CORATA Belgique

4ème Congrès de Biologie Clinique

28 - 29 septembre 2016

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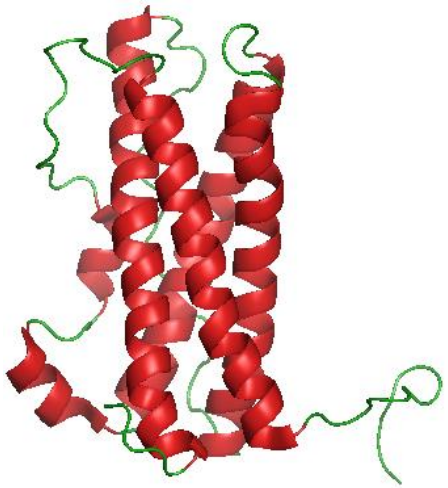
Recherche de la macroprolactine: état des lieux en 2016

Favresse Julien

Assistant Biologie Clinique 2ème année

Cliniques universitaires SAINT-LUC UCL BRUXELLES

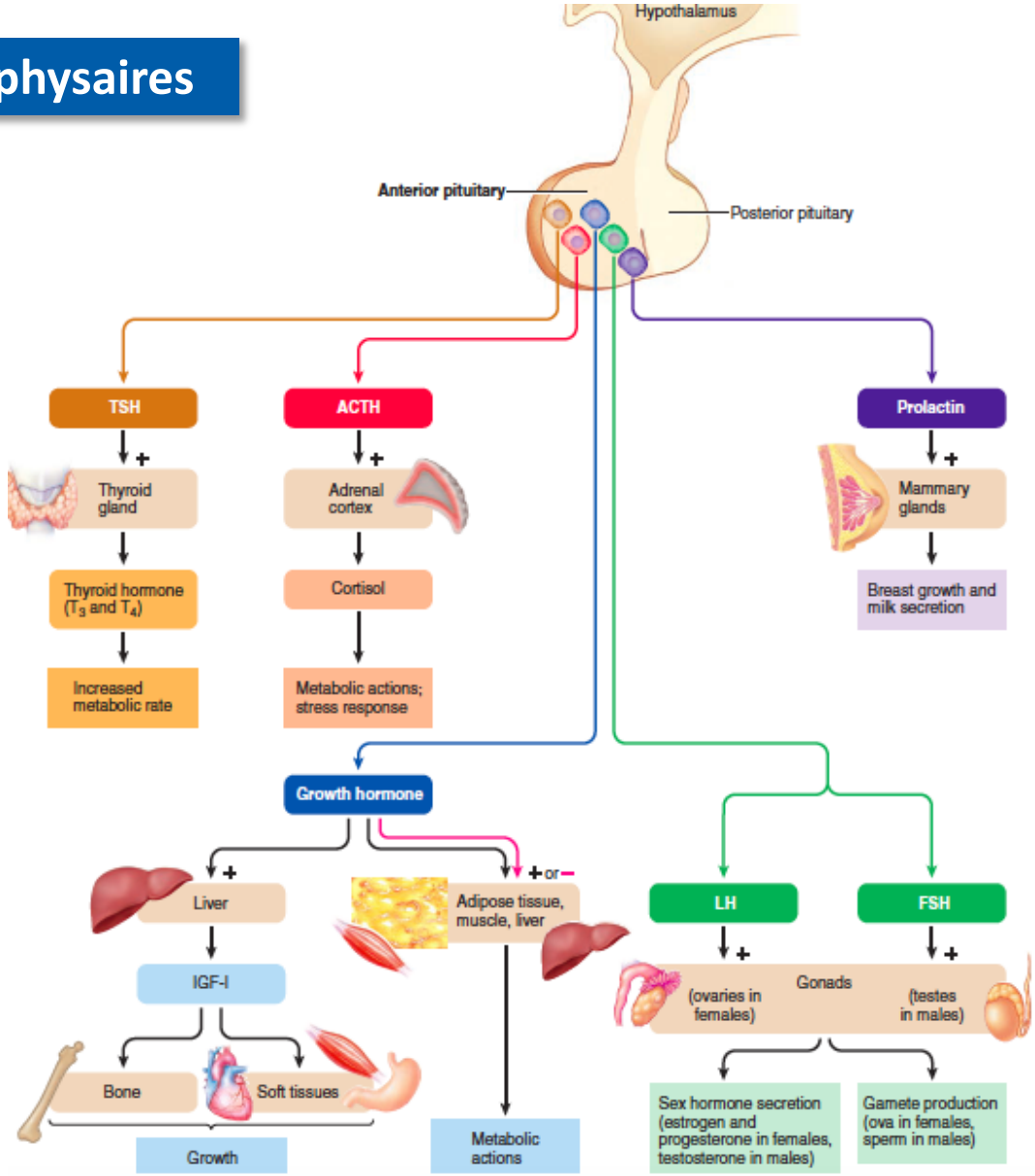
Plan de présentation



- **Rappels prolactine**
  - Hormones hypophysaires
  - Physiologie de la prolactine
  - Causes et symptômes d'hyperprolactinémie
  - Structure prolactine
- **Macroprolactine**
  - Quelques chiffres
  - Immunodosages
  - Rechercher la macroprolactine
  - Validation vs CHU Liège
- **Macrocalcitonine?**

Rappels prolactine

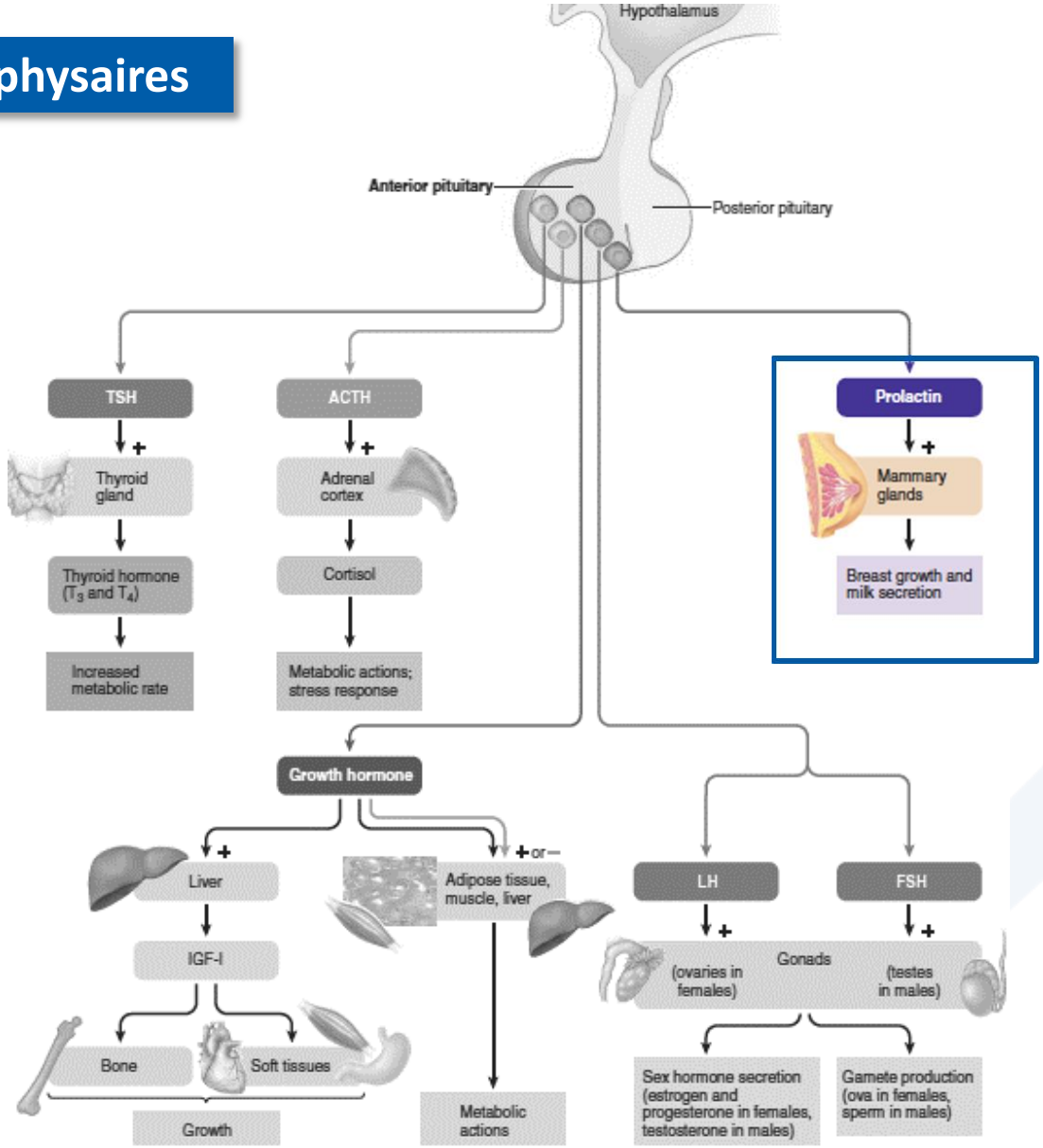
Hormones hypophysaires



Source: Sherwood L et al (2011) Human Physiology: from cells to systems, 8th

Rappels prolactine

Hormones hypophysaires



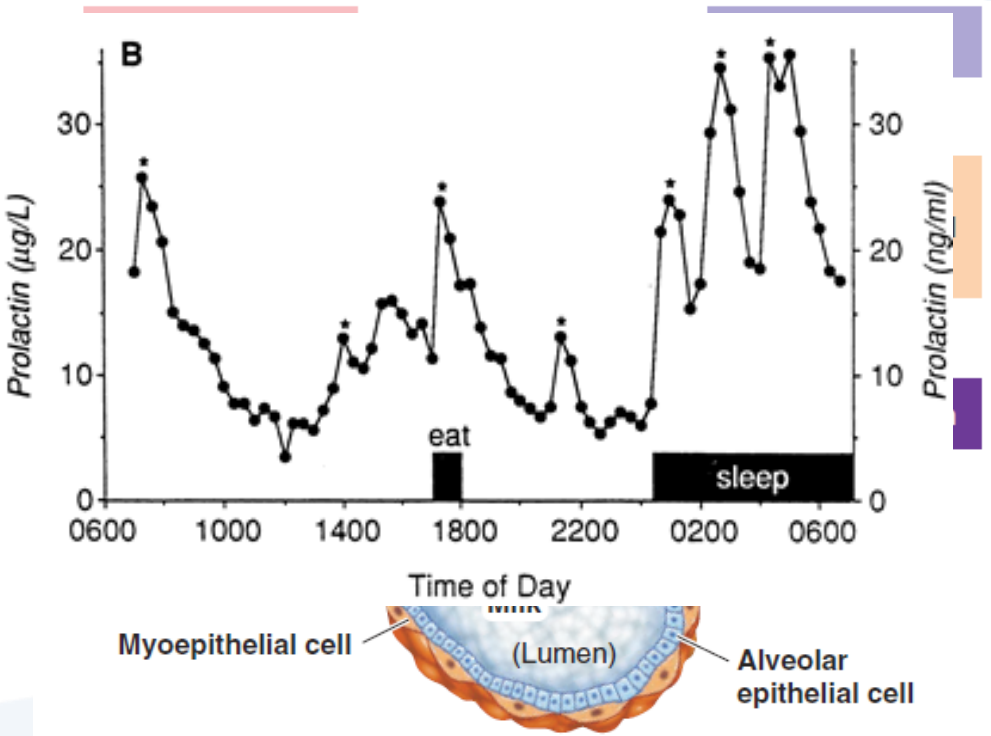
Source: Sherwood L et al (2011) Human Physiology: from cells to systems, 8th

Rappels prolactine

Physiologie de la prolactine

Prolactin-Releasing Hormone (+TRH) (+) → **Prolactine** ← (-) **Prolactin-Inhibiting Hormone (Dopamine)**

- Sécrétion pulsatile
- Stimule développement glandes mammaires
- Stimule production et sécrétion du lait par alvéoles mammaires
- Fonction chez l'homme peu connu
- Renforce SI des deux sexes?



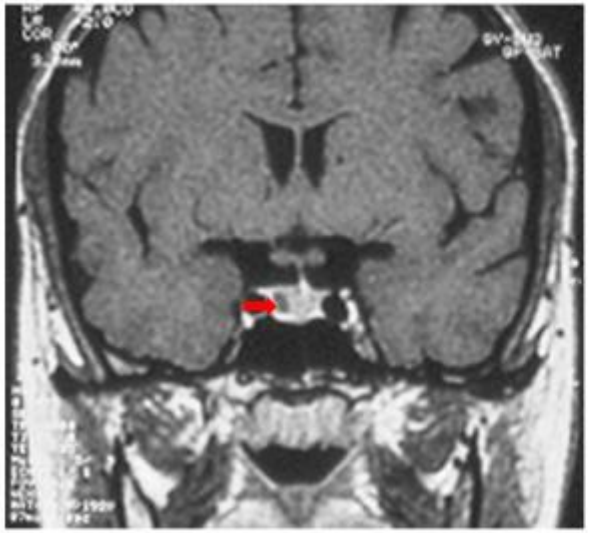
Source: Sherwood L et al (2011) Human Physiology: from cells to systems, 8th

Rappels prolactine

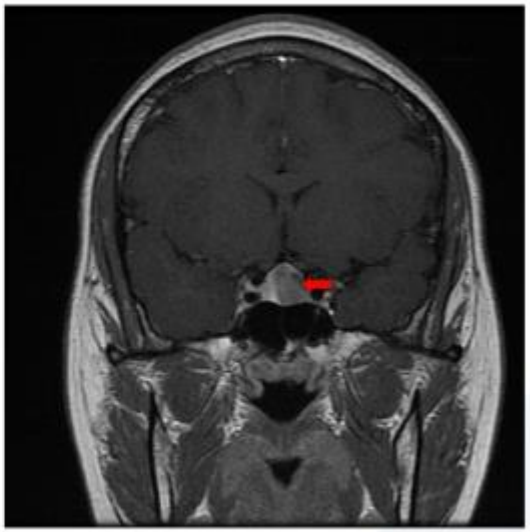
Causes d'hyperprolactinémie

- **Prolactinome**: tumeur pituitaire bénigne sécrétant de la prolactine ou adénome hypophysaire mixte (GH, ACTH, …)

Microadénome < 10 mm



Macroadénome > 10 mm



- Lésior
- Hypot
- Troub
- Lésior
- « Idiopathiques » (29% selon littérature comme microadénome non détecté par l'imagerie)

Source: Maiter D (2014) Apport de la biologie clinique aux principales maladies endocriniennes

Rappels prolactine

Causes d'hyperprolactinémie

Médicaments

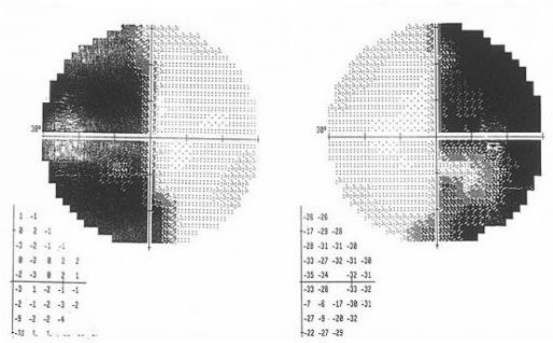
S. Nerveux	S. Gastro-intestinal	S. Cardiovasculaire	S. Hormonal
Neuroleptiques: - Classiques (sulpiride) - Atypiques - (risperid. > olenzapine > quétiapine)	**Antiémétiques:** Métoclopramide, dompéridone, alizapride	**Antihypertenseurs:** - Antagonistes du Ca^{2+} (vérapamil) - Action centrale (α-méthyldopa)	**Œstrogènes**
Antidépresseurs: Tricycliques, SSRI et IMAO	**Anti-H2 et IPP:** Cimétidine, ranitidine, oméproazole, …		**Progestérone**
Cocaïne			

Source: Maiter D (2014) Apport de la biologie clinique aux principales maladies endocriniennes

Rappels prolactine

Symptômes hyperprolactinémie

Femmes	Hommes
Oligo-aménorrhée (90%)	Gynécomastie
Galactorrhée (50%)	↘ caractères sexuels
Infertilité, ostéopénie	Infertilité, ostéopénie
↘ Libido, retard pubertaire, …	↘ Libido, impuissance
Symptômes compression	Symptômes compression ++

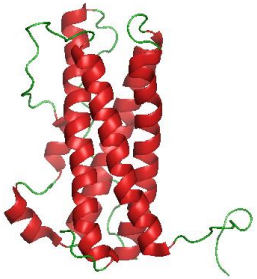


Source: Maiter D (2014) Apport de la biologie clinique aux principales maladies endocriniennes

Rappels prolactine

Structure prolactine

Gène prolactine



Polypeptide 227 a.a.

Prolactine 199 a.a.

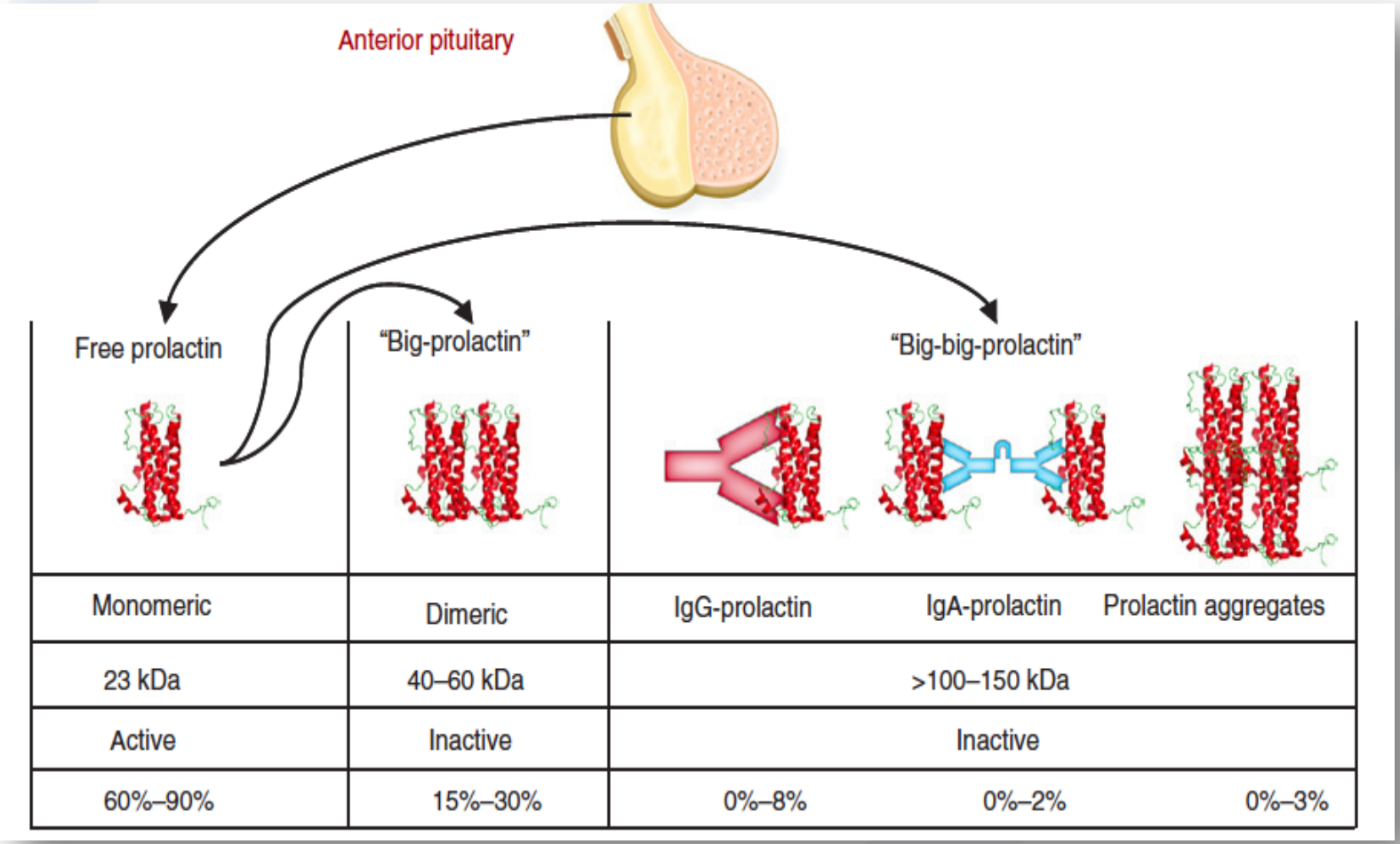
Peptide signal 28 a.a.

Monomérique	**23 kDa (65-85%) active**
Monomérique glycosylée	**25 kDa (25%) moins active**
Dimérique « Big prolactin »	**50-60 kDa (10-20%) inactive**
Macroprolactine « Big big prolactin »	**>150 kDa (<10%) inactive**

Source: Samson et al, Endocrine Practice Vol 21 No. 12 December 2015

Rappels prolactine

Structure prolactine



Monomeric	Dimeric	IgG-prolactin	IgA-prolactin	Prolactin aggregates
23 kDa	40–60 kDa	>100–150 kDa		
Active	Inactive	Inactive		
60%–90%	15%–30%	0%–8%	0%–2%	0%–3%

Source: Lippi and Plebani (2016) CCLM 54(4): 519-522

Macroprolactine

Quelques chiffres

- « Big big prolactin » de **150 kDa**
- Décrire pour la 1ère fois par ***Soong et al*** en **1982**
- Terme « Macroprolactinémie » utilisé la 1ère fois **par *Jackson et al*** en **1985**

  « Prédominance de formes circulantes avec un haut PM »
- **Prévalence**

  <1-4% dans p

  4-40% dans le
- **Inactive in vivo**

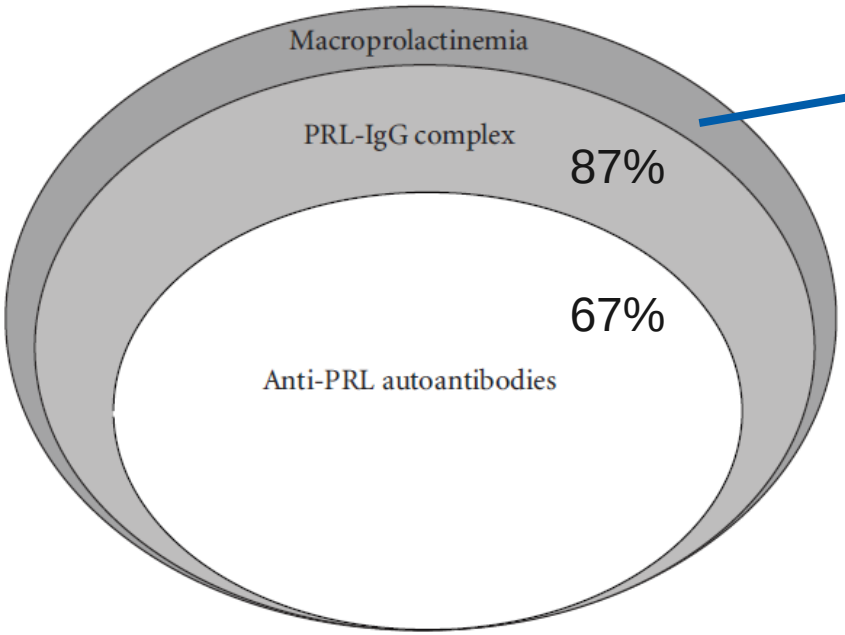
  Confinée en ir

  Ac interfèrent
- **Genèse**

  Impact de la p

  Hypo

  Circulation: sérine 195

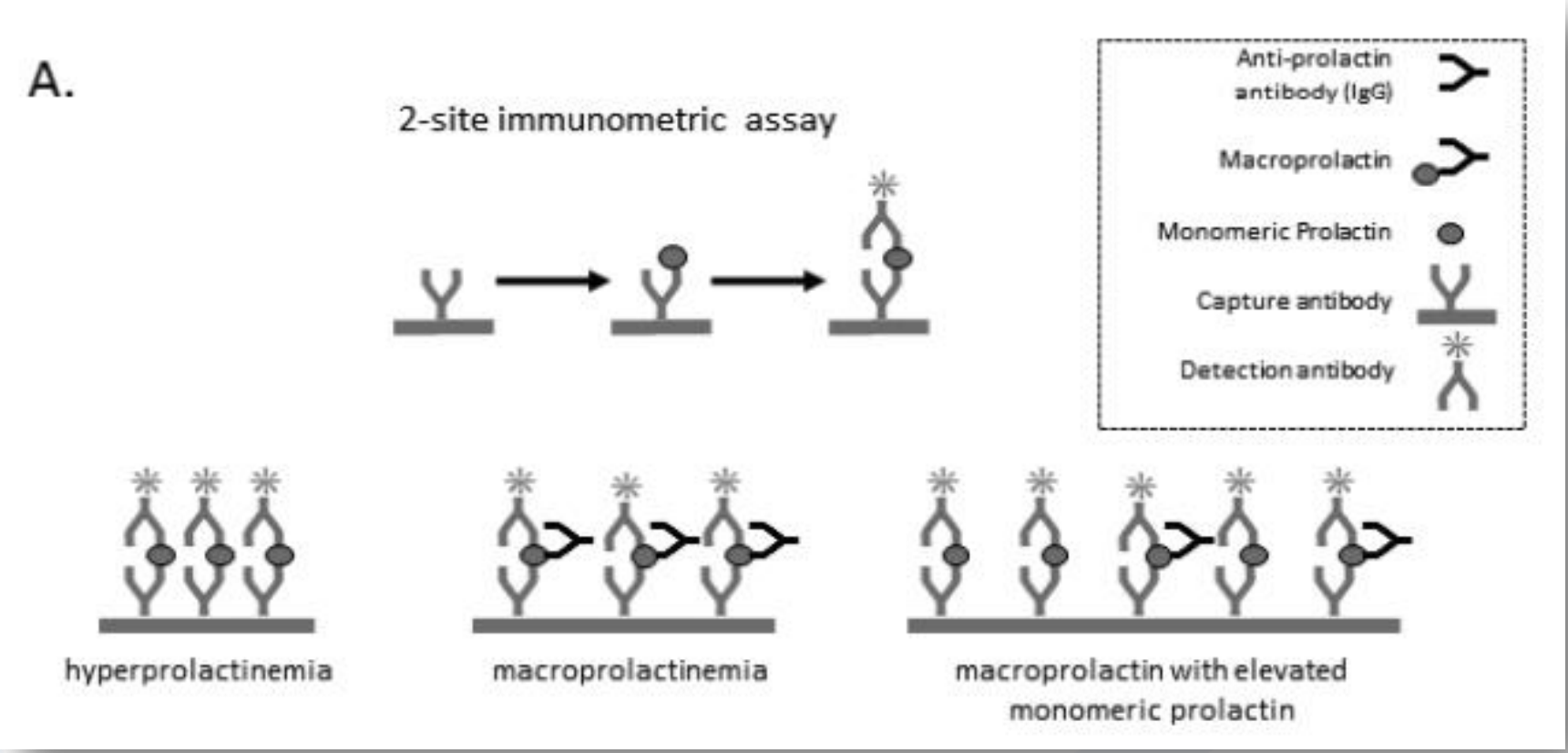


Complexe hyperglycosylé (**200-669** kDa)

Source: Shimatsu and Hattori (2012) Clin and Dev Imm, review article

Macroprolactine

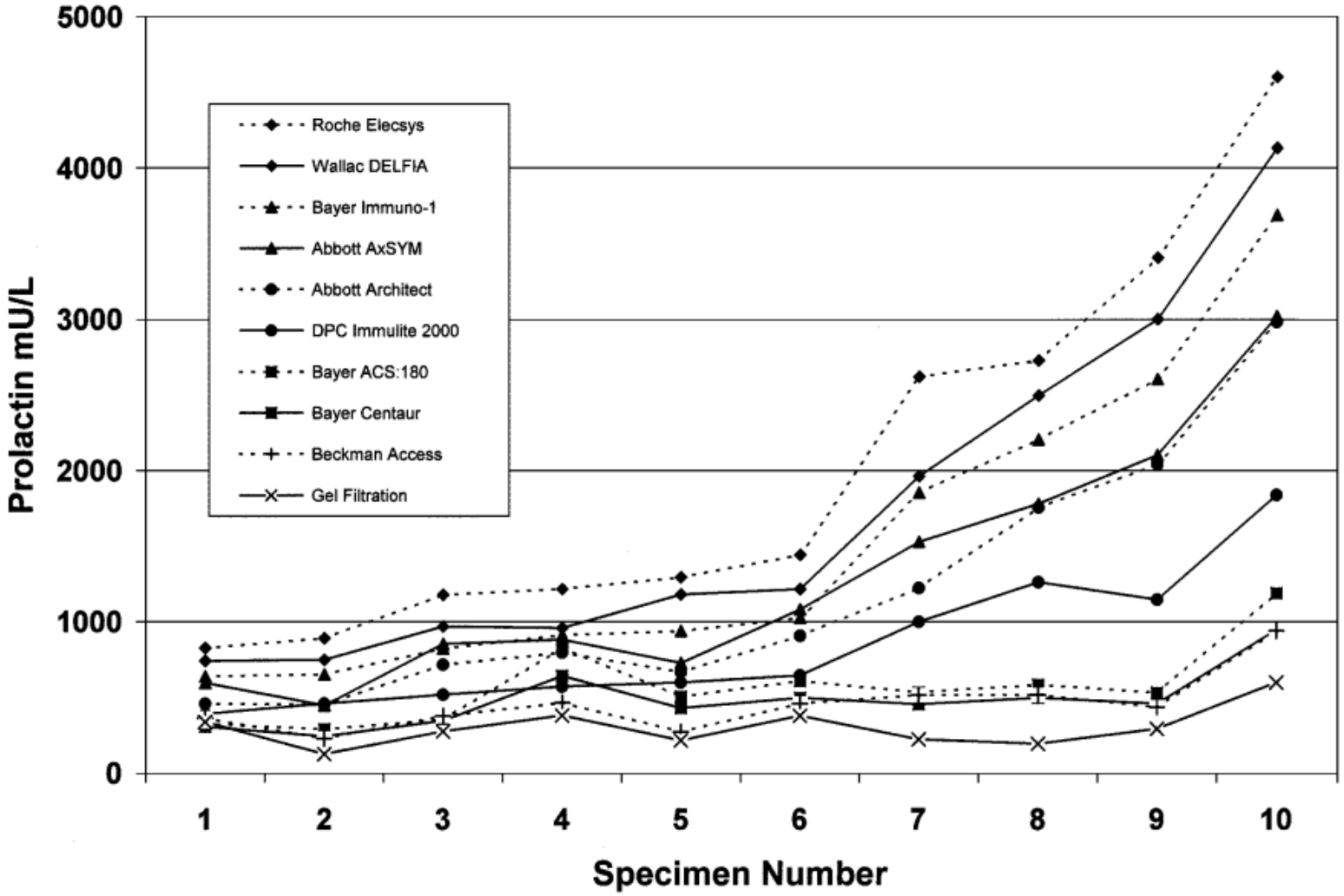
Immunodosages



Source: Samson et al, Endocrine Practice Vol 21 No. 12 December 2015

Macroprolactine

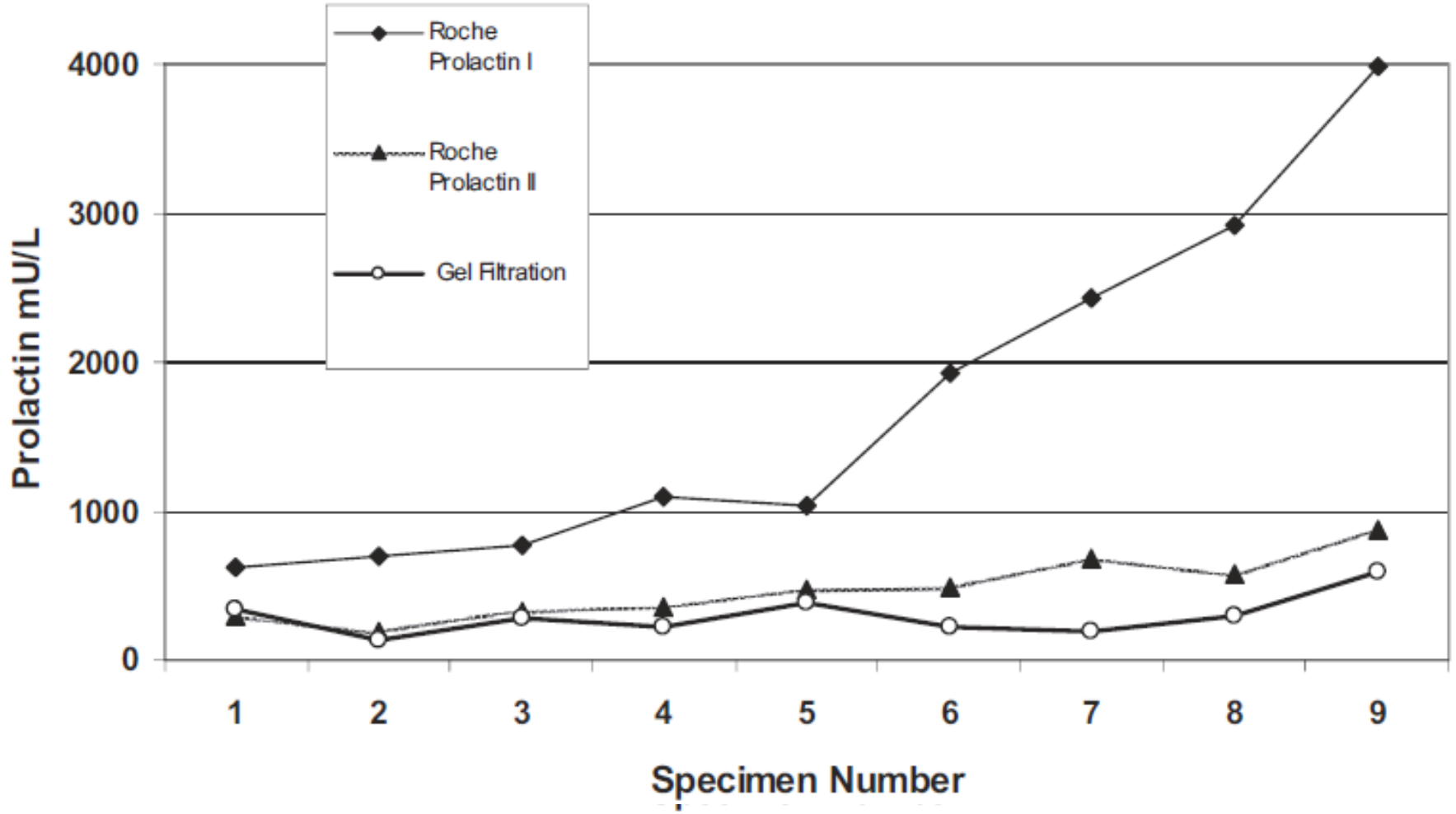
Immunodosages



Source: Smith et al (2002) J Clin Endocrinol Metab 87 (12):5410-5415

Macroprolactine

Immunodosages



Source: Fahie-Wilson et al (2013) Best Pr & Research Cl Endo & Met 27, 725-742

Macroprolactine

Immunodosages

Situation 1

PRL augmentée

+

MPRL absente

↓

HyperPRL vraie

↓

Prise en charge requise

Situation 2

PRL normale

+

MPRL présente

↓

HyperPRL fausse

↓

Prise en charge inutile

Source: Samson et al, Endocrine Practice Vol 21 No. 12 December 2015

Macroprolactine

Intérêts

- Imageries coûteuses
- Coûts de laboratoire
- Traitements pharmacologiques et actes chirurgicaux inappropriés

Recommandations

- **McCudden et al. 2010:** ≤ 85 ng/mL
- **Beda-Maluga et al. 2014:** ≤ 100 ng/mL
- **The Pituitary Society:** 25-150 ng/mL
- **The Endocrine Society:** seulement les cas asymptomatiques
- **AACE/ACE Disease State 2015:** dans tous les cas d'hyperPRL
    - Haute prévalence (**4-40%**)
    - Mauvaise discrimination sur base de la clinique seule (Gibney 2005, Alfonso 2006)

      Estradiol, LH, LH/FSH

      Oligo/aménorrhée et galactorrhée

Source: Samson et al, Endocrine Practice Vol 21 No. 12 December 2015

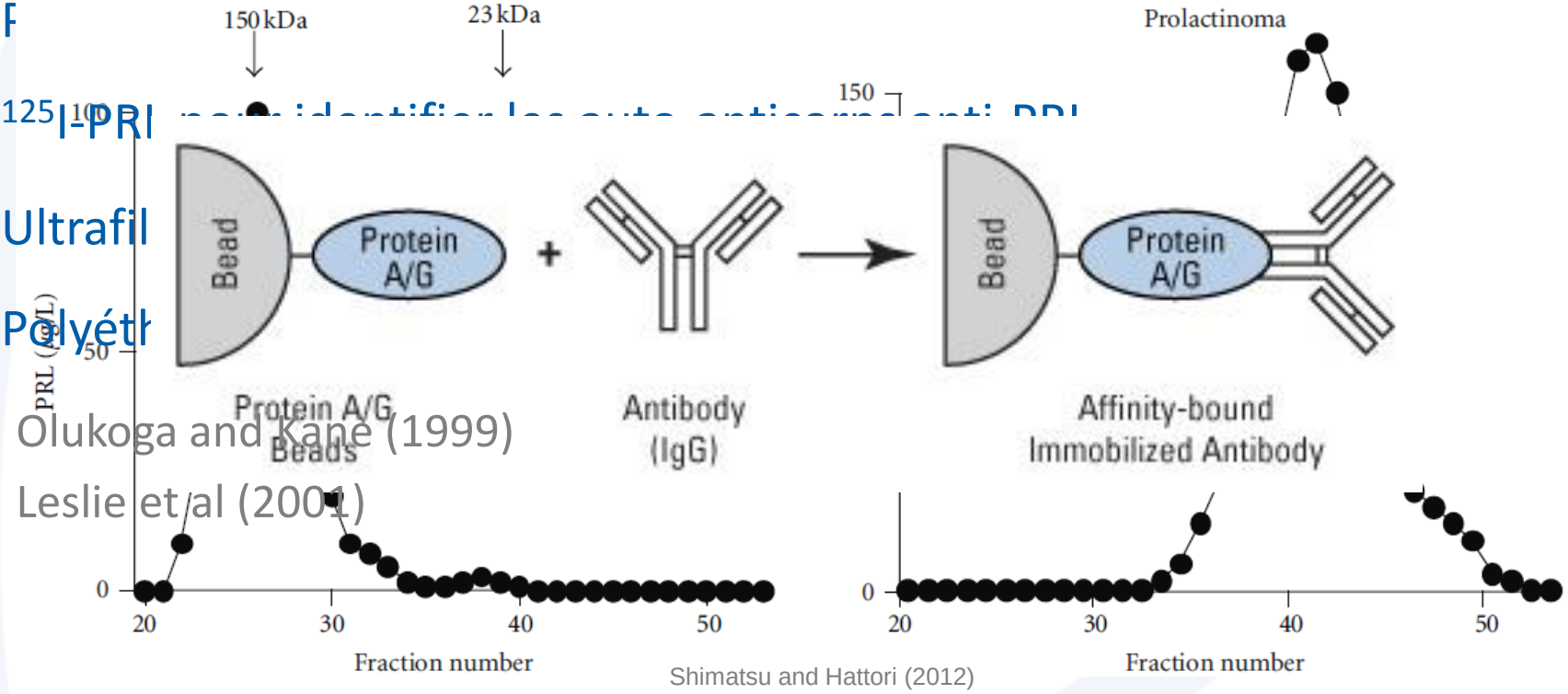
Macroprolactine

Rechercher la MPRL

- Chromatographie filtration sur gel (GFC) « Gold Standard »
- F
- 125-PRL pour identifier les auto anticorps anti-PRL
- Ultrafil
- Polyéth

Olukoga and Kane (1999)

Leslie et al (2001)



Shimatsu and Hattori (2012)

Source: Shimatsu and Hattori (2012) Clin and Dev Imm, review article

Macroprolactine

Rechercher la MPRL

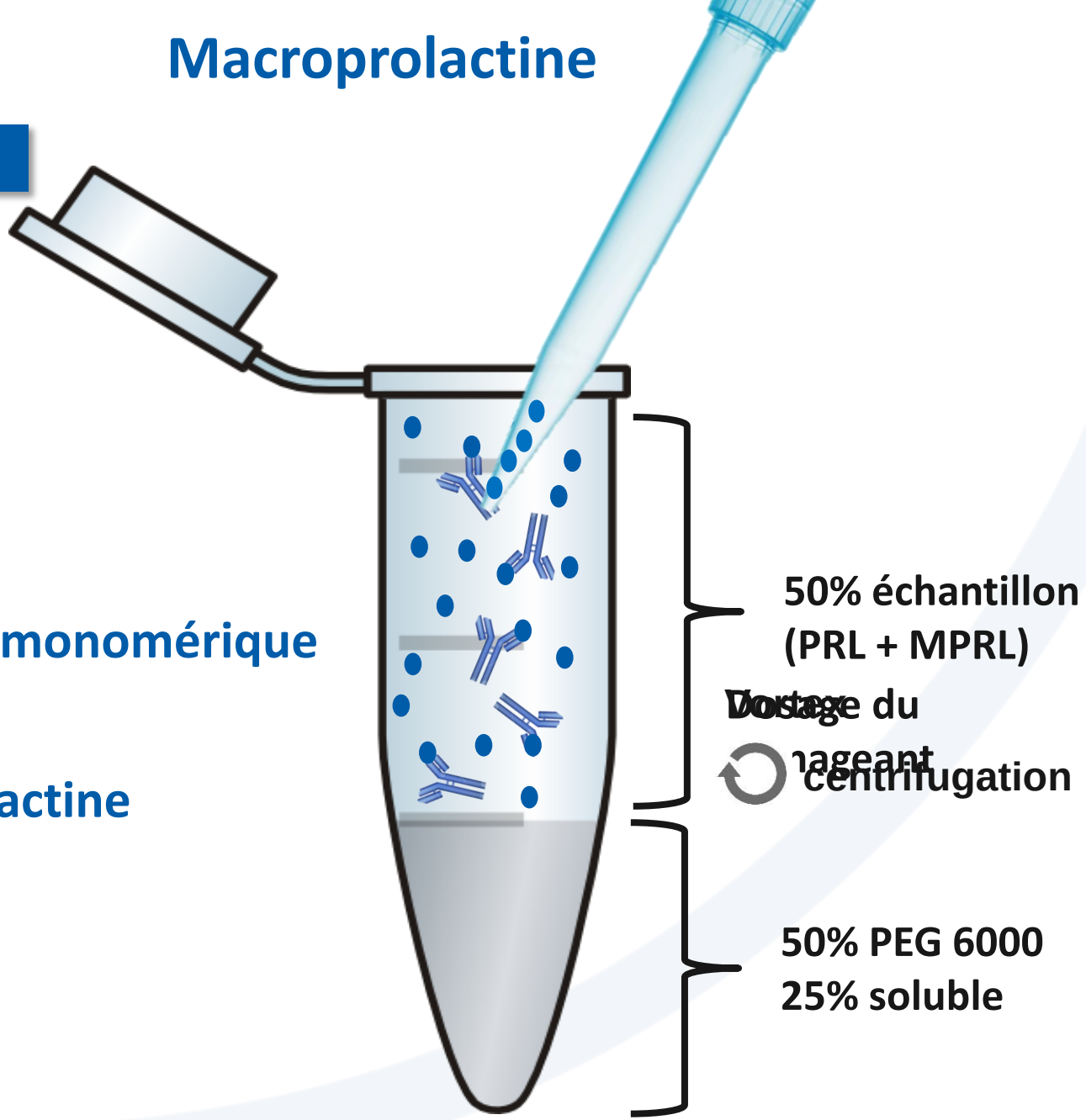
Table 1. Comparative mean (SD) values for prolactin together with method correlation coefficients and cost in the 42 macroprolactinemic sera subjected to a variety of separation procedures.

Separation method	Monomeric prolactin, mIU/L	Residual prolactin		Correlation coefficient vs GFC	Cost per specimen, US $
		mIU/L	%		
GFC	290 (108)		100		275.00
PEG		218 (90)	75	0.80	11.00
UF		324 (194)	112	0.61	16.00
PA		517 (283)	178	0.72	26.00
PG		438 (194)	151	0.78	28.00
Anti-hIgG		516 (190)	178	0.70	20.00

Source: Kavanagh (2006) Clinical Chemistry 52, No. 7

Macroprolactine

Rechercher la MPRL

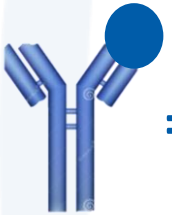


= Prolactine monomérique

= Macroprolactine

Macroprolactine

Rechercher la MPRL



= Prolactine monomérique

= Macroprolactine

Dosage

Macroprolactine

Rechercher la MPRL

1. Calcul d'un Recovery (%)

$$\frac{(\text{Concentration PRL postPEG} * 2)}{\text{Concentration PRL prépEG}}$$

- Exemple:

- **1er** dosage en prolactine à **70 ng/mL**
- Traitement PEG6000
- **2ème** dosage du surnageant à **9 ng/mL**
- Calcul du Recovery:

  [(9*2)/70]*100 = **25,7%**

Macroprolactine

Rechercher la MPRL

1. Calcul d'un Recovery (%)

$$\frac{(\text{Concentration PRL postPEG} * 2)}{\text{Concentration PRL prépEG}}$$

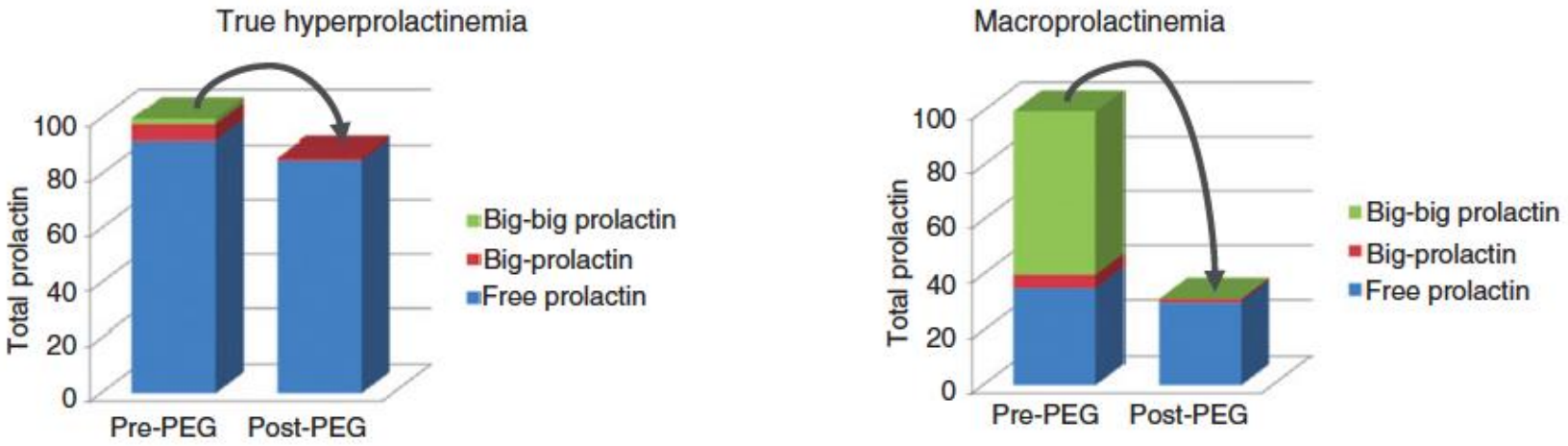


Figure 1: Synthesis and structure of free (monomeric) prolactin, big-prolactin and big-big-prolactin. PEG, poly-ethylene-glycol.

Source: Lippi and Plebani (2016) CCLM 54(4): 519-522)

Macroprolactine

Rechercher la MPRL

1. Calcul d'un Recovery (%)

$$\frac{(\text{Concentration PRL postPEG} * 2)}{\text{Concentration PRL prépEG}}$$

1) **Recovery < 40%**
= Macroprolactinémie significative

2) **Recovery 40 – 60%**
= Macroprolactinémie possible

?????

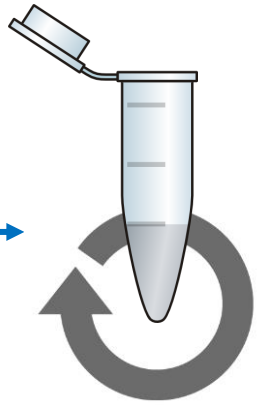
3) **Recovery > 60%**
= Absence de macroprolactinémie

Macroprolactine

Rechercher la MPRL

2. Valeurs référence post-PEG

Population sujets sains



Echantillon patient + PEG (50/50)

Valeurs de référence post-PEG (déterminé dans le surnageant)

>< valeurs référence fournisseurs car perte de 20-25% en PRL monomérique active !!!!

1) Valeur patient post-PEG comprise dans l'intervalle → Absence d'hyperPRLémie

2) Valeur patient post-PEG supérieur aux VR → HyperPRLémie vraie

Macroprolactine

Rechercher la MPRL

2. Valeurs référence post-PEG

Sexe	Race	Age		pré-PEG (ng/mL)	post-PEG (ng/mL)	post-PEG*2 (ng/mL)	pré-PEG (mIU/L)	post-PEG (mIU/L)	post-PEG*2 (mIU/L)
H	Caucasian	26	**C1**	6,19	2,27	4,54	131,228	48,124	96,248
H	Caucasian	52	**C2**	8,82	3,42	6,84	186,984	72,504	145,008
F	Caucasian	37	**C3**	32,32	13,63	27,26	685,184	288,956	577,912
F	Caucasian	31	**C4**	10,44	4,61	9,22	221,328	97,732	195,464
H	Caucasian	43	**C5**	4,03	1,86	3,72	85,436	39,432	78,864
H	Caucasian	30	**C6**	4,04	1,76	3,52	85,648	37,312	74,624
F	Caucasian	23	**C7**	7,52	3,12	6,24	159,424	66,144	132,288
F	Caucasian	34	**C8**	4,89	2,11	4,22	103,668	44,732	89,464
H	Caucasian	36	**C9**	3,98	1,58	3,16	84,376	33,496	66,992
F	Caucasian	54	**C10**	8,97	3,62	7,24	190,164	76,744	153,488
F	Caucasian	44	**C11**	6,6	2,69	5,38	139,92	57,028	114,056
F	Caucasian	55	**C12**	10,27	4,09	8,18	217,724	86,708	173,416
F	Caucasian	25	**C13**	6,37	2,63	5,26	135,044	55,756	111,512
F	Caucasian	37	**C14**	5,88	2,42	4,84	124,656	51,304	102,608
F	Caucasian	52	**C15**	6,39	2,62	5,24	135,468	55,544	111,088
F	Caucasian	27	**C16**	5,33	2,18	4,36	112,996	46,216	92,432

Macroprolactine

Rechercher la MPRL

2. Valeurs référence post-PEG

Table 3. Parametric reference intervals for post-PEG prolactin (mIU/L) in male and female sera for each immunoassay platform.

	Male range		Female range	
Analyzer	Lower	Upper	Lower	Upper
Centaur	61	196	66	278
Elecsys	63	245	75	381
Access	70	301	92	469
Architect	72	229	79	347
AIA	73	247	83	383
Immulite	78	263	85	394

Source: Bestran et al (2008) Clin Chem 54/10, 1673-1681

Macroprolactine

Défaut recovery (%)

Situation 1

PRL augmentée

+

MPRL absente

↓

HyperPRL vraie

↓

Prise en charge requise

Situation 2

PRL normale

+

MPRL présente

↓

HyperPRL fausse

↓

Prise en charge inutile

Situation 3

PRL augmentée

+

MPRL présente

↓

HyperPRL vraie

↓

Prise en charge requise

Source: Samson et al, Endocrine Practice Vol 21 No. 12 December 2015

Macroprolactine

Défaut recovery (%)

Beda-Maluga et al 2014 (Immulite 1000®)

245 patients (PRL > 30ng/mL)

21 patients (Recovery ≤ 40%)

224 patients (Recovery > 40%)

14 avec **hyperPRL**

219 avec **hyperPRL**
5 avec **pseudohyperPRL**

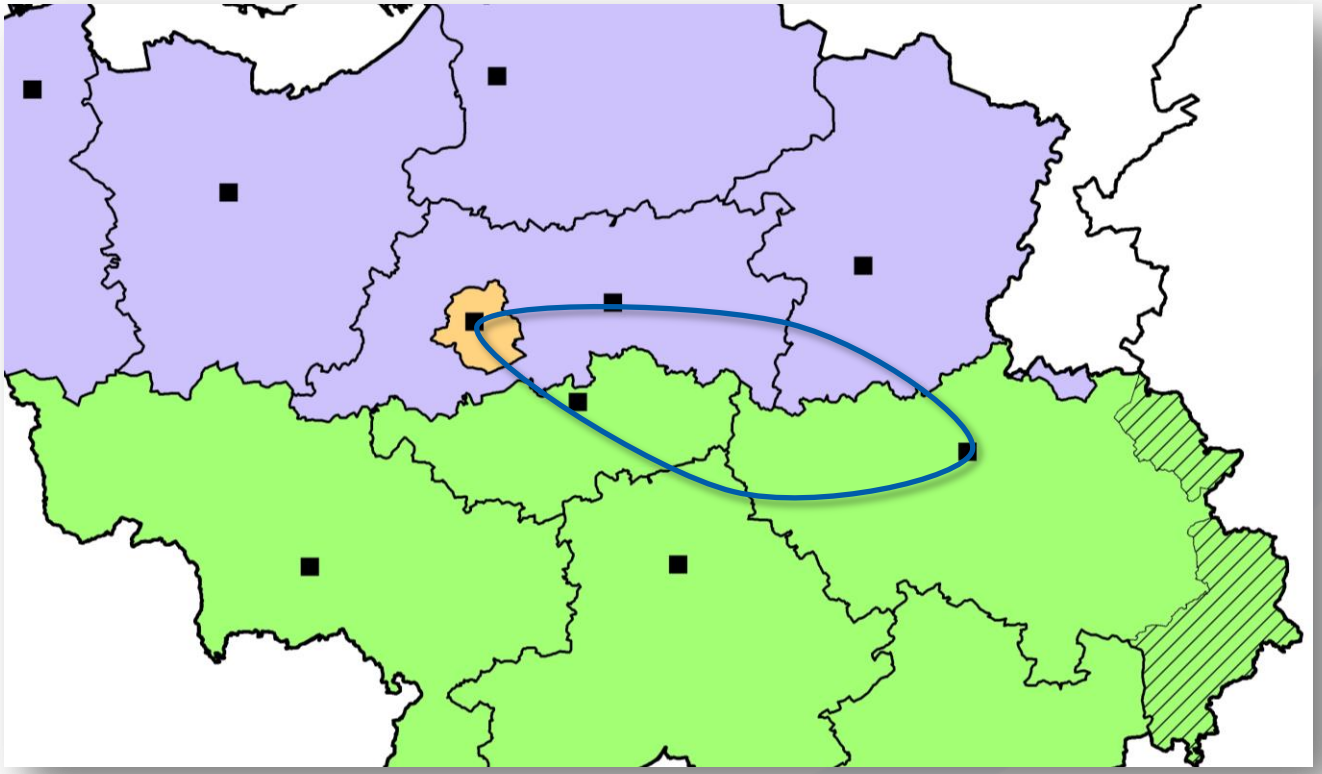
	Women	Men
Manufacturer's reference ranges for PRL [ng/mL]	1.9 – 25	2.5 – 17
Ranges for PRL concentration after macroforms separation [ng/mL]	1.5 – 20	2 – 13.6

Source: Beda-Maluga et al, Journal of Physiology and Pharmacology Vol 65 No. 3, 359-364, 2014

Macroprolactine

Validation

- **Sous-traitance CHU Liège**



Source: http://www.enseignement.be/index.php?page=23827&do_id=3143&do_check=

Macroprolactine

Validation

- **Sous-traitance CHU Liège**

Intervalle screening	30-100 ng/mL
Dosage	ECLIA module E170
Volume échantillon	300 µL
Traitement PEG	2 minutes, 14.500 rpm
Stabilité PEG	7 jours
Rendu des résultats	Recovery (%)

Macroprolactine

Validation

- **Multitude de méthodes de précipitation au PEG**

Vieira 1998
To 250 mL of se
mixed them for
temperature). PE

Olukoga 1999
Polyethylene glycol, 200 µl, molecular weight 6000 (PEG 6000) (25% w/w) was added to 200
r 30 min at 4°C.

Sapin 2001
PEG precipitation was performed according to Fahie-Wilson and Soule [10]. Five hundred
C. Prolactin was
microliters of a 25% PEG 6000 solution was added at room temperature (20–25°C) to 500 µL serum. Prolactin
of serum and af

Leslie 2001
) and patients'

Beltran 2008
All sera were also treated with PEG (15). Briefly, 250µL of sera, mixed with an equal volume
as measured in
of PEG 6000 (VWR International UK, product 29577), 250 g/L in PBS (Sigma, 137 mmol/L
obtained from
sodium chloride, 10 mmol/L sodium phosphate), pH 7.4, was incubated for 10 min at room
temperature. T

Shimatsu 2012
prolactin meas
To determine free PRL concentrations, serum samples (50 µL) are mixed vigorously with 50 µL
than 14 days a
of cold PEG (molecular weight 6000, 25% in water) and centrifuged at 9,100 ×g for 10 min to

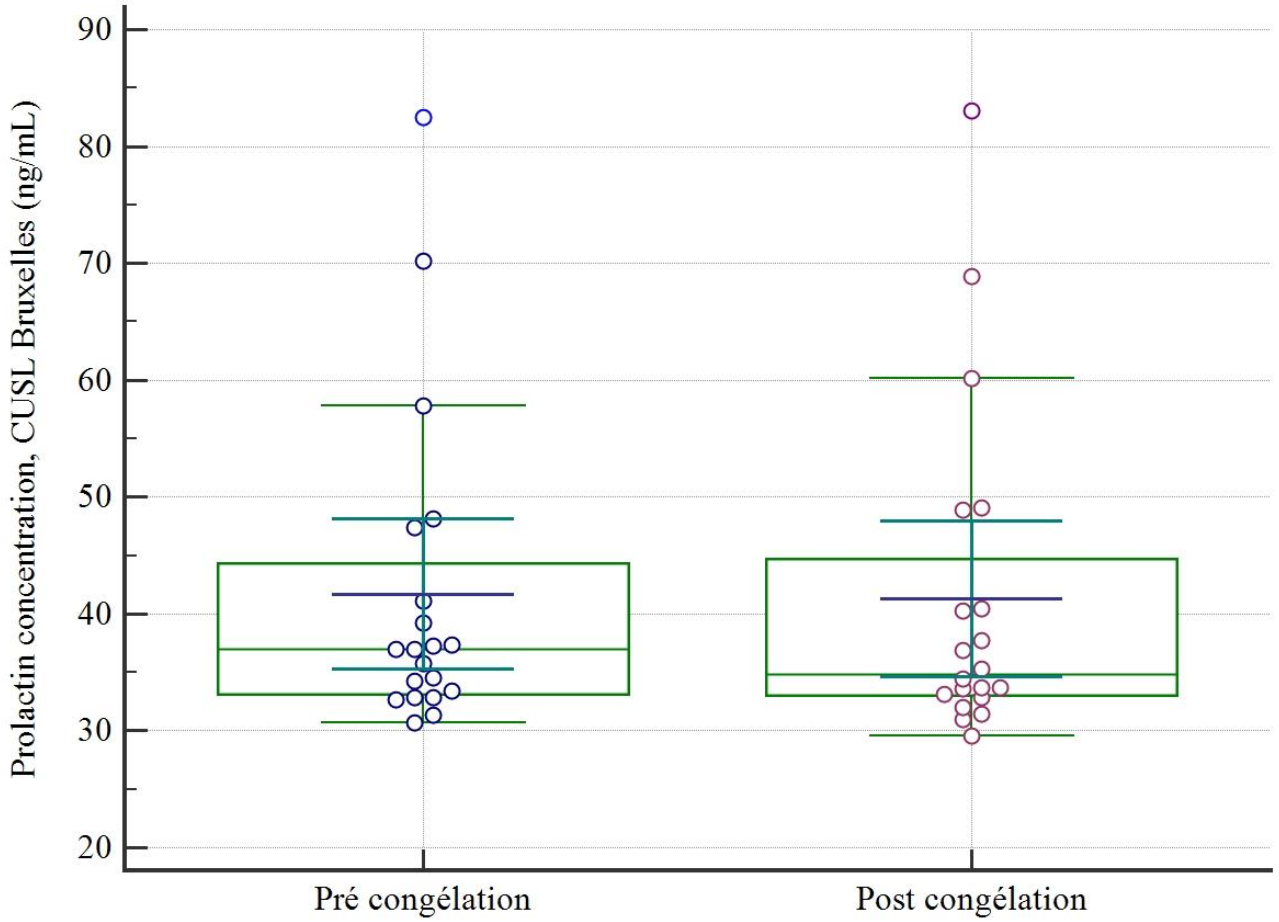
Beda-Maluga 2014
Equal volumes o
temperature for 1
after this procedu

Chen 2016
PEG treatment of serum samples and calculations of PRL recovery: An equal quantity of 25% PEG was added to 200 µl of the PRL-elevated serum sample. After full mixing, the mixture was centrifuged at 1500xg for 30 minutes, and then the supernatant was isolated for PRL analysis. The PRL recovery was calculated using the following formula: (2xPRL level following PEG treatment/PRL level before PEG treatment) x 100%.

Macroprolactine

Validation

- **Décongélation**



Wilcoxon test
P = 0.81
n = 20

Macroprolactine

Validation

Solution PEG

Reporting of post-polyethylene glycol prolactin: precipitation by polyethylene glycol 6000 or polyethylene glycol 8000 will change reference intervals for monomeric prolactin.

Veljkovic K[1], Servedio D, Don-Wauchope AC.

⊕ Author information

Abstract

BACKGROUND: When screening for macroprolactin, many laboratories use precipitation by polyethylene glycol (PEG) with molecular weight 6000 (PEG6000) or 8000 (PEG8000), and report the percentage prolactin recovery. It has been proposed that reporting of percentage prolactin recovery should be replaced by absolute post-PEG prolactin; however, the post-PEG prolactin reference interval has been established using PEG6000 only. We sought to determine whether the use of PEG8000, instead of PEG6000, changed post-PEG prolactin concentrations.

METHODS: We compared the post-PEG6000 and post-PEG8000 prolactin concentrations in hyperprolactinaemic serum samples referred for macroprolactin screening (n=40), using Passing-Bablok regression analysis and Bland-Altman difference plot.

RESULTS: The median (25th-75th percentile, range) total prolactin, post-PEG6000 and post-PEG8000 prolactin concentrations were, respectively, 36 (31-46, 23-83) µg/L, 27 (20-38, 18-72) µg/L and 24 (18-35, 16-64) µg/L for male serum samples (n=5); and 56 (39-83, 24-596) µg/L, 45 (31-67, 8-503) µg/L and 41 (28-62, 6-457) µg/L for female serum samples (n=35) (mIU/L conversion factor: 21.2). The Passing-Bablok analysis demonstrated a significant constant bias of -1.27 and a non-significant proportional bias of 0.96. The Bland-Altman plot showed a bias of -8.2% (95% limits of agreement -19.3-2.9%).

CONCLUSIONS: There is a significant constant bias between the two macroprolactin precipitation methods. We changed our PEG precipitation to a PEG6000 method. Laboratories that use PEG8000 should consider the transference of the reference interval established with PEG6000 carefully.

Macroprolactine

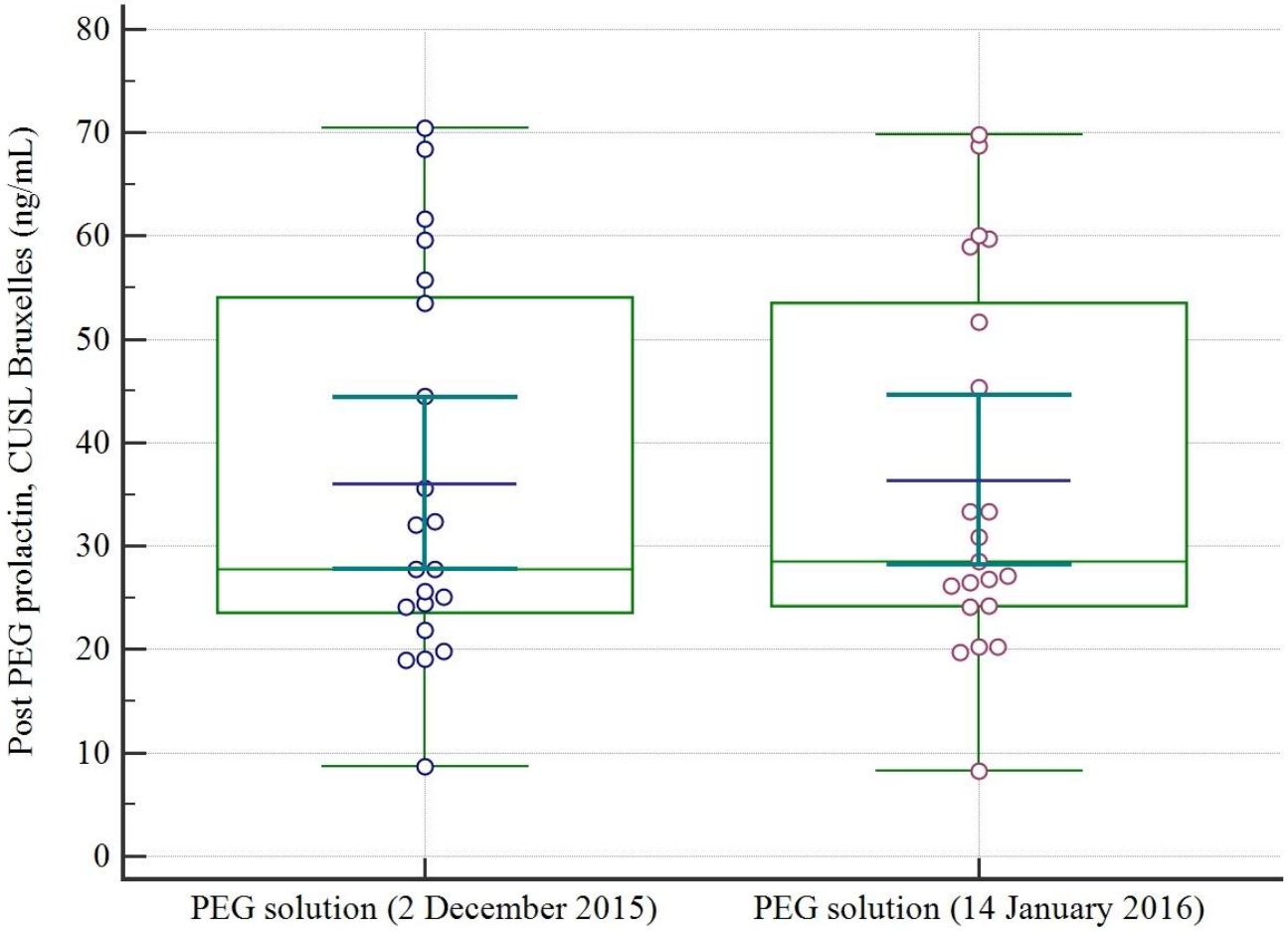
Validation

10 minutes

Macroprolactine

Validation

- **Stabilité solution PEG 6000 – 44 jours**

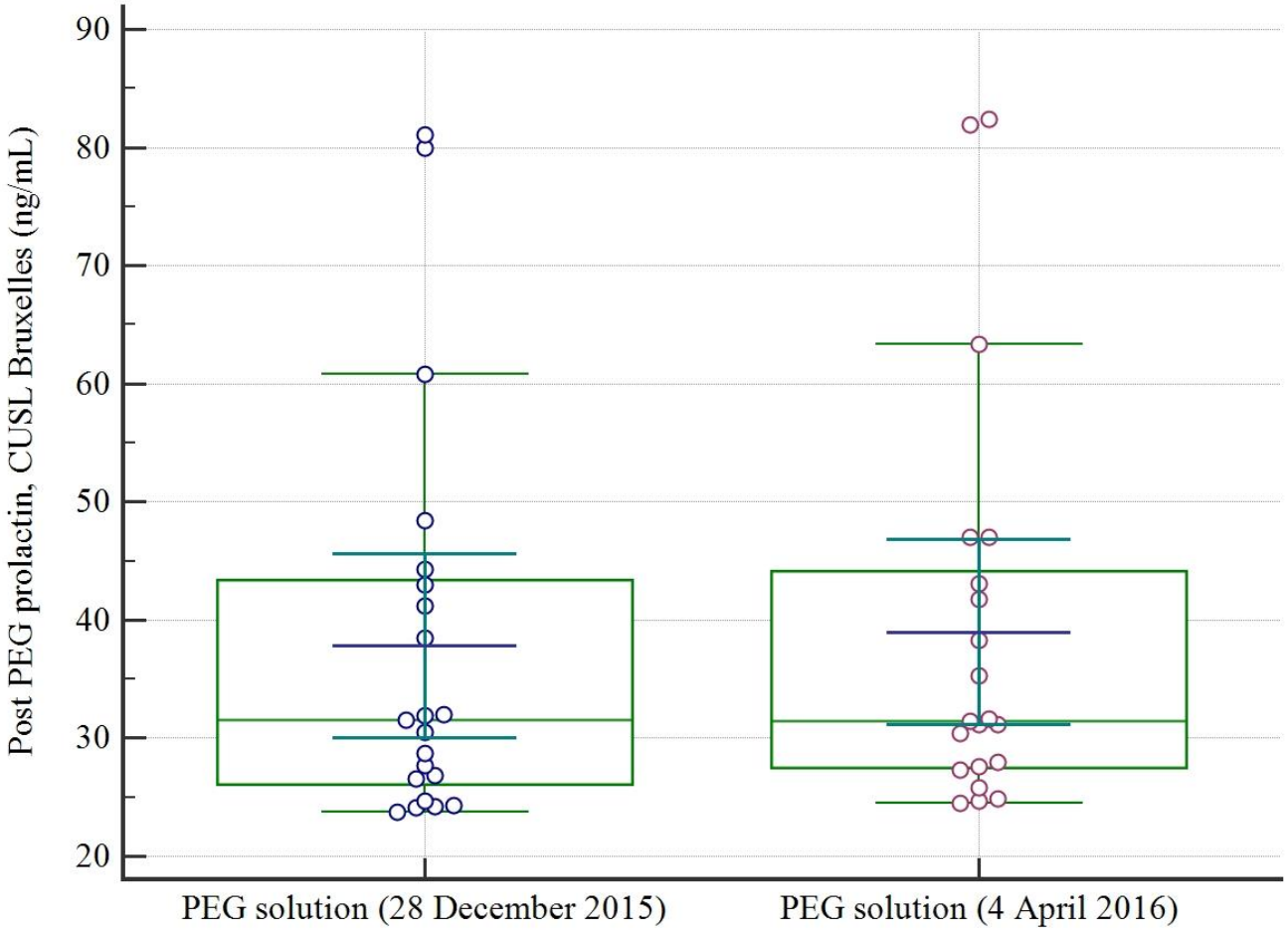


Paired samples
t-test
P = 0.48
n = 21

Macroprolactine

Validation

- **Stabilité solution PEG 6000 – 99 jours**



Paired samples t-test
P = 0.02
n = 21

Macroprolactine

Validation

- **Stabilité solution PEG 6000 – 99 jours**


JAMES WESTGARD

Desirable Specifications for Total Error, Imprecision, and Bias, derived from intra- and inter-individual biologic variation

This most recent and extensive listing of biologic goals has been provided by Ricos C, Alvarez V, Cava F, Garcia-Lario JV, Hernandez A, Jimenez CV, Minchinela J, Perich C, Simon M. "Current databases on biologic variation: pros, cons and progress." Scand J Clin Lab Invest 1999;59:491-500. *This database was most recently updated in 2014.*

	Analyte	Number of papers	Biological Variation		Desirable specification		
			CV_I	CVg	I(%)	B(%)	TE(%)
S-	Prolactin	4	23.0	35.0	11.5	10.5	29.4

Macroprolactine

Validation

- **Comparaison CUSL Bruxelles – standard method (*Leslie et al. 2001*)**

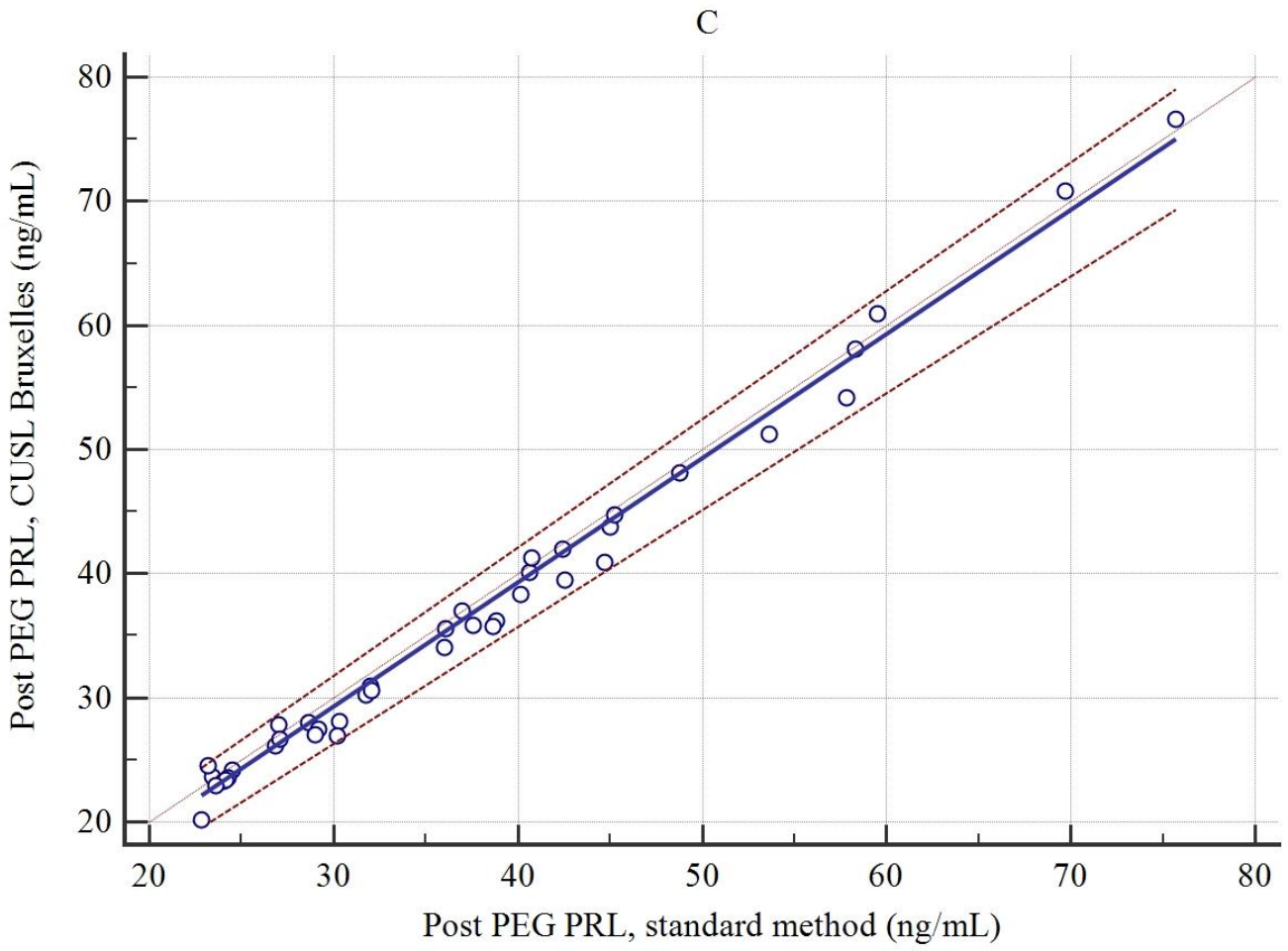
PEG precipitation test

Equal volumes (200 µL) of a 25% solution of PEG (molecular mass 6000 kDa) and patients' sera were mixed and centrifuged at 1500 × *g* for 30 min. Immunoreactive PRL was measured in the supernatant, and the results after correction for dilution compared with those obtained from unprecipitated serum. The results were expressed as the percent of PRL recovery. Recovery less than or equal to 40% was taken as evidence that a significant level of macroprolactin was present in the serum. Two patient samples, with macroprolactin present, were each submitted to 10 PEG precipitation tests. The within-assay CV for PRL recoveries were 3.7% and 2.7%, respectively.

Macroprolactine

Validation

- **Comparaison CUSL Bruxelles – standard method (*Leslie et al. 2001*)**



n = 40

Macroprolactine

Validation

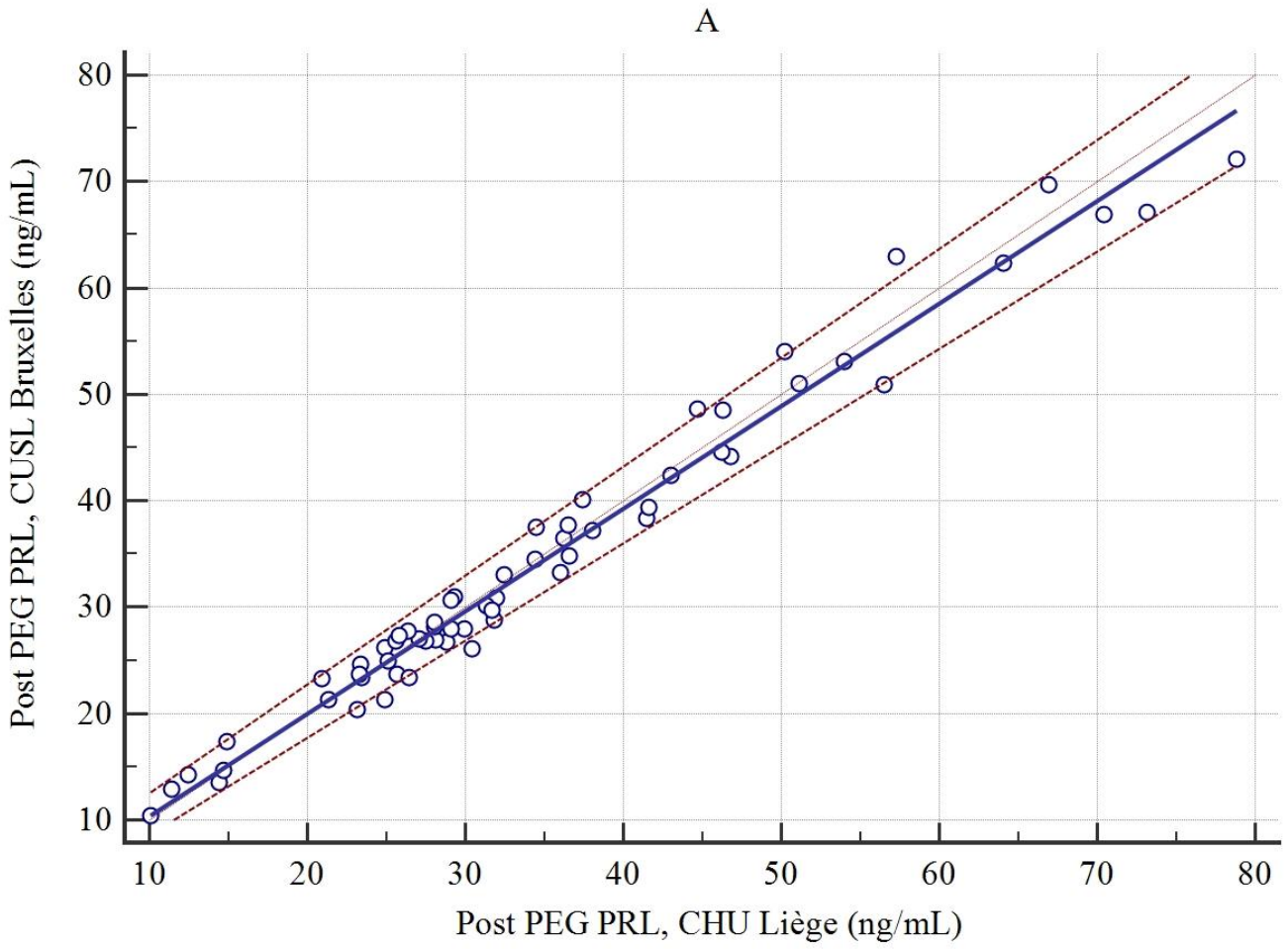
- **Comparaison CUSL Bruxelles – CHU Liège**

	CHU Liège	CUSL Bruxelles
Dosage	ECLIA module E170	ECLIA module E602
Volume échantillon	300 µL	100 µL
Traitement PEG	2 minutes, 14.500 rpm	2 minutes, 14.500 rpm
Stabilité PEG	7 jours	99 jours
Rendu des résultats	Recovery (%)	Recovery (%) & valeurs référence post PEG

Macroprolactine

Validation

- **Comparaison CUSL Bruxelles – CHU Liège**

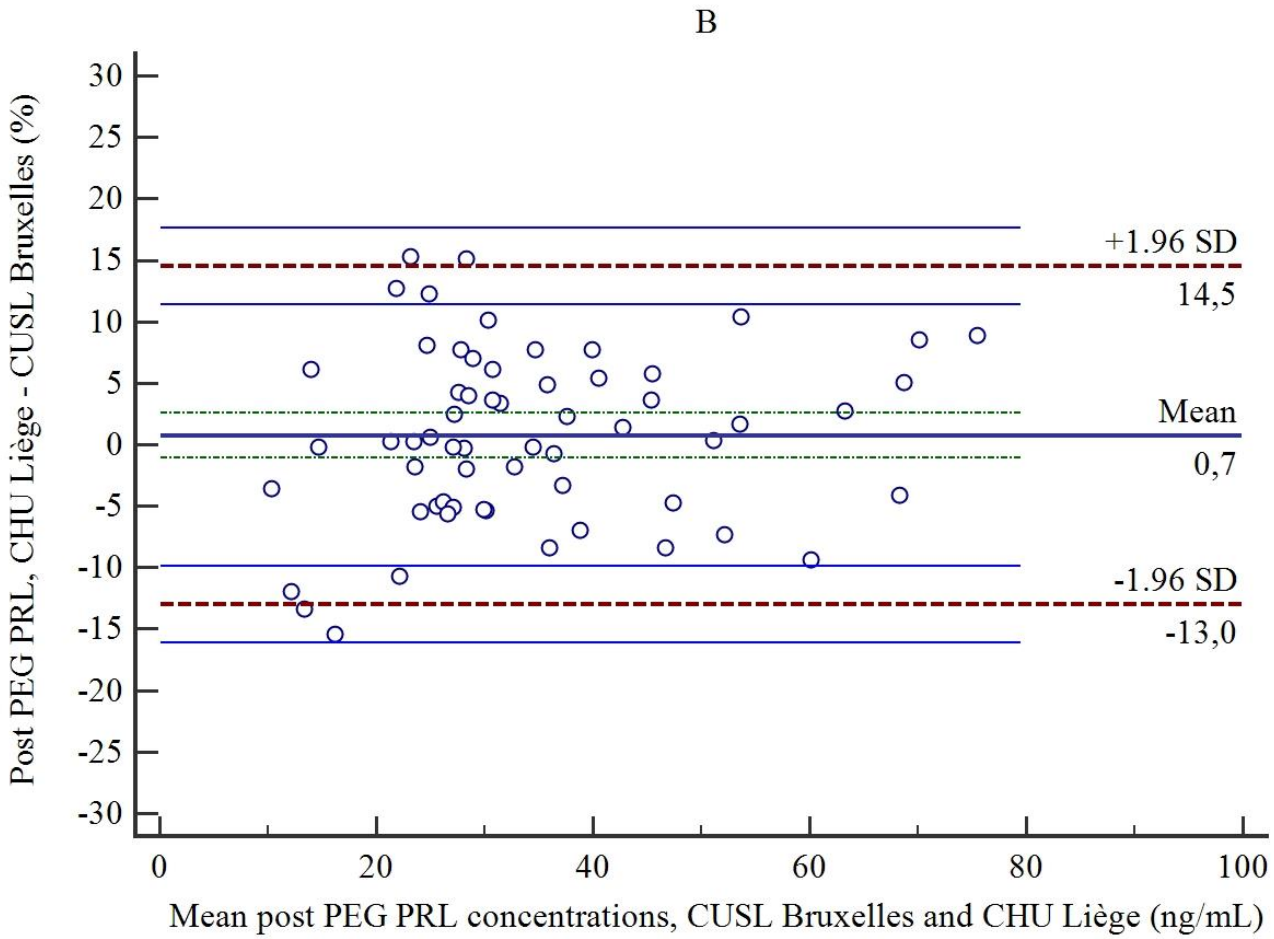


r = 0.975
n = 61

Macroprolactine

Validation

- **Comparaison CUSL Bruxelles – CHU Liège**



Macroprolactine

Validation

Comparaison CUSL Bruxelles – CHU Liège

Patient	Pré PEG PRL (ng/mL)	Recovery, Bxl (%)	Recovery, Liège (%)	Post PEG PRL, Bxl (ng/mL)	Post PEG PRL, Liège (ng/mL)
1	32,06	54,34	46,55	17,42	14,92
2	43,45	32,73	28,64	14,22	12,44
3	43,91	56,21	53,22	24,68	23,37
4	43,25	61,97	59,16	26,8	25,59
5	68,88	41,52	40,72	28,6	28,05
6	32,29	41,87	44,53	13,52	14,38
7	31,11	33,56	32,39	10,44	10,08
8	38,84	37,80	37,72	14,68	14,65
9	31,01	41,47	36,81	12,86	11,42

Valeurs de référence post PEG

- Informations plus pertinentes (40-60%)
- Evite les MPRL associée à une vraie hyperPRL

Macroprolactine

Cas clinique

- Femme de 37 ans, 55 kg, 1m 59
- Hyperprolactinémie à trois reprises (**38,3 ng/mL** le 25/11/2015; **38,9 ng/mL** le 9/12/2015 et **29,4 ng/mL** le 4/02/2016)
- LH, FSH, thyroïde, cycles, médicaments, etc…: **RAS**.
- PDF du rapport IRM hypophyse.
- Prescription de Sosital 0,5 mg ½ co 2x/sem.
- Recovery = **37,8%**, valeur prolactine post PEG = **14,65 ng/mL**.

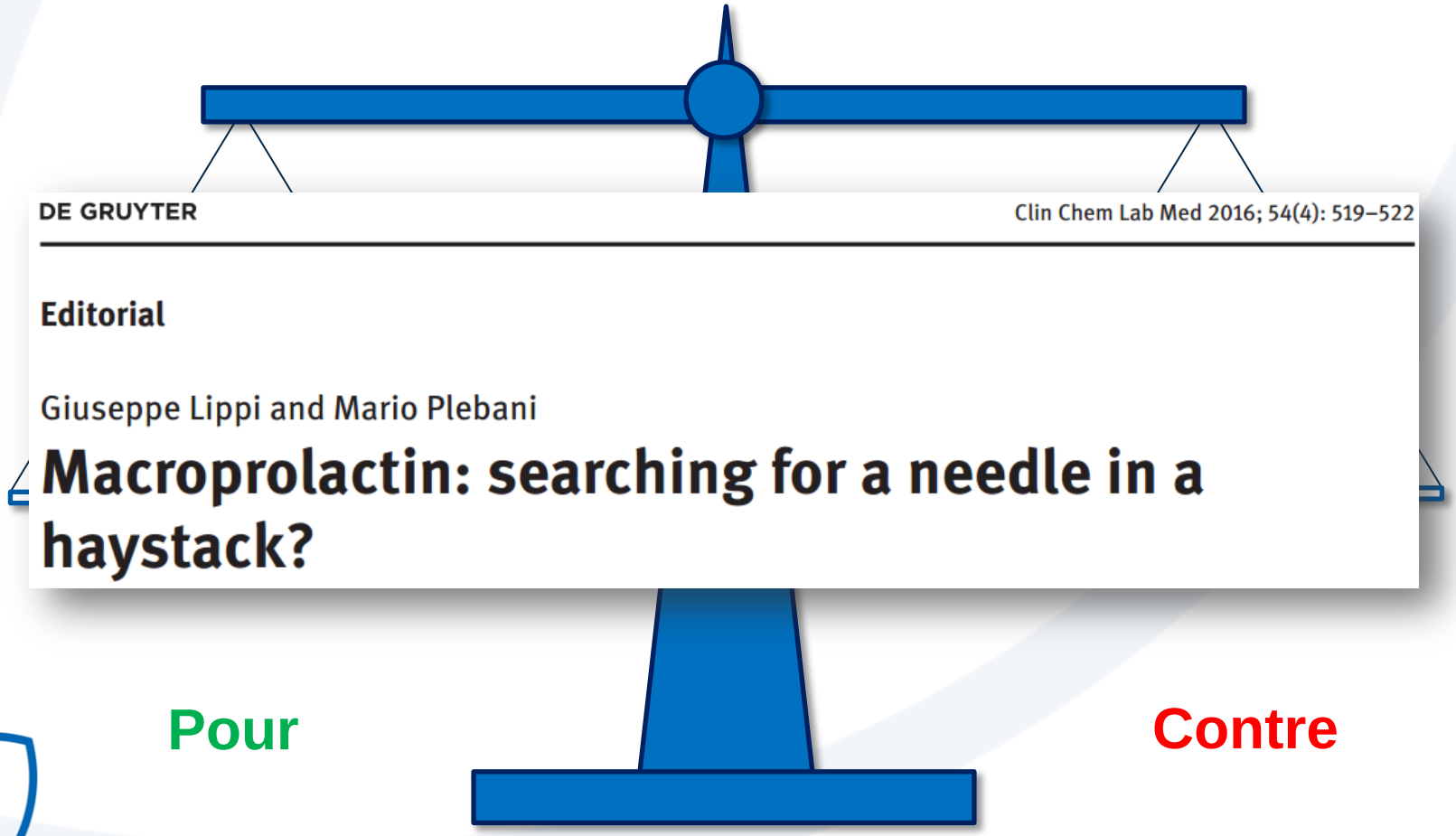
- MPRL et ratio PRL stable jusqu'à 17 ans.

Source: Shimatsu and Hattori (2012) Clin and Dev Imm, review article

Macroprolactine

Validation

- **Comparaison CUSL Bruxelles – CHU Liège**



DE GRUYTER Clin Chem Lab Med 2016; 54(4): 519–522

Editorial

Giuseppe Lippi and Mario Plebani

Macroprolactin: searching for a needle in a haystack?

Pour

Contre

Conclusion

1. Prévalence variable (**4-40%**)
2. Rechercher la MPRL chez **tous les cas** d'hyperPRL?
3. Screening avec le **PEG 6000** (meilleur rapport qualité/prix)
4. Confirmation toujours possible par **GFC** (Gold Standard)
5. Préférer les valeurs de références **postPEG** au **Recovery**
    a) Valeurs de référence littérature
    b) Valeurs de référence home-made

Macrocalcitonine?

Intérêts recherche MC

Macrocalcitonin is a novel pitfall in the routine of serum calcitonin immunoassay

Thalita G. Alves[1,2], Teresa S. Kasamatsu[1], Ji H. Yang[1], Maria Cecília Z. Meneghetti[2], Aline Mendes[2], Ilda S. Kunii[1], Susan C. Lindsey[1], Cléber P. Camacho[1], Magnus R. Dias da Silva[1], Rui M. B. Maciel[1], José Gilberto H. Vieira[1], João Roberto M. Martins[1,2]

[1] Thyroid Disease Center and Laboratory of Molecular and Translational Endocrinology, Division of Endocrinology, Department of Medicine, Escola Paulista de Medicina, Universidade Federal de São Paulo, Brazil. Rua Pedro de Toledo, 669 11th floor, 04039–032, São Paulo, SP, Brazil, Tel: +55 11 5084 5231.; [2] Molecular Biology Division, Department of Biochemistry, Escola Paulista de Medicina, Universidade Federal de São Paulo, Brazil. Rua Três de Maio, 100, fourth floor, 04044–020, São Paulo, SP, Brazil, Tel: +55 11 5579–3175.

Seul article avec « Macrocalcitonin » sur PubMed

Source: Thalita et al (2015) JCEM

Macrocalcitonine?

Intérêts recherche MC

- Sélection de 3 échantillons
- 250µL PEG 6000 25% + 250µL échantillon
- Vortex 1min
- Centrifugation 9500g 5min à 25°C
- Mesure sur Liaison XL®
- Calcul d'un Recovery (%)

?????

Echantillon	Pré-PEG (pmol/mL)	Post-PEG (pmol/mL)
CALPEG	28.3	63.6
CALPEG	173.0	211.0
CALPEG	13.9	59.1

Macrocalcitonine?

Intérêts recherche MC

- 250µL PEG 6000 25% + 250µL sérum phy
- Vortex 1min
- Centrifugation 9500g 5min à 25°C
- Mesure sur Liaison XL®

Test	Résultat
C-peptide	0.00642 pmol/mL
Insuline	< 1.434 pmol/L
Phosphatase alcaline	< 1.50 µg/L
Calcitonine1	**85.6 pg/mL!**
Calcitonine2	**75.9 pg/mL!**
Calcitonine3	**87.3 pg/mL!**