



LABORATOIRE HOSPITALIER UNIVERSITAIRE DE BRUXELLES

LHUB-ULB

UNIVERSITAIR LABORATORIUM BRUSSEL

Intérêt du dosage de hCG dans le cadre des processus tumoraux et des grossesses anormales

Fleur Wolff, LHUB-ULB, CORATA 2017

Plan



1. Structure
2. Formes
3. Rôles
4. Métabolisme
5. Méthodes analytiques
 - 5.1. Historique
 - 5.2. Différences observées entre les méthodes
6. Applications cliniques
7. Etude locale
 - 7.1. Objectifs
 - 7.2. M&M
 - 7.3. Résultats et conclusions

Plan



1. Structure

2. Formes

3. Rôles

4. Métabolisme

5. Méthodes analytiques

5.1. Historique

5.2. Différences observées entre les méthodes

6. Applications cliniques

7. Etude locale

7.1. Objectifs

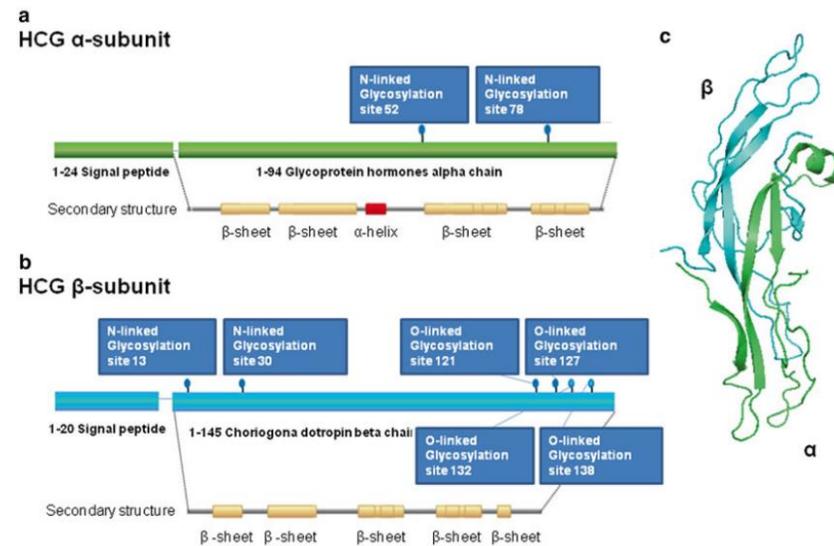
7.2. M&M

7.3. Résultats et conclusions

1. Structure

- LHCG: structure glycoprotéique

- ✓ Sous-unité α : 92 aa et sous-unité β : 145 aa
- ✓ Interagit avec le récepteur LH/hCG



Plan



1. Structure

2. Formes

3. Rôles

4. Métabolisme

5. Méthodes analytiques

5.1. Historique

5.2. Différences observées entre les méthodes

6. Applications cliniques

7. Etude locale

7.1. Objectifs

7.2. M&M

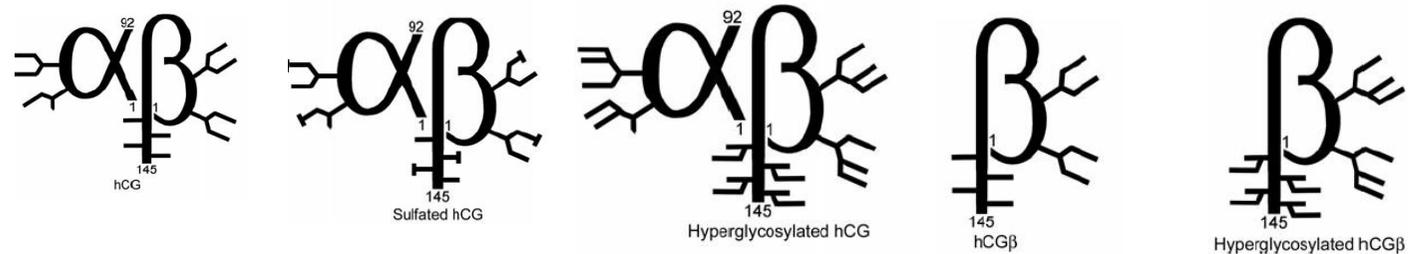
7.3. Résultats et conclusions



2. Formes

- hCG: terme générique comportant 5 formes principales

Parameter	hCG	Sulfated hCG	Hyperglycosylated hCG	hCGβ	Hyperglycosylated hCGβ
Source cell of synthesis	Syncytiotrophoblast	Gonadotrope	Cytotrophoblast	Advanced malignancies	Advanced malignancies
Mode of action	Endocrine	Endocrine	Autocrine	Autocrine	Autocrine
Site of action	LH/hCG receptor	LH/hCG receptor	TGFβ antagonism	TGFβ antagonism	TGFβ antagonism
Components:					
1. Amino acids α-subunit	92	92	92	–	–
2. Amino acids β-subunit	145	145	145	145	145
3. O-linked sugar units	4	4	4	4	4
4. N-linked sugar units	4	4	4	2	2
Peptide molecular weight	26,200	26,200	26,200	16,000	16,000
Molecular weight sugars	10,980	9950	16,600	7300	11,600
Total molecular weight	37,180	36,150	42,800	23,300	27,600
Percentage sugars	30%	28%	39%	31%	42%
Metabolic clearance rate	36 h	20 h	Not known	0.72 h	Not known



Plan



1. Structure

2. Formes

3. Rôles

4. Métabolisme

5. Méthodes analytiques

5.1. Historique

5.2. Différences observées entre les méthodes

6. Applications cliniques

7. Etude locale

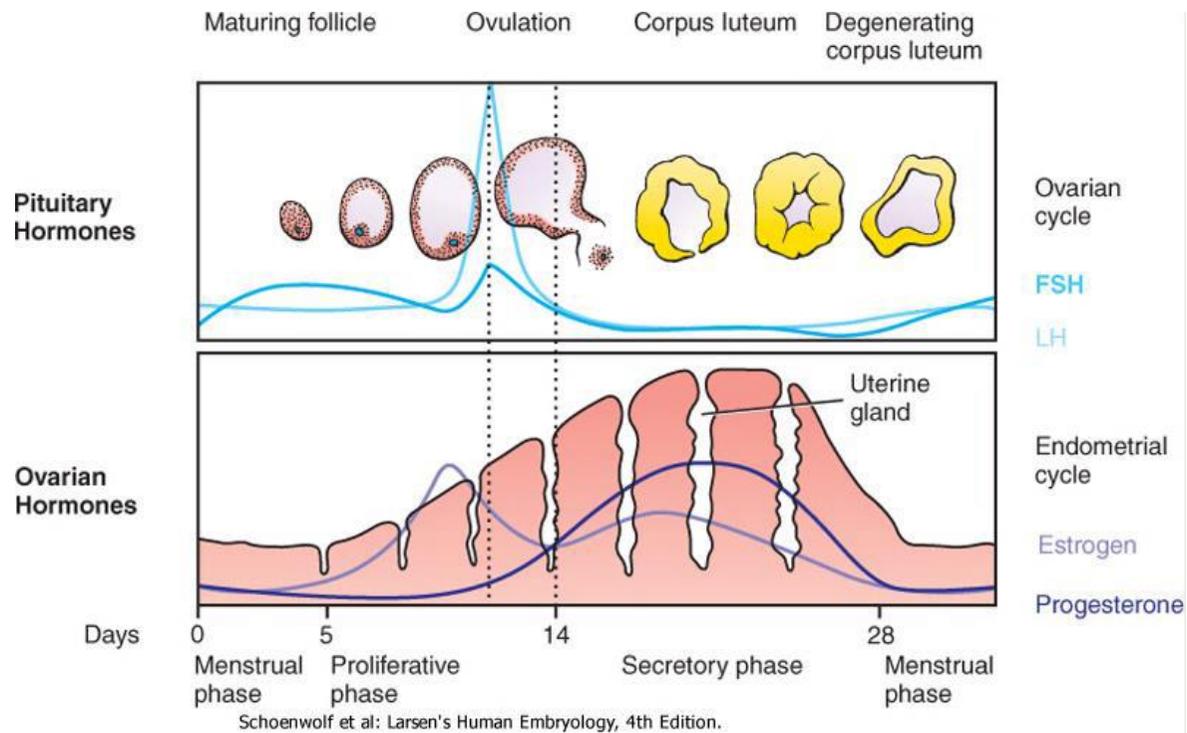
7.1. Objectifs

7.2. M&M

7.3. Résultats et conclusions

3. Rôles

- hCG et hCG hyperglycosylée: rôles durant la grossesse

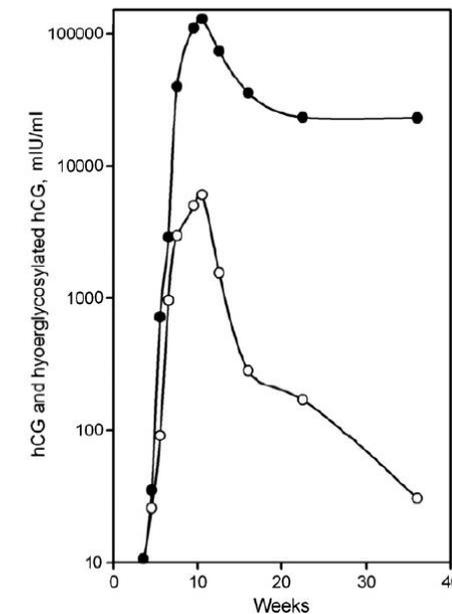


3. Rôles

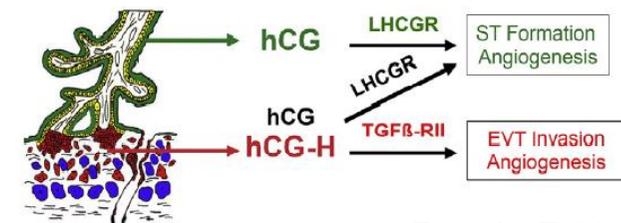
○ hCG et hCG hyperglycosylée: rôles durant la grossesse

Table 4 The biological functions of hCG during pregnancy

Function
A. hCG
1. Promotion of corpus luteal progesterone production
2. Angiogenesis of uterine vasculature
3. Cytotrophoblast differentiation
4. Immuno-suppression and blockage of phagocytosis of invading trophoblast cells
5. Growth of uterus in line with fetal growth
6. Quiescence of uterine muscle contraction
7. Promotion of growth of fetal organs
8. Umbilical cord growth and development
9. Blastocysts signals uterine decidua prior to invasion regarding pending implantation
10. hCG in sperm and receptors found in fallopian tubes suggesting pre-pregnancy communication
11. hCG receptors in hippocampus and brain stem, may cause nausea and vomiting in pregnancy
B. Hyperglycosylated hCG
1. Stimulates implantation by invasion of cytotrophoblast cells as occurs at implantation of pregnancy
2. Stimulates growth of placenta by promoting growth of cytotrophoblast cells
C. hCG and hyperglycosylated hCG together
1. Drives hemochorial placentation



Cole L, 2012



Fournier T, 2015

3. Rôles

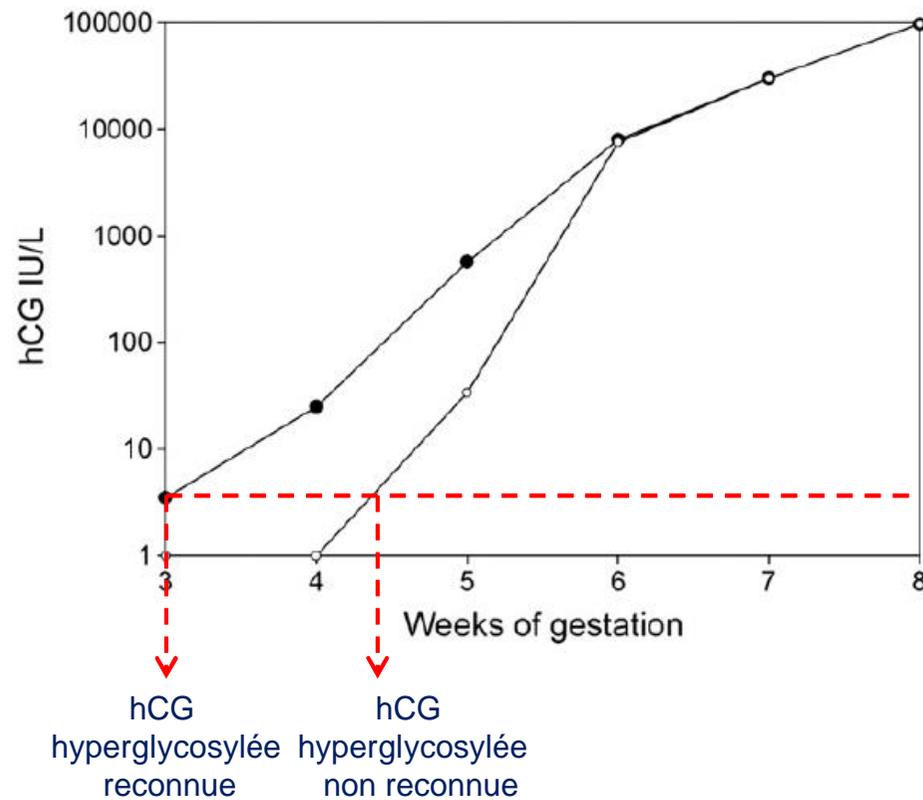
- hCG hyperglycosylée: forme prédominante en début de grossesse

Table 2 Concentration of total hCG and hyperglycosylated hCG (hCG-H) in 496 serum samples from 310 women with term pregnancies measured using the Siemens Immulite 1000 total hCG assay

Gestation age (weeks since start of menstrual period)	N	Median Total hCG ng/ml	Range Total hCG ng/ml (variation)	Median hCG-H ng/ml	Range hCG-H ng/ml (variation)	hCG-H %
3-weeks (3 weeks 0 days - 6 days)	n = 42	0.26 (16 of 42 < 0.1 ng/ml)	0.04 - 5.5	0.20(16 of 42 < 0.1 ng/ml)	0.01 - 6.45 (645X)	87%
4 weeks	n = 42	3.4	0.21 - 173 (824X)	2.5	0.18 - 160 (888X)	51%
5 weeks	n = 67	65	1.86 - 1308 (704X)	8.6	0.96 - 698 (731X)	43%
6-weeks	n = 29	252	3.80 - 855 (225X)	86	0.76 - 629 (827X)	36%
7 weeks	n = 30	3,278	203 - 7,766 (38X)	359	27 - 931 (34X)	16%
8 weeks	n = 33	4,331	1,064 - 10,057 (9.4X)	386	67 - 1050 (15.6X)	7.0%
9 weeks	n = 24	5,832	1,031 - 11,586 (11.2X)	430	102 - 1158 (11.3X)	5.1%
10 weeks	n = 20	10,352	1,952 - 19,958 (10.2X)	521	188 - 1855 (9.9X)	4.3%
11 - 13 weeks	n = 41	5,953	1,440 - 15,318 (10.6X)	137	24 - 330 (13.7X)	2.3%
14 - 17 weeks	n = 57	2,934	311 - 4,757 (15.2X)	26	6.7 - 129 (19.3X)	1.3%
18 - 26-weeks	n = 62	1,931	210 - 6,223 (30.3X)	15.8	5.3 - 95 (17.9X)	0.65%
27 - 40 weeks	n = 49	1,911	184 - 8,530 (46.4X)	2.95	0.3 - 12.2 (40.6X)	0.14%

3. Rôles

- hCG hyperglycosylée: forme prédominante en début de grossesse



3. Rôles

- hCG sulfatée
 - ✓ Sécrétion parallèle à celle de la LH
 - ✓ Production stimulée lors de:
 - “ Ménopause
 - “ Préménopause
 - “ Ovariectomie

#	Age	Total hCG IU/L
1	68	2.5
2	69	3.5
3	52	3.7
4	51	4.1
5	65	4.5
6	55	4.6
7	52	4.8
8	55	5.3
9	53	5.9
10	54	6.0
11	54	6.1
12	54	6.7
13	69	6.9
14	53	7.0
15	51	7.3
16	51	7.3
17	56	7.3
18	51	7.4
19	58	7.4
20	52	7.5
21	57	7.9
22	54	8.0
23	55	8.0
24	55	8.0
25	51	8.1
26	52	9.0
27	55	9.2
28	53	9.3
29	54	9.5
30	57	10
31	52	10
32	53	11
33	52	11
34	54	12
35	53	11
36	52	11
37	54	12
38	50	12
39	54	13
40	50	13
41	51	14
42	51	15
43	52	15
44	59	16
45	60	22
Median		8.0

3. Rôles

- hCG et hCG hyperglycosylée

Table 2

Use of serum free β -subunit (hCG β plus hyperglycosylated hCG β) and urine β -core fragment as tumor markers for detection of malignancies. All averages are determined by combining total positive cases from multiple reports [65–92].

Malignancy	hCG β as a tumor marker		β -core fragment as a tumor marker	
	Number of cases	Serum hCG β (>3 pmol/L)	Number of cases	Urine β -core fragment (>3 pmol/L)
Bladder cancer	170	35%	102	48%
Cervical cancer	60	37%	410	48%
Colorectal cancer	436	17%		
Endometrial cancer	55	33%	157	47%
Lung cancer	243	18%	122	45%
Ovarian cancer	150	38%	207	66%
Pancreatic cancer			29	55%
Vulvar	64	41%		
TOTAL	1164	Mean 30%	1027	Mean 48%

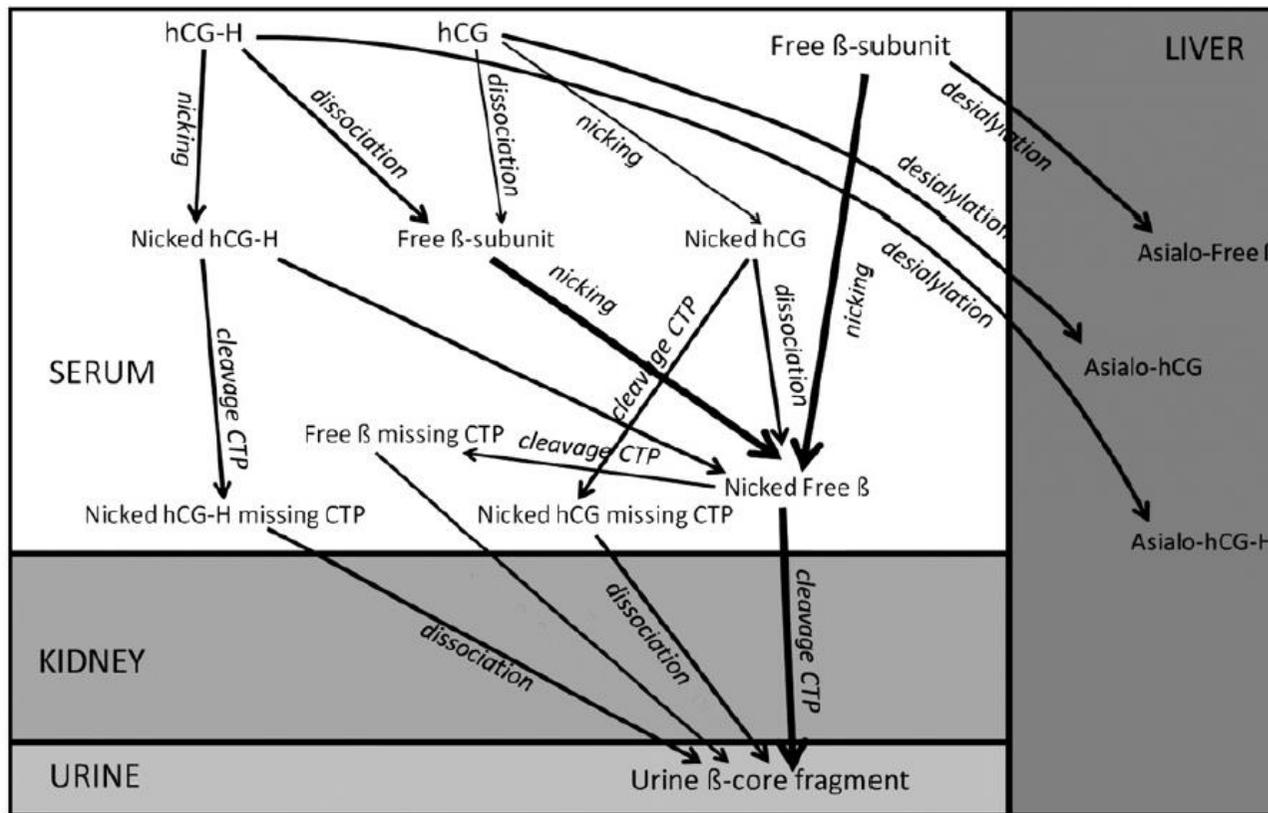
Plan



1. Structure
2. Formes
3. Rôles
- 4. Métabolisme**
5. Méthodes analytiques
 - 5.1. Historique
 - 5.2. Différences observées entre les méthodes
6. Applications cliniques
7. Etude locale
 - 7.1. Objectifs
 - 7.2. M&M
 - 7.3. Résultats et conclusions

4. Métabolisme

- Plasmatique-hépatique-rénal



4. Métabolisme



○ Métabolites de hCG . utilités cliniques

Molecule	Relationship to total hCG	Detection in serum and urine
hCG	Independent molecule with separate biological functions. It promotes progesterone production, uterine angiogenesis during pregnancy, uterine quiescence, umbilical cord growth, fetal growth, and uterine growth during pregnancy [1].	1. Produced during the length of pregnancy
Hyperglycosylated hCG	Independent molecules, separate biological functions. It promotes invasion as in implantation and growth of cytotrophoblast cells [6].	1. Principal hCG molecule in early pregnancy 2. Elevated in trisomy pregnancies 3. Principal molecule produced in choriocarcinoma, gestational trophoblastic neoplasm, and persistent hydatidiform mole. 4. Critical in Down syndrome screening
Nicked hCG	hCG cleaved by macrophage or leukocyte enzymes such as elastase, cleavage at β 47-48. Biologically inactive degradation product of hCG.	1. Present in pregnancy serum and urine. 2. Significant component of hCG following evacuation of an ectopic pregnancy or spontaneous abortion, or parturition.
Nicked hyperglycosylated hCG	Hyperglycosylated hCG is rapidly nicked by macrophages of leukocyte enzymes such as elastase, cleavage at β 47-48 [10].	1. Principal molecule produced in choriocarcinoma, gestational trophoblastic neoplasm, and persistent hydatidiform mole.
Nicked hCG missing β CTP	Further cleavage of nicked hCG by macrophage or leukocyte enzymes such as elastase. C-terminal peptide is cleaved from β -subunit at 92-93. Biologically inactive degradation product of hCG [10].	1. Commonly detected in serum and urine of patients with hydatidiform mole or choriocarcinoma. 2. Detected in serum and urine following evacuation of an ectopic pregnancy or spontaneous abortion, or parturition. 3. Produced in Familial hCG syndrome.
Asialo hCG	recombinant hCG standard incubated with Neuraminidase to remove sialic acid.	1. hCG with variable sialic acid content produced in pregnancy and gestation trophoblastic disease. Standard hCG has full complement of sialic acid, this has none representing other extreme of normality.
hCG β	Dissociation product of hCG and independent molecule with separate biological functions produced by cancer cells. It promotes growth and invasion of cancer cells producing this molecule [8] [13].	1. Dissociation product is critical in early pregnancy and in Down syndrome screening. 2. hCG β or hyperglycosylated hCG β produced by most advanced malignancies, detected as β -core fragment in urine. 3. Detected in Familial hCG syndrome.
Nicked hCG β	hCG β cleavage enzymes such as elastase, cleavage at β 47-48. Rapid cleavage occurs in blood. Degradation product of hCG β [8,10,13].	1. Nicked hCG β or nicked hyperglycosylated hCG β present in serum and urine of most cases with advanced malignancies.
β -core fragment	A urine terminal degradation product of nicked hCG missing C-terminal peptide. β -core fragment comprises hCG β residues 6-40 disulfide linked to residues 55-92 [10].	1. β -core fragment detected in urine of most cases with advanced malignancies. 2. Detected in urine following evacuation of an ectopic pregnancy or spontaneous abortion, or following parturition.

Plan



1. Structure

2. Formes

3. Rôles

4. Métabolisme

5. Méthodes analytiques

5.1. Historique

5.2. Différences observées entre les méthodes

6. Applications cliniques

7. Etude locale

7.1. Objectifs

7.2. M&M

7.3. Résultats et conclusions

5. Méthodes analytiques

5.1. Historique

Year published	Description	Authors and reference
1930	First pregnancy test, the Zondek-Aschein Pregnancy Test	Zondek B, Aschein S [55]
1960	First immunological pregnancy test, an antibody agglutination test	Wide L, Gemzell CA [56]
1967	First hCG radioimmunoassay	Aono T, Goldstein DP, Taymor ML, Dolch K [57]
1972	Discovery of hCG β radioimmunoassay, assay only detects hCG	Vaitukaitis JL, Braunstein GD, Ross GF [58]
1984	First hCG radio-immunometric assay	Armstrong EG, Ehrlich PH, Birken S, Schlatterer JP, Siris E, Hembree WE, Canfield RE [59]
1995	Automated hCG chemiluminescent-immunometric assay	Vankrieken L, Hertogh RE [60]



5. Méthodes analytiques

5.2. Différences observées entre les méthodes

- ✓ Reconnaissance variable des 5 formes d'hCG et de leurs métabolites
- ✓ Applications cliniques différentes

	Abbott Architect	Abbott AxSYM	Beckman Access 2	Beckman Dxl 800	Ortho Vitros ECIQ	Roche Elecsys hCG + β	Siemens ACS180	Siemens Centaur	Siemens Dimension	Siemens Immulite	Siemens Stratus	Tosoh AIA
Serum standards												
hCG	96%	103%	103%	100%	112%	109%	105%	104%	96%	96%	92%	95%
Hyperglycosylated hCG	86%	85%	120%	98%	68%	78%	102%	81%	67%	105%	66%	nd
Nicked hCG	70%	99%	84%	71%	80%	69%	85%	66%	65%	115%	8%	nd
Nicked hCG missing CTP	0%	0%	0%	0%	0%	12%	0%	0%	10%	109%	28%	16%
Nicked hyperglycosylated hCG	40%	46%	46%	51%	80%	100%	70%	40%	80%	103%	88%	70%
Asialo hCG	35%	69%	48%	46%	85%	46%	81%	39%	65%	114%	73%	59%
hCG β	87%	94%	142%	136%	47%	102%	126%	47%	47%	111%	73%	66%
Nicked hCG β	33%	51%	56%	63%	19%	53%	72%	19%	41%	107%	70%	60%
β -core fragment	1%	1%	1%	1%	1%	16%	0%	1%	1%	35%	1%	1%
Poor detection	6 of 9	5 of 9	6 of 9	7 of 9	5 of 9	5 of 9	5 of 9	7 of 9	7 of 9	1 of 9	7 of 9	6 of 7
LH crossreactivity	0.01%	0.01%	0.01%	0.01%	0.32%	0.01%	0.01%	0.01%	0.01%	0.04%	0.53%	0.01%
Applications (based on detection)												
Pregnancy (6 weeks - term)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Early pregnancy (3/4/5 weeks)	✓	✓	✓	✓		✓	✓	✓		✓		✓
Abnormal pregnancy										✓		
Down syndrome screening		✓	✓				✓			✓		✓
Non trophoblastic cancer										✓		
Gestational trophoblastic disease		✓	✓				✓			✓		✓

5. Méthodes analytiques

- 5.2. Différences observées entre les méthodes
 - ✓ Préparation Internationale de référence variable selon le test utilisé
 - ✓ Tests commerciaux calibrés par rapport au 3^{ème} ou 4^{ème} (75/589) Standard International
 - ✓ IFCC working group: développement d'un nouveau réactif international de référence pour hCG et pour 5 de ses variants/métabolites

Table 2. Nomenclature and description of the current International Standard (IS) and the International Reference Reagents (IRR) for hCG and hCG-related variants [6,8,64]

Symbol	WHO code	Content/ampoule	Molecular description ^a
hCG	Fifth IS 07/364	0.39 nmol or 179 IU	Intact hCG – α/β heterodimer; bioactive
hCG	First IRR 99/688	1.88 nmol	
hCGn	First IRR 99/642	0.78 nmol	Nicked hCG – α/β heterodimer; aa <i>hCGβ44–48</i> (nicks)
hCG β	First IRR 99/650	0.84 nmol	Free beta-subunit of hCG; aa <i>hCGβ1–145</i>
hCG β n	First IRR 99/692	0.88 nmol	Nicked free beta-subunit of hCG, aa <i>hCGβ44–48</i> (nicks)
hCG β cf	First IRR 99/708	0.33 nmol	Beta-core fragment of hCG; aa <i>hCGβ6–40</i> linked to <i>hCGβ55–92</i>
hCG α	First IRR 99/720	1.02 nmol	Free alpha-subunit of hCG; aa <i>hCGα1–92</i>

Plan



1. Structure
2. Formes
3. Rôles
4. Métabolisme
5. Méthodes analytiques
 - 5.1. Historique
 - 5.2. Différences observées entre les méthodes
- 6. Applications cliniques**
7. Etude locale
 - 7.1. Objectifs
 - 7.2. M&M
 - 7.3. Résultats et conclusions

6. Applications cliniques

- Détection et suivi de grossesse
- Dépistage prénatal (syndrome de Down)
- Suivi de la clairance de β hCG après grossesse extra-utérine, fausse couche, accouchement
- Prise en charge des maladies trophoblastiques gestationnelles (GTD: môle hydatiforme, choriocarcinome)
- Marqueur tumoral (tumeur des cellules germinales et autres)
- Surveillance du dopage en médecine sportive (http://www.wada-ama.org/Documents/World_Anti-Doping_Program/WADP-Prohibited-list/2014/WADA-prohibited-list-2014-EN.pdf)



5. Applications cliniques

- Détection et suivi de grossesse
- Dépistage prénatal (syndrome de Down)
- Suivi de la clairance de hCG après grossesse extra-utérine, fausse couche, accouchement
- Prise en charge des maladies trophoblastiques gestationnelles (GTD: môle hydatiforme, choriocarcinome)
- Marqueur tumoral (tumeur des cellules germinales et autres)
- Surveillance du dopage en médecine sportive (http://www.wada-ama.org/Documents/World_Anti-Doping_Program/WADP-Prohibited-list/2014/WADA-prohibited-list-2014-EN.pdf)



5. Applications cliniques

- Suivi de la clairance de hCG après grossesse extra-utérine, fausse couche, accouchement
 - ✓ Formes et métabolites de hCG important à quantifier
 - hCG clivée
 - hCG clivée dépourvue du fragment C-terminal

Table 1. Requirements of hCG methods in pregnancy and oncology (Table updated from that in [1] and reproduced with permission)

Clinical application	Method of choice	Type of specimen	Specificity required	Desirable detection limit ^a	Timing/frequency/rapidity required
Ectopic pregnancy	Quantitative immunoassay	Serum or urine	hCG or hCG + hCG β + hCG β cf	2 U/l	Serial measurements at 48–72 h intervals until level is within normal limits
Detection of retained products of conception	Quantitative immunoassay	Serum	hCG + hCG β	2 U/l	Serial measurements

5. Applications cliniques

- Prise en charge des maladies trophoblastiques gestationnelles
 - ✓ Quantification de I_{hCG} (International Federation of Gynecology and Obstetrics)
 - Au démarrage du traitement
 - Suivi hebdomadaire
 - Rémission définie par 3 concentrations successives <5 UI/L
 - Suivi mensuel durant 1 an (môle complète)
 - Chimiothérapie indiquée sur base de la cinétique d_{hCG} (Mangili G, 2014)

TABLE 1. Indications for chemotherapy after a molar pregnancy

Weekly hCG rising* for at least 3 consecutive measurements for a period of at least 2 wk (days 0, 7, and 14)

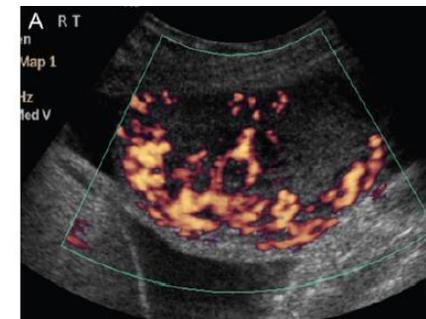
Weekly hCG plateauing† for at least 4 consecutive measurements for a period of at least 3 wk (days 0, 7, 14, and 21)

Persistence of hCG more than 6 months after evacuation

Histological diagnosis of choriocarcinoma

*A rising hCG is usually defined as a more than 10% increase over the previous weekly value.

†A plateauing hCG concentration is defined as a less than 10% change over the previous weekly value.



5. Applications cliniques



- Prise en charge des maladies trophoblastiques gestationnelles
 - ✓ Formes et métabolites de hCG important à quantifier:
 - hCG hyperglycosylée
 - hCG clivée hyperglycosylée
 - hCG clivée
 - hCG clivée dépourvue du fragment C-terminal

5. Applications cliniques

- Marqueur tumoral (tumeur des cellules germinales)
 - ✓ Recommandations pour les tumeurs testiculaires (European Association of Urology)
 - Au moment du diagnostic . Stade

Table 1 – Recommended tests for staging at diagnosis

Test	Recommendation
Serum tumour markers	α-Fetoprotein hCG Lactate dehydrogenase
Abdominopelvic CT	All patients
Chest CT	All patients
Testis ultrasound (bilateral)	All patients
Bone scan or spinal MRI	In the case of symptoms
Brain scan (CT/MRI)	In the case of symptoms and patients with metastatic disease with multiple lung metastases and/or high β-hCG levels

-Après traitement . Fréquence variable selon le type de tumeur et son agressivité

Table 12 – Recommended minimum follow-up schedule in a surveillance policy for stage I nonseminoma [103]

Procedure	Year			
	1	2	3	4-5
Physical examination	Four times	Four times	Four times	Once/yr
Tumour markers	Four times	Four times	Four times	Once/yr
Plain radiography of the chest	Twice	Twice	Twice	Twice
Abdominopelvic computed tomography	Twice (at 3 and 12 mo)	Once (at 24 mo)	Once (at 36 mo)	

Plan



1. Structure

2. Formes

3. Rôles

4. Métabolisme

5. Méthodes analytiques

5.1. Historique

5.2. Différences observées entre les méthodes

6. Applications cliniques

7. Etude locale

7.1. Objectifs

7.2. M&M

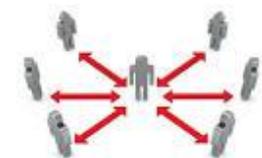
7.3. Résultats et conclusions

7. Etude locale

7.1. Objectifs

- Centraliser les tests d'hCG sur la même plateforme analytique quelle que soit l'indication clinique

	Roche hCG + β	RIA-ELSA-F- β hCG	Siemens hCG
Principe de dosage	Immunologique-chemiluminescence	Immunoradiométrique-sandwich	Immunologique-chemiluminescence



7. Etude locale

7.1. Objectifs

- Données discordantes dans la littérature concernant les métabolites de hCG reconnus par le test Roche Elecsys hCG+ et ses applications cliniques
 - ✓ Cole *et al*, 2011 faible détection de hCG clivée, hCG clivé CG clivée dépourvue du fragment C-terminal

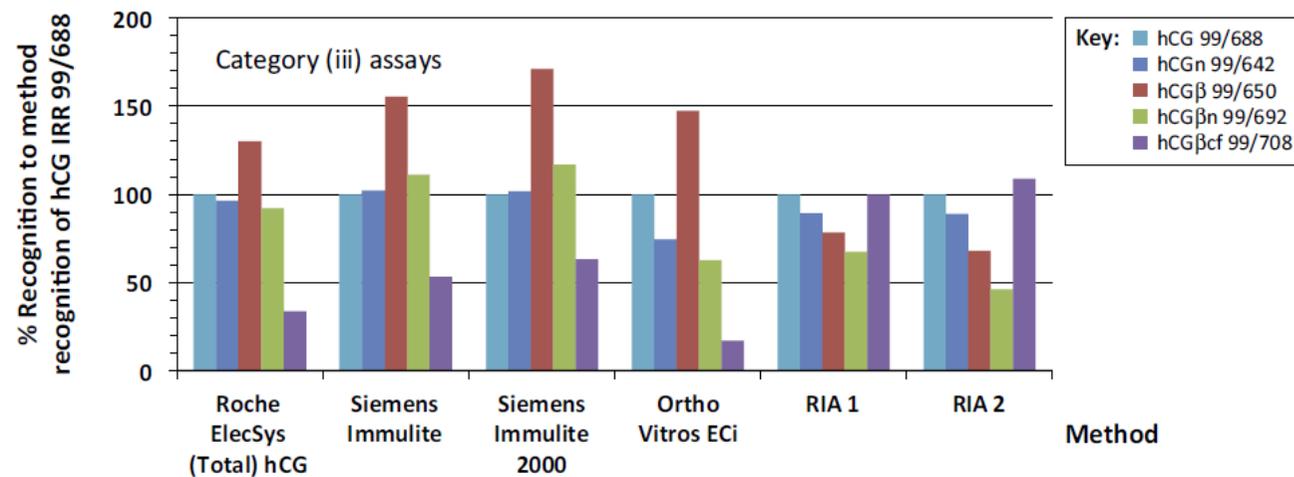


	Abbott Architect	Abbott AxSYM	Beckman Access 2	Beckman Dxl 800	Ortho Vitros ECIQ	Roche Elecsys hCG + β	Siemens ACS180	Siemens Centaur	Siemens Dimension	Siemens Immulite	Siemens Stratus	Tosoh A1A
Serum standards												
hCG	96%	103%	103%	100%	112%	109%	105%	104%	96%	96%	92%	95%
Hyperglycosylated hCG	86%	85%	120%	98%	68%	78%	102%	81%	67%	105%	66%	nd
Nicked hCG	70%	99%	84%	71%	80%	69%	85%	66%	65%	115%	8%	nd
Nicked hCG missing CTP	0%	0%	0%	0%	0%	12%	0%	0%	10%	109%	28%	16%
Nicked hyperglycosylated hCG	40%	46%	46%	51%	80%	100%	70%	40%	80%	103%	88%	70%
Asialo hCG	35%	69%	48%	46%	85%	46%	81%	39%	65%	114%	73%	59%
hCGβ	87%	94%	142%	136%	47%	102%	126%	47%	47%	111%	73%	66%
Nicked hCGβ	33%	51%	56%	63%	19%	53%	72%	19%	41%	107%	70%	60%
β-core fragment	1%	1%	1%	1%	1%	16%	0%	1%	1%	35%	1%	1%
Poor detection	6 of 9	5 of 9	6 of 9	7 of 9	5 of 9	5 of 9	5 of 9	7 of 9	7 of 9	1 of 9	7 of 9	6 of 7
LH crossreactivity	0.01%	0.01%	0.01%	0.01%	0.32%	0.01%	0.01%	0.01%	0.01%	0.04%	0.53%	0.01%
Applications (based on detection)												
Pregnancy (6 weeks - term)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Early pregnancy (3/4/5 weeks)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Abnormal pregnancy										✓		
Down syndrome screening		✓	✓				✓			✓		✓
Non trophoblastic cancer										✓		
Gestational trophoblastic disease		✓	✓				✓			✓		✓

7. Etude locale

7.1. Objectifs

- ✓ Whittington *et al*, 2010 reconnaissance de α hCG clivée (95.8%), hCG clivée (92.5%)



7. Etude locale

7.1. Objectifs

- Evaluer le degré de concordance entre le test Roche Elecsys hCG+ et Siemens Immulite 2000 (Gold Standard) dans le suivi de grossesses EU, biochimiques, de fausse couches, de GTD, de processus tumoraux d'origine trophoblastique ou non-trophoblastique
- Evaluation de la précision intermédiaire des 2 tests



7. Etude locale

7.2. M&M . Méthodes

- Récolte des échantillons de novembre 2014 à février 2017
 - ✓ 152 échantillons . suivi de grossesses (EU, fausse-couche, biochimique), de GTD, de processus tumoraux d'origine trophoblastique ou non-trophoblastique
 - ✓ 44 échantillons . suivi de processus tumoraux d'origine trophoblastique ou non-trophoblastique
- Réalisation d'un pool avec une concentration en hCG proche du seuil de normalisation
 - ✓ Analyse en duplicat durant 21 jours

7. Etude locale

7.2. M&M - Méthodes

- Siemens Immulite 2000
- Roche Elecsys hCG+

	Siemens Immulite 2000 hCG	Roche Elecsys hCG+
Methodology	Chemiluminescent immunometric assay	Chemiluminescent immunometric assay
Units	UI/L	UI/L
Reference material	WHO 3rd International Standard (75/537)	WHO 4th International Standard (N°75/589)
Limit of quantification	0.4	0.6
Reference values provided by the manufacturer	-Women (P100):<5.3 -Men (P100):<2.5	-Non menopausal women (95% confidence interval (P97.5)):<5.3 -Menopausal women (95% confidence interval (P97.5)):<8.3 -Men (95% confidence interval (P97.5)):<2.6
Package insert informations (hCG variants recognition)	None	hCG, nicked hCG, hCG and nicked hCG

7. Etude locale

7.2. M&M . Méthodes

N:152

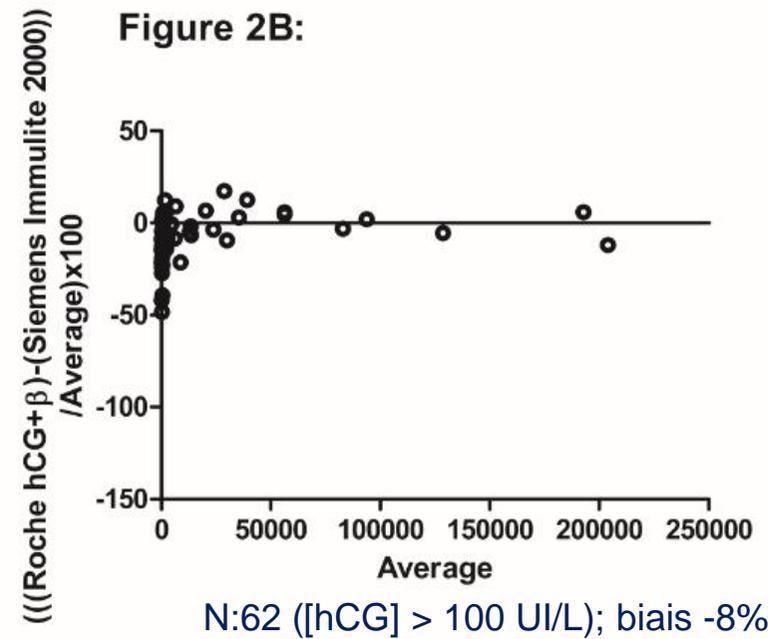
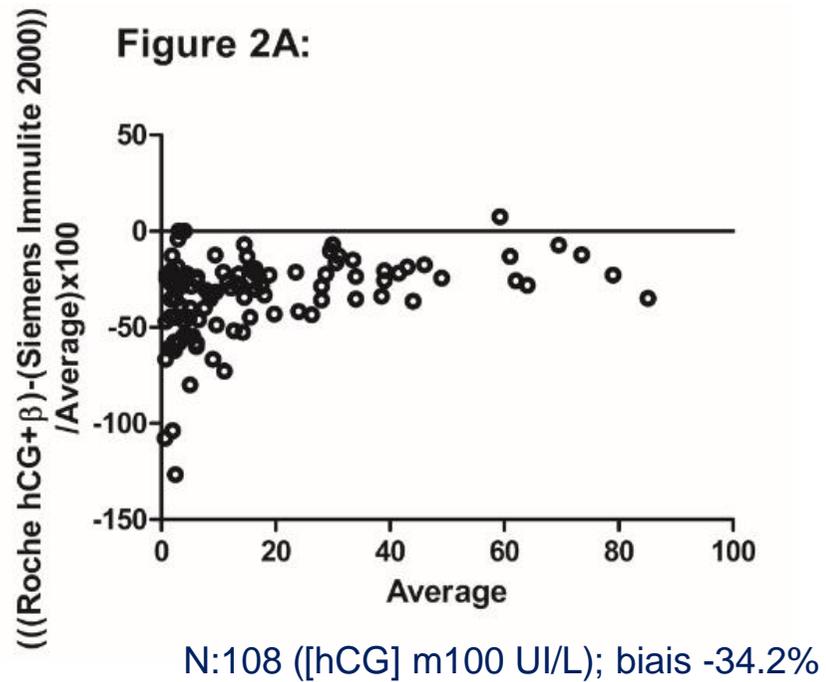
Gender	Final diagnosis	Number of patients	Number of patients for whom hCG concentrations were tested until normalization
Abnormal pregnancies			
F	Ectopic pregnancy	5	5
F	Biochemical pregnancy	4	4
F	Spontaneous abortion	18	18
Gestational trophoblastic disease			
F	Invasive mole (complete)	2	2
F	Invasive mole (incomplete)	1	1
Gonadal germ cell tumoral process			
F	Ovarian yolk sac tumor	1	0
Non-trophoblastic tumoral process			
F	Endocrine tumor	1	0
Gonadal germ cell tumoral processes			
M	Testis tumor (seminomas)	5	2
M	Testis tumor (nonseminomatous or mix tumor)	9	5
Non-trophoblastic tumoral process			
M	Bladder tumor	1	1

N:44

7. Etude locale

7.3. Résultats et conclusions

- Bland-Altman



7. Etude locale

7.3. Résultats et conclusions

○ Femmes

✓ Taux de concordance de 96.1%

N:152		Siemens Immulite 2000	
		<5.3	≥ 5.3
Roche Elecsys	<5.3	43	6
	≥ 5.3	0	103

- ✓ Six discordances observées:
- ” 3 dans le suivi de môle complète
 - ” 2 dans le suivi de fausse couche
 - ” 1 dans le suivi d'une tumeur ovarienne

7. Etude locale

7.3. Résultats et conclusions

- Hommes

- ✓ Taux de concordance de 97.7%

N:44		Siemens Immolute 2000	
		<2.5	≥ 2.5
Roche Elecsys	<2.6	14	1
	≥ 2.6	0	29

- ✓ Une discordance observée dans le suivi d'une tumeur testiculaire (séminome)

7. Etude locale

7.3. Résultats et conclusions

Gender	Final diagnosis	hCG (UI/L) Siemens Immolute 2000	hCG (UI/L) Roche Elecsys hCG+	Bias (%)
F	Spontaneous abortion	7	3.2	-54.3
F	Spontaneous abortion	6	4.5	-25.0
F	Invasive mole (complete)	7	3.9	-44.3
F	Invasive mole (complete)	7	3.2	-54.3
F	Invasive mole (complete)	6	3.4	-43.3
F	Ovarian yolk sac tumor	8	4.4	-45.1
M	Testis tumor (seminomas)	3	1.6	-47.3

7. Etude locale

7.3. Résultats et conclusions

- Adaptation de la valeur seuil Roche Elecsys hCG+ : 5.3 → 3.2 UI/L:
 - ✓ Taux de concordance de 98.7%

N:152		Siemens Immulate 2000	
		<5.3	≥ 5.3
Roche Elecsys	<3.2	41	0
	≥ 3.2	2	109

7. Etude locale

7.3. Résultats et conclusions

- Adaptation de la valeur seuil Roche Elecsys hCG+ : 2.6 → 1.6 UI/L
 - ✓ Taux de concordance de 100%

N:44		Siemens Immulite 2000	
		<2.5	≥ 2.5
Roche Elecsys	<1.6	14	0
	≥ 1.6	0	30

7. Etude locale

7.3. Résultats et conclusions

- Précision intermédiaire

- ✓ Coefficient de variation (Siemens Immulite 2000): 10.5% (9 UI/L)
- ✓ Coefficient de variation (Roche Elecsys hCG+): 2.8% (7 UI/L)

Conclusions

- Hétérogénéité des concentrations mesurées d'hCG selon le test commercial
- Concentrations en hCG plus basses sur Roche
- Par diminution de la valeur seuil à 3.2 UI/L (au lieu de 5.3 UI/L) et à 1.6 UI/L (au lieu de 2.6 UI/L), observation d'un meilleur taux de concordance [(96.1% - 98.7%) - (97.7% - 100%)] avec le test Siemens
- Excellente précision du test Roche Elecsys hCG+ à une concentration proche de la valeur seuil

Merci pour votre attention

