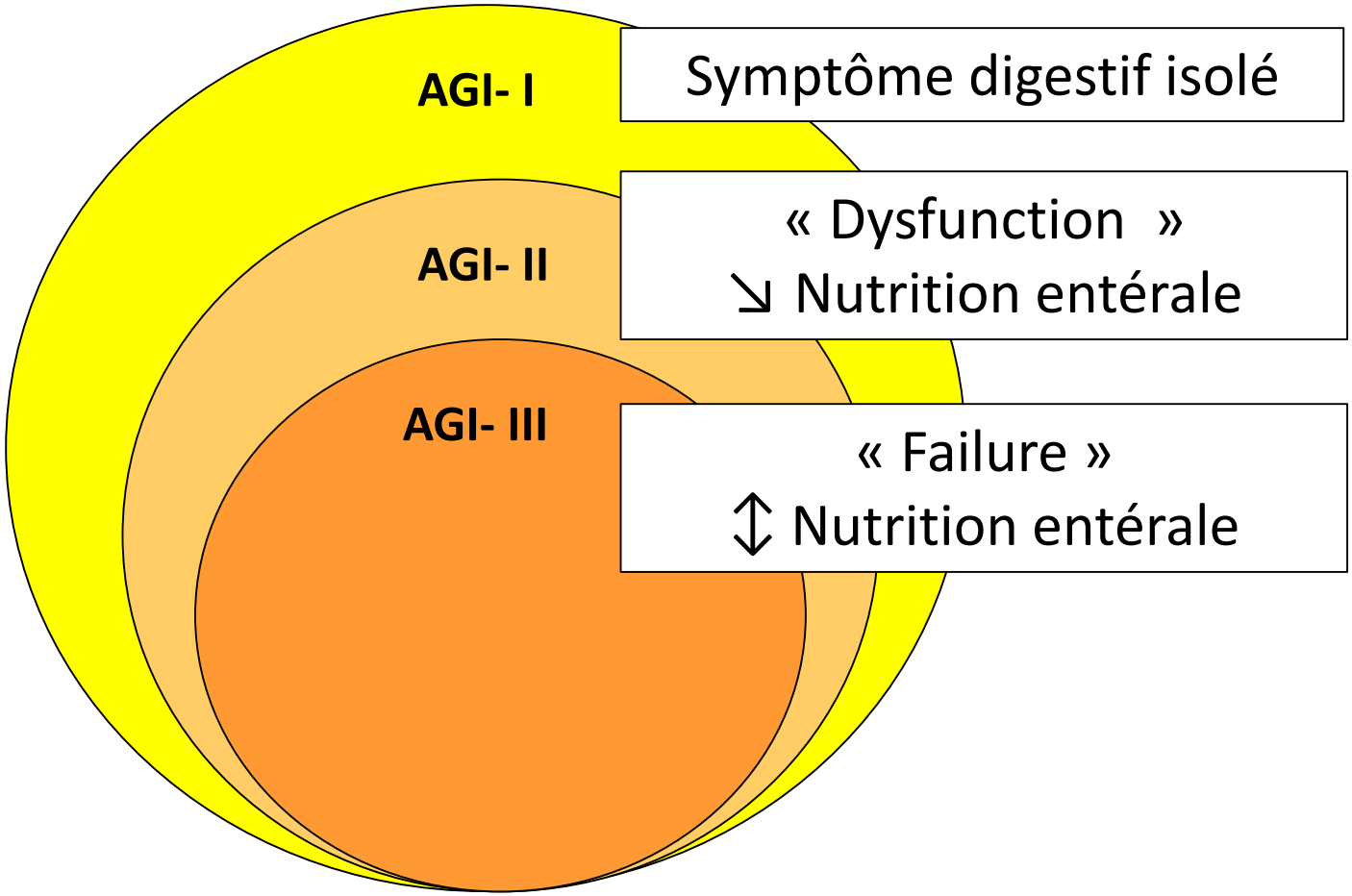


Symptôme digestif isolé

« Dysfunction »
↘ Nutrition entérale

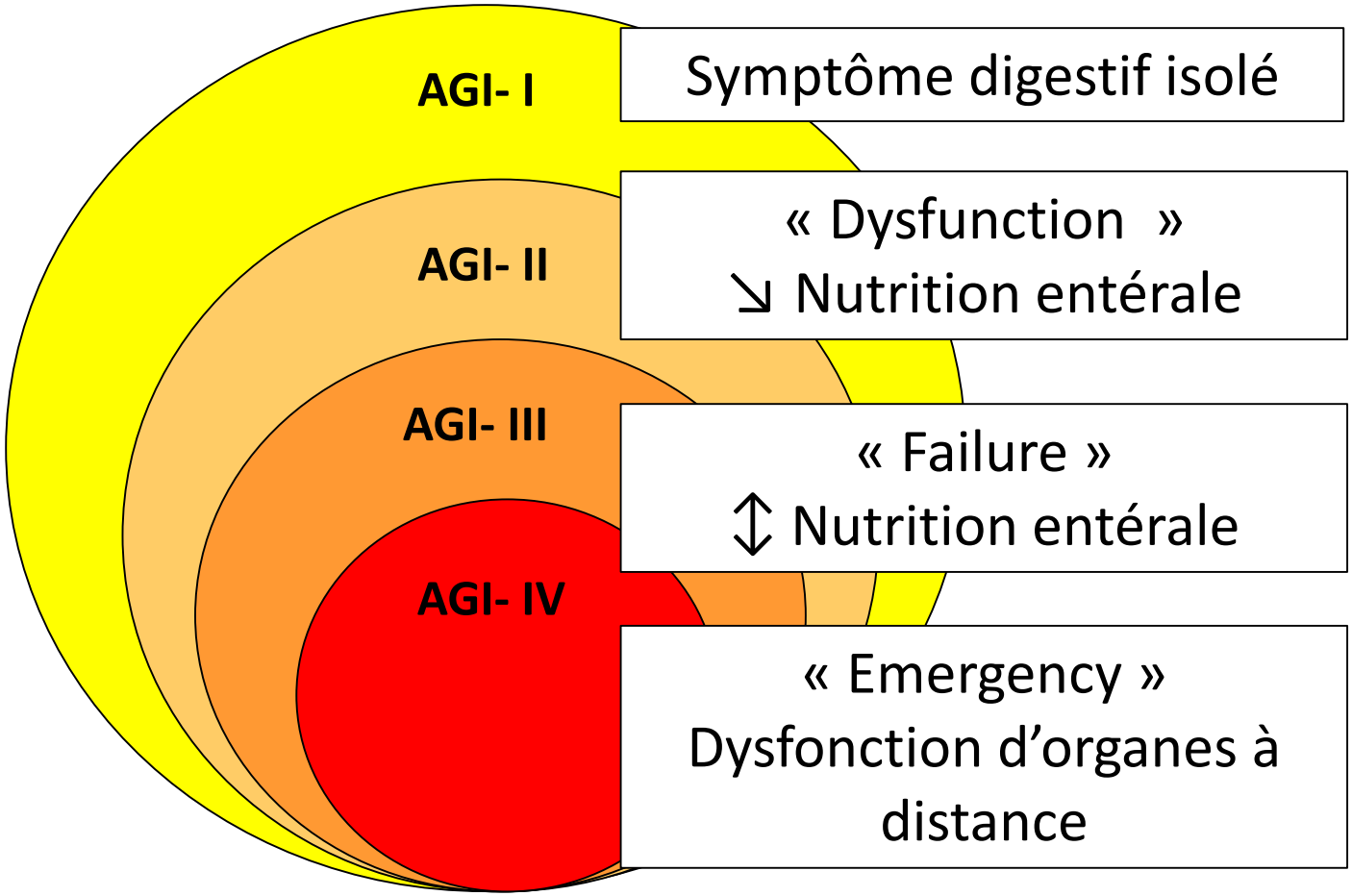
Reintam et al, ICM 2012

Acute Gastrointestinal Injury



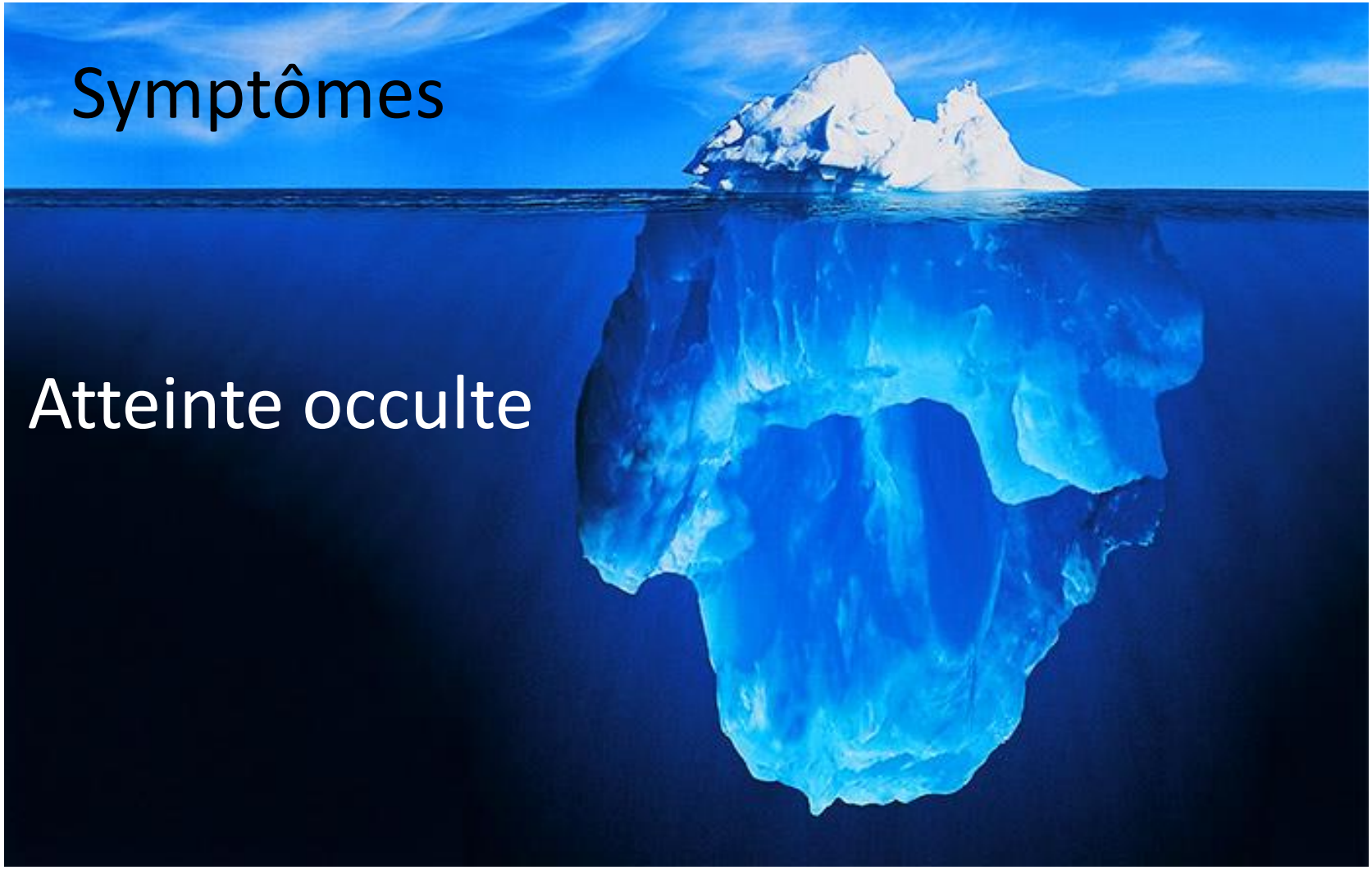
Reintam et al, ICM 2012

Acute Gastrointestinal Injury



Reintam et al, ICM 2012

L’évaluation intestinale est difficile



Peut-on définir l'insuffisance intestinale à l'échelle de l'entérocyte ?

Acute intestinal failure

=

Acute reduction of enterocyte mass

± loss of gut barrier function

Piton, ICM 2011

Peut-on définir l'insuffisance intestinale à l'échelle de l'entérocyte ?

Acute reduction of enterocyte mass

± loss of gut barrier function

	Citrulline	IFABP
Enterocyte Destruction	↓	↑
Enterocyte dysfunction	↓	N

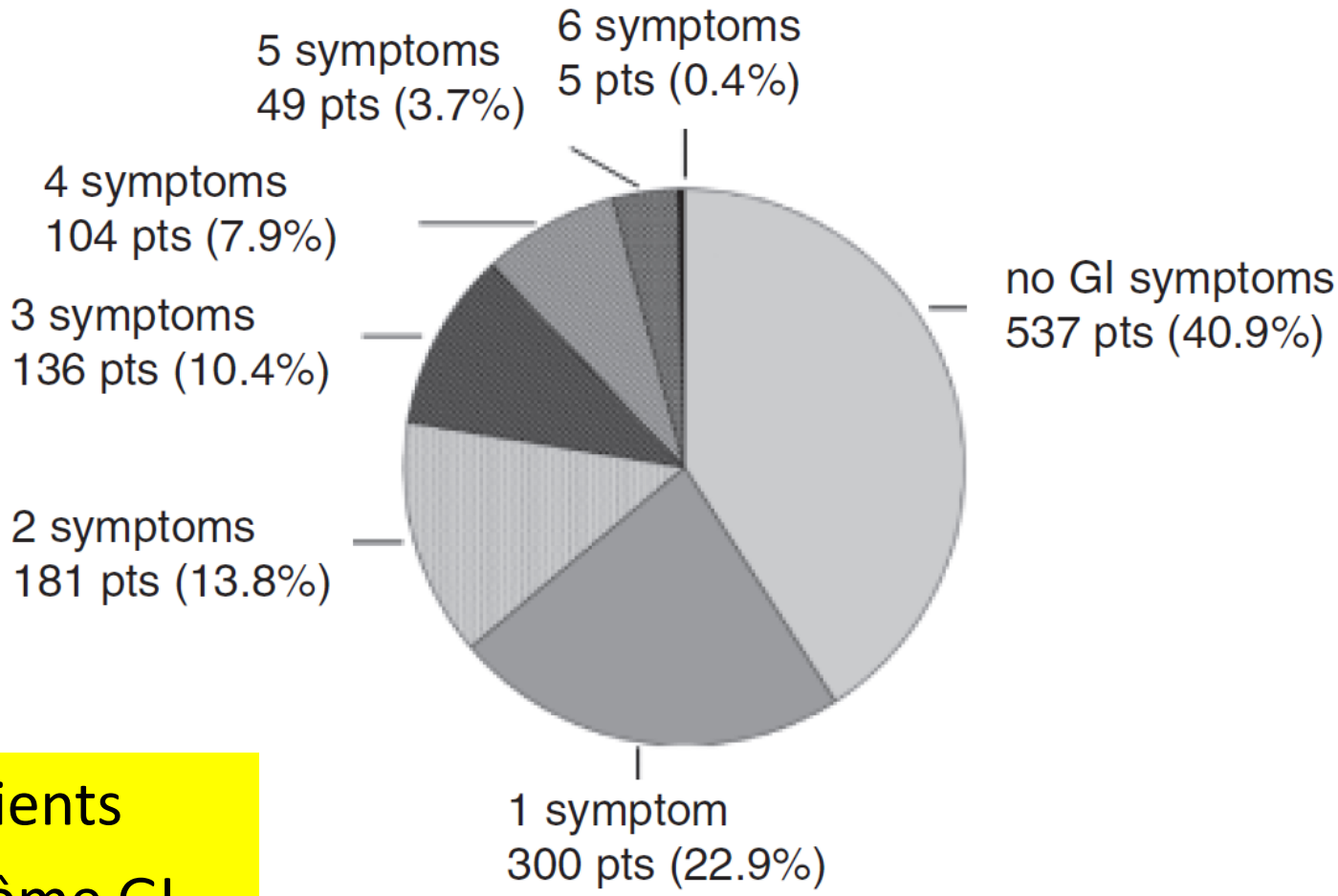
Piton, ICM 2011

Partie 1

Introduction

b) Epidémiologie de l'insuffisance intestinale

Symptômes digestifs en réanimation

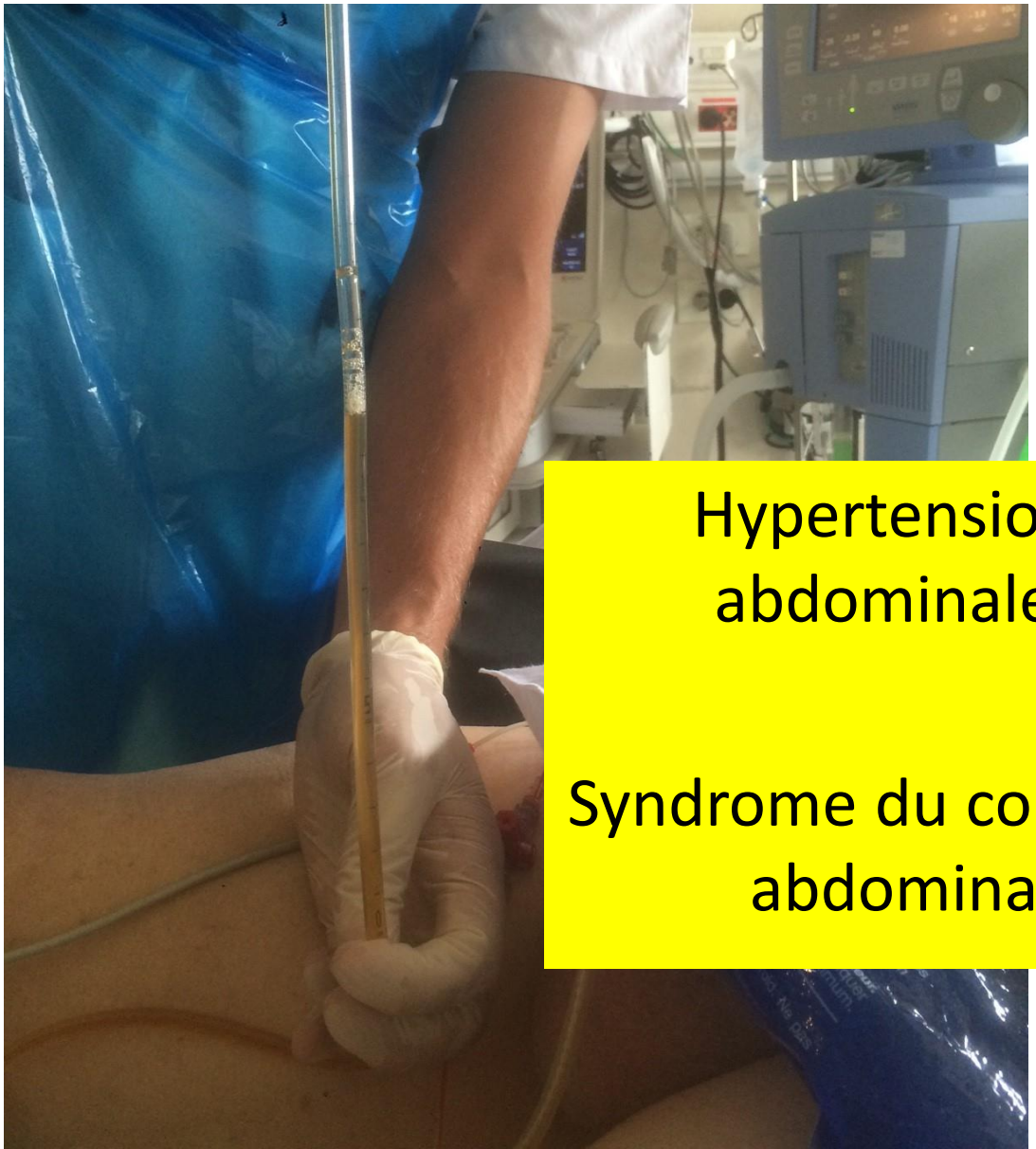


60% patients

≥ 1 symptôme GI

Reintam et al, Acta Anaesthesiol Scand 2009

Hypertension intra abdominale



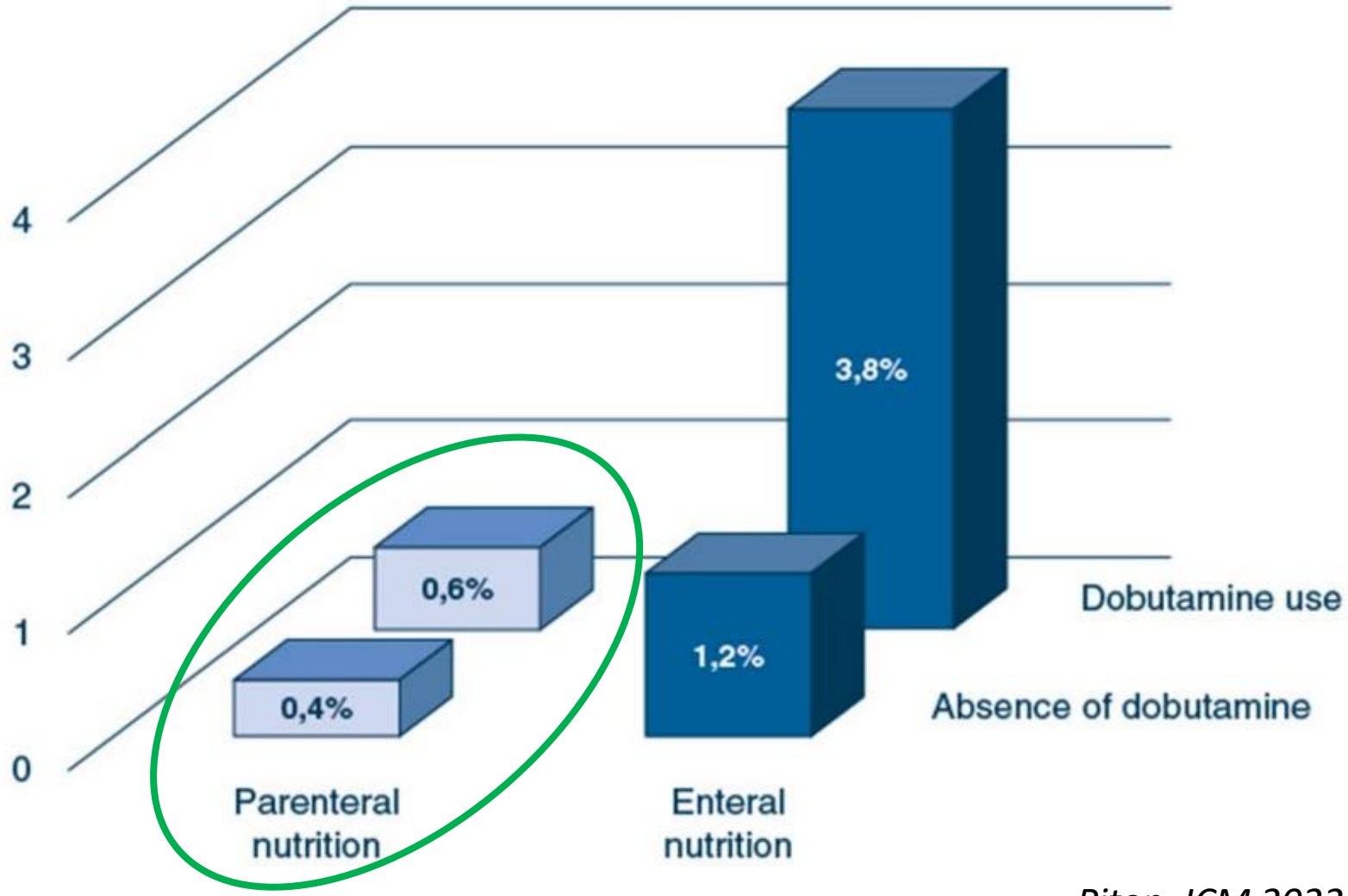
Hypertension intra-abdominale : 50%

Syndrome du compartiment abdominal : 5%

Ischémie mésentérique aigue en réanimation

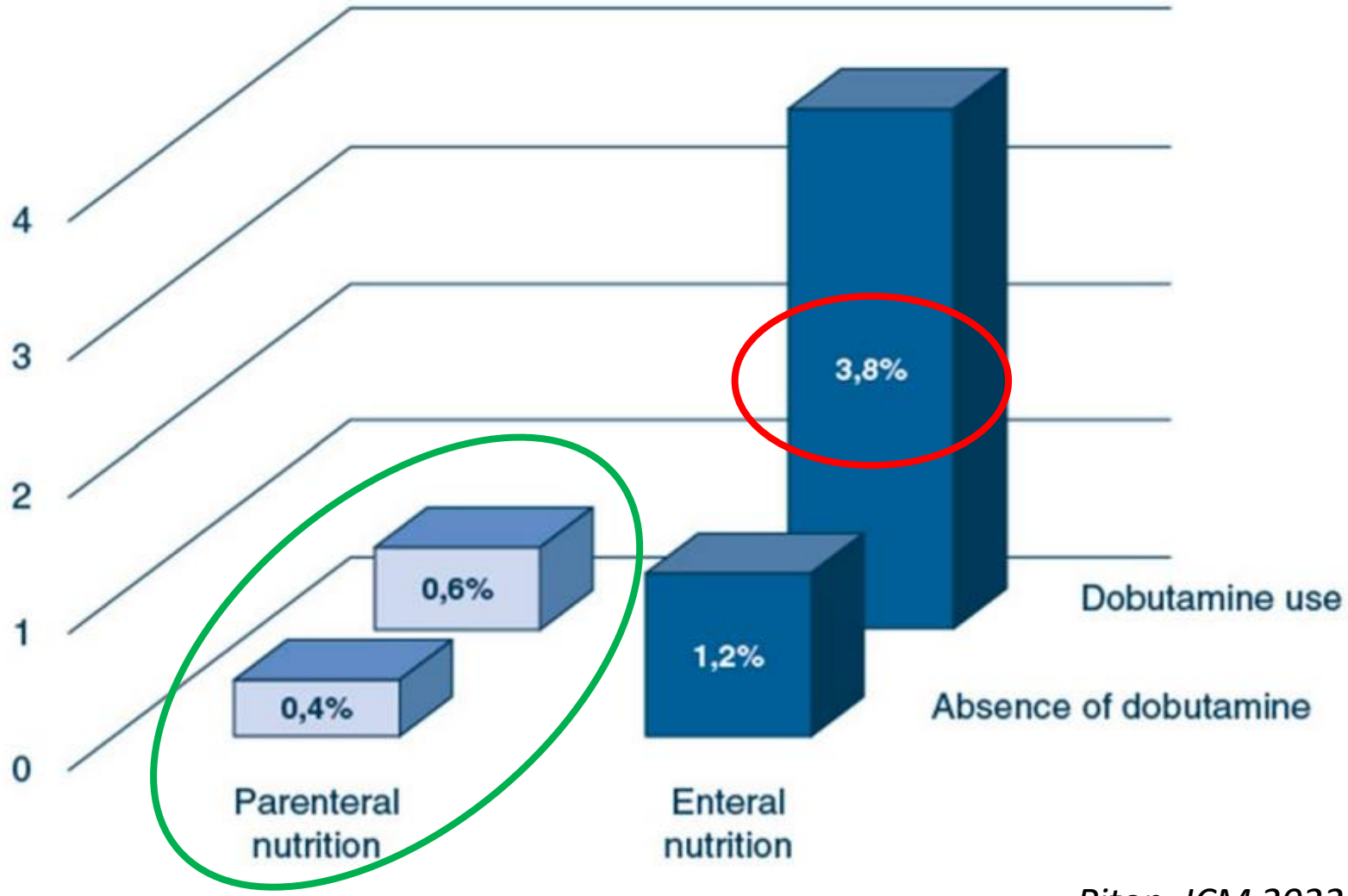
Reignier, Lancet 2017

Ischémie mésentérique aigue chez le patient intubé ventilé en choc



Piton, ICM 2022

Ischémie mésentérique aigue chez le patient intubé ventilé en choc



Piton, ICM 2022

Partie 1

Introduction

c) Pronostic de l’insuffisance intestinale

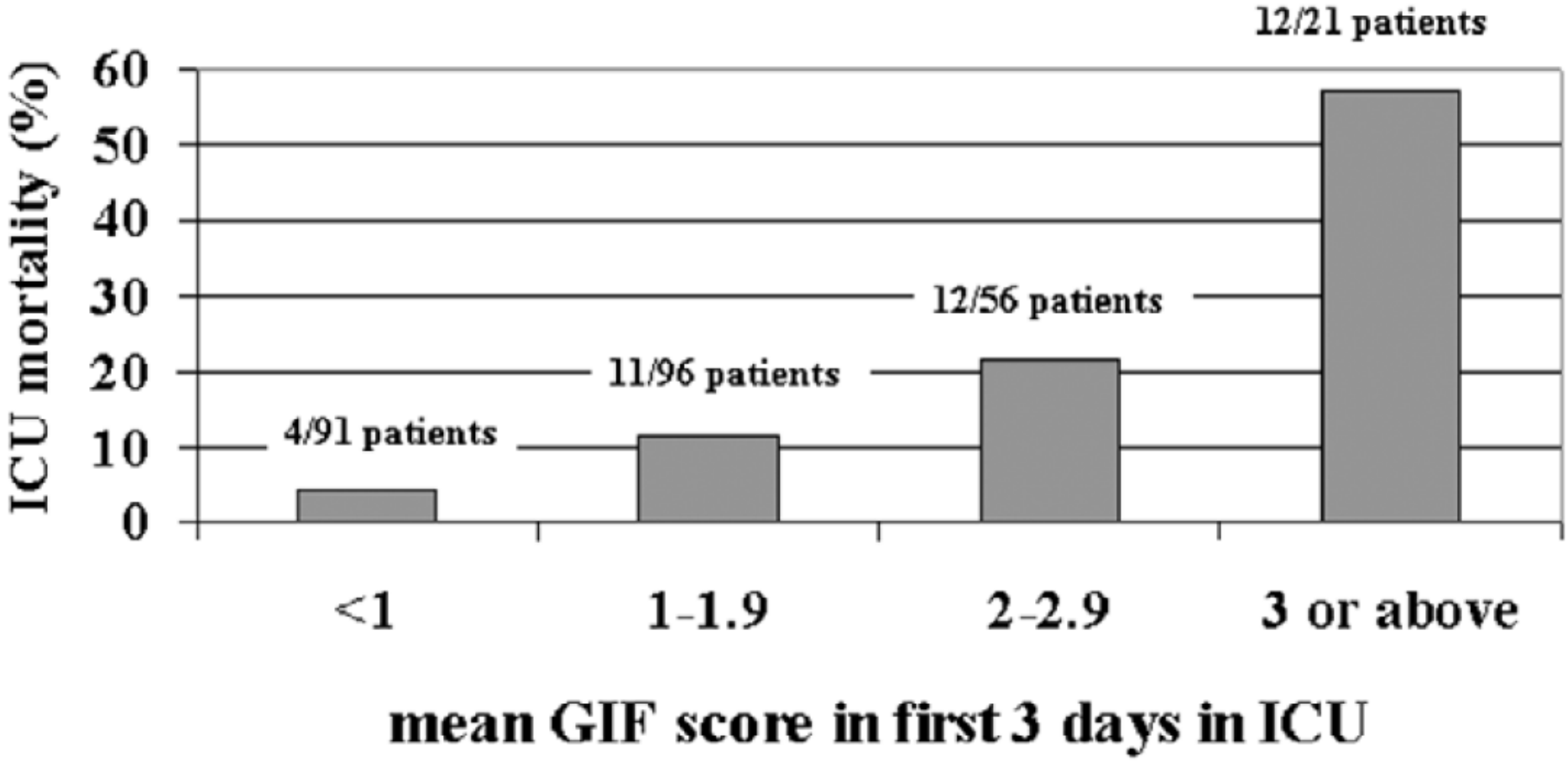
Valeur pronostique des symptômes digestifs

Mean SOFA during the ICU stay and GI symptoms in prediction of mortality.

	P-value	OR	95% CI
Mean SOFA	<0.001	1.49	1.41–1.56
Absent/abnormal bowel sounds	<0.001	3.16	2.08–4.80
GI bleeding	0.016	1.94	1.13–3.32
Bowel distension	0.097	1.54	0.93–2.56

Reintam et al, Acta Anaesthesiol Scand 2009

Valeur pronostique du score AGI



Reintam, Critical Care 2008

Vers un « intestinal-SOFA » ?

Etude prospective multicentrique
540 patients
11 services de réanimation
9 pays

Reintam, Clinical nutrition, 2021

Vers un « intestinal-SOFA » ?

Multivariate analyses		
	Mortality during 28 days n = 539; 79 died	
Covariates	HR (95% CI)	P-value
Model 1: SOFA total + descriptive AGI grading		
SOFA total	1.22 (1.15; 1.29)	<0.001
AGI grade	1.39 (1.05; 1.84)	0.020

Reintam, Clinical nutrition, 2021

Vers un « intestinal-SOFA » ?

Multivariate analyses		
	Mortality during 28 days n = 539; 79 died	
Covariates	HR (95% CI)	P-value
Model 1: SOFA total + descriptive AGI grading		
SOFA total	1.22 (1.15; 1.29)	<0.001
AGI grade	1.39 (1.05; 1.84)	0.020
Model 2: SOFA subscores + descriptive AGI grading		
SOFA cardiovascular	1.15 (0.96; 1.38)	0.116
SOFA respiratory	1.15 (0.89; 1.48)	0.279
SOFA hematological	0.91 (0.66; 1.26)	0.584
SOFA renal	1.44 (1.17; 1.77)	<0.001
SOFA hepatic	0.93 (0.65; 1.33)	0.690
SOFA neurological	1.60 (1.32; 1.94)	<0.001
AGI grade	1.51 (1.16; 1.95)	0.002

Reintam, Clinical nutrition, 2021

Pronostic de l’ischémie mésentérique en réa

28-day mortality 60%

Leone ICM 2015
Guillaume, Shock 2017
Piton, ICM 2022

Dysfonction intestinale en réanimation

1- Difficile à identifier

2- Fréquente

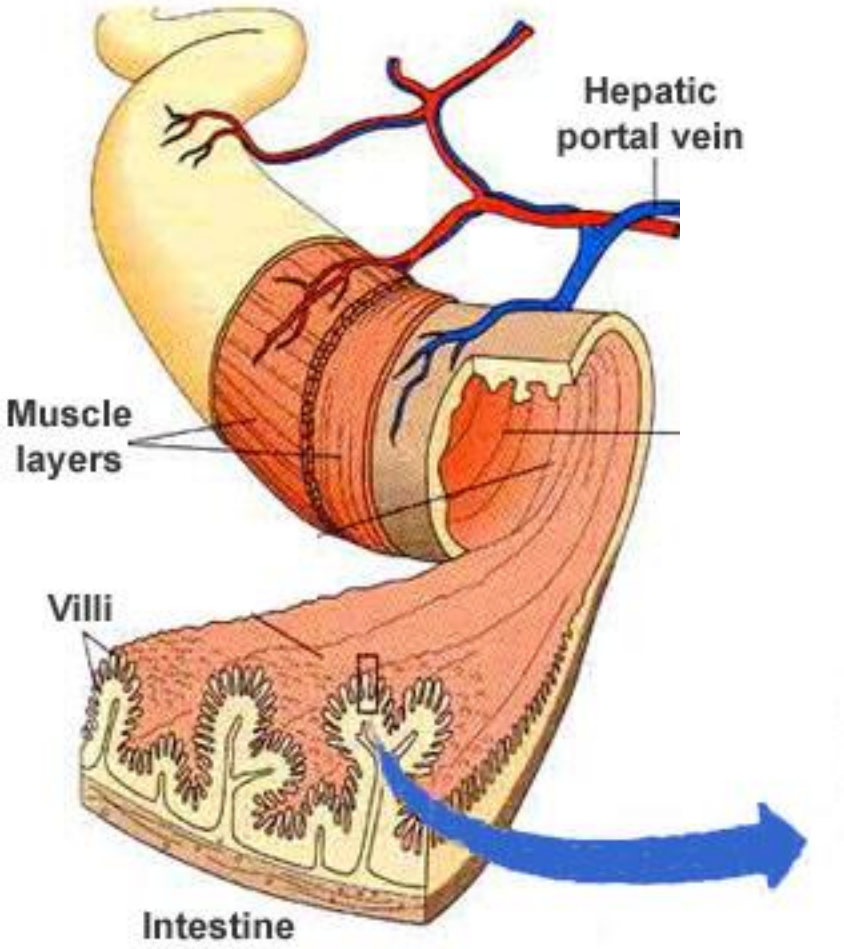
3- Associée à un mauvais pronostic

→ Le réanimateur devrait s'y intéresser !

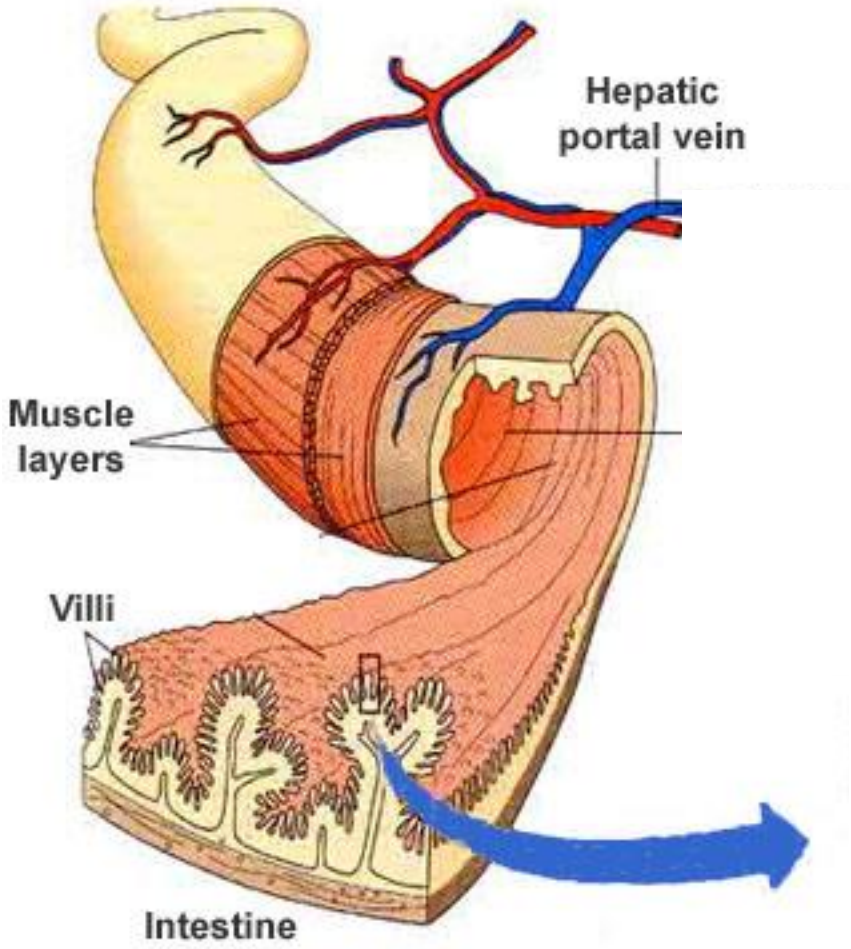
2

Physiopathologie

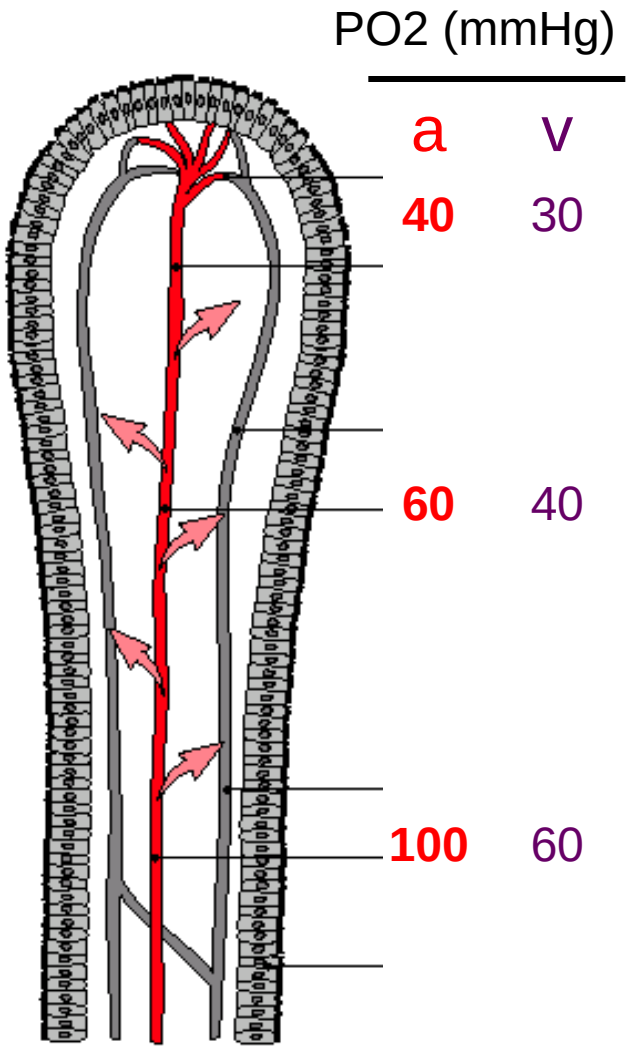
Force
Surface 250 m^2



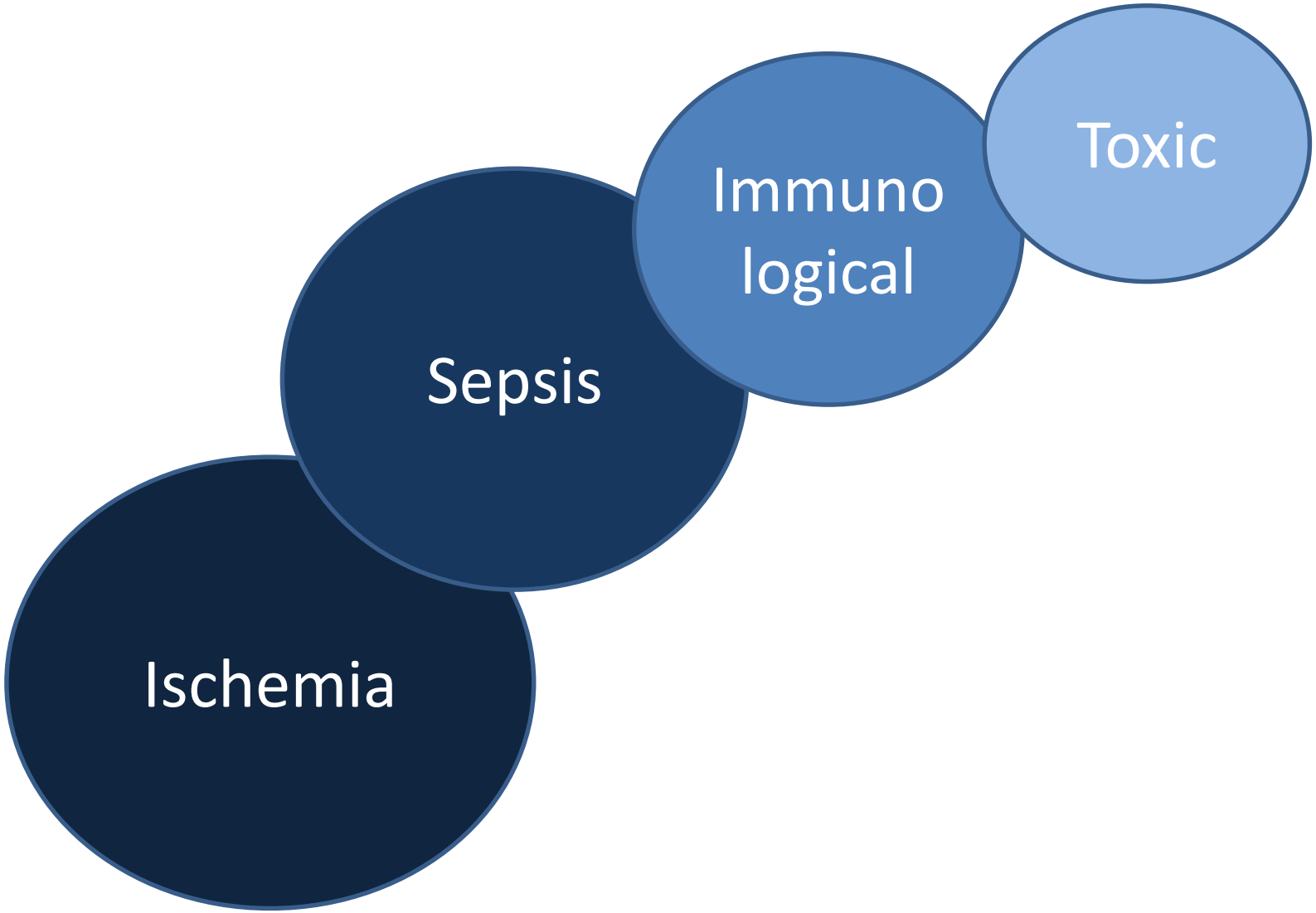
Force
Surface 250 m^2



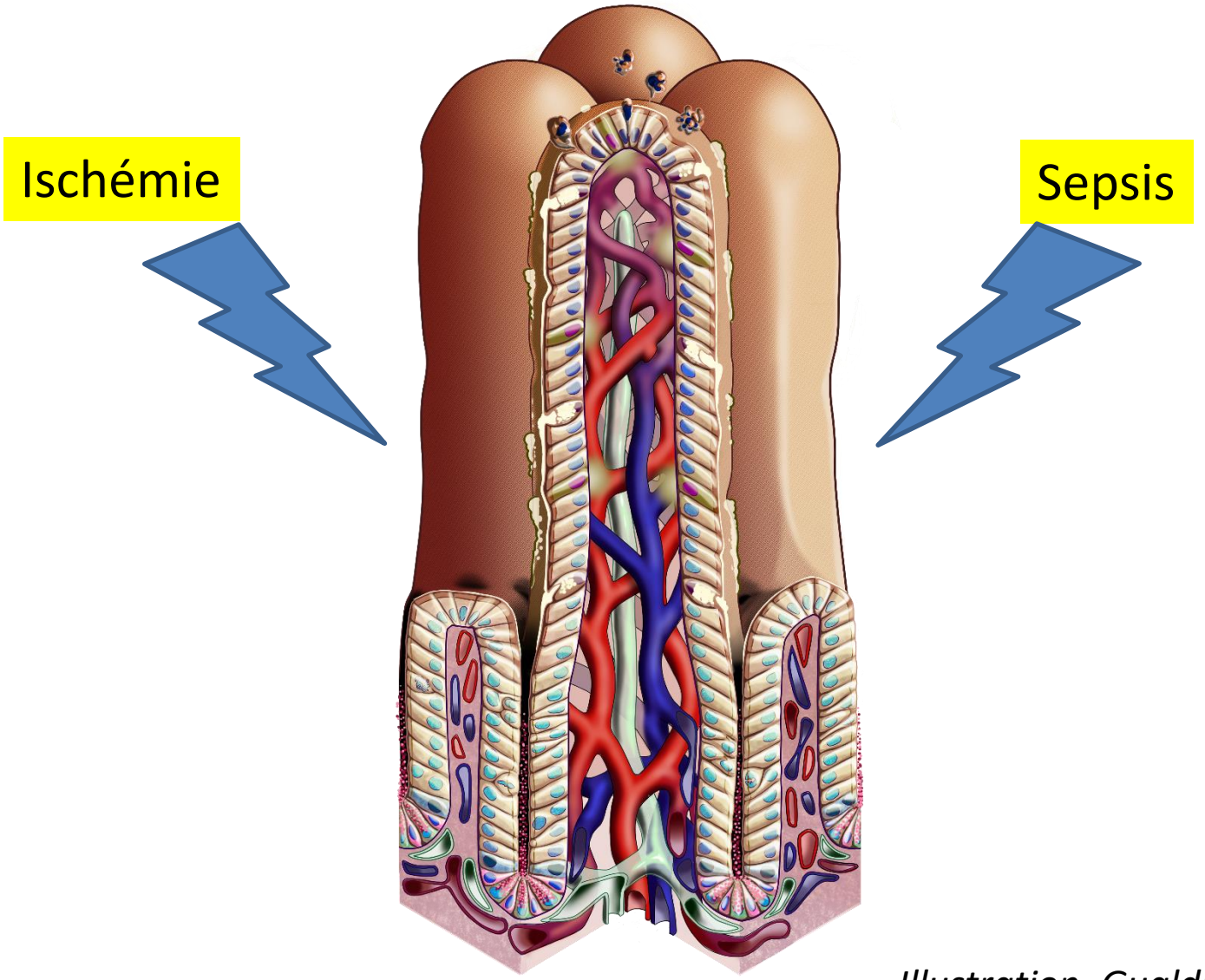
Faiblesse
Circulation contrecourant



Mécanismes de l’atteinte intestinale



2 modèles d'atteinte intestinale

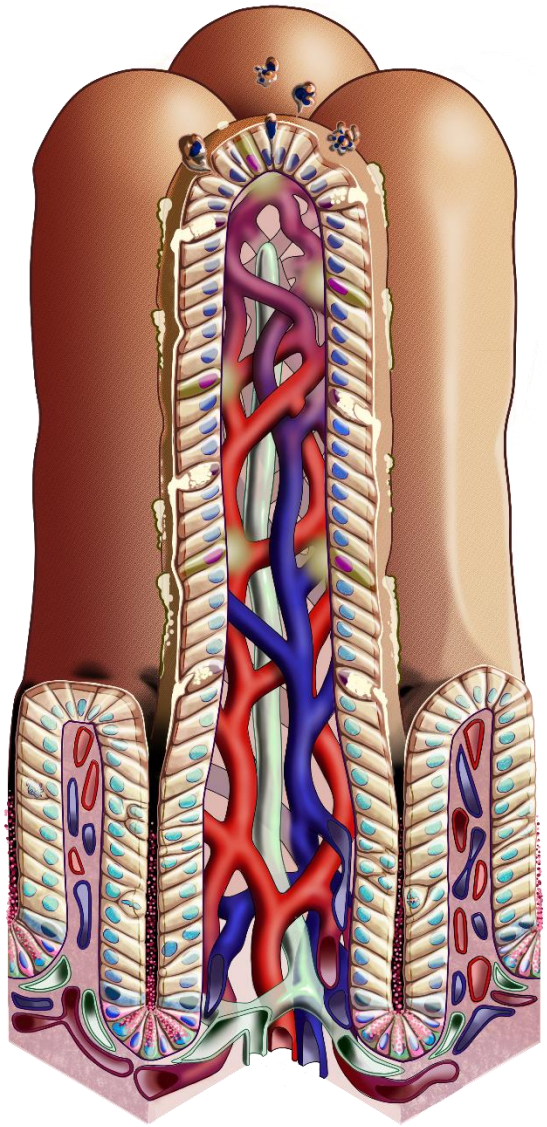


Illustration, Gualdi, Besançon

Ischémie

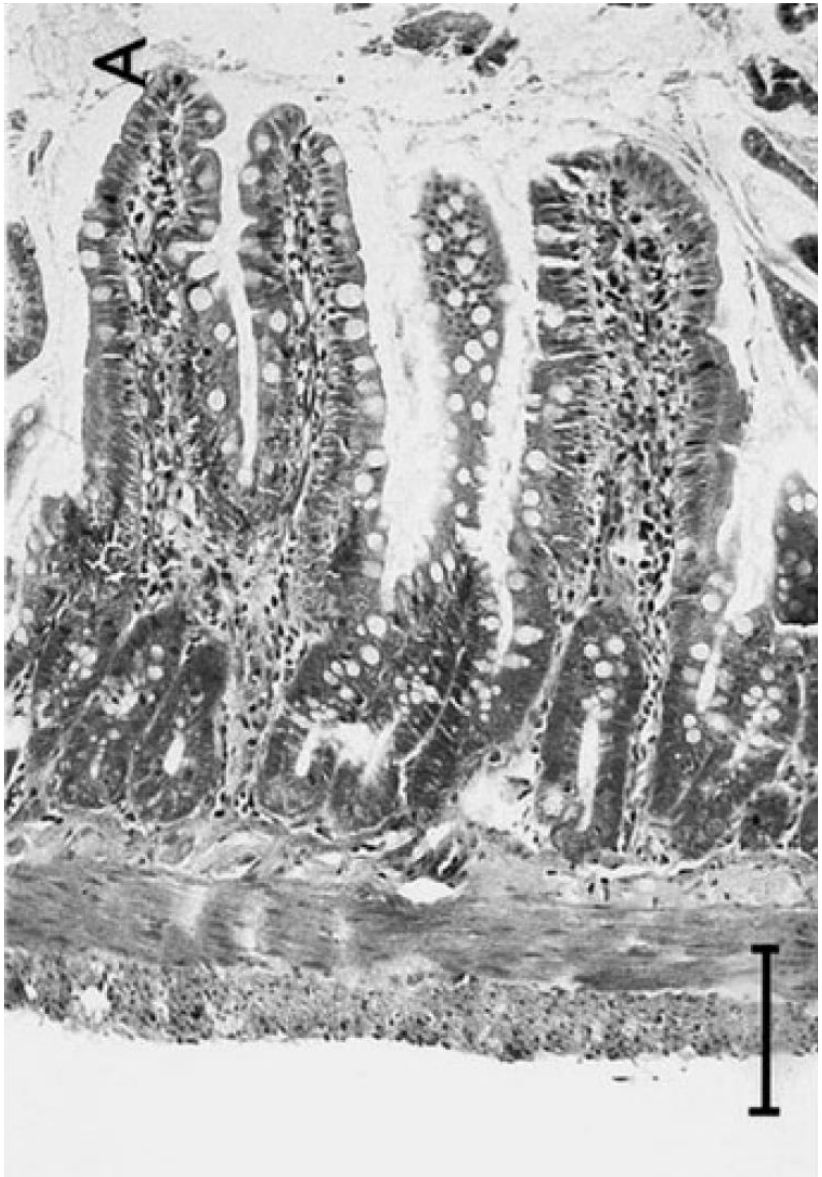
Le principal mécanisme

Ischémie



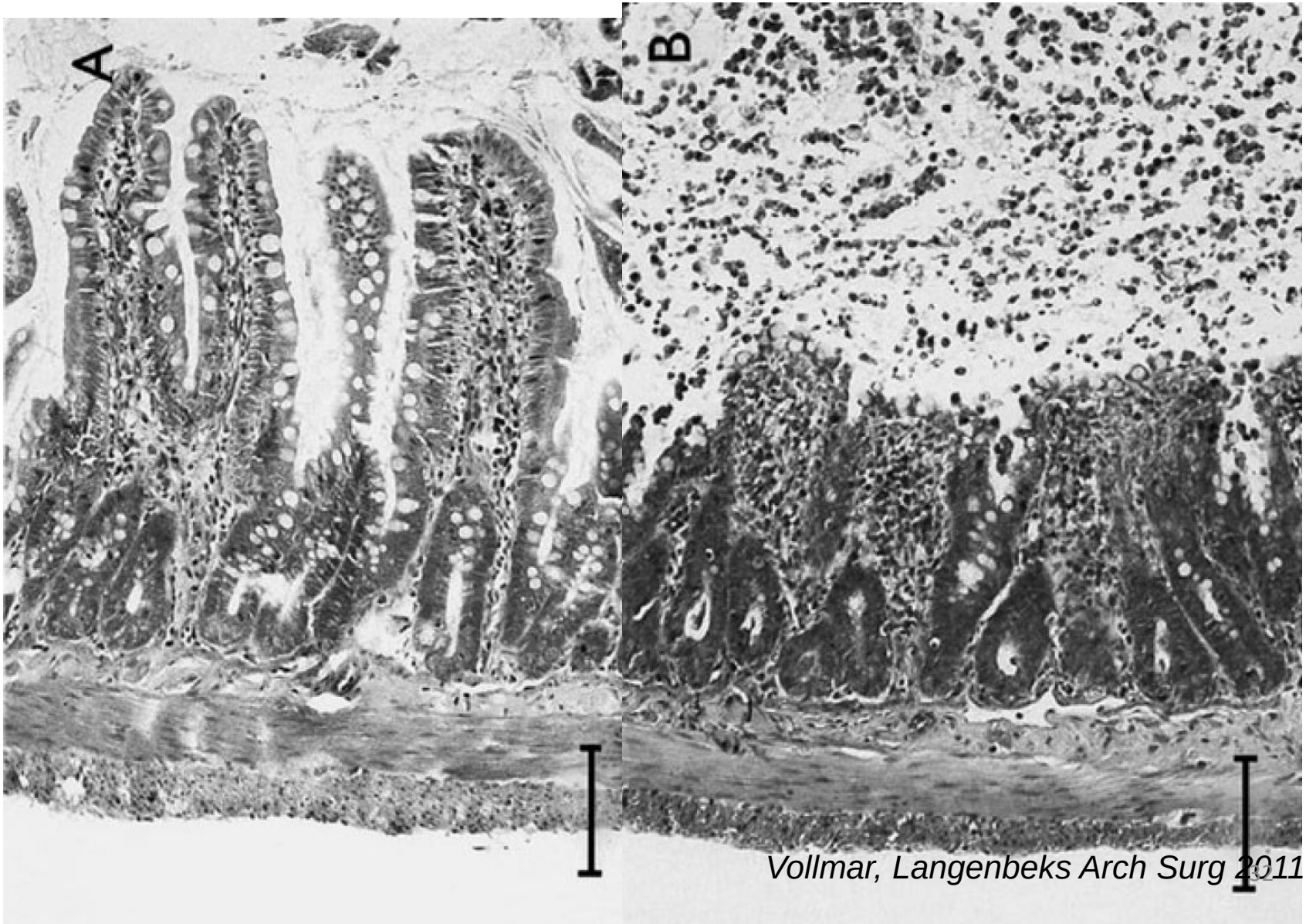
Illustration, Gualdi, Besançon

Effet de l’ischémie reperfusion sur la villosité



Vollmar, Langenbeks Arch Surg 2011

Effet de l’ischémie reperfusion sur la villosité



Vollmar, Langenbeks Arch Surg 2011

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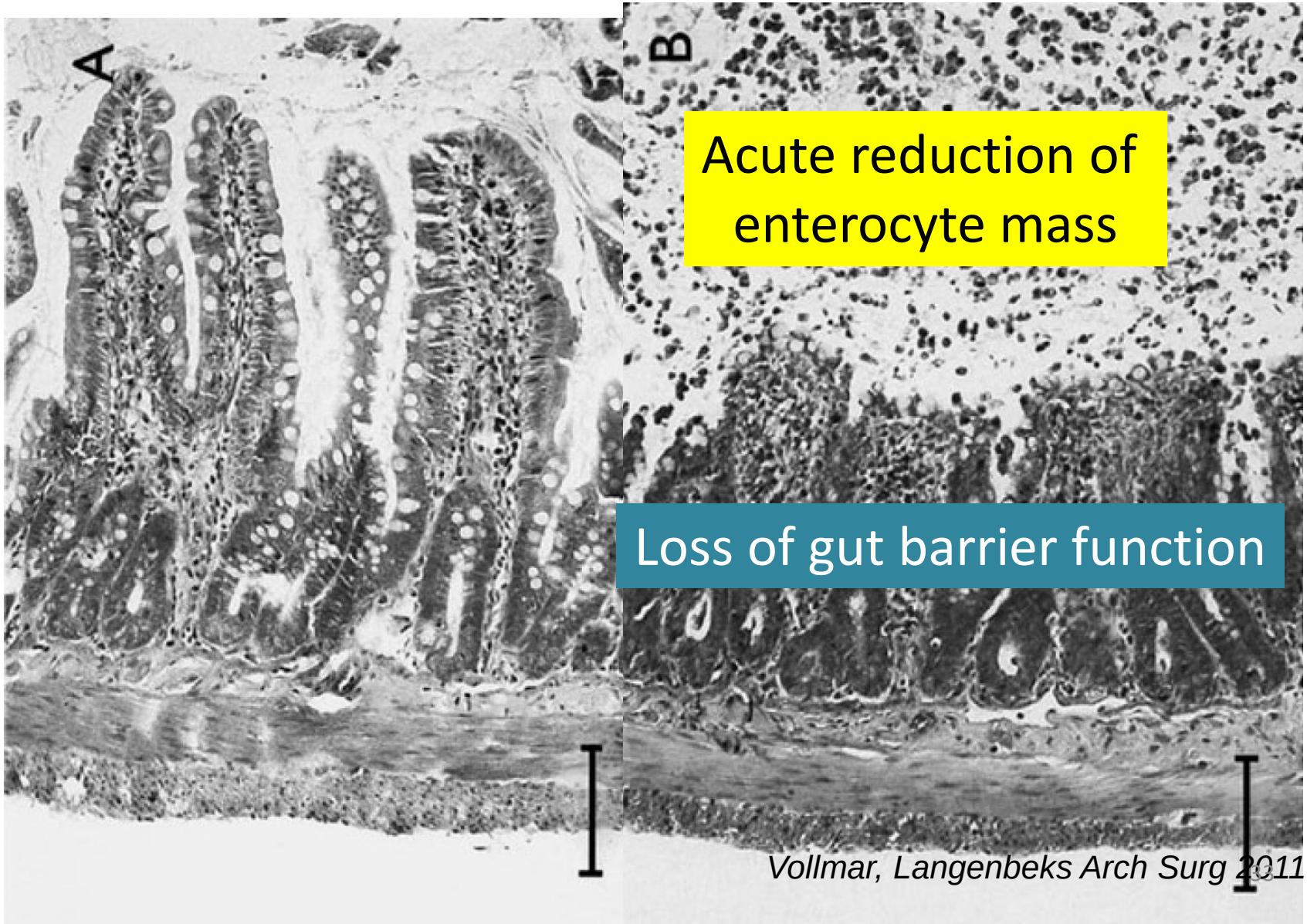
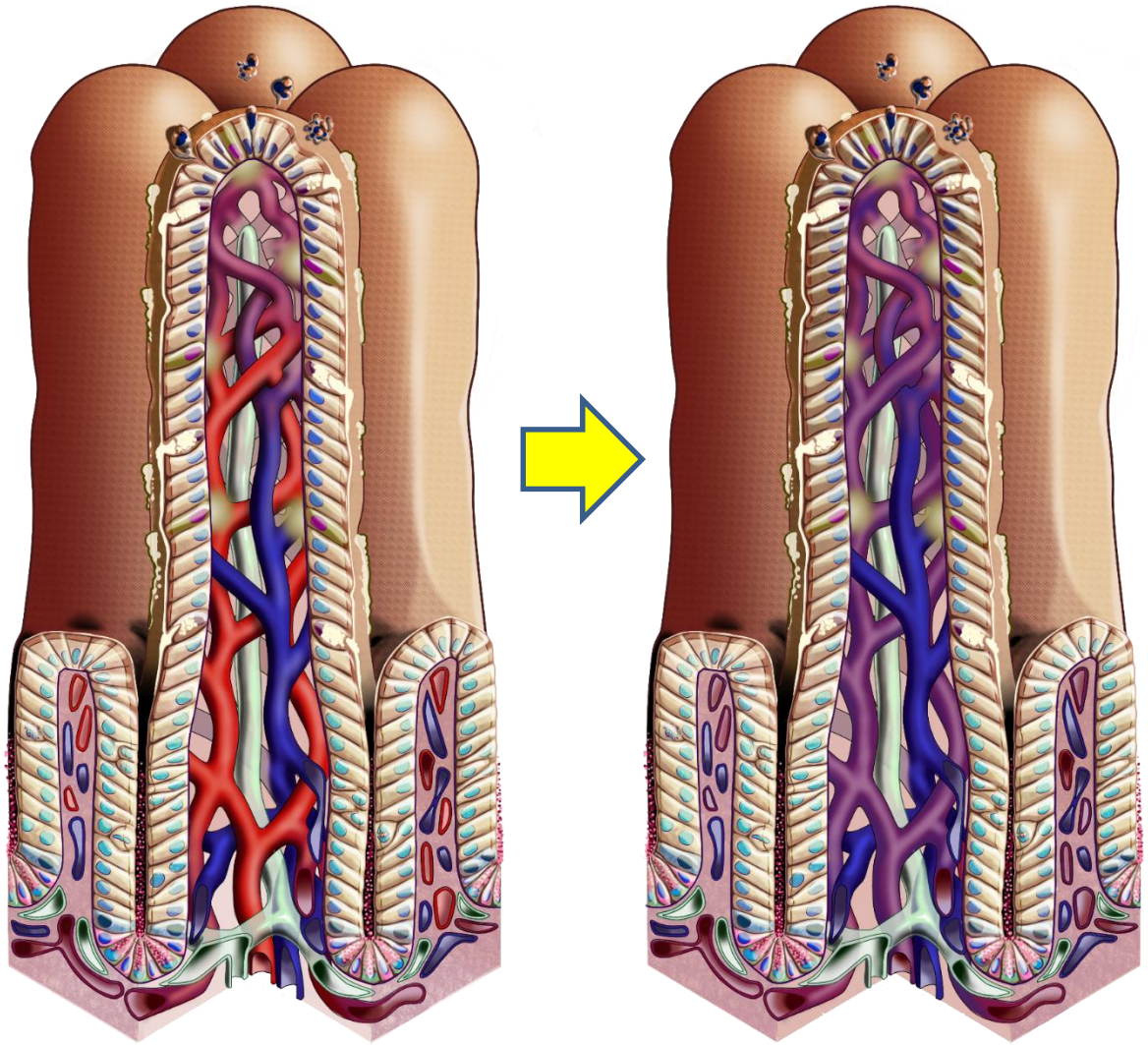


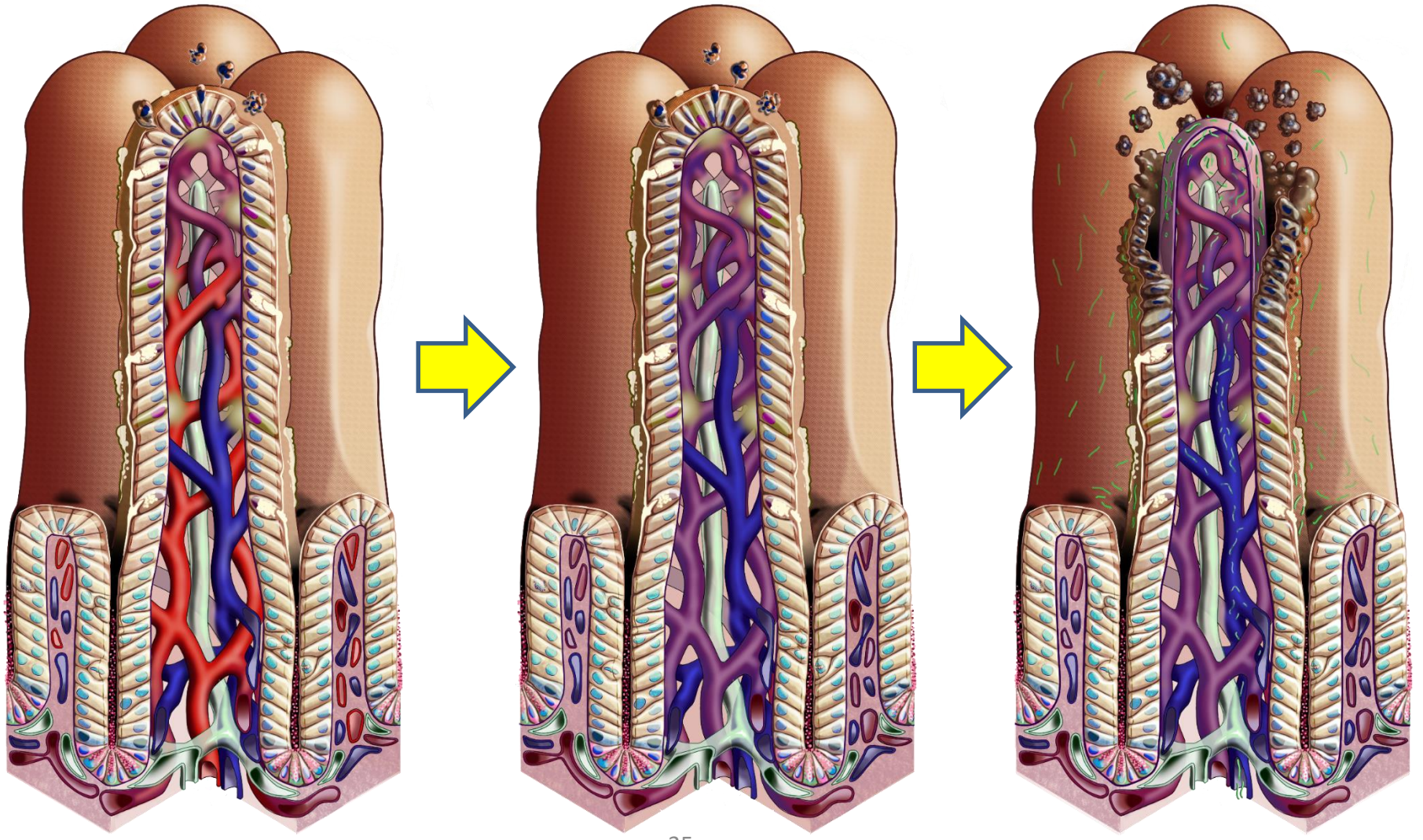
Vollmar, Langenbeks Arch Surg 2011

Modèle d'ischémie intestinale



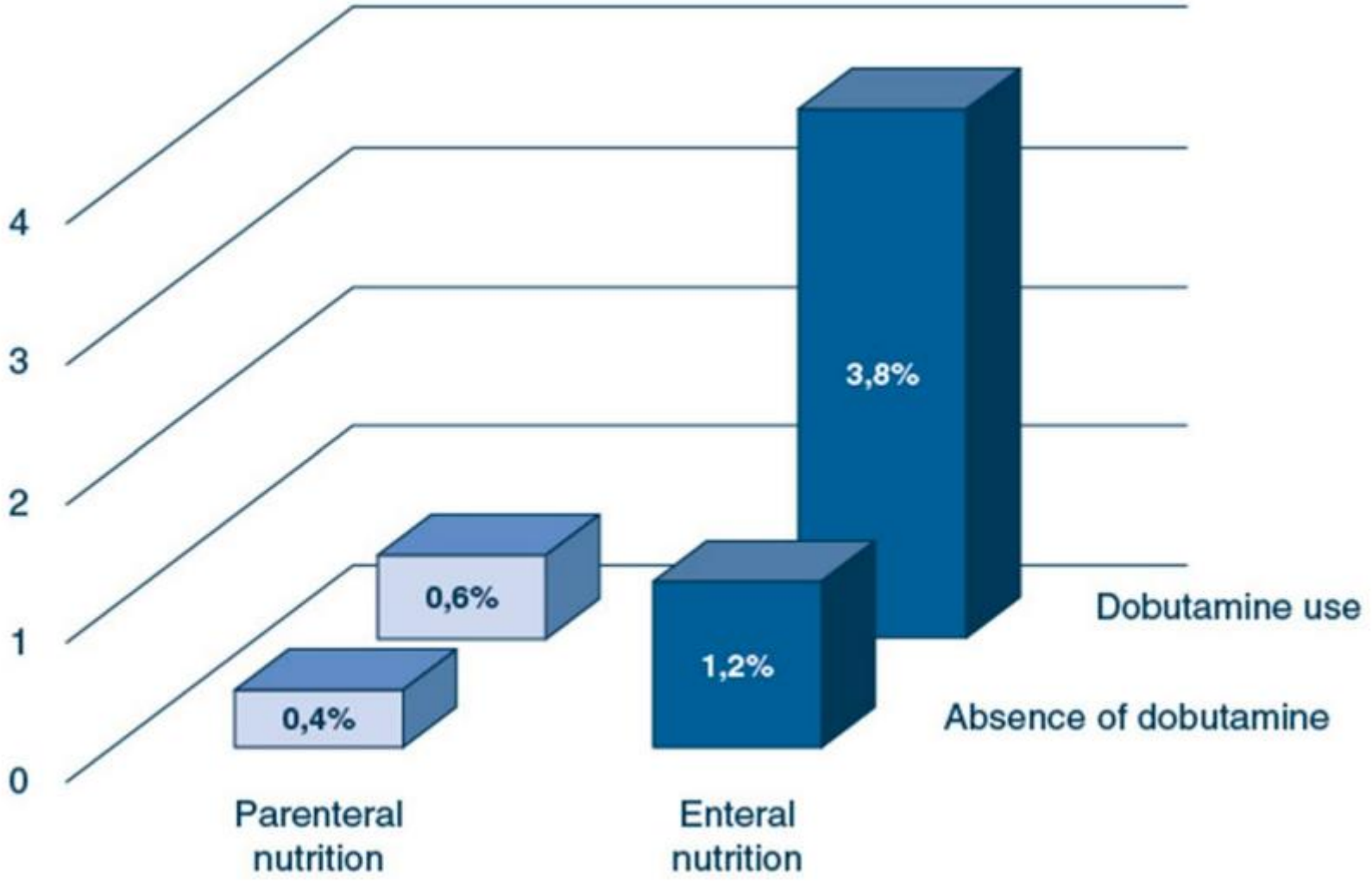
Illustration, Gualdi, Besançon

Modèle d’ischémie intestinale



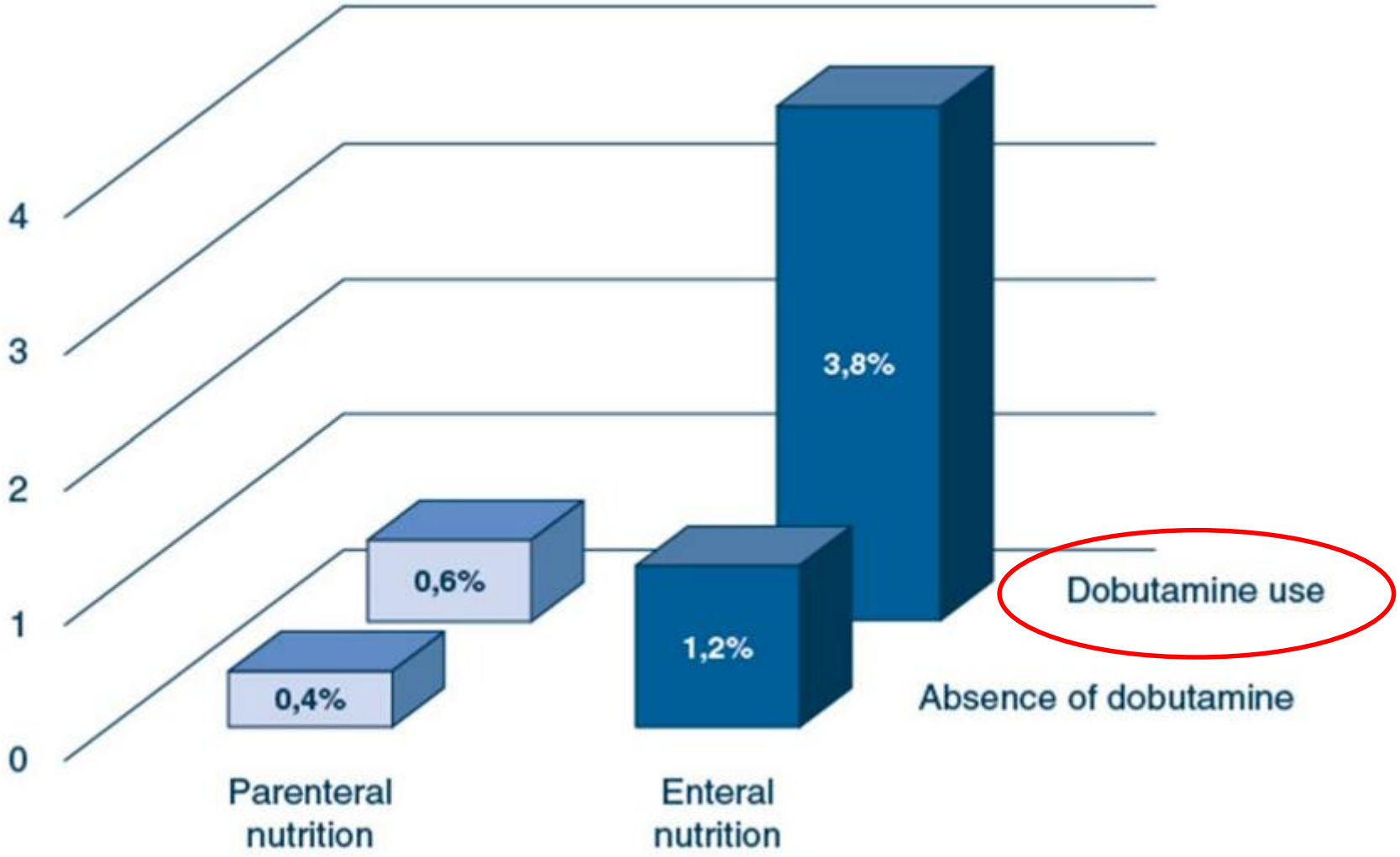
Illustration, Gualdi, Besançon

Physiopathologie du NOMI



Piton, ICM 2022

Physiopathologie du NOMI



Piton, ICM 2022

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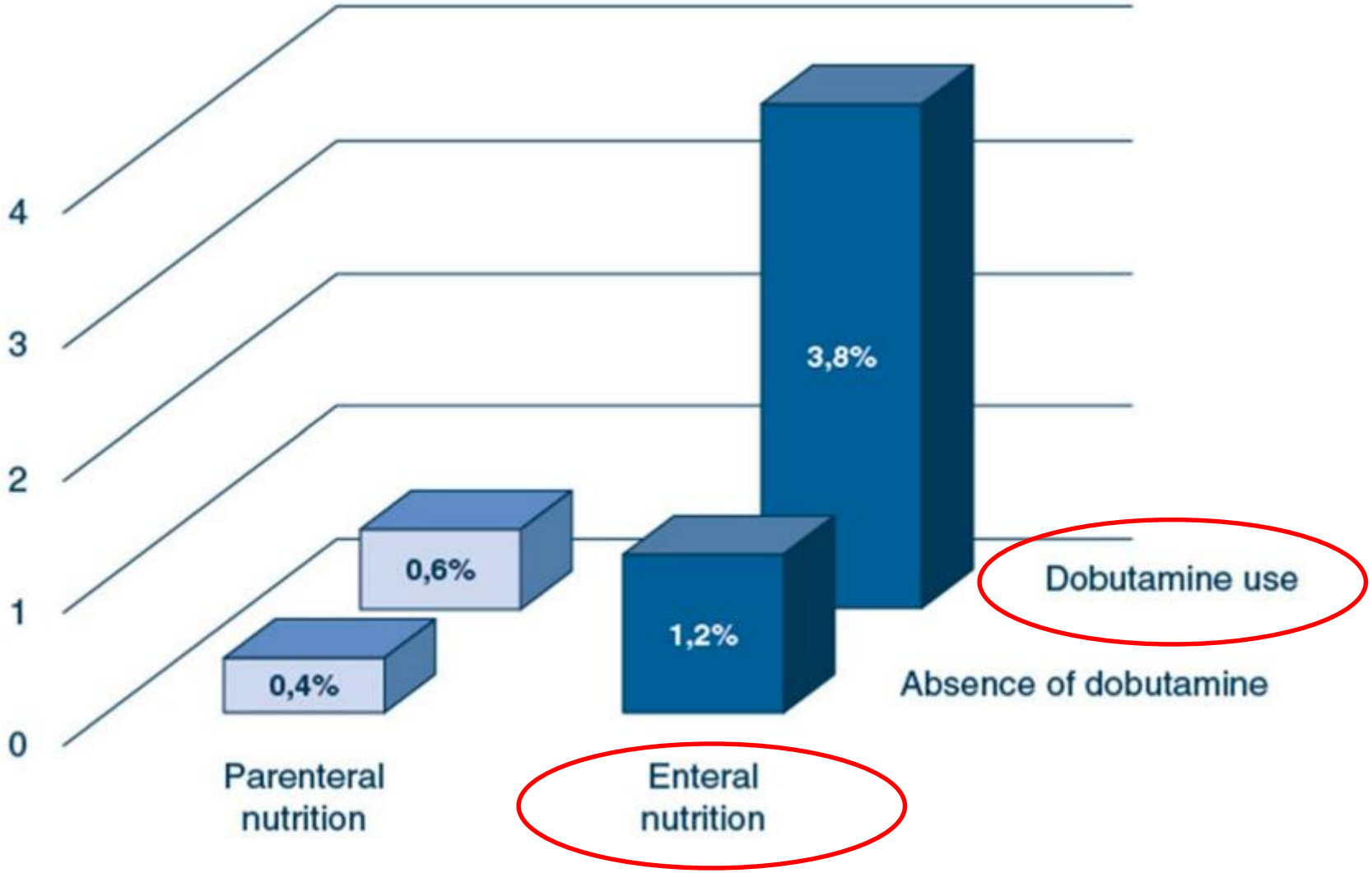
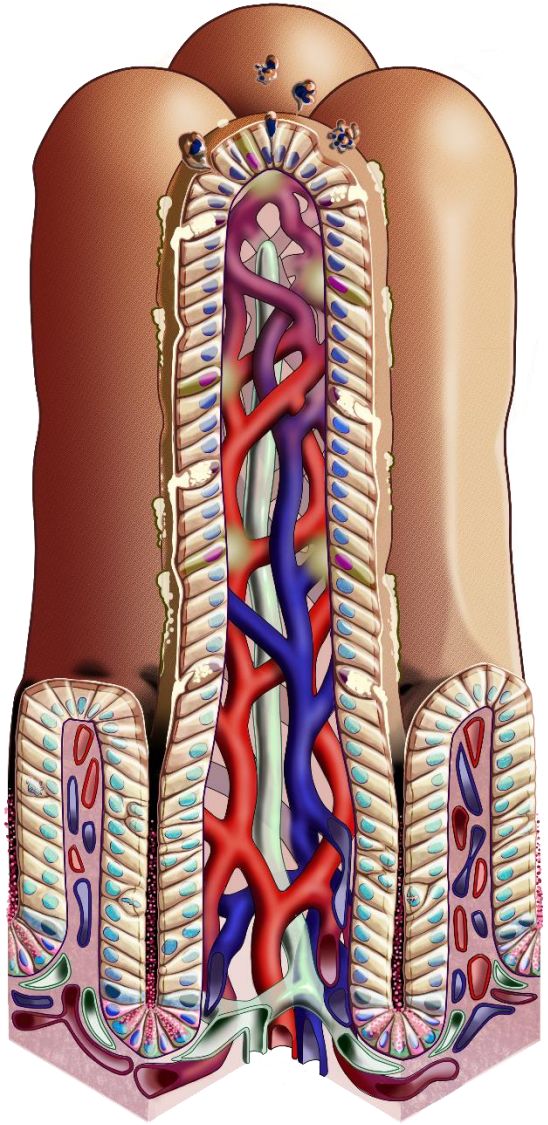


Piton, ICM 2022

Sepsis

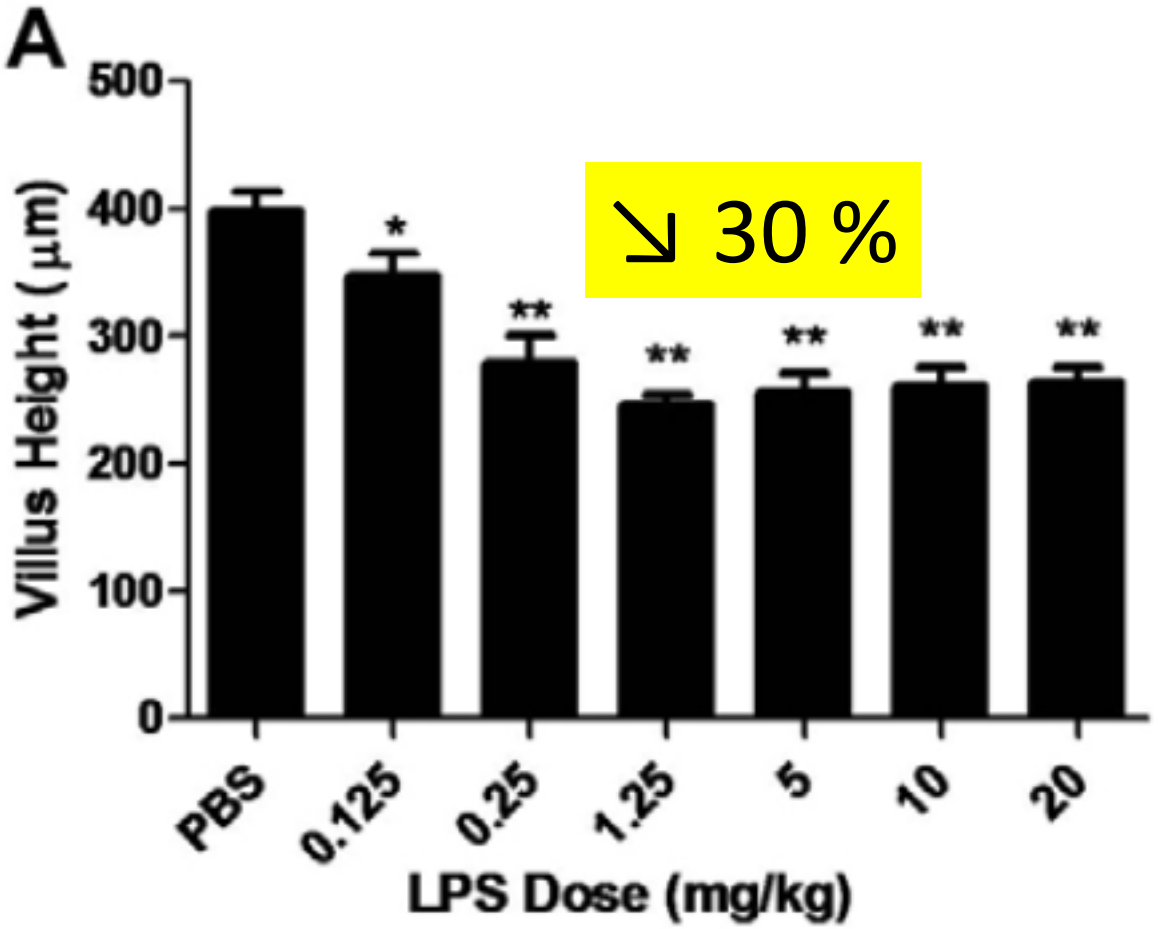
Un mécanisme sous-estimé



Sepsis

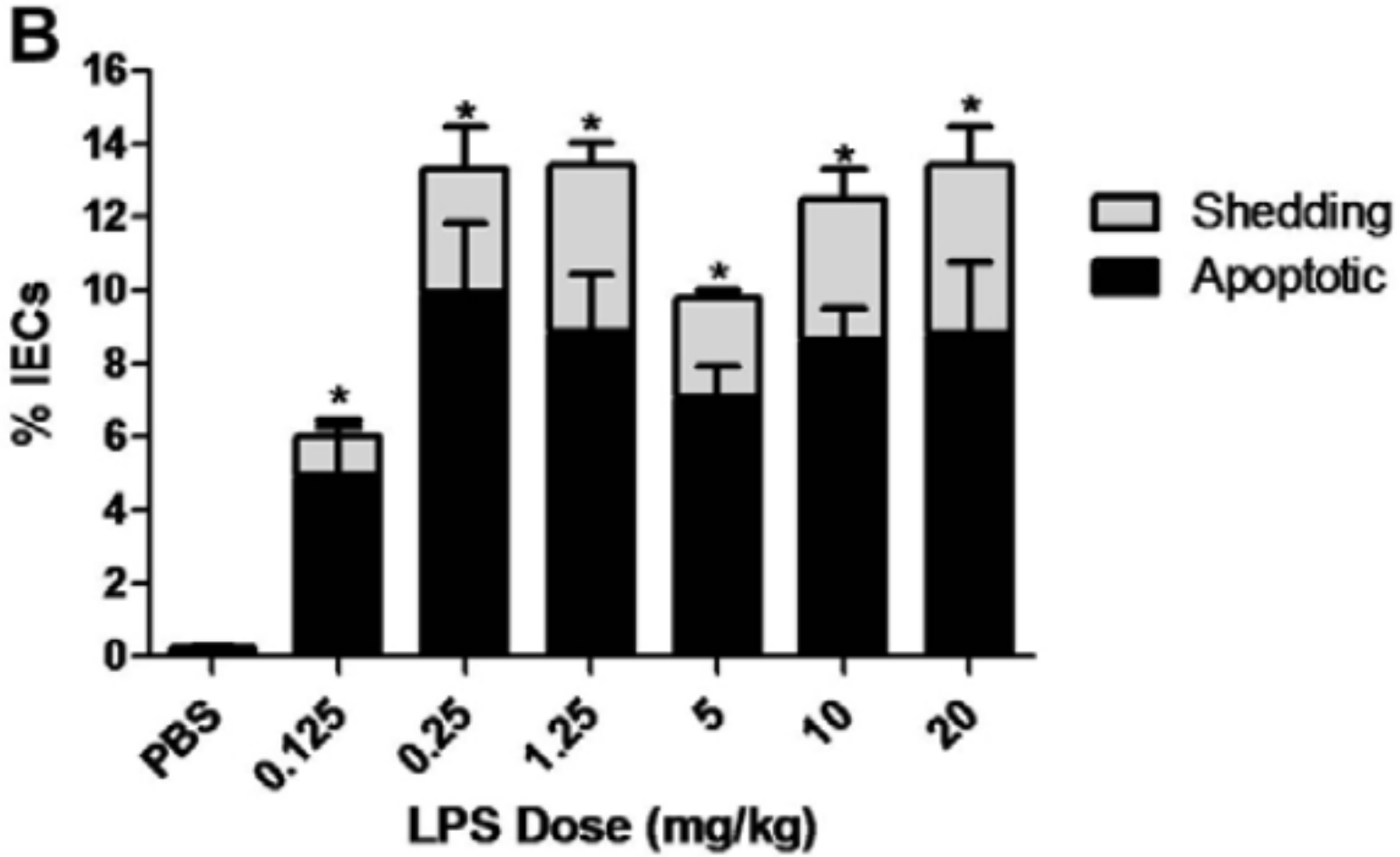
Illustration, Gualdi, Besançon

Effet de l’injection du LPS sur la longueur villositaire



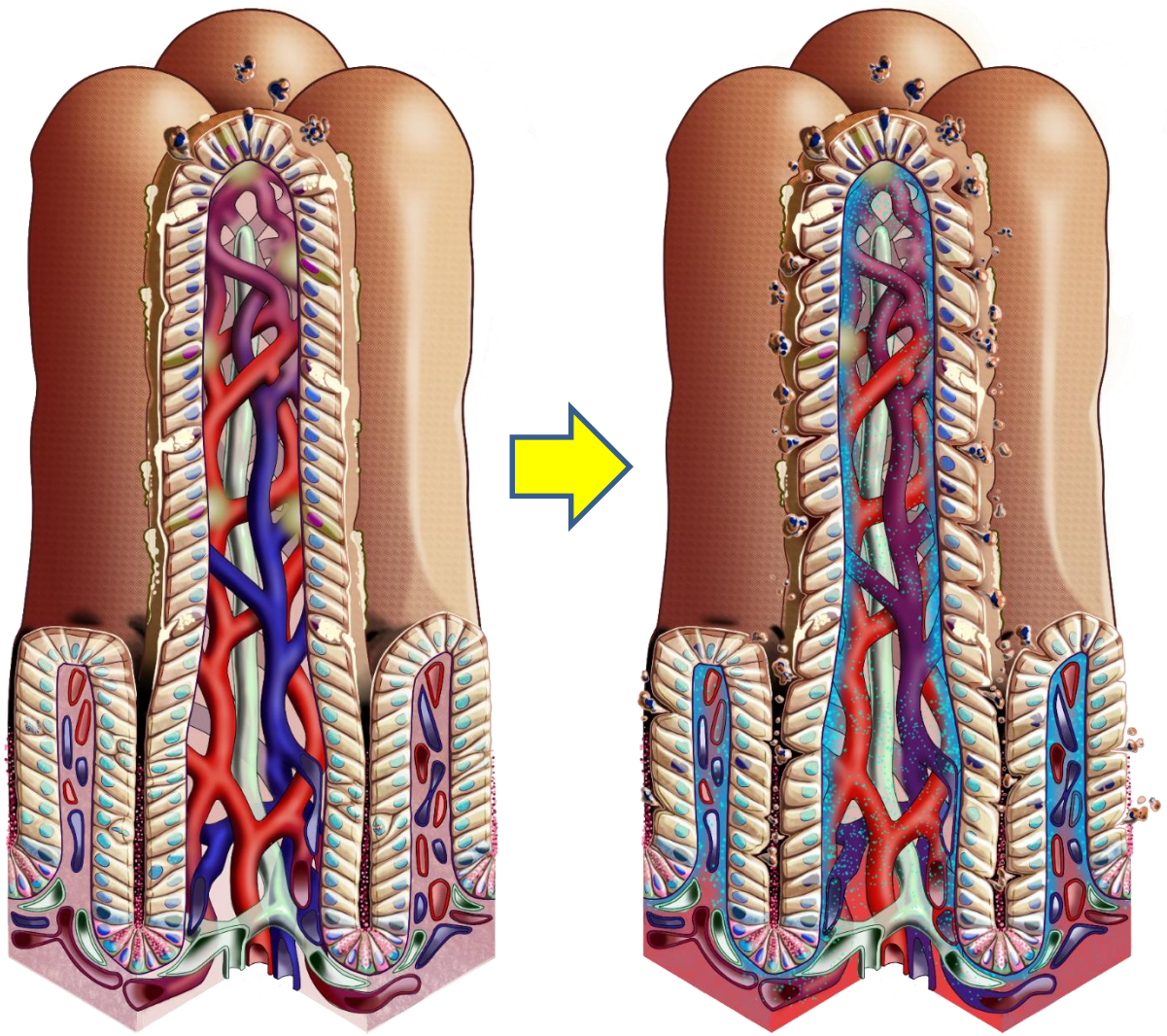
Williams, Disease Model and Mechanism, 2013

Effet de l'injection de LPS sur l'apoptose villositaire



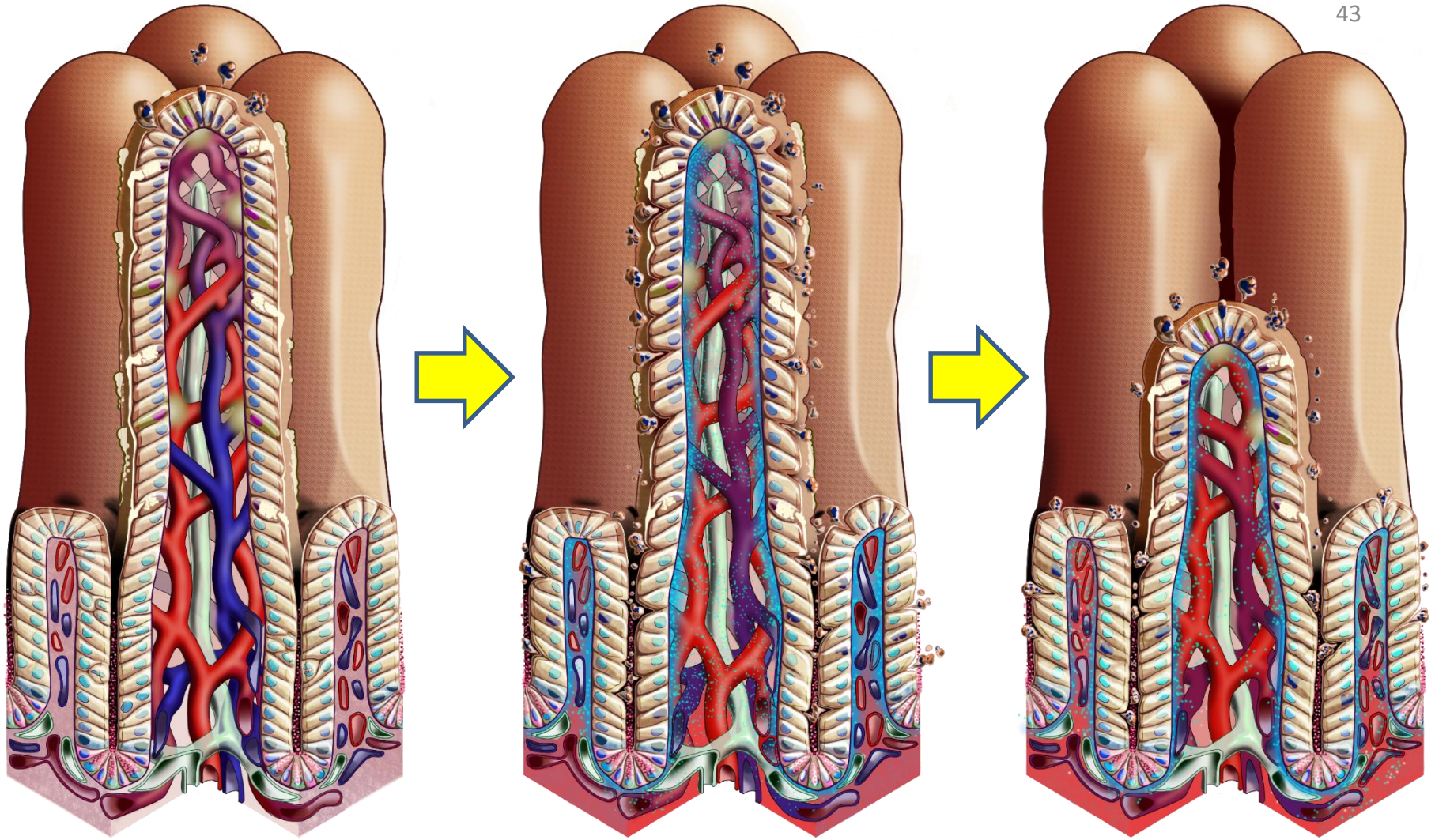
Williams, Disease Model and Mechanism, 2013

Gut-sepsis model



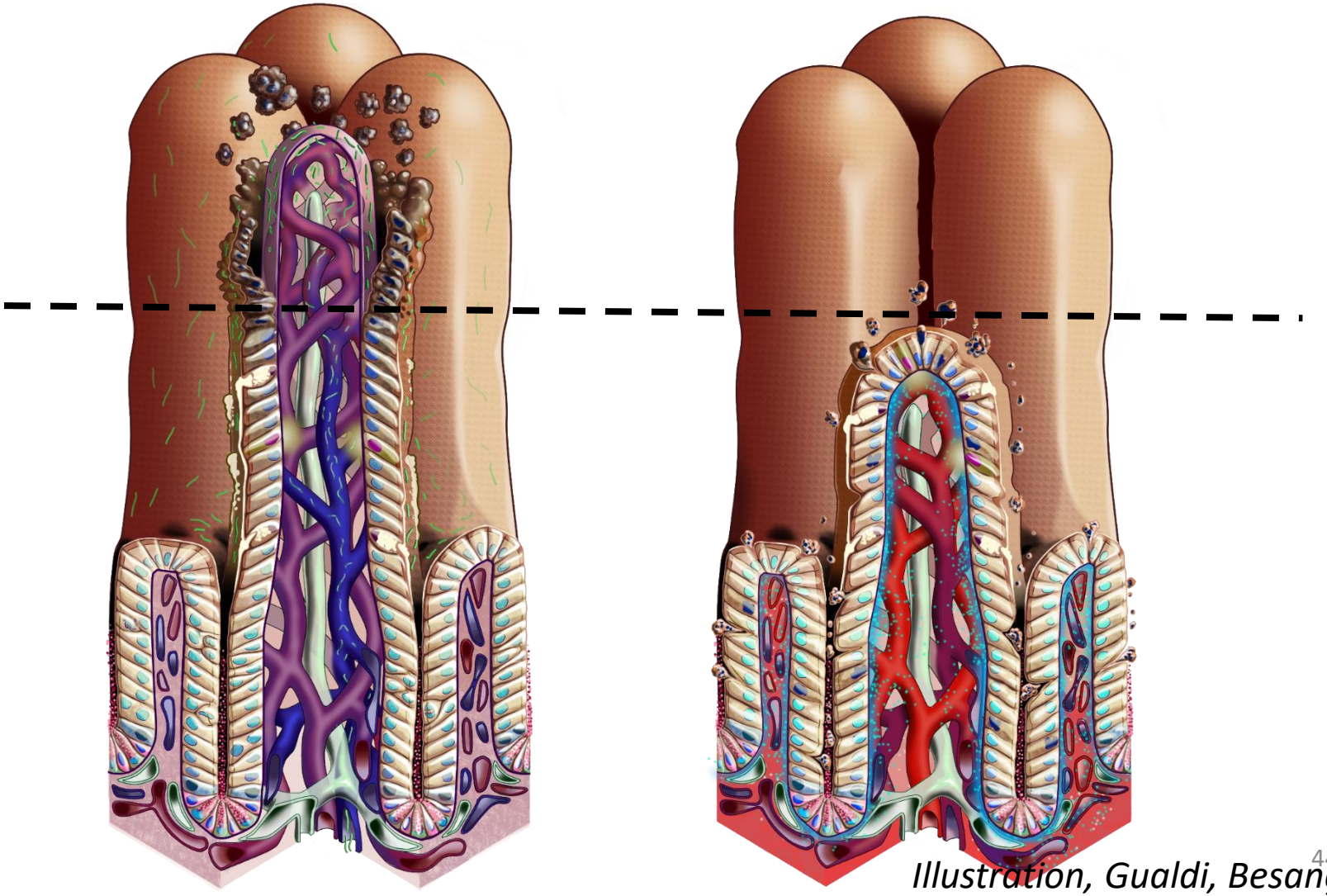
Illustration, Gualdi, Besançon

Gut-sepsis model



Illustration, Gualdi, Besançon

2 mécanismes → 1 conséquence



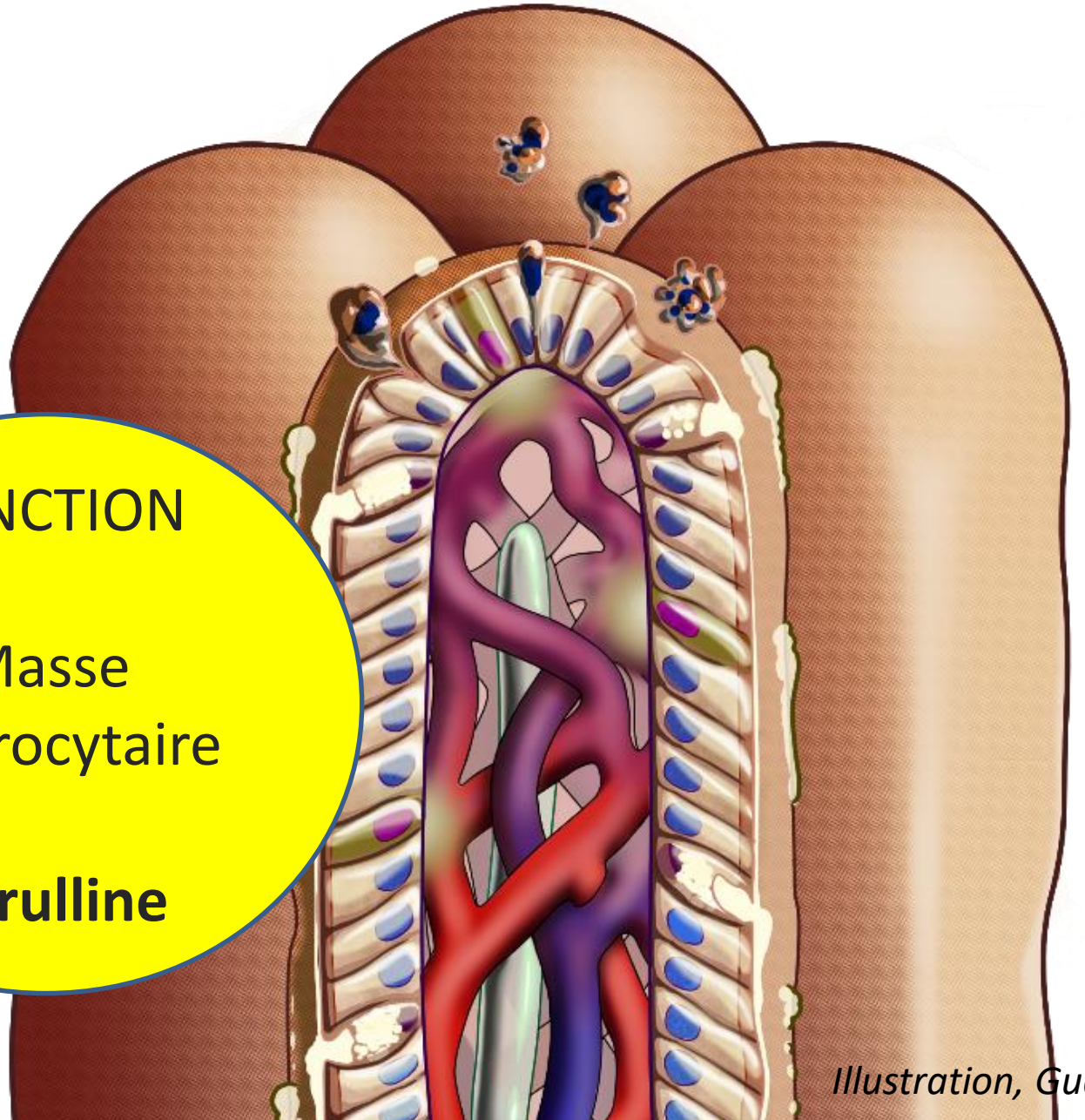
Illustration, Gualdi, Besançon

10’

3

Biomarqueurs entérocytaires

Biomarqueurs entérocytaires

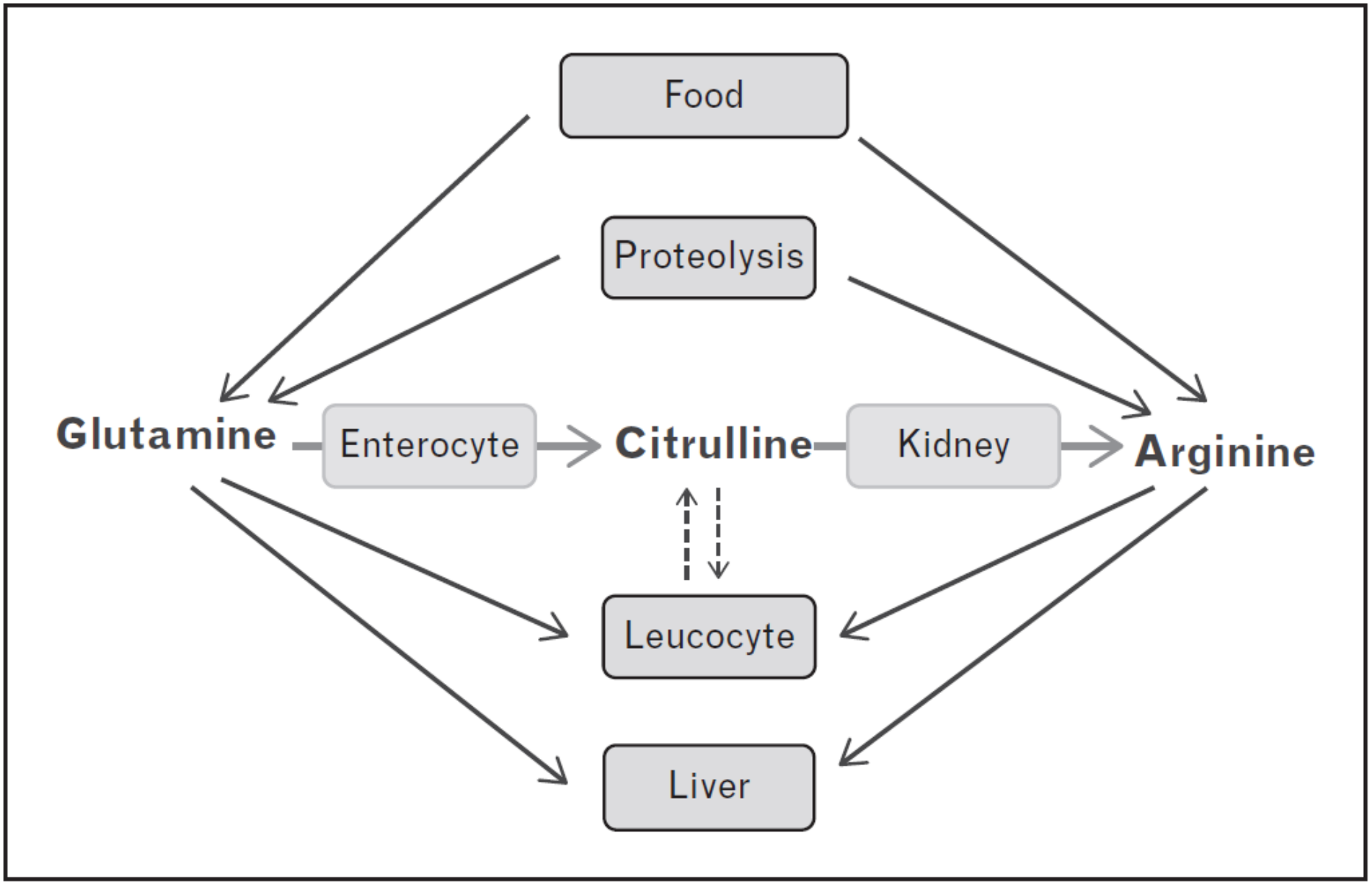


FONCTION

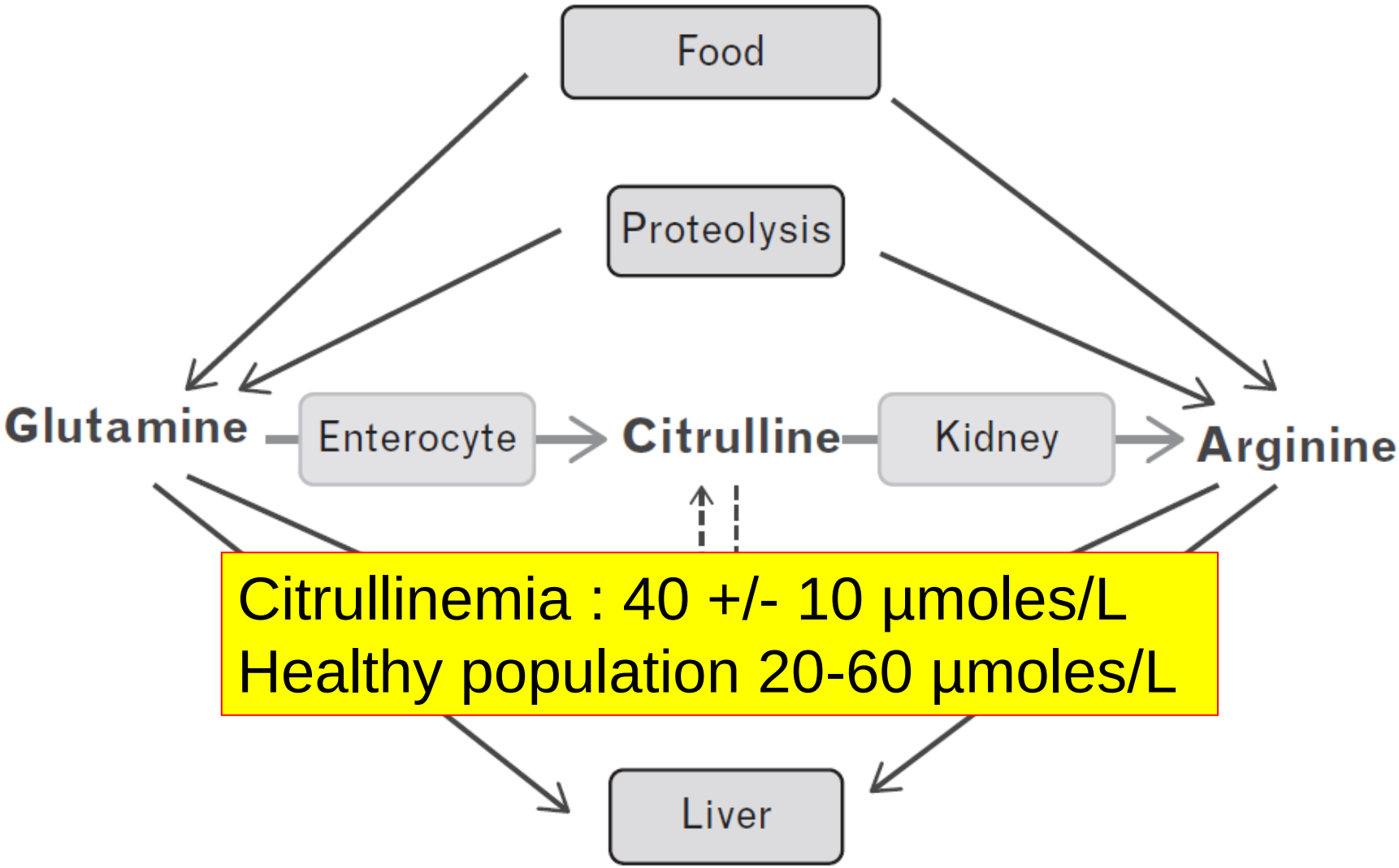
Masse entérocytaire

Citrulline

Illustration, Gualdi, Besançon



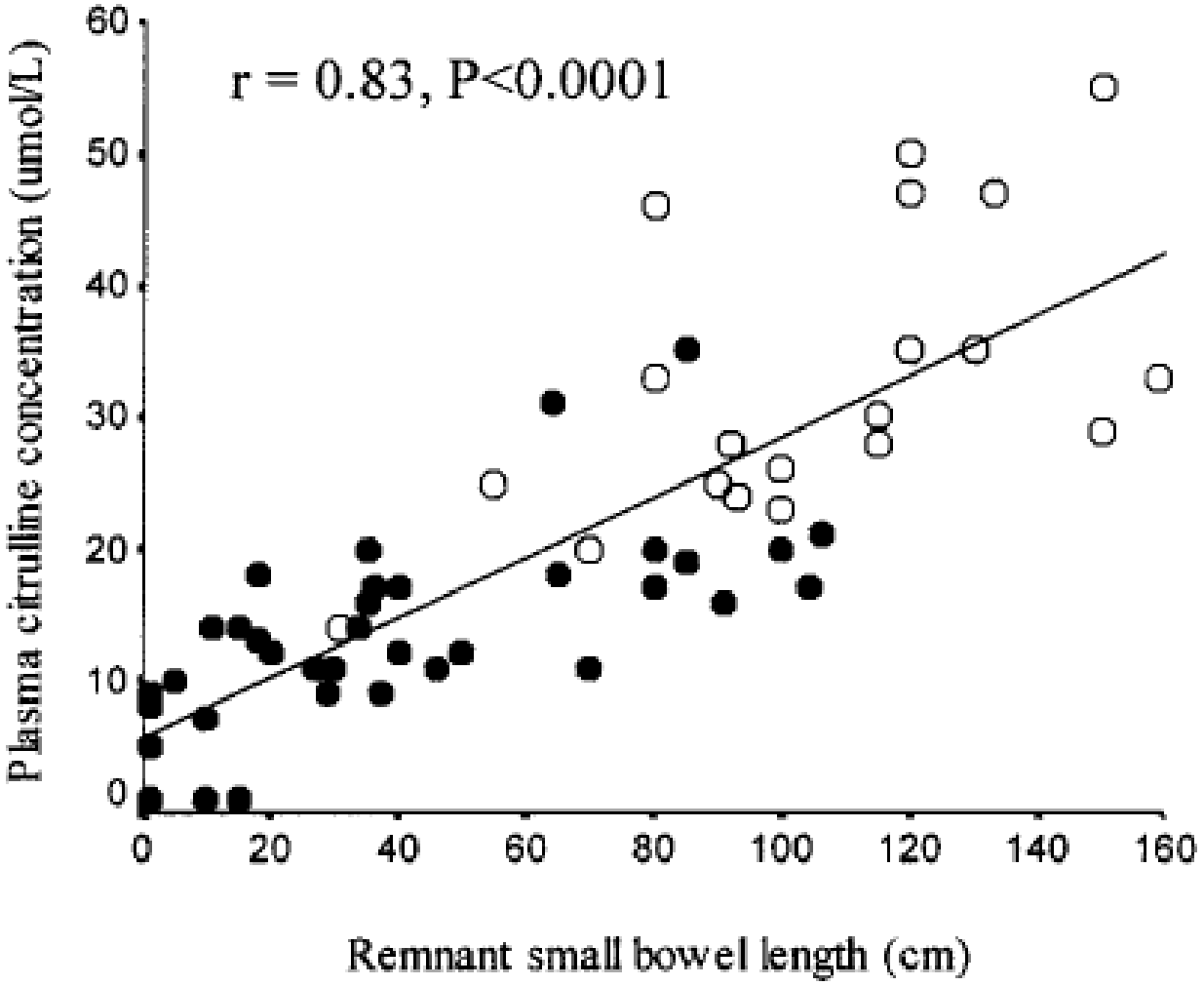
Piton, Curr Opinion Critical Care, 2016



Citrullinemia : 40 +/- 10 µmoles/L
Healthy population 20-60 µmoles/L

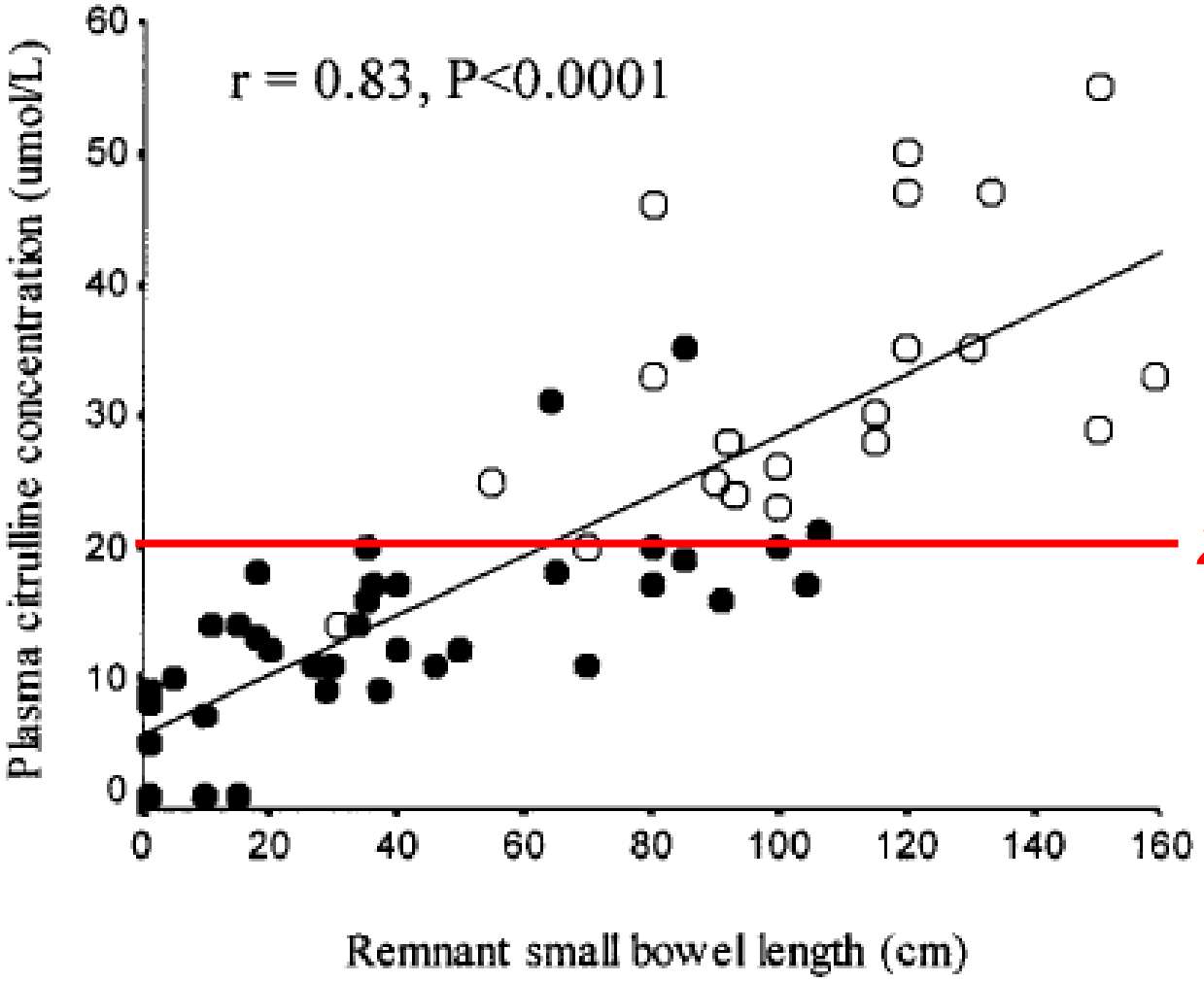
Piton, Curr Opinion Critical Care, 2016

Syndrome de grêle court



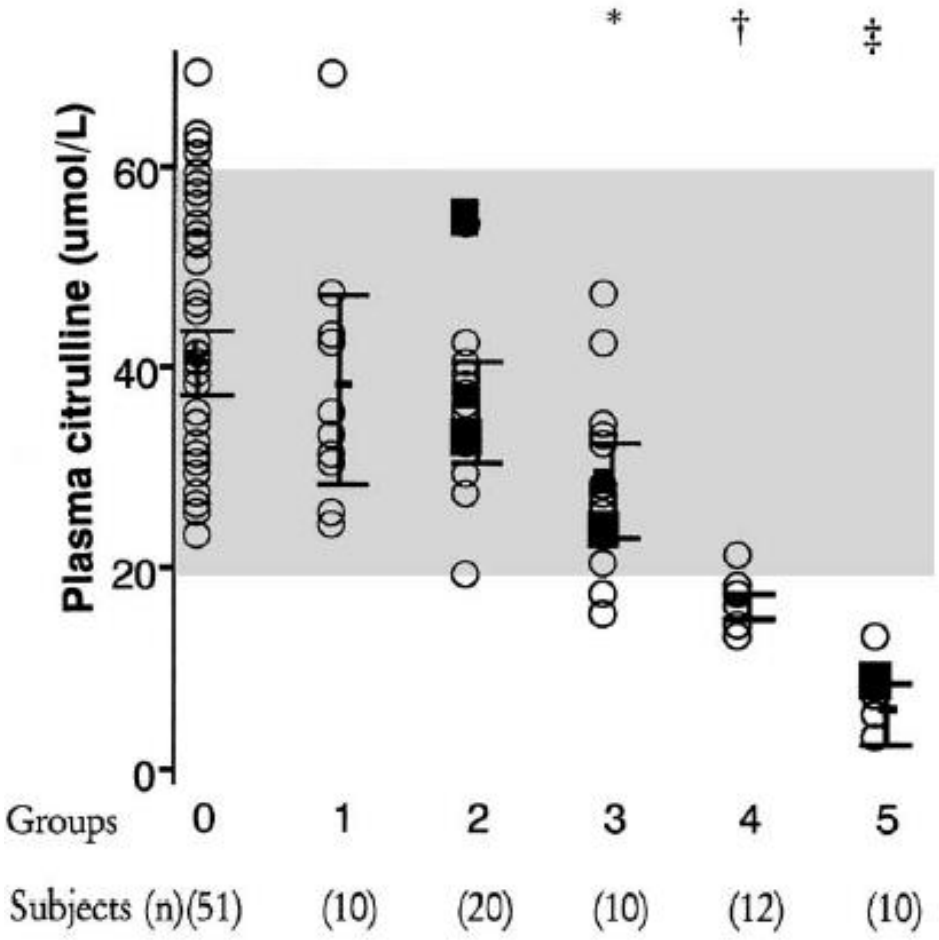
Crenn et al, Gastroenterology 2000

Syndrome de grêle court



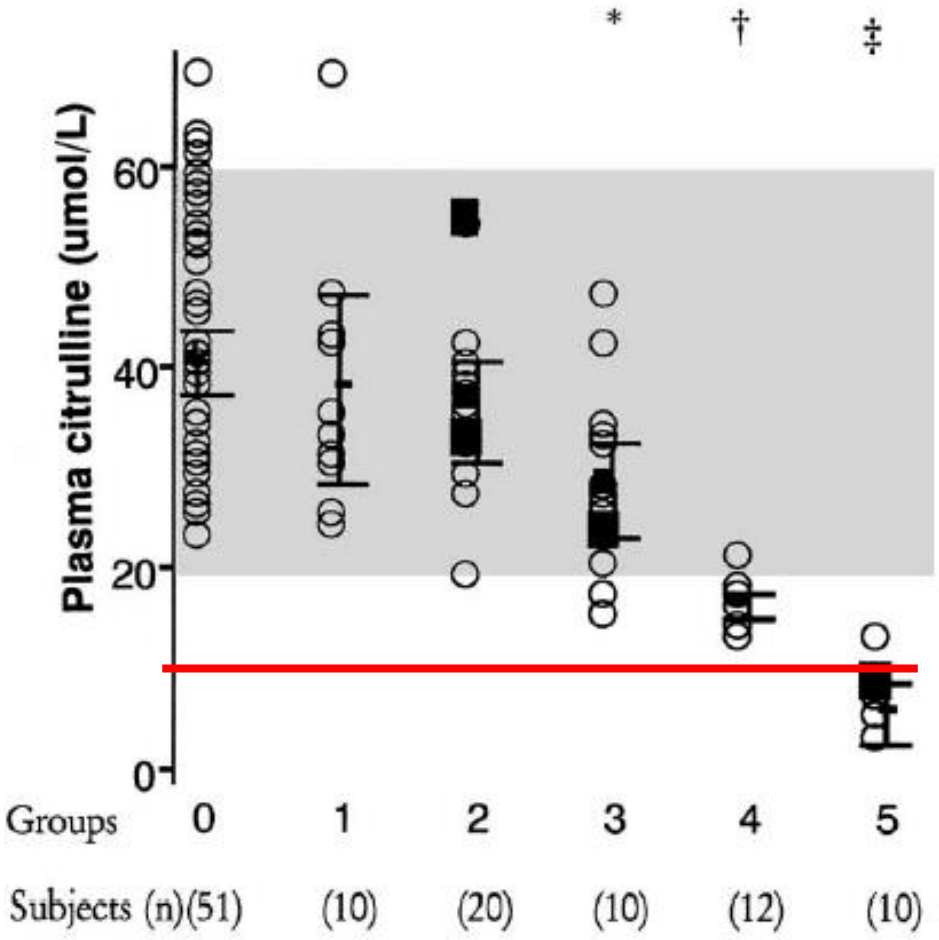
Crenn et al, Gastroenterology 2000

Atrophie villositaire



Crenn et al, Gastroenterology 2003

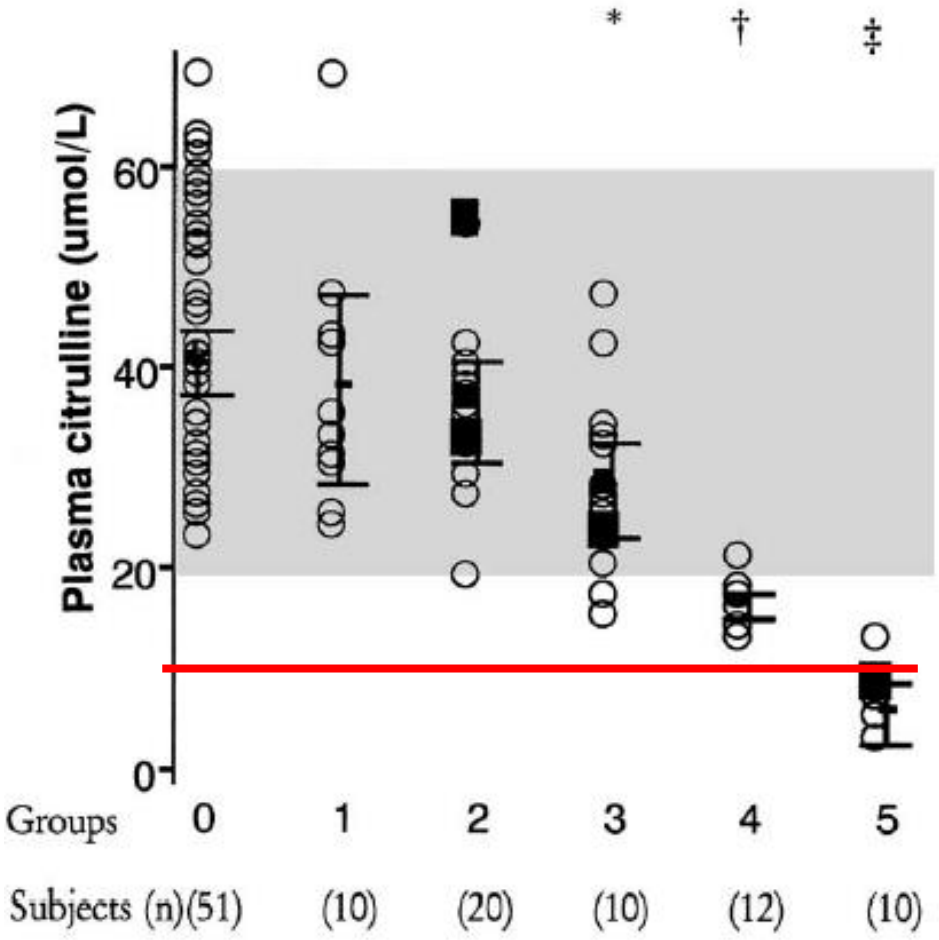
Atrophie villositaire

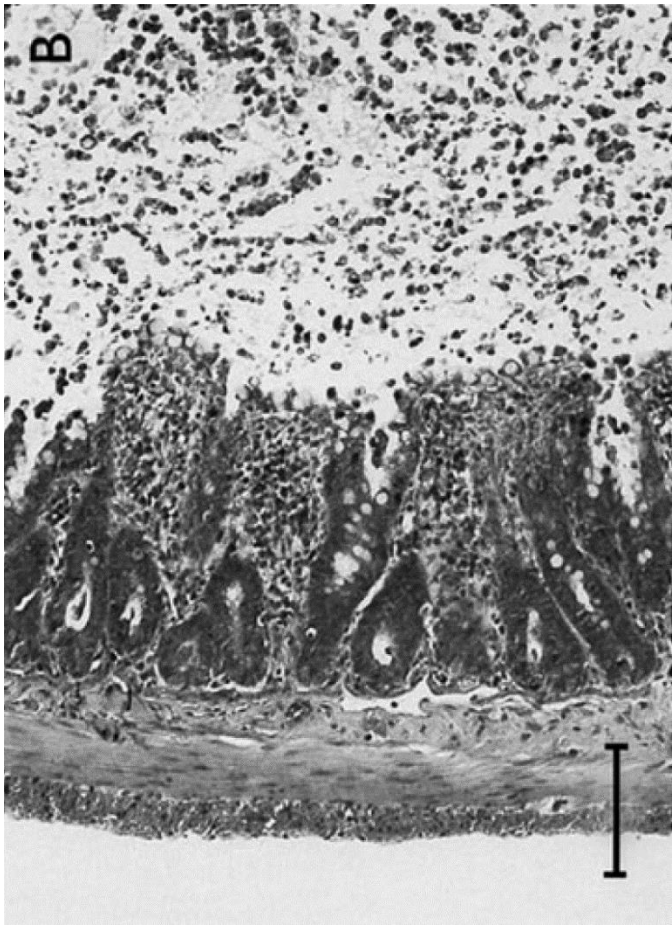


10 µmol.L^{-1}

Crenn et al, Gastroenterology 2003

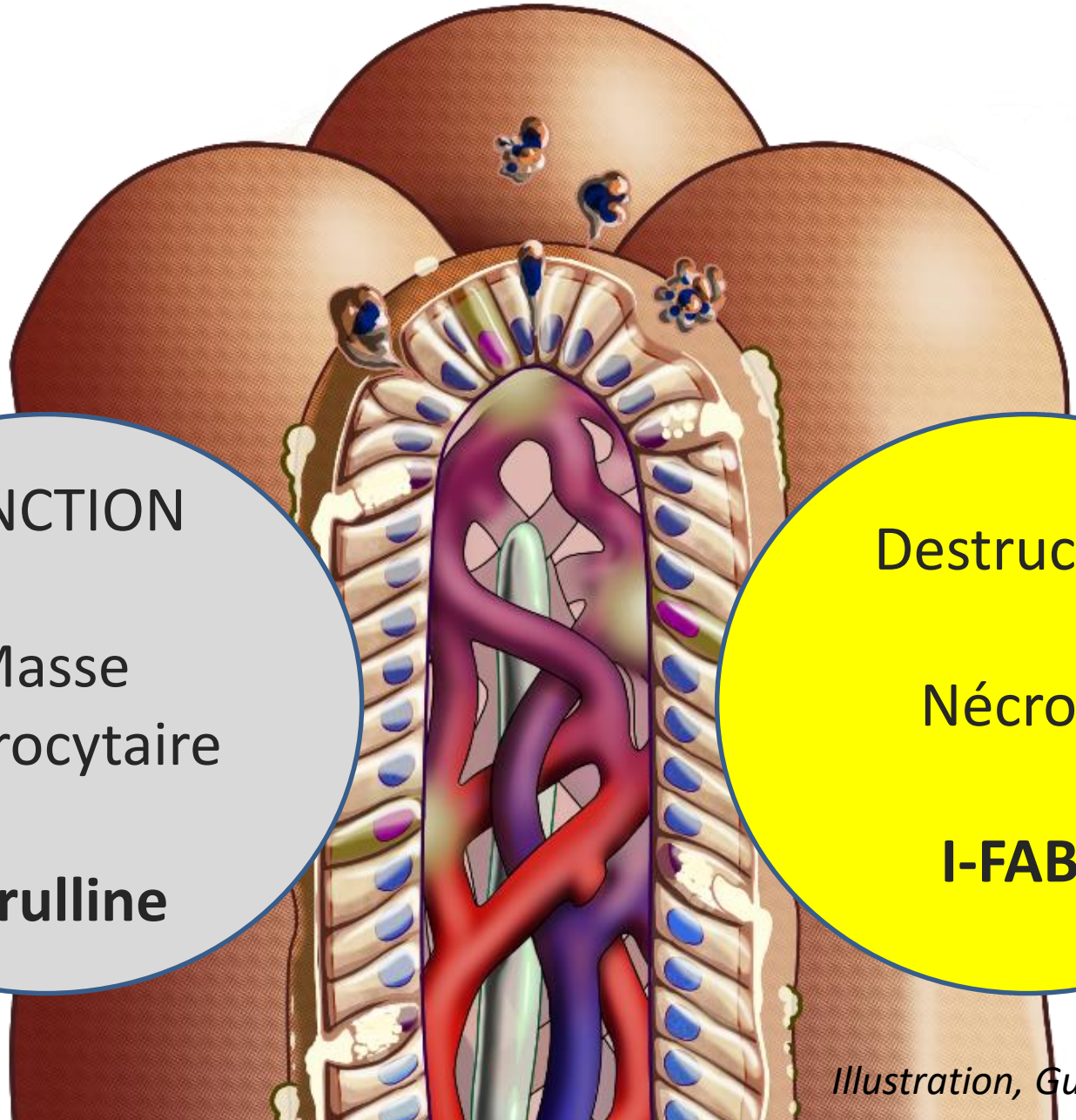
Atrophie villositaire





Crenn et al, Gastroenterology 2003

Biomarqueurs entérocytaires



FONCTION

Masse entérocytaire

Citrulline

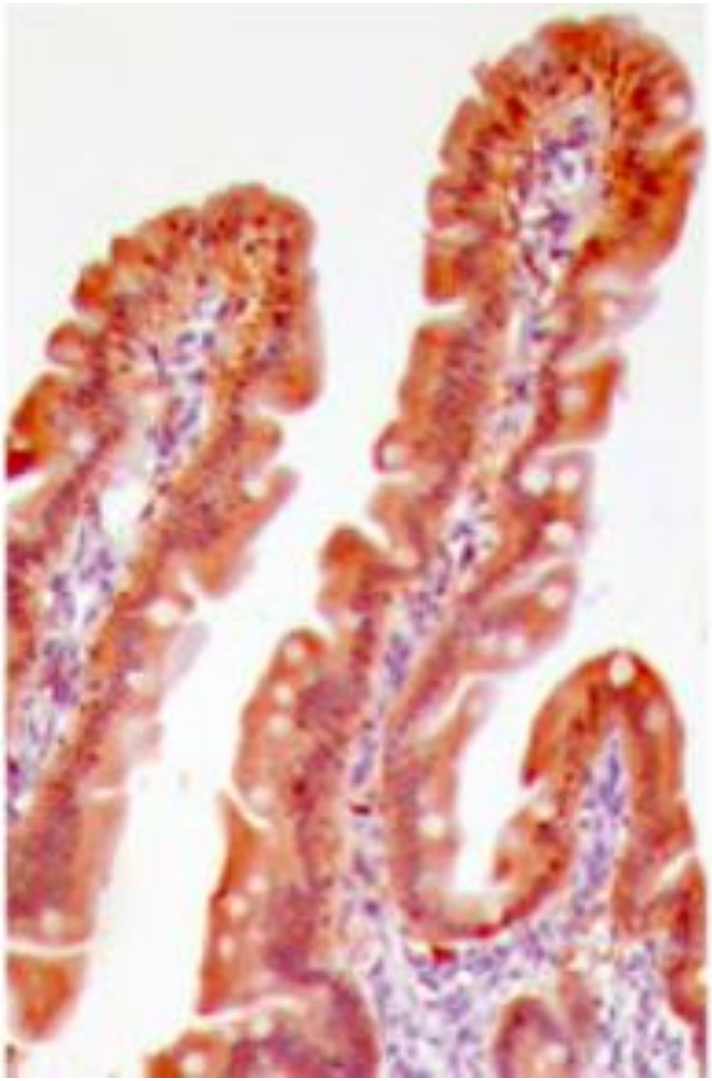
Destruction

Nécrose

I-FABP

Illustration, Gualdi, Besançon

I-FABP (Intestinal fatty acid-binding protein)



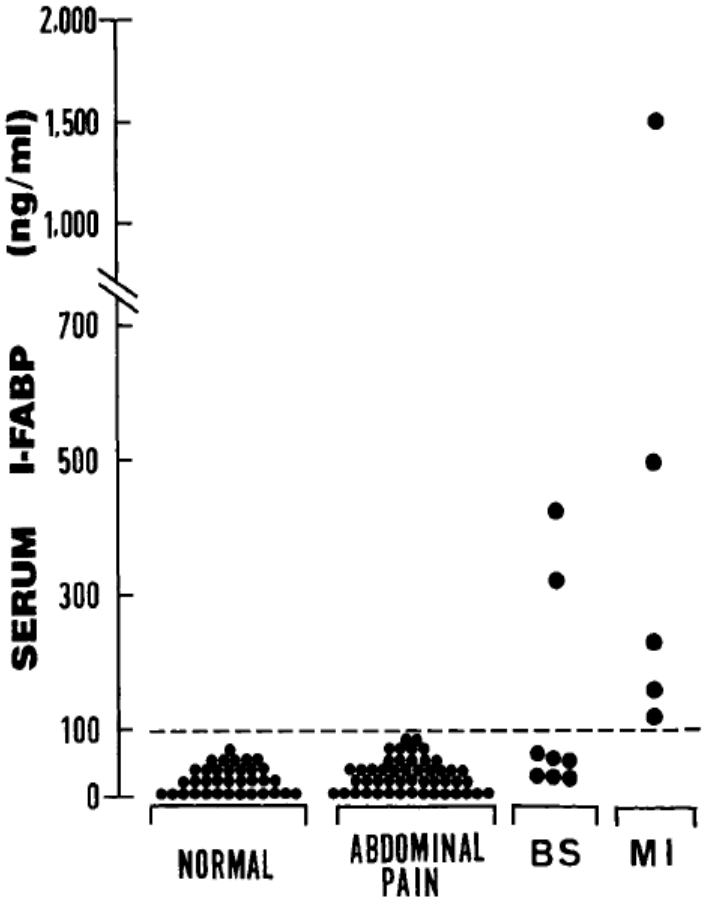
Petite protéine cytosolique
« Gut troponin »

immunohistochimie
Derikx JP et al, Plos one 2008

Intestinal Fatty Acid–Binding Protein Is a Useful Diagnostic Marker for Mesenteric Infarction in Humans

TATSUO KANDA,* HIROSHI FUJII,† TATSUO TANI,* HIROSHI MURAKAMI,* TAKEYASU SUDA,* YASUO SAKAI,* TERUO ONO,† and KATSUYOSHI HATAKEYAMA*

Departments of *Surgery and †Biochemistry, Niigata University School of Medicine, Niigata, Japan



IFABP = 100 ng/ml

Gastroenterology 1996

IFABP et ischémie mésentérique

	Mean control[a]	Mean AMI[b]	*p* value	Cut-off level
I-FABP Uden kit (ng/mL)				
Block et al. [37]	0.050 (0.0–0.197)	0.186 (0.0–0.613)	0.58	N/A
Cronk et al. [40]	0.281	1.772	N/A	0.1
Güzel et al. [41]	0.08 (0.0		<0.001	0.09
Thuijls et al. [46][f]	0.109 [0.		0.02	0.268
Uzun et al. [47]	0.170 ± 0.543	0.709 ± 0.669	N/A	0.145
Vermeulen Windsant et al. [48]	N/A	N/A	N/A	0.815
van der Voort et al. [39][f]	1.020	2.872	0.98	N/A
I-FABP Osaka kit (ng/mL)				
Kanda et al. [15]	25.1 ± 3.6	265.8 ± 111.3	<0.0	100
Kanda et al. [42]	5.8 ± 15.6		<0.0001	3.1
Kittaka et al. [43]	1.6		<0.001	6.5
Matsumoto et al. [44]	2.5 (0.2–56.7)	31.0 (1.1–498.4)	<0.01	9.1
Matsumoto et al. [45]	3.2 [1.7–6.7]	15.5 [5.3–52.9]	<0.001	9.7
Shi et al. [38]	33.9 ± 12.6	113.8 ± 46.3	<0.001	93.07

100 to 815 pg/mL

3.1 to 100 ng/mL

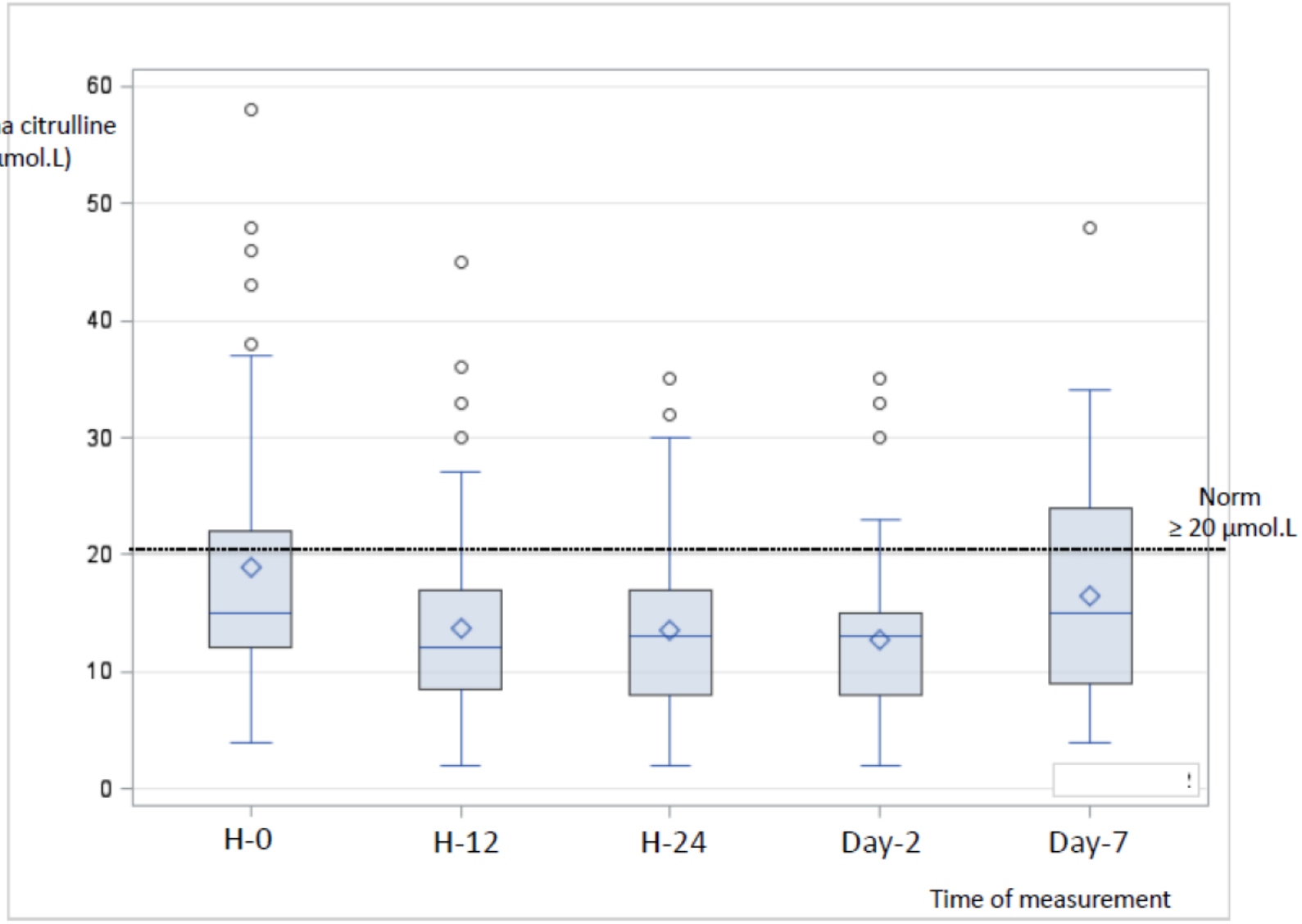
Treskes, Intern Emerg Med 2017

Partie 3

Biomarqueurs entérocytaires

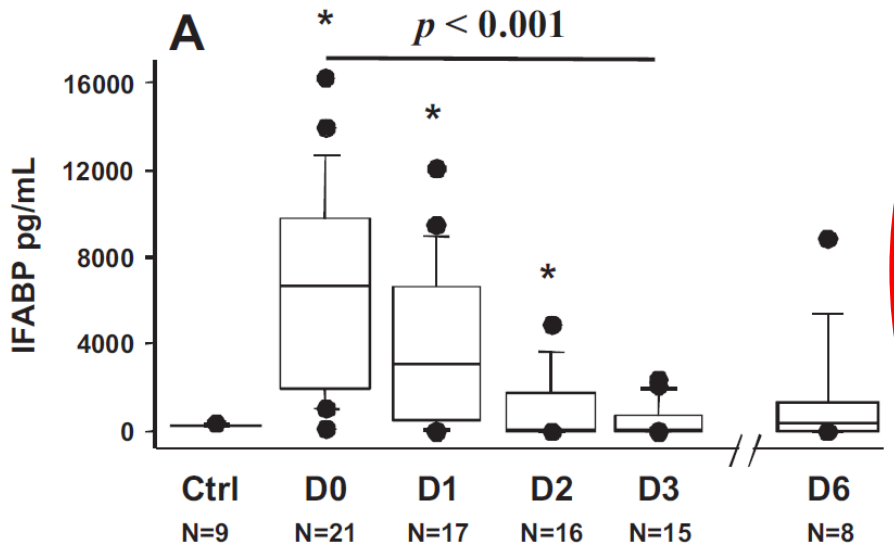
Intérêt en réanimation ?

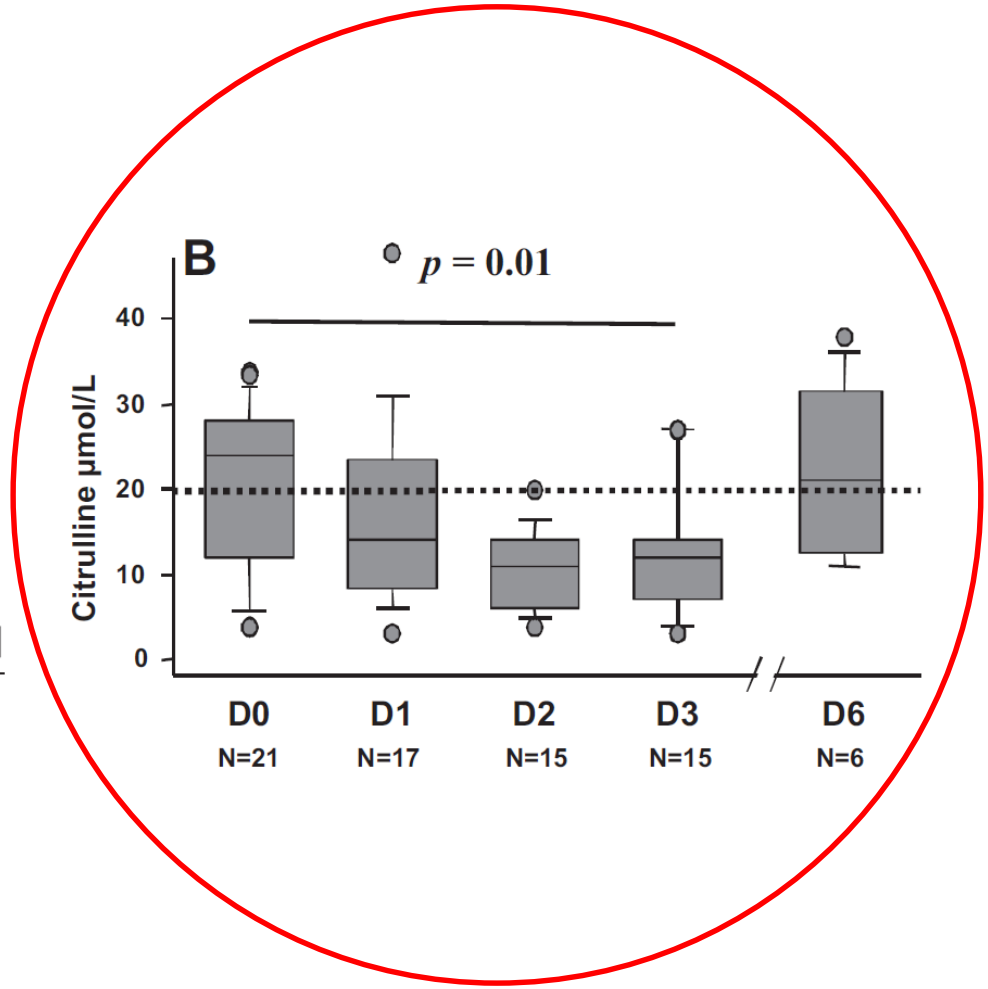
Citrullinémie en réa = Courbe en U



Piton, Intensive Care Med, 2010

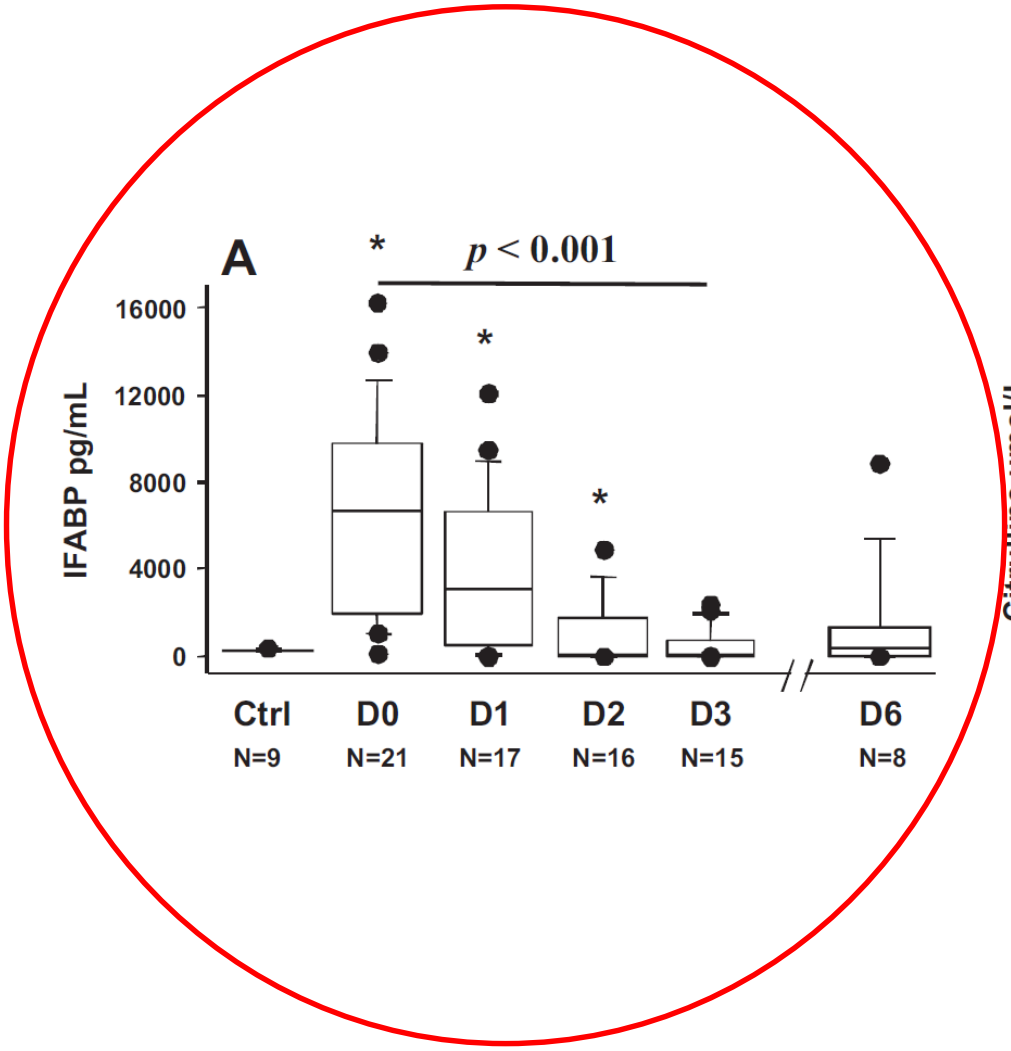
Biomarqueurs entérocytaires après un ACR

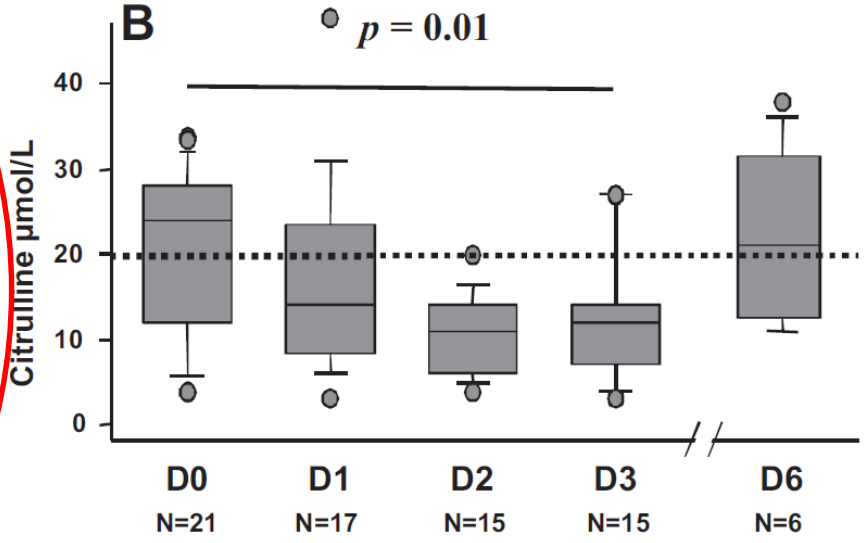




Grimaldi, Resuscitation 2012

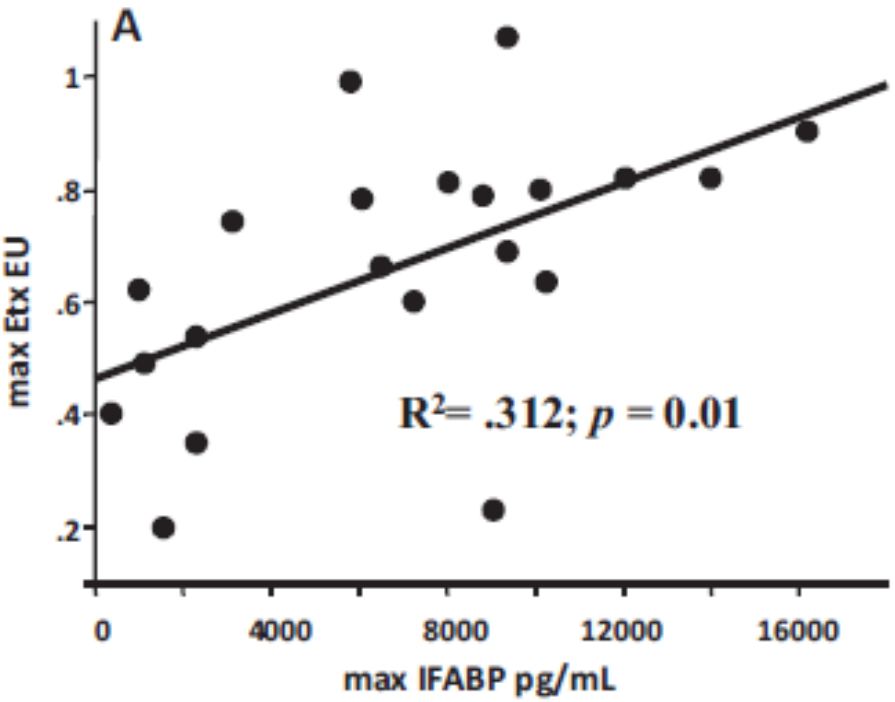
Biomarqueurs entérocytaires après un ACR

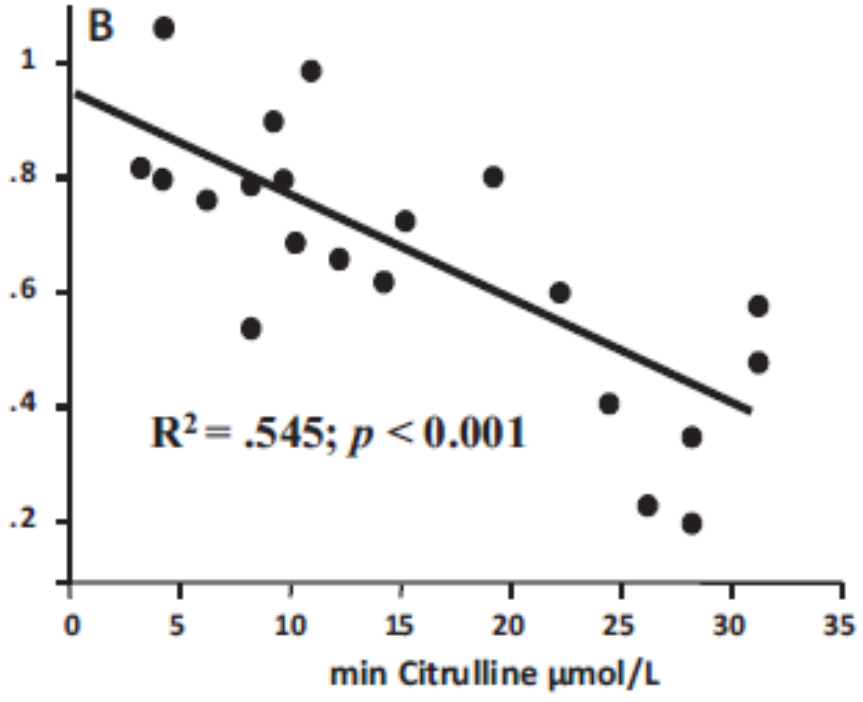




Grimaldi, Resuscitation 2012

Biomarqueurs entérocytaires et translocation





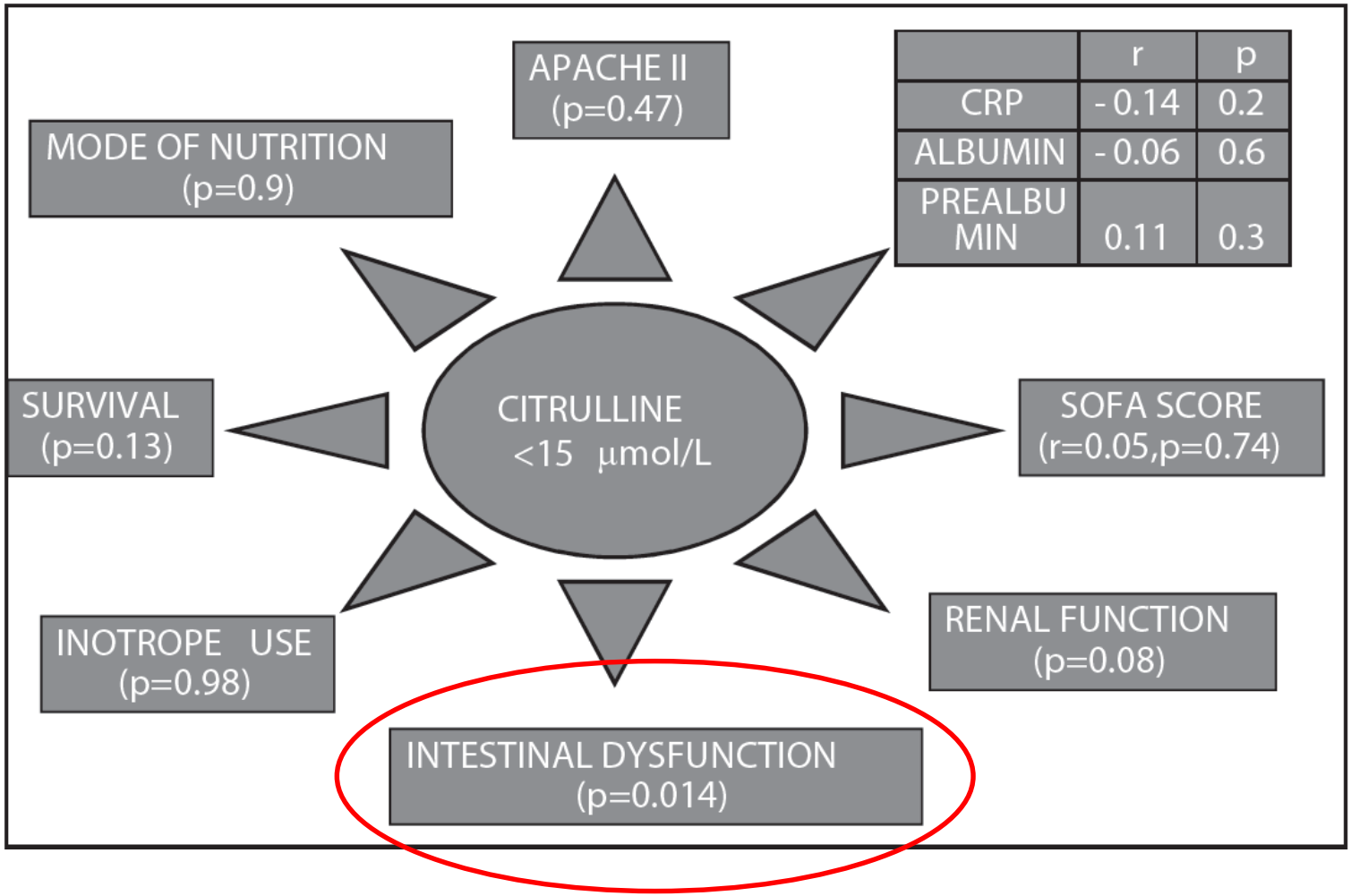
Grimaldi, Resuscitation 2012

Citrullinémie et bactériemie (Translocation)

	Translocation (n = 12)	No translocation (n = 4)
Plasma citrulline nadir (μmol/L)	13 ± 6*	29 ± 7
Glutamine (μmol/L)	330 ± 208	496 ± 184
Arginine (μmol/L)	31 ± 27	57 ± 58
CRP (ng/mL)	189 ± 129	110 ± 103
TNF-α (pg/mL)	42 (3-1100)	28 (21-69)
IL-10 (pg/mL)	16 (4-718)	56 (4-311)
TNF-α/IL-10	1.7 (0.29-275)	0.38 (0.22-15)
Albumin (g/L)	19 ± 8	16 ± 2
Transthyretin (g/L)	0.11 ± 10	0.05 ± 0.01

Crenn, J Crit Care, 2014

Citrullinémie et dysfonction intestinale

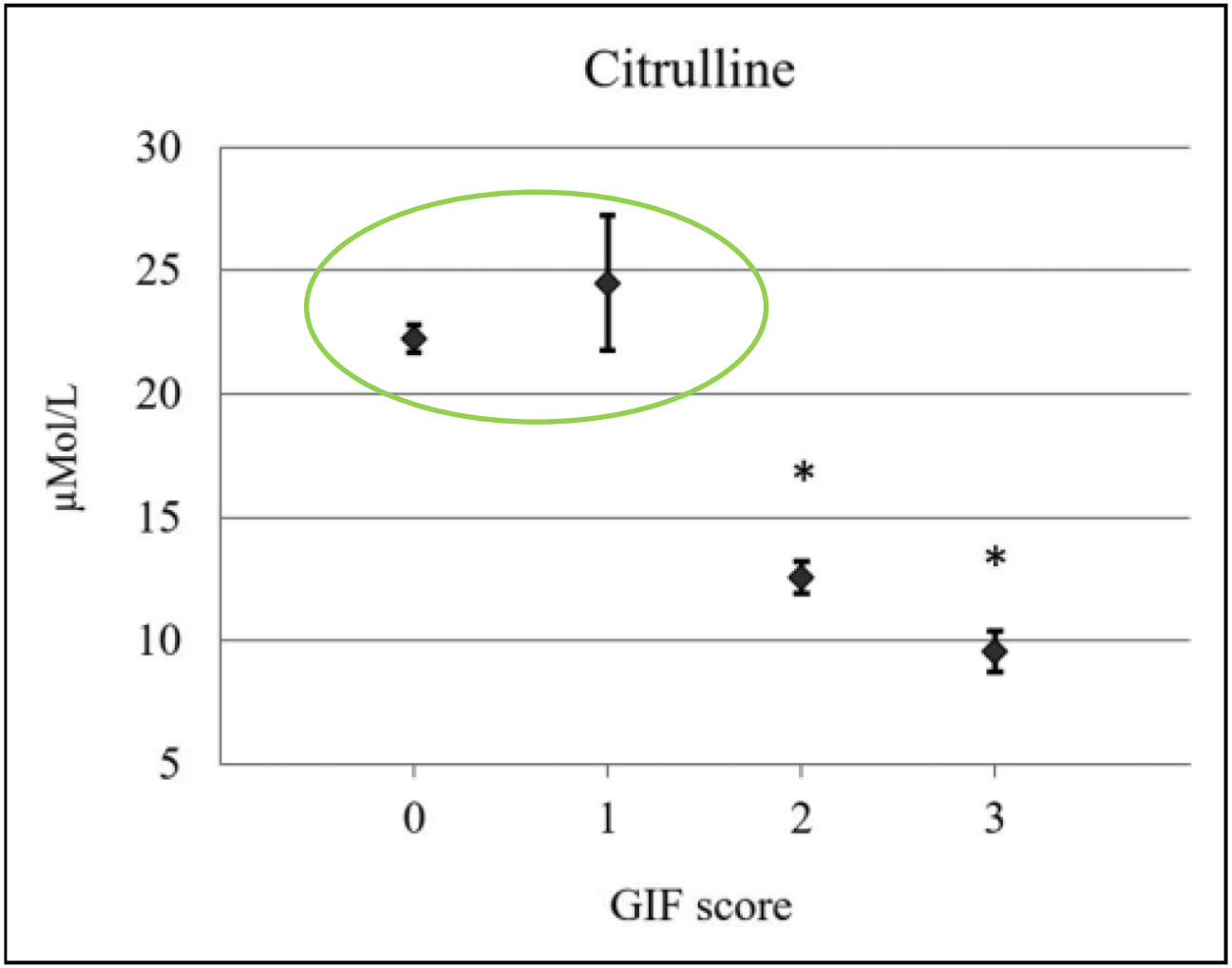


Noordally,Nutr Clin Pract 2012

AGI score et citrullinémie

15’

n = 39

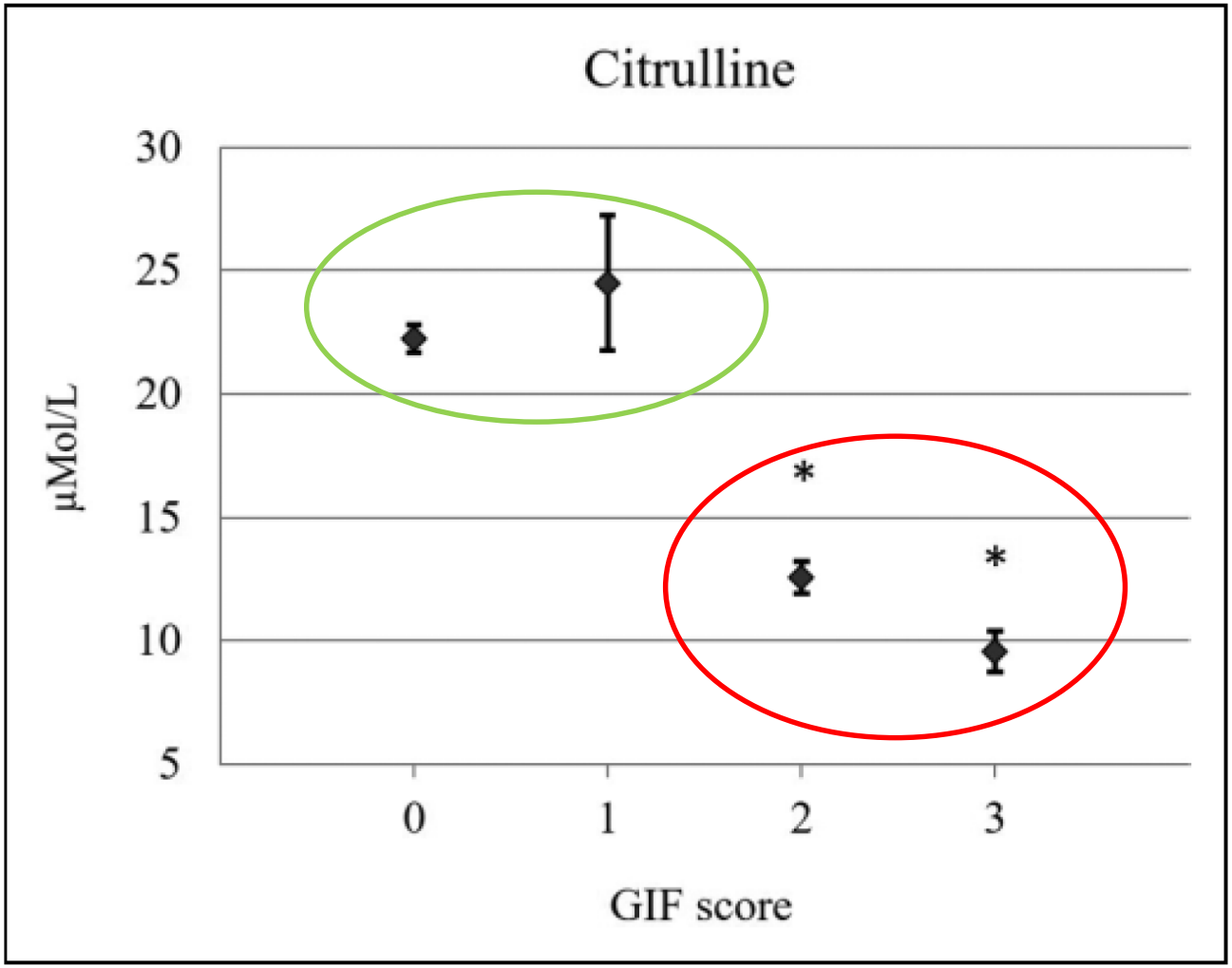


Fagoni, J Intens Care Med 2017

AGI score et citrullinémie

15’

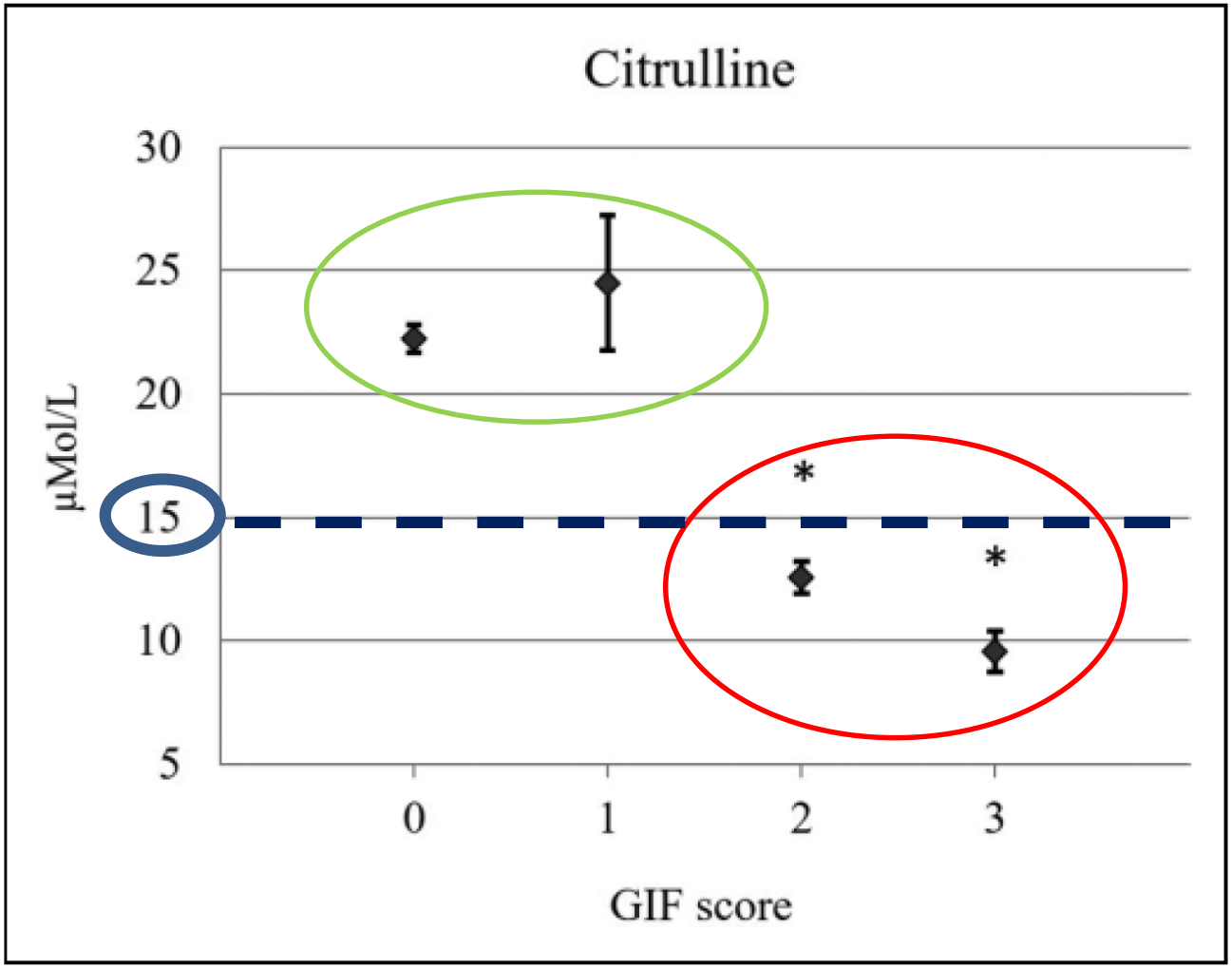
n = 39



Fagoni, J Intens Care Med 2017

AGI score et citrullinémie

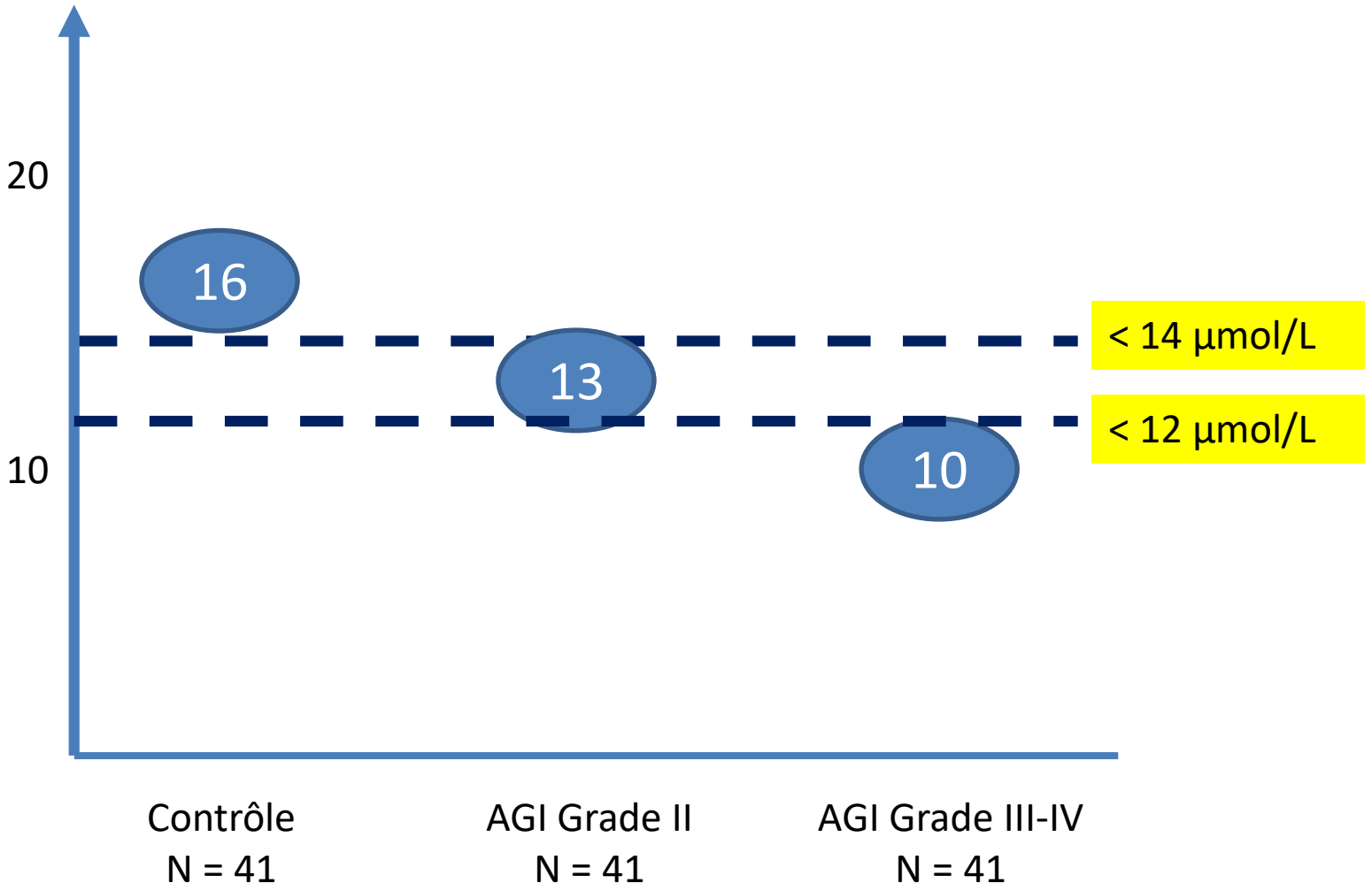
n = 39



Fagoni, J Intens Care Med 2017

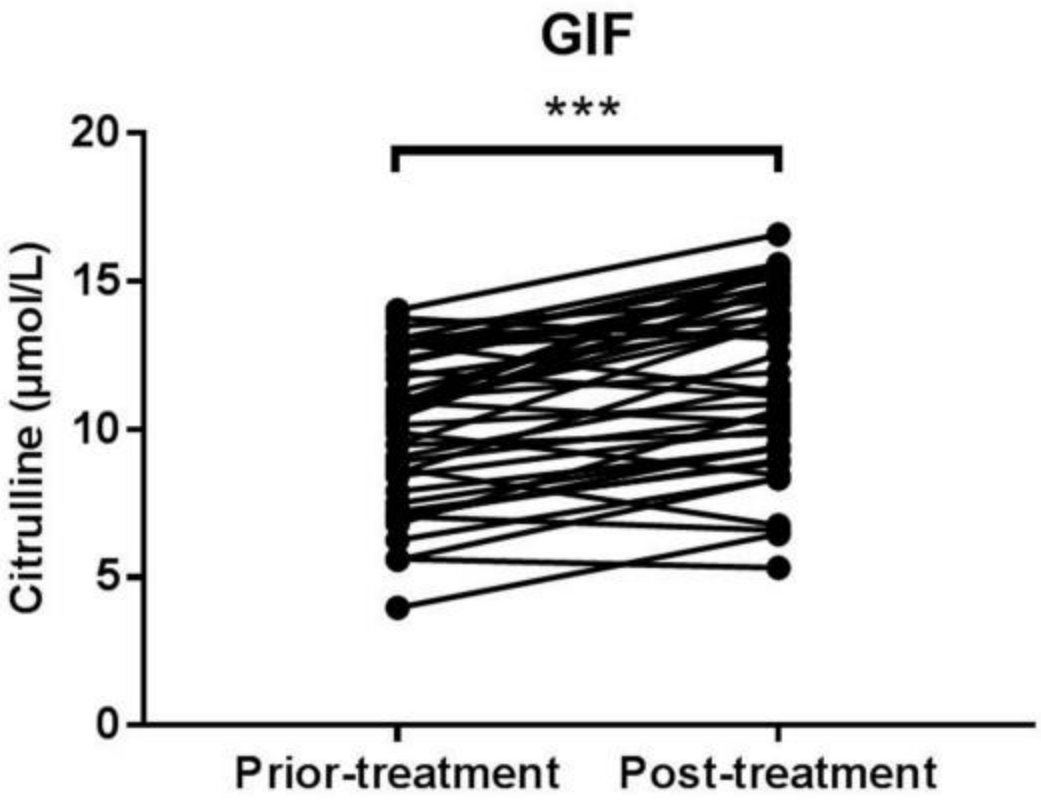
AGI et citrullinémie

n = 110



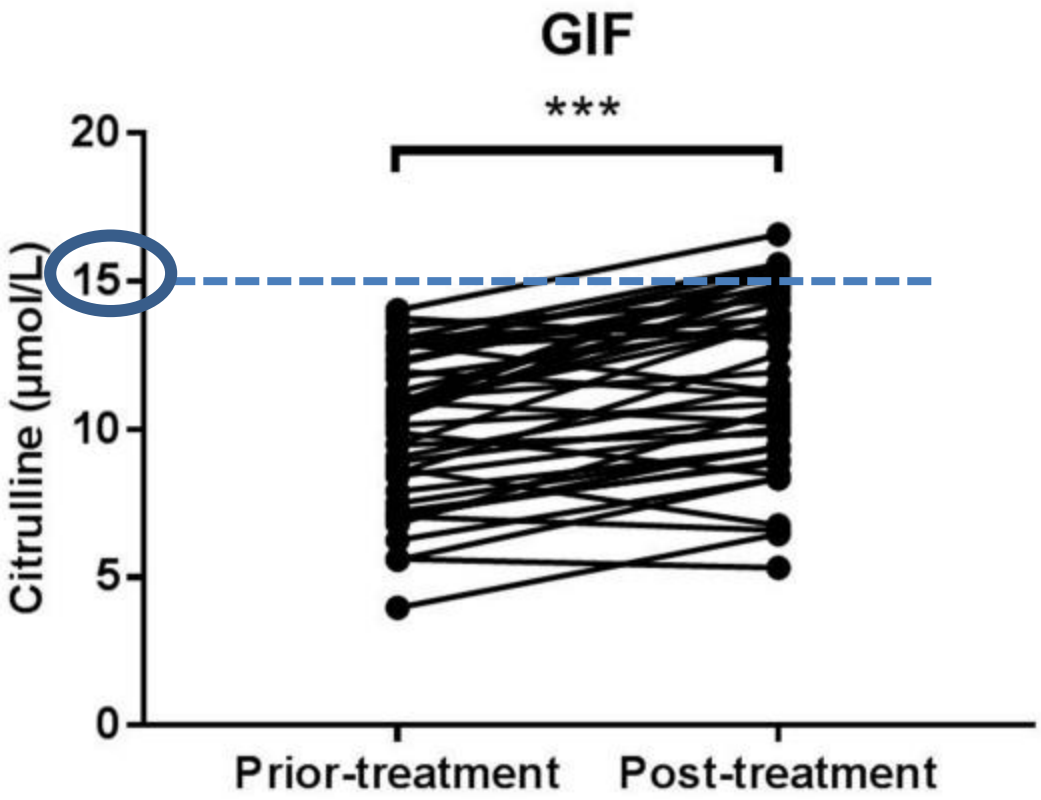
Teng, Int J General Med 2021

AGI III-IV et citrulline



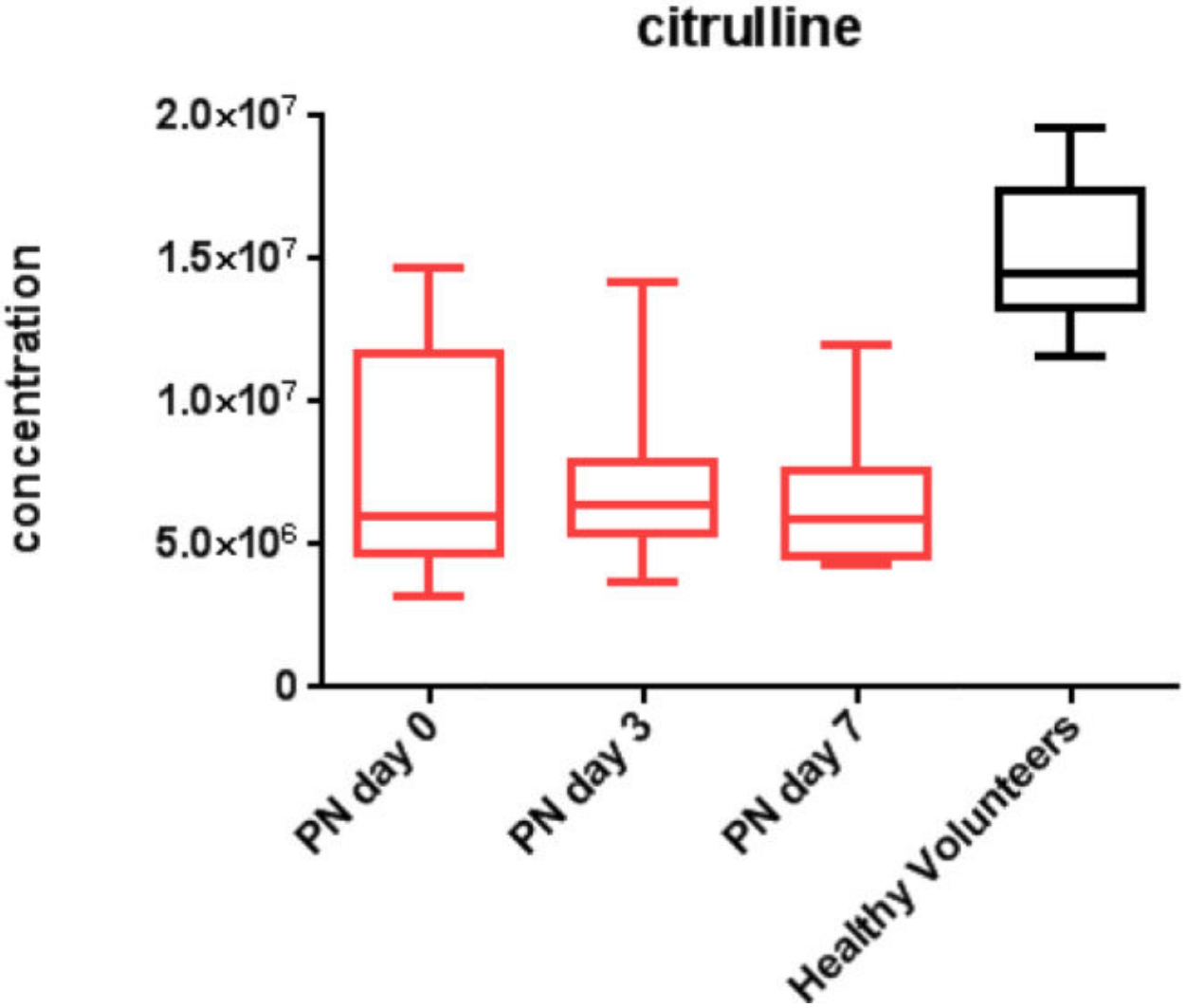
Teng, Int J General Med 2021

AGI III-IV et citrulline



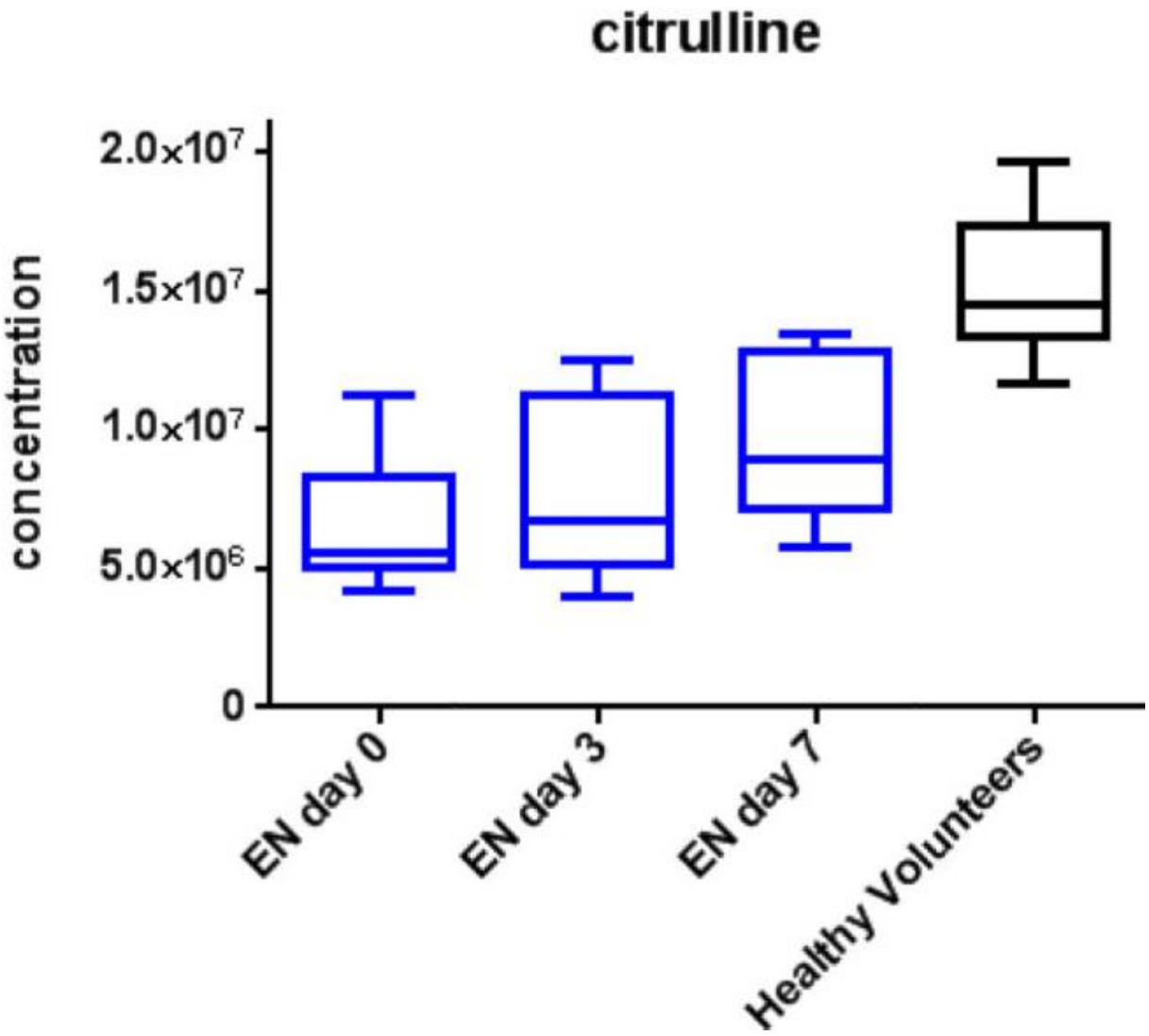
Teng, Int J General Med 2021

Citrullinémie reste basse sous NP



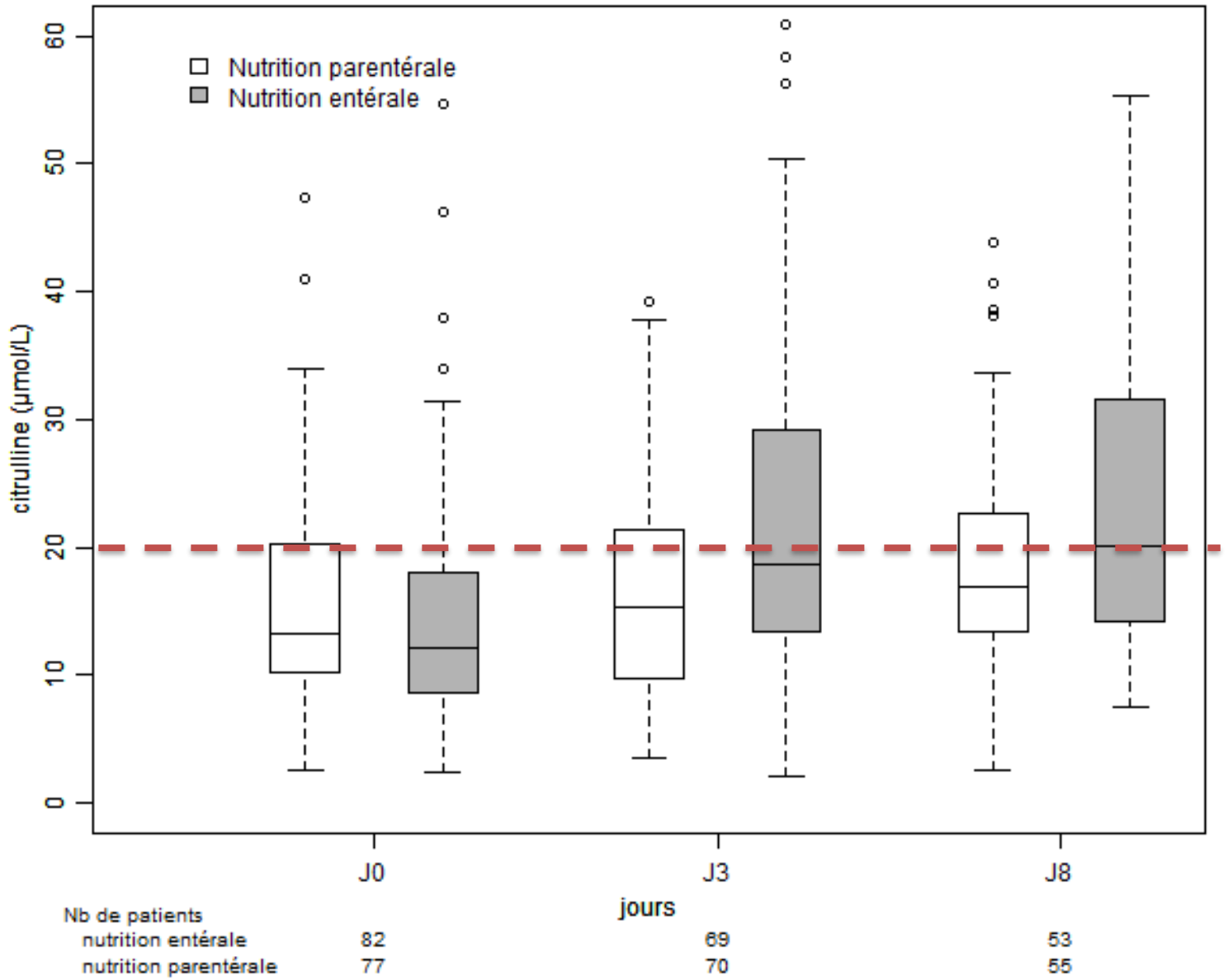
Parent, J Trauma Acute Care Surg 2017

Citrullinémie remonte sous NE



Parent, J Trauma Acute Care Surg 2017

Citrullinémie remonte plus vite sous NE



Piton, Intensive Care Medicine 2019

Citrulline interpretation is not so easy !

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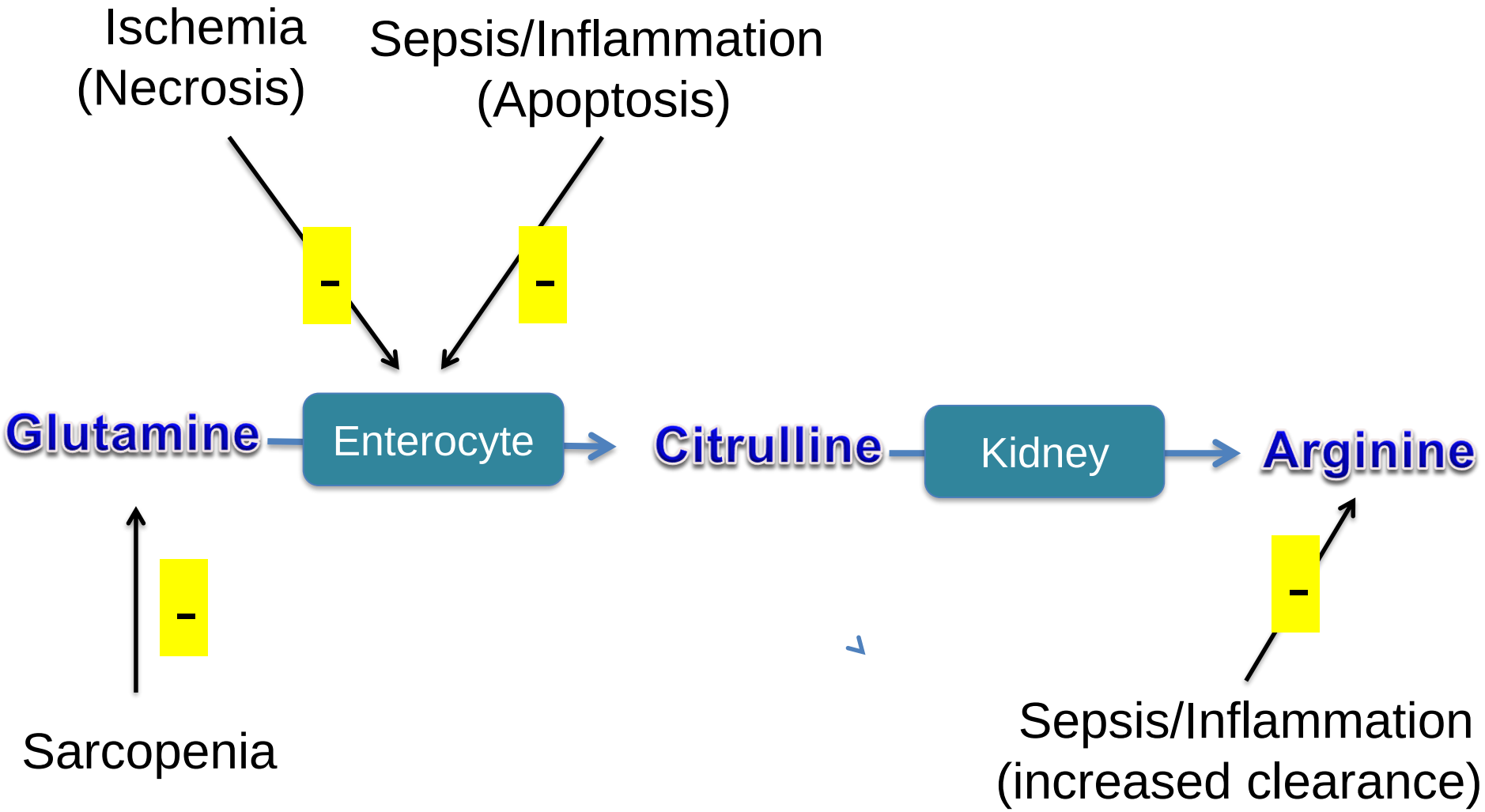
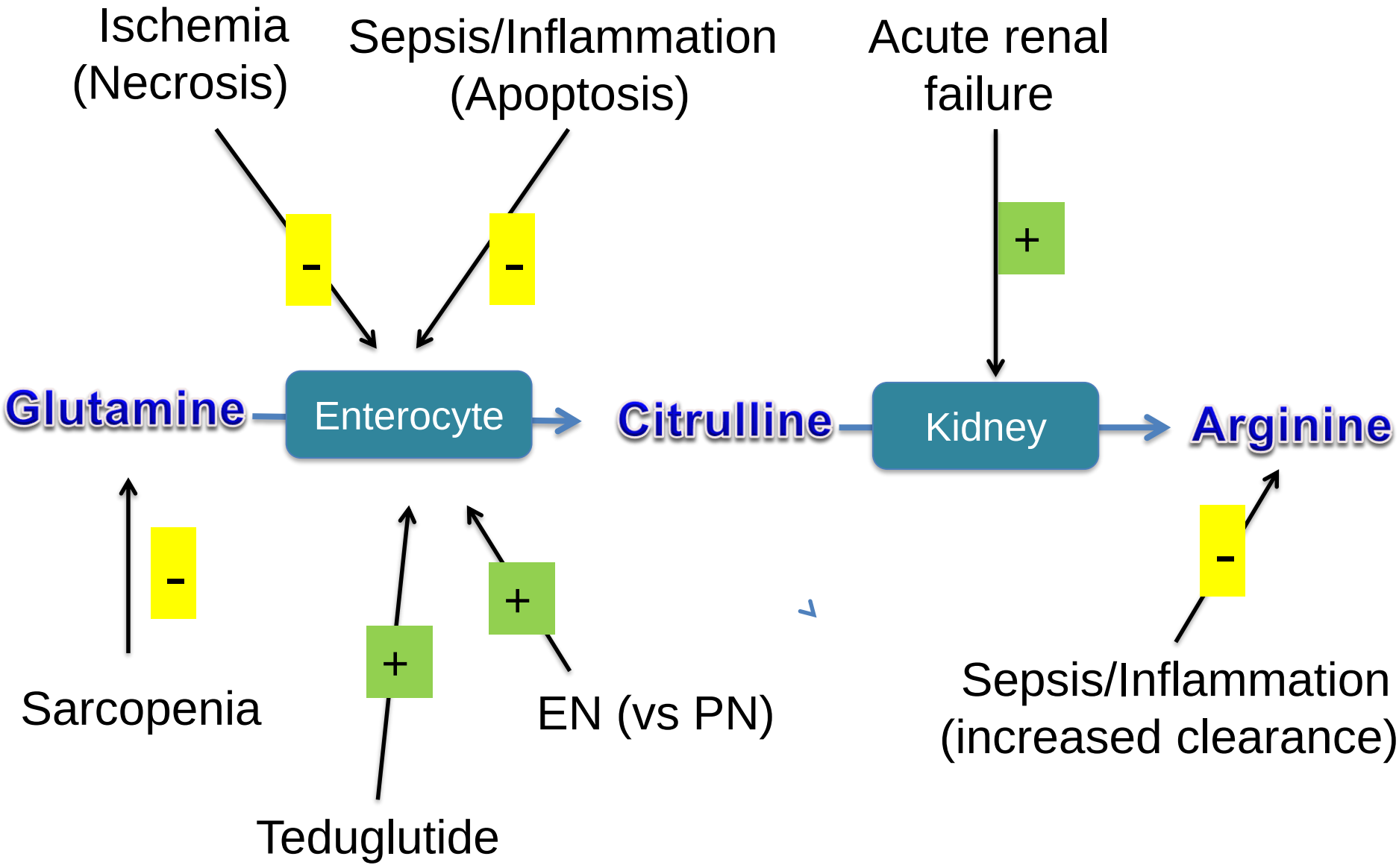


Citrulline interpretation is not so easy !



The End

Conclusion et perspectives

19’

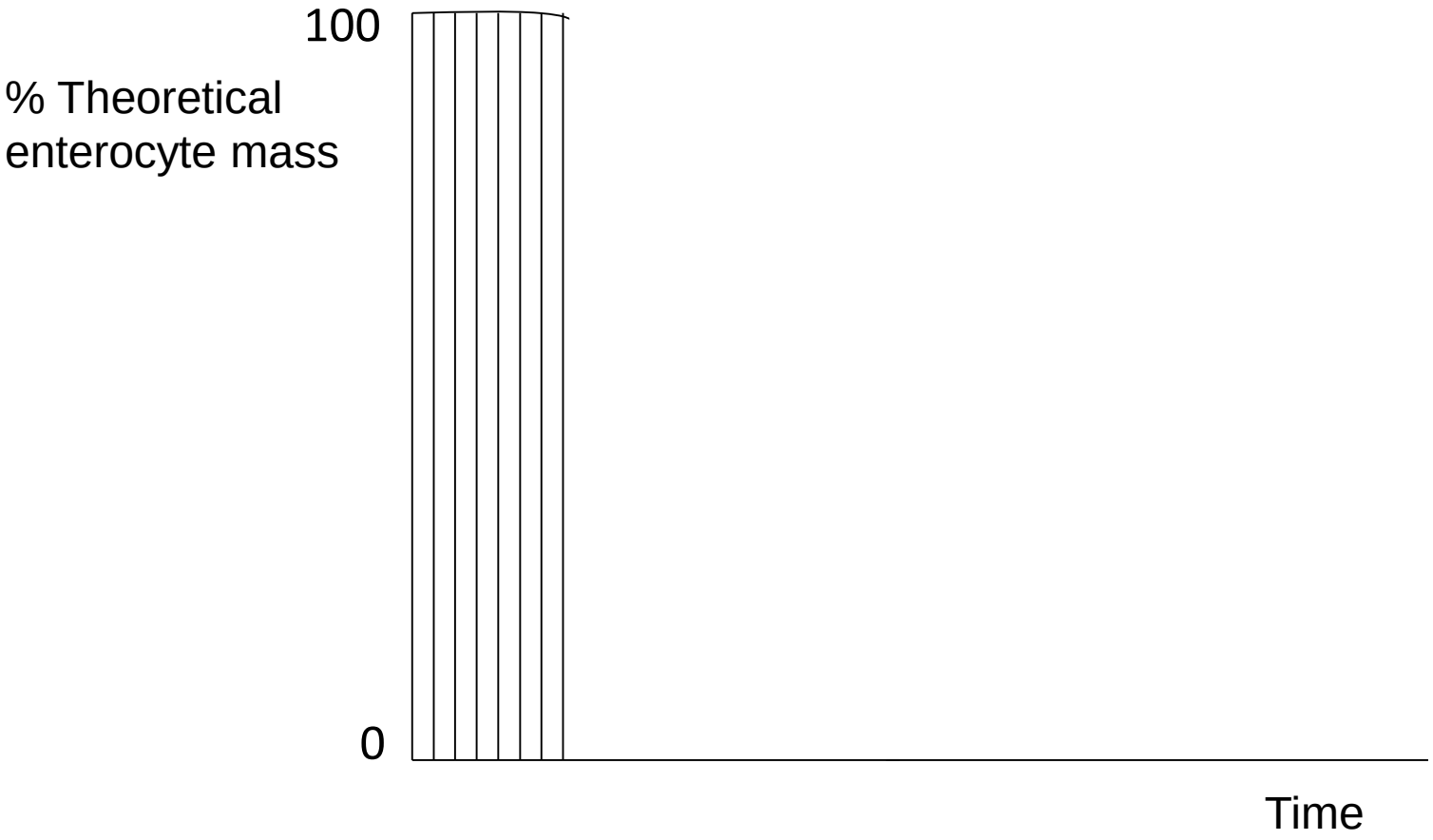
Atteinte intestinale est fréquente

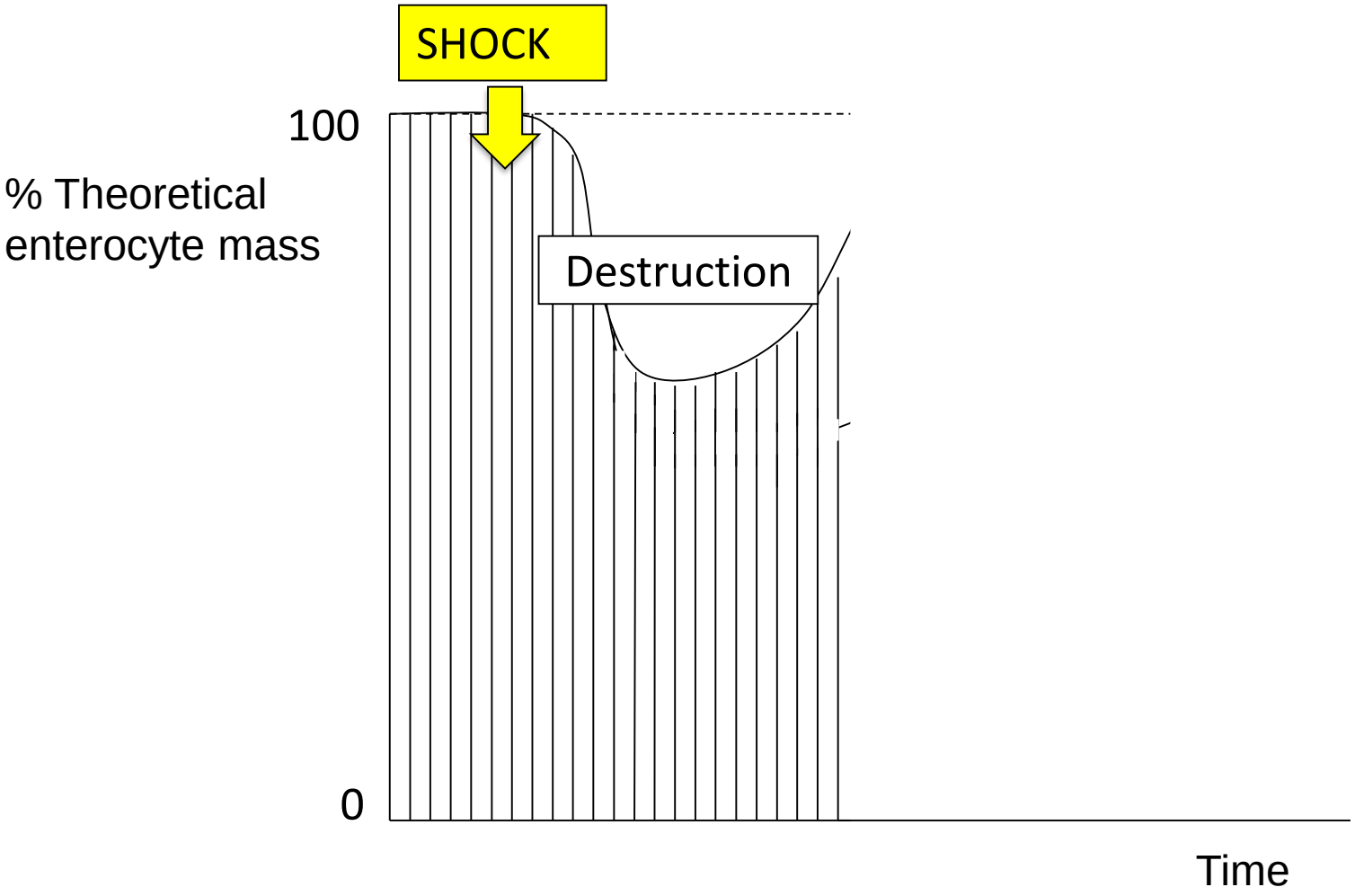
- Primaire
- Secondaire +++ (ischémie, sepsis)

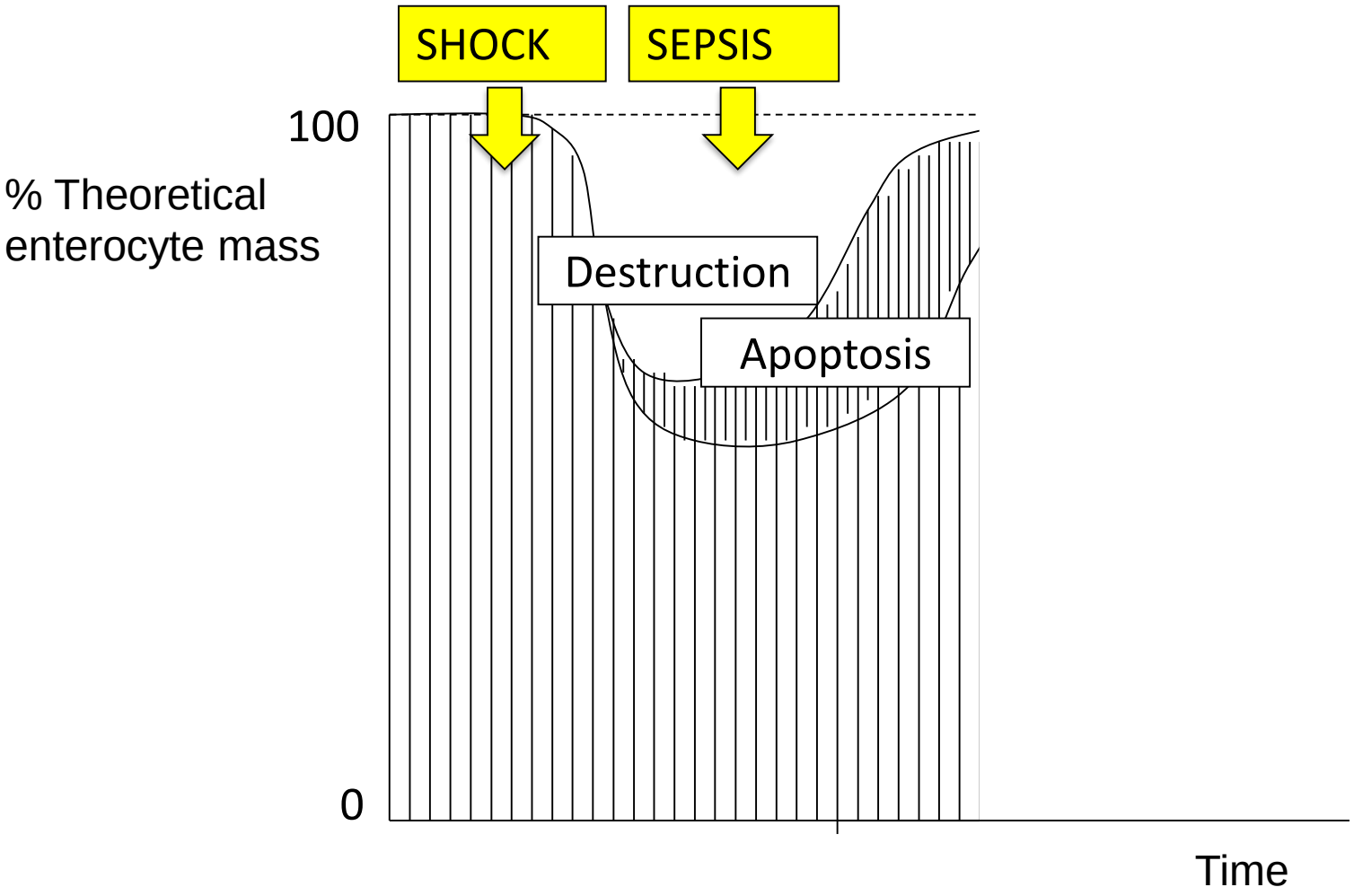
Valeur pronostique propre

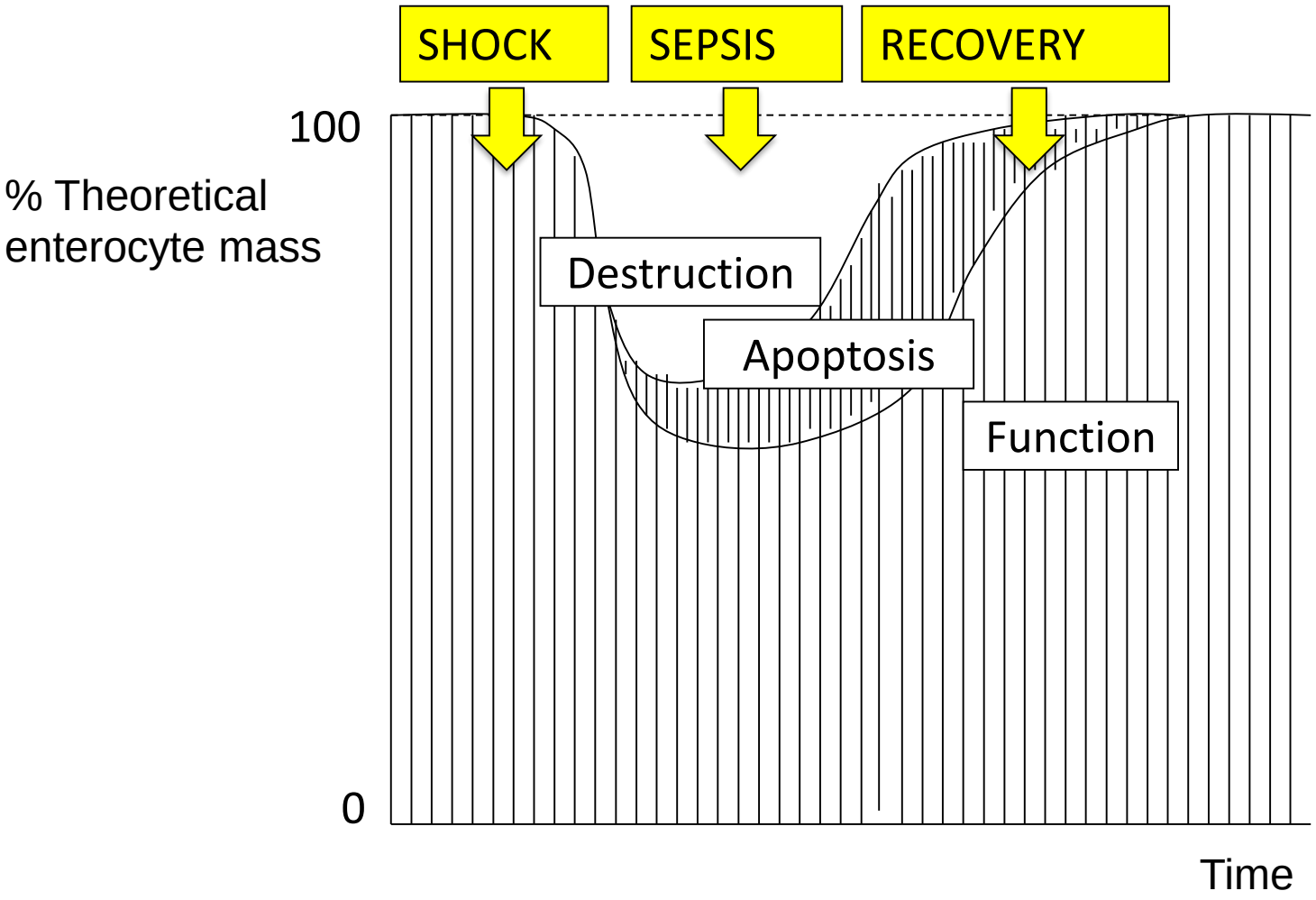
Biodisponibilité/interprétation biomarqueurs ?

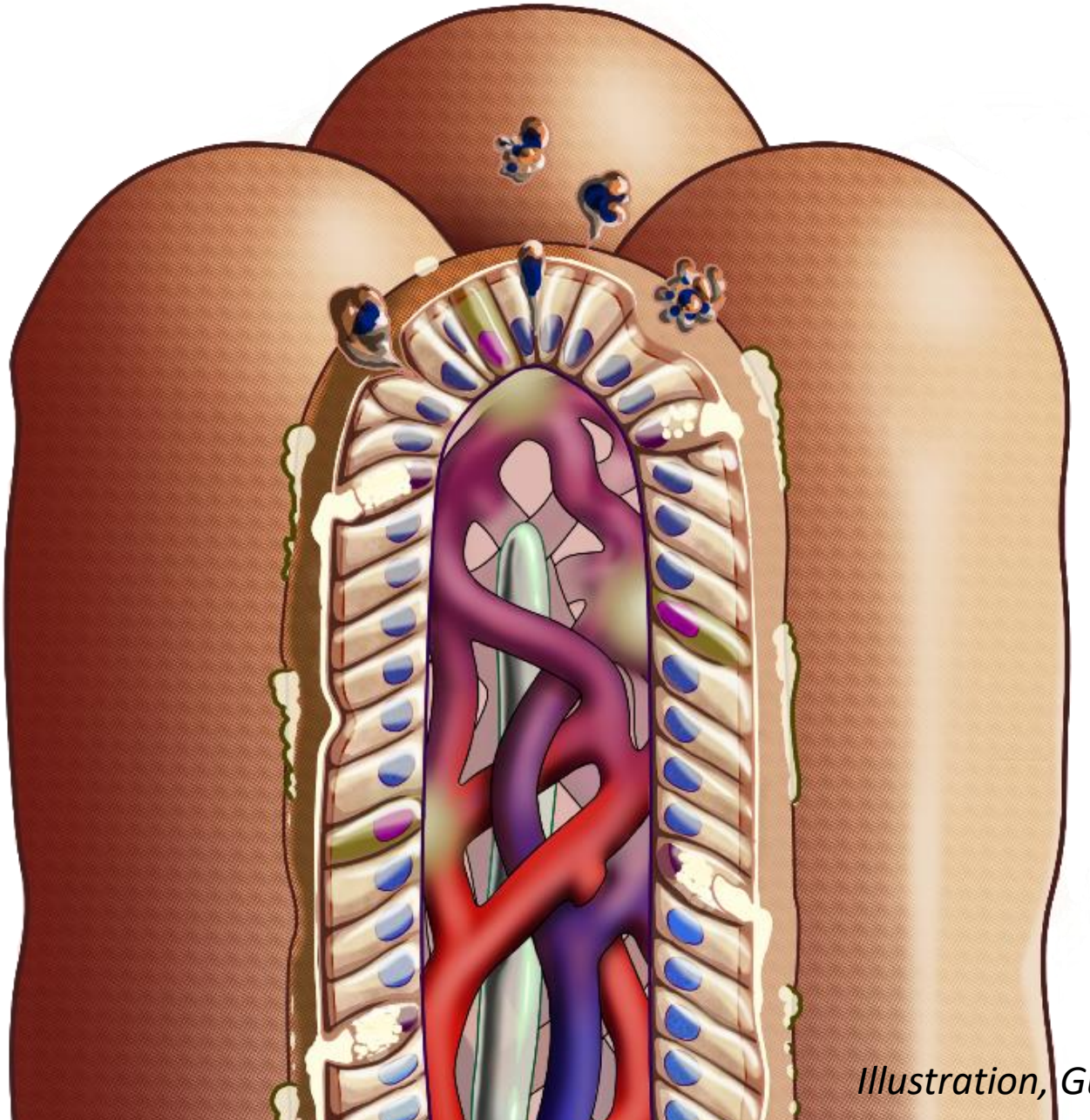
Réfléchir sur un modèle ?


100
% Theoretical
enterocyte mass
0
Time

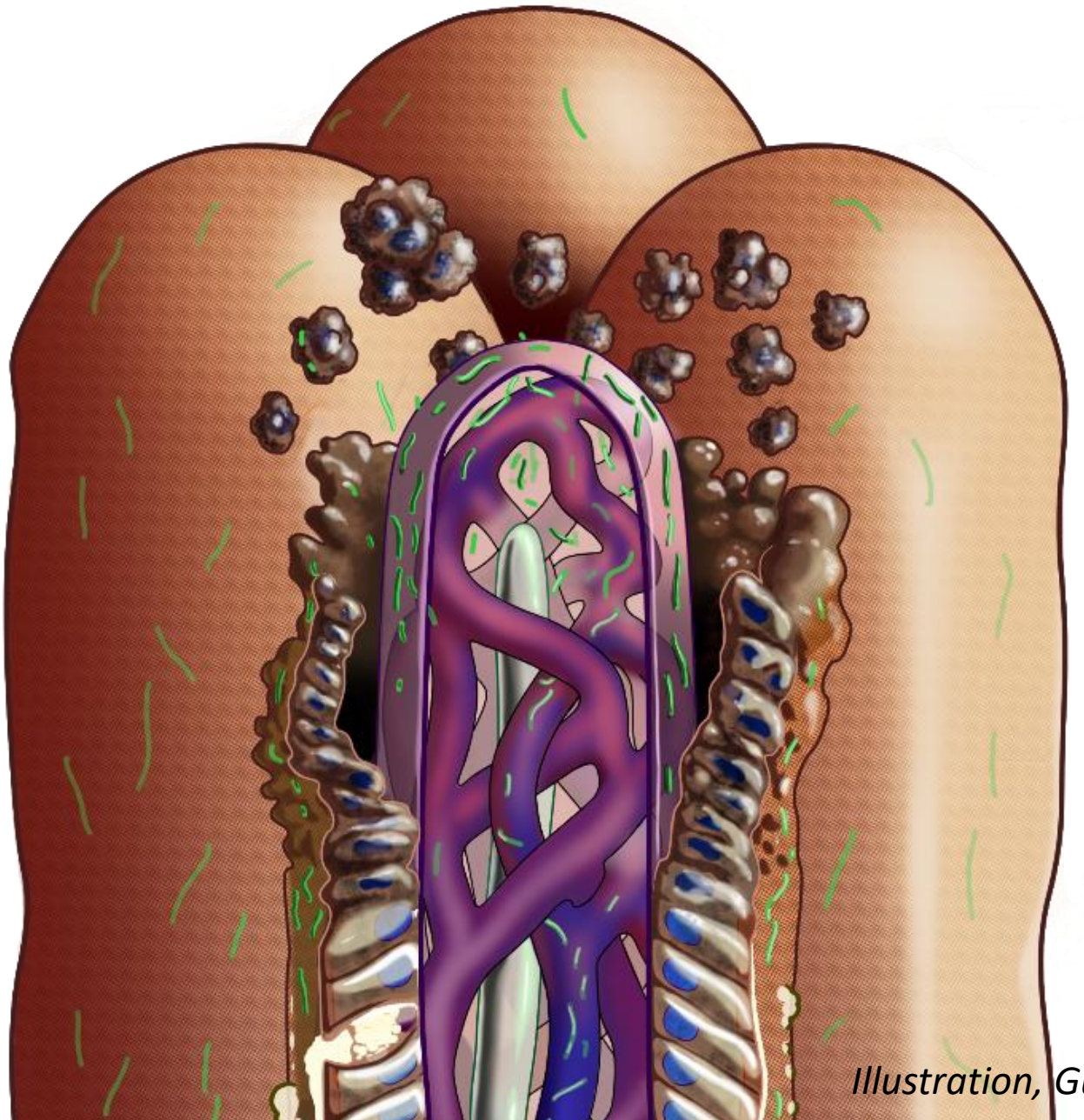

SHOCK
100
% Theoretical
enterocyte mass
Destruction
0
Time


SHOCK
SEPSIS
100
% Theoretical
enterocyte mass
Destruction
Apoptosis
0
Time


SHOCK
SEPSIS
RECOVERY
100
% Theoretical enterocyte mass
Destruction
Apoptosis
Function
0
Time

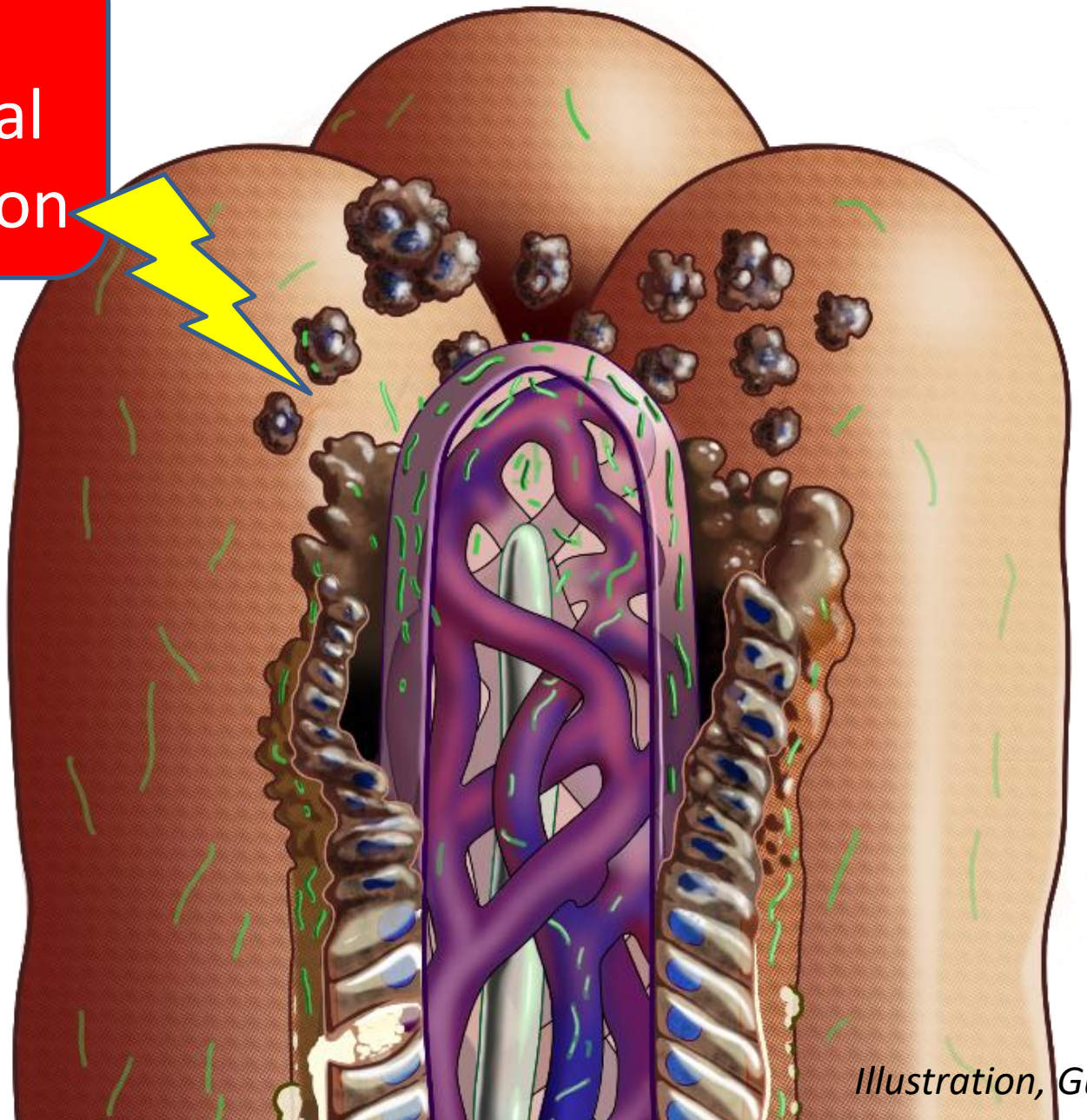


Illustration, Gualdi, Besançon



Illustration, Gualdi, Besançon

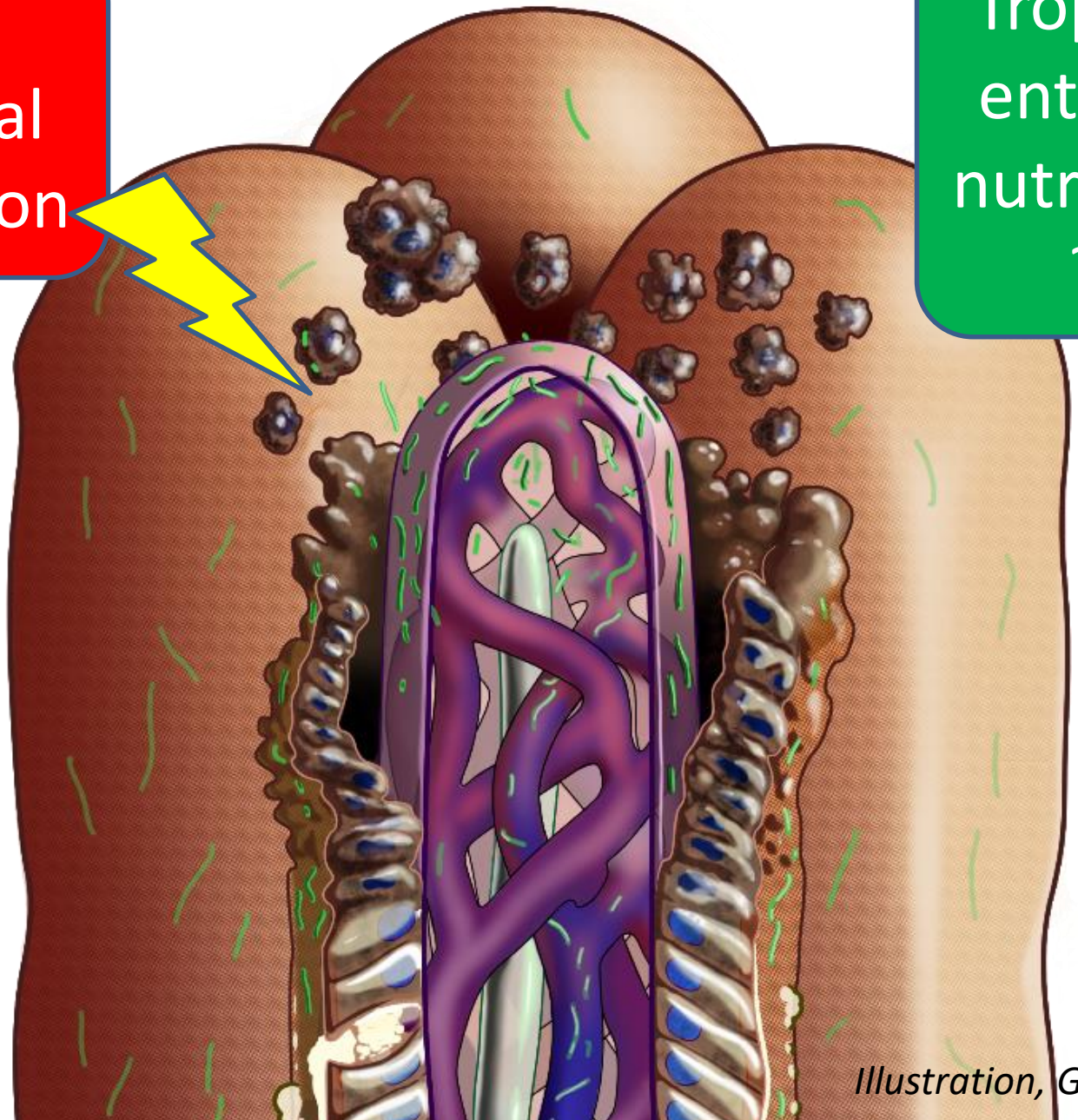
Full enteral nutrition



Illustration, Gualdi, Besançon

Full enteral nutrition

Trophic enteral nutrition ?

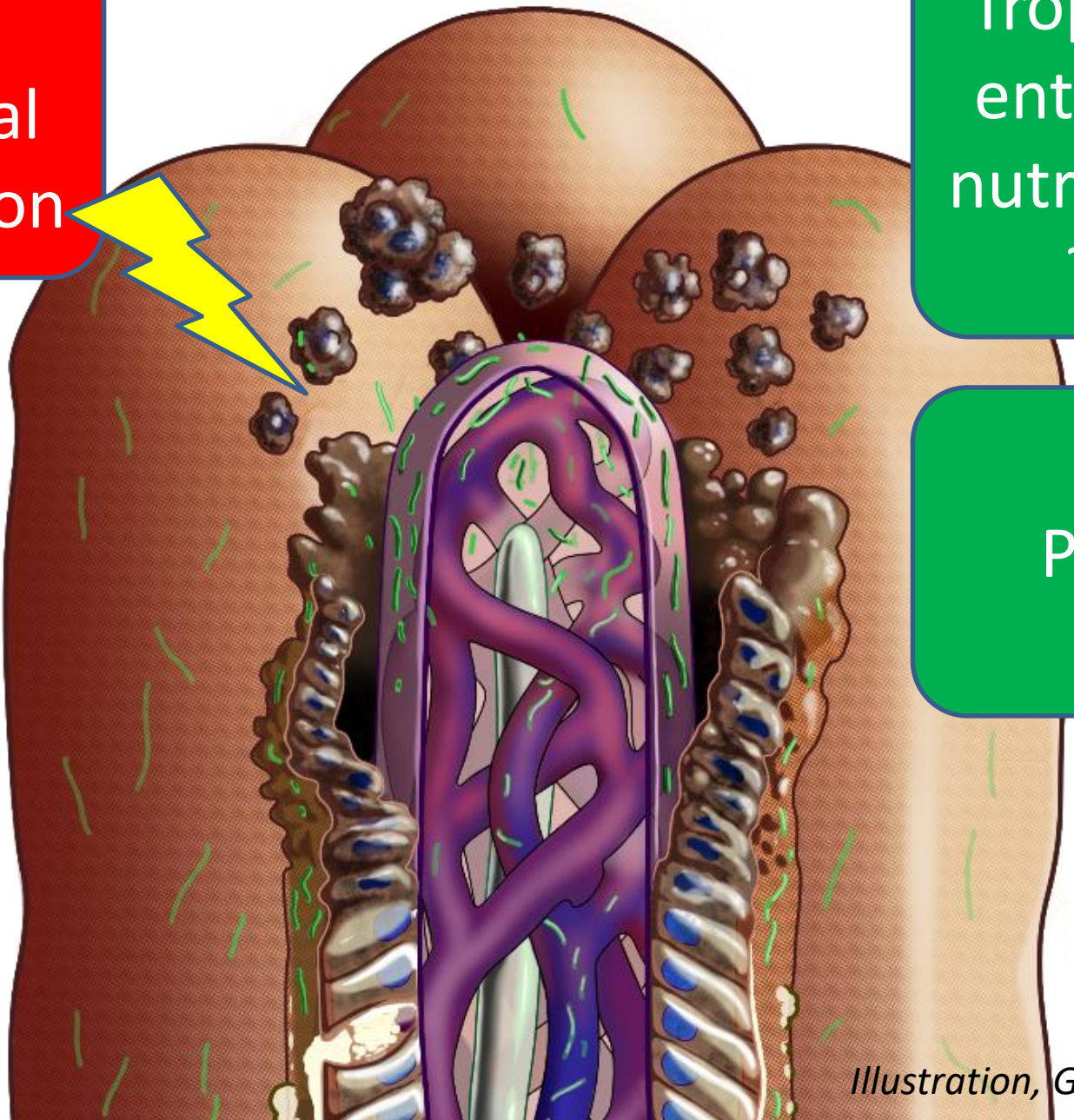


Illustration, Gualdi, Besançon

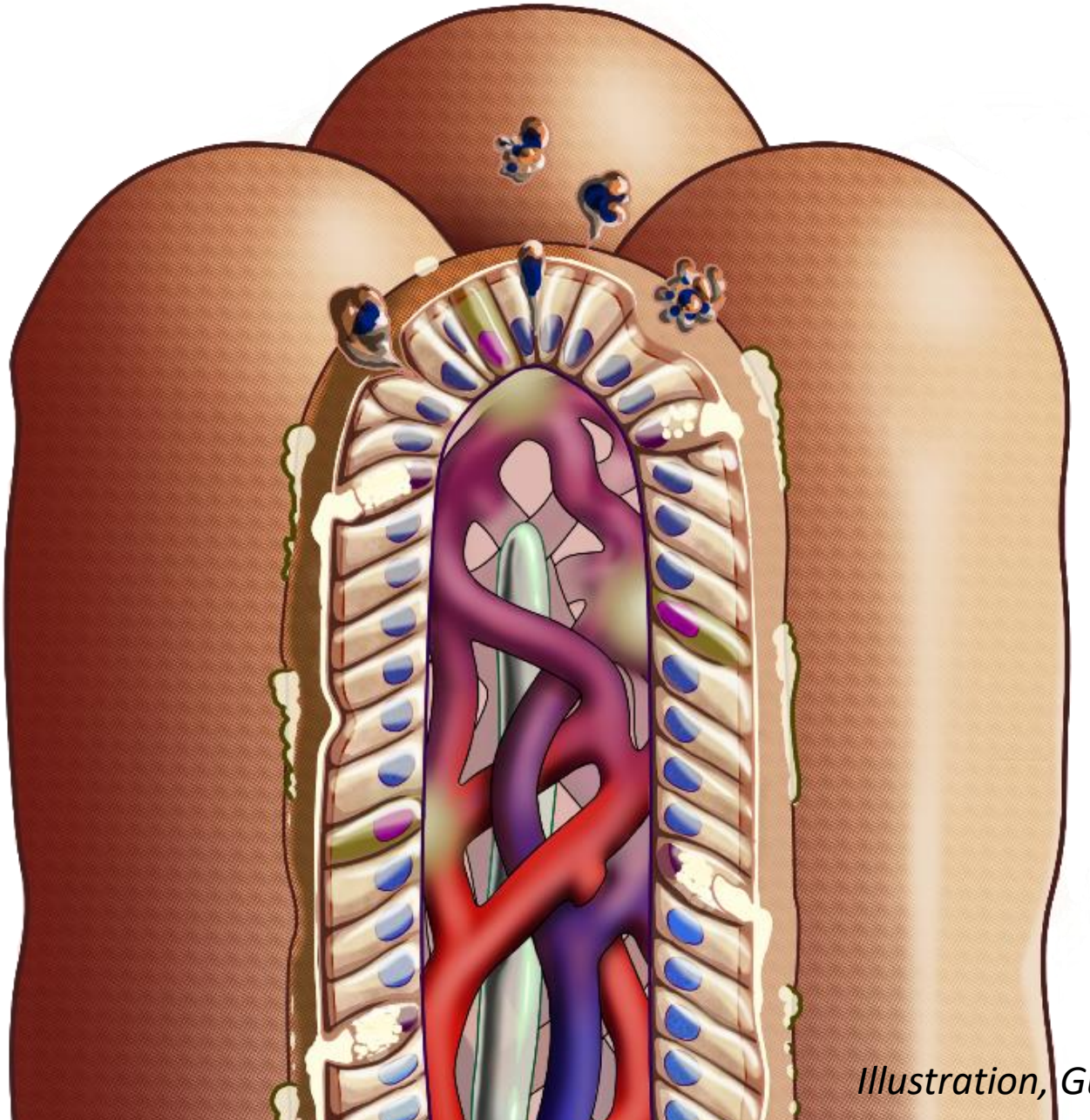
Full enteral nutrition

Trophic enteral nutrition ?

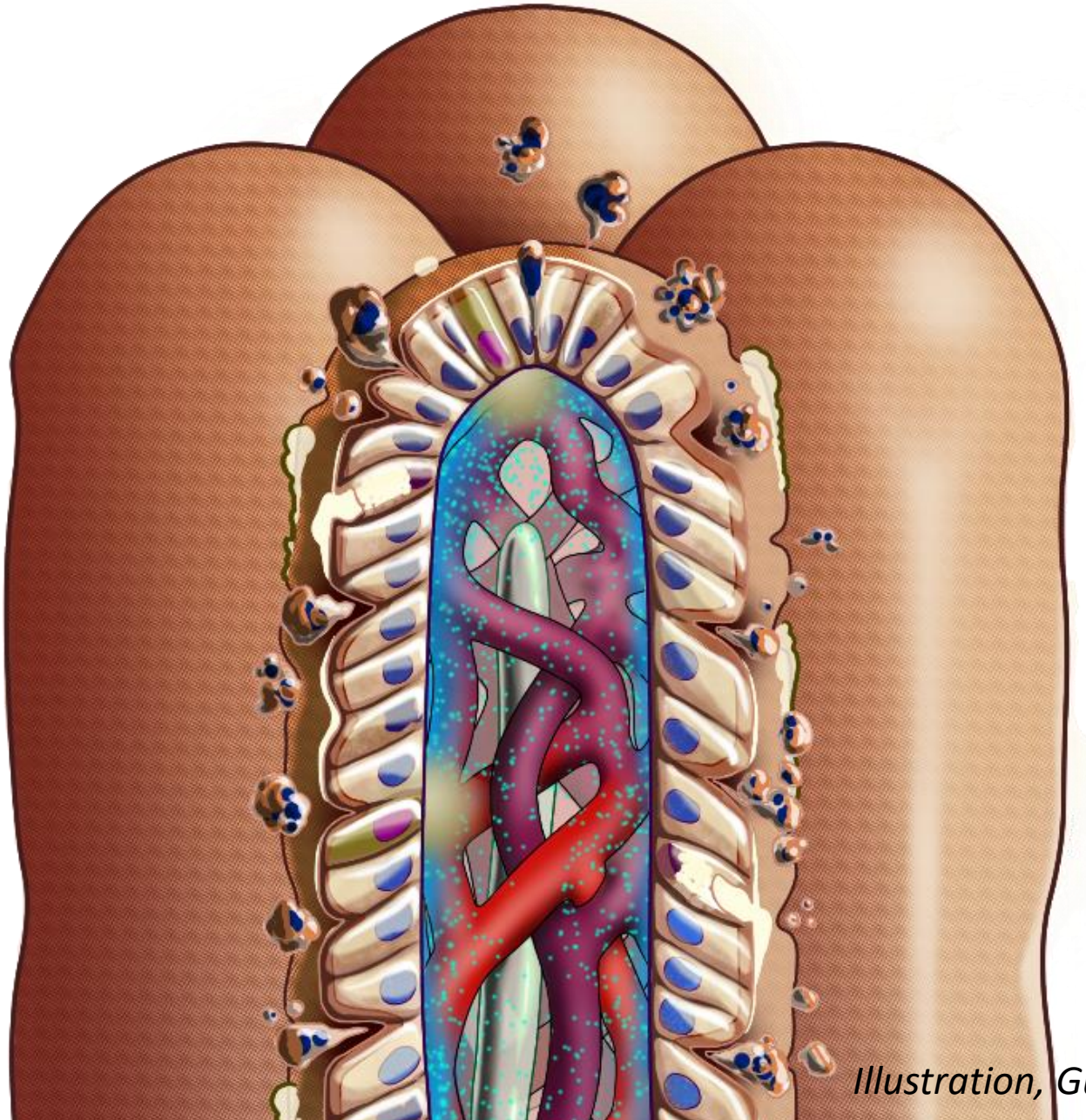
PN



Illustration, Gualdi, Besançon



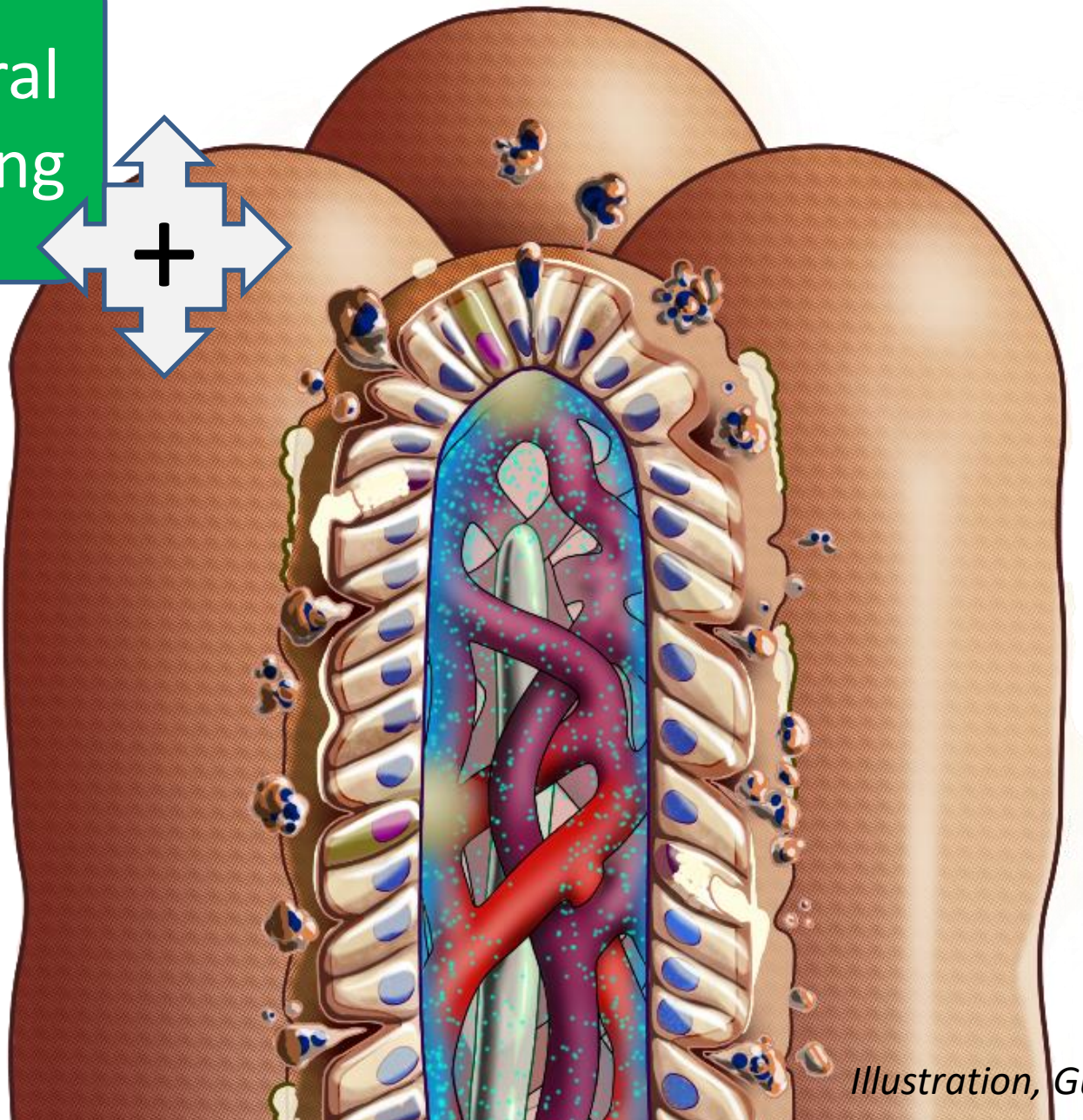
Illustration, Gualdi, Besançon



Illustration, Gualdi, Besançon

Enteral feeding

+



Illustration, Gualdi, Besançon

Enteral feeding

+

Illustration, Gualdi, Besançon

Merci pour votre attention