Diabète Gestationnel: Intérêt d'un suivi nutritionnel après la grossesse ?

Vincent Rigalleau

Symposium FNAMN-SFN 2011, Reims

Conflits d'intérêts

- **1996: prix de recherche en nutrition CIDEF* (50000 FF) pour le projet "Rôle des interactions lipides-glucides … »**
- **1999: prix de recherche en nutrition de l'Institut Appert (50000 FF) et subvention du conseil Régional d'Aquitaine (40000 FF) pour le projet "Effet des acides gras … »**
- **2011: Président comité de Titration essai GALAPAGOS (Sanofi-Aventis)**
- Bourses : Servier, Roche, Merck-Lipha
- Partenariats : Bayer, GSK, Novo, Lilly, Pfizer, Takeda, Scherring-Plough, MSD, Novartis

- * CIDEF: Comité Interprofessionnel de la Dinde en France

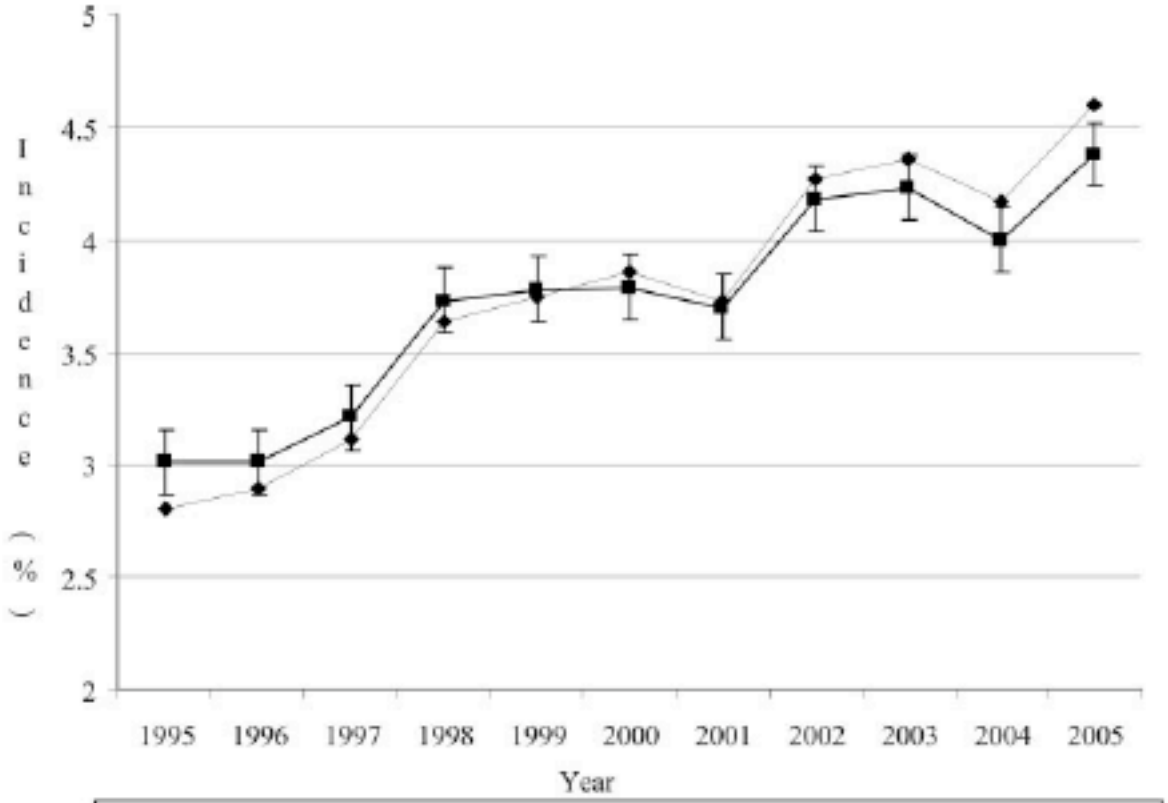
- Le Diabète Gestationnel
  - Physiopathologie
  - Assurer le diagnostic !
  - Conseil diététique
- Après la grossesse:
  - La femme, l'enfant
  - La prochaine grossesse

Diabète gestationnel

- « Intolérance au glucose survenue ou reconnue pendant la grossesse »
- 3-6% en France, en augmentation

L ’augmentation

(New South wale-Australie-*Vibeke DCare 2008*)



86646	85750	87352	85635	86864	87444	85346	85380	85687	84930	89713
29.1	29.2	29.3	29.4	29.6	29.8	30.0	30.2	30.4	30.6	30.7

Number of births and median age of women for each year in Figure 1.

Figure 1—*Annual crude and adjusted incidence of GDM, number of births, and annual median age of women.* ◆, *crude incidence;* ■, *age- and ethnicity-adjusted incidence and 95% CI.*

Pourquoi ça augmente ?

- Surpoids maternel
  - BMI+1 = prévalence DG +1%
- Âge maternel
  - 1977: 26 ans --> 2009: 30ans
  - Risque X2,5 si 30-35 ans, X4 si 35-40 ans
    - Par rapport à: 1,8% des grossesses à 20-24ans
    - *(Vibeke DCare 2008)*

Nouvelles recommandations (SFD-CNGOF, Mars 2010)

- Dépistage si un FR majeur:
  - âge>35, BMI>25, ATCD 1°DT2, ATCD personnel de DG ou macrosomie
- Sur GàJ au 1er Trimestre (ou avant conception):
  - GàJ≥ 92mg/dL = DG; GàJ≥126 = DT2
- Et sur HGPO 75g à S24-S28
  - G≥ 92mg/dL (T0) ou ≥180 (T60) ou ≥153 (T120)

Conséquences foetales

Mère **Placenta** **Enfant**

« Pedersen Hypothesis »

Glycémie ↗ → **Glycémie ↗**

↓

Insulinémie ↗

↓

HypoG néonatales
Macrosomie

Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study

Associations With Neonatal Anthropometrics

CONCLUSIONS—These findings confirm the link between maternal glucose and neonatal adiposity and suggest that the relationship is mediated by fetal insulin production and that the Pedersen hypothesis describes a basic biological relationship influencing fetal growth. ***Diabetes*** **58:453–459, 2009**

AGL
TG
Inflammation ?

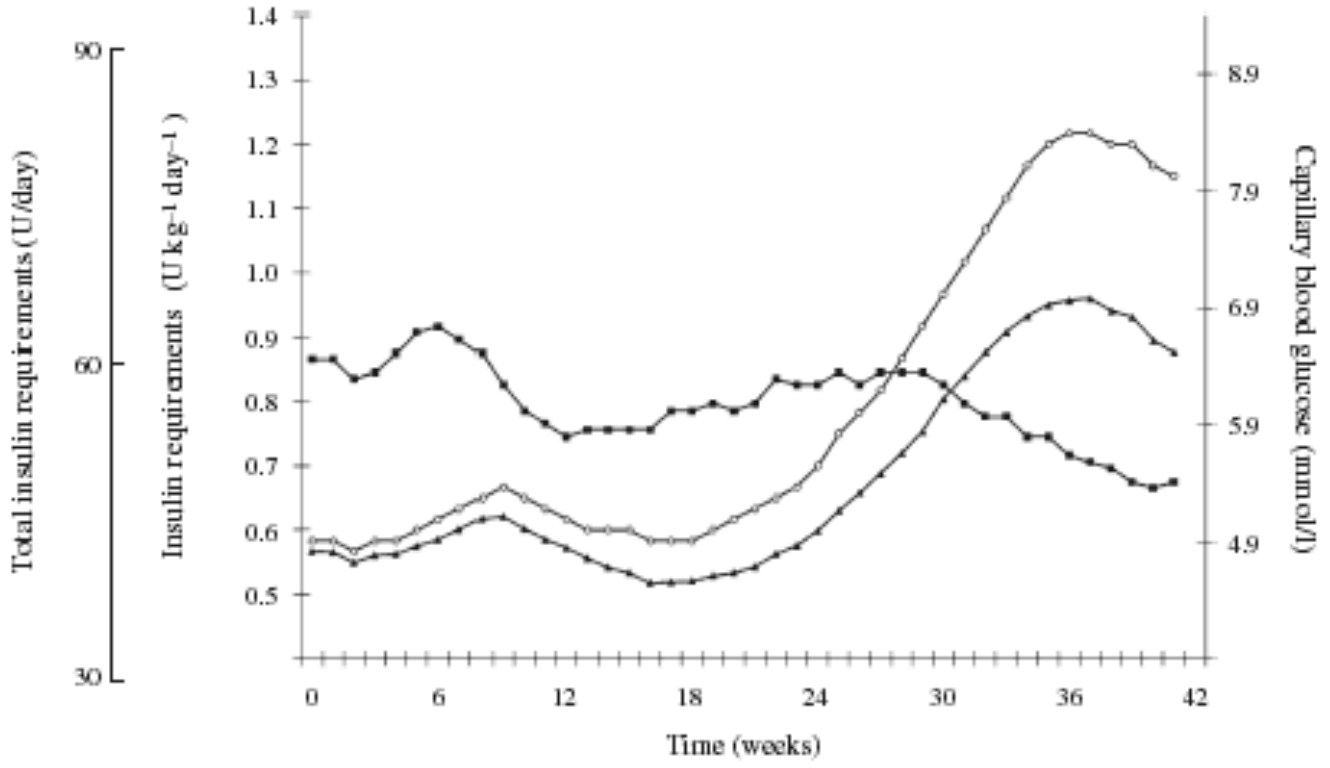
? LPL → Adiposité foetale

Causes (1)
L ’insulinorésistance maternelle

Garcia-patterson

Diabetologia (2010) 53:446–451

Fig. 1 Mean insulin requirements and self-monitored blood glucose in type 1 diabetic pregnant women. Square, capillary blood glucose; circle, total insulin requirement; triangle, insulin requirements



Causes (2) L'insulinopénie maternelle

Impaired β-cell function in lean normotolerant former gestational diabetic women

A. Tura*, A. Mari*, C. Winzer†, A. Kautzky-Willer† and G. Pacini*

Materials and methods To assess insulin sensitivity and β-cell function in fGDM uncomplicated by obesity and hyperglycaemia, we studied 24 lean fGDM women and 23 control women matched for age (30·7 ± 0·7 years, whole cohort), body mass index (22·2 ± 0·3 kg m^{-2}), and indistinguishable for plasma glucose both at fasting and at 120 min.

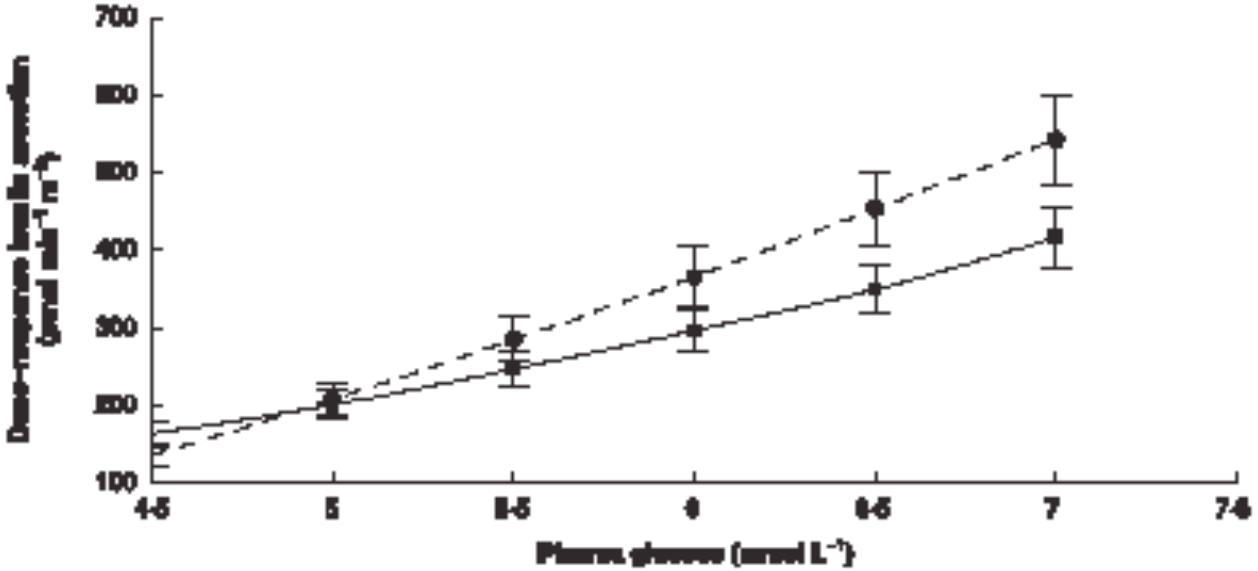


Figure 2 Dose–response curve of glucose-induced insulin secretion during the oral glucose tolerance test in 24 former gestational diabetic women (solid line) and 23 control women (dashed line).

Eur J Clin Invest 2008

Assurer le diagnostic : Cas clinique

- Femme de 37 ans
- ATCD familiaux = 0
- Une grossesse normale à 32 ans
- FIV il y a 5 mois , grossesse gémellaire
- Poids 49 kg (BMI 19)
- Nausées, soif depuis la veille
- Glycémie 31 mM

Japonaise

Fulminant Diabetes Mellitus Associated with Pregnancy: Case Reports and Literature Review

TAKESHI INAGAKI, YUTAKA NISHII*, NAOMI SUZUKI, SATORU SUZUKI, YOICHI KOIZUMI*, TORU AIZAWA AND KIYOSHI HASHIZUME

- *Endocrine jounal 2002*

- pH 7,1
- HbA1C 5,7%
- AntiGAD -
- Amylase, lipase élevées
- Pertes fœtales à J3

Assurer le diagnostic : DT1 ?

Presence of GAD Antibodies During Gestational Diabetes Mellitus Predicts Type 1 Diabetes

Nilsson, DCare 2007

385 DG --> 24 antiGAD+ (6%)
--> 12 DT1 dans les 8 ans, 6 dans les 6 mois

Facteurs +
Järvela DCare 2006

Table 1—*Characteristics for the autoantibody-positive women and GDM control subjects*

	Antibody-positive women with GDM	Antibody-negative women with GDM	*P*
n	24	48	
Age (years)*	29.5 (27.0–34.0)	30.0 (27.0–34.0)	NS
BMI (kg/m^2)†	24.5 (22.4–28.4)	25.4 (21.9–30.1)	NS
Heredity‡	15 (62.5)	22 (45.8)	NS
Ethnicity			
Scandinavian	21 (87.5)	37 (77.1)	NS
Non-Scandinavian	3 (12.5)	11 (22.9)	NS
OGTT value during pregnancy§	10.0 (9.4–12.0)	9.5 (9.1–10.4)	NS
GDM during previous pregnancy	8 of 19 (42.1)	9 of 42 (45.2)	NS
Insulin during the pregnancy	14 (58.3)	18 (37.5)	NS

Assurer le diagnostic : DT2 ?

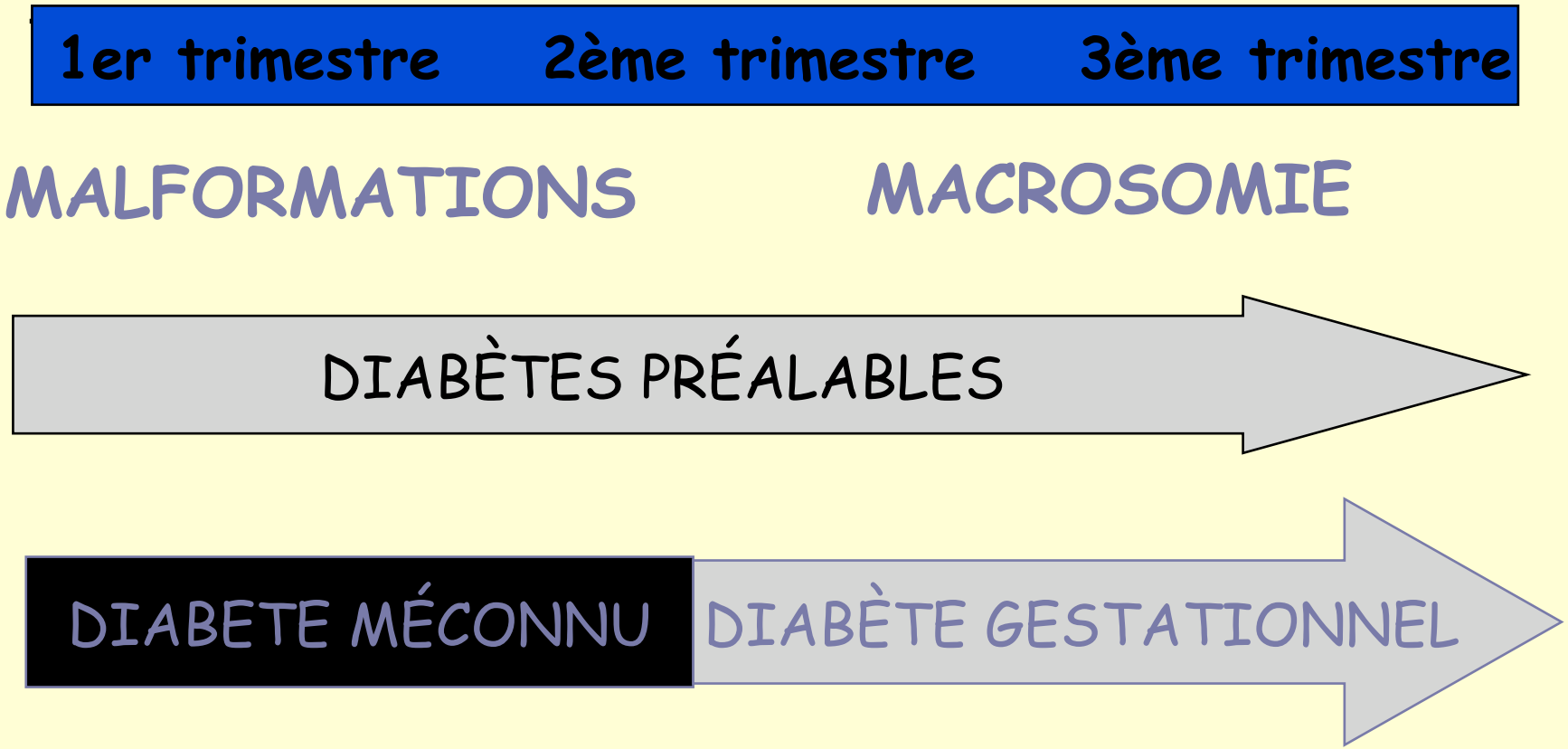
- *Jovanovic JCEM 2010:*

Two percent of pregnant women have undiagnosed T2DM, 5% have GDM when tested in the second trimes-

- *Verier-Mine D&M 2010:*

Total number of women studied	Mean follow-up (SD)	Definition of T2DM	% T2DM
318	6 (5-9) weeks	WHO	1.3%
605	13 weeks	WHO	5.5%
5857	1 to 26 weeks	ADA	1.1%
470	1 year	WHO	8.1%

Diabètes et malformations : l'hyperglycémie est délétère pour l'embryon et le fœtus



Poor Pregnancy Outcome in Women With Type 2 Diabetes

TINE D. CLAUSEN, MD[1] ELLINOR HELLMUTH, MD[1]

DiabetesCare 2002

- Mortalité périnatale X 3 - 6
- Malformations X 6 - 11
  - GàJ au 1er trimestre > 105 mg/dL: malformations X 6
- Obésité et malformations *(Stothard, JAMA 2009)*
  - DFTN X 1,9
  - Malformation cardiaques X1,3

Penser au DT2 chez une femme enceinte

- La femme:
  - Obèse
  - ***ATCD DG***
  - Acanthosis nigricans, OPK
  - Minorité ethnique
- Son diabète « gestationnel »
  - Précoce (avant S24)
  - Très hyperglycémique, ++ à jeun (HbA1C ≥5,3%)
  - Nécessitant rapidement de fortes doses d'insuline

Conseil diététique

(Hone & Jovanovic, JCEM 2010)

- 1-Individualisé, avec diététicienne
- 2-Correction des erreurs
  - « Avoid sweets and highly processed food »
  - 5 boissons sucrées/semaine = +22%DG *(Chen, DCare 2009)*
- 3-Contrôle des glucides
  - ≥ 175 g/j ? (<35% possible: « vegetables and diary products »)
  - « Small frequent meals to avoid G excursions », small breakfast
- 4-Modération calorique
  - ≥1800Cal/j ? 1200 possible
- +10-15kg **BMI18,5** +5-9kg **BMI25** +5kg
  - *(Stotland, DNCB 2009)*

Le DG, état pré-diabétique

Outcomes in women with a history of gestational diabetes. Screening and prevention of type 2 diabetes. Literature review

O. Verier-Mine

D&M 2010

- Risque X 7
- En augmentation *(Lauenborg DCare 2004):*
  - 1978-1985: 18% à 10 ans
  - 1987-1996: 41% à 10 ans
- DIAGEST2: 18% à 7 ans
  - *(Vambergue, Diab Med 2008)*

Prévenir le DT2 après DG

Prevention of Diabetes in Women with a History of Gestational Diabetes: Effects of Metformin and Lifestyle Interventions

Robert E. Ratner, Costas A. Christophi, Boyd E. Metzger, Dana Dabelea, Peter H. Bennett, Xavier Pi-Sunyer, Sarah Fowler, Steven E. Kahn, and The Diabetes Prevention Program Research Group*

TABLE 2. Effect of DPP treatment on incidence of diabetes

	Placebo		Metformin		ILS	
	GDM (n = 122)	No GDM (n = 487)	GDM (n = 111)	No GDM (n = 464)	GDM (n = 117)	No GDM (n = 465)
Incidence of diabetes (number of cases per 100 person-years)[a]	15.2[b]	8.9	7.8	7.8	7.4	4.7
Reduction in incidence (compared with placebo)[a]			50.4[c]	14.4	53.4[c]	49.2[c]
Number needed to treat (to prevent one case in 3 yr compared with placebo)[a]			6.1	24.0	5.3	9.0

[a] Adjusted for age.

[b] $P < 0.05$ compared with non-GDM group.

[c] $P < 0.05$ compared with placebo.

TRIPOD: -55% DT2 après DG sous Troglitazone
PIPOD: -66% DT2 après DG sous Pioglitazone

Prévenir le DT2 après DG: la réalité

- *Stage E, Diab Res Clin Pract 2004*
- N=121 femmes informées après DG, revues à 2 ans:
  - activité physique non augmentée,
  - apports lipidiques non diminués

- *Verier-Mine, D&M 2010*:
- « Sparse literature… appears to indicate inefficacy. »

Barriers to and Facilitators of Postpartum Follow-Up Care in Women with Recent Gestational Diabetes Mellitus: A Qualitative Study

Wendy L. Bennett, M.D., M.P.H.,[1,2] Christopher S. Ennen, M.D.,[3] Joseph A. Carrese, M.D., M.P.H.,[1] Felicia Hill-Briggs, Ph.D.,[1] David M. Levine, M.D., M.P.H., Sc.D.,[1] Wanda K. Nicholson, M.D., M.P.H.,[4] and Jeanne M. Clark, M.D., M.P.H.[1,5]

I guess [I didn't come] cause [I was] seeing the baby every day . . . It's the only thing I did, see the baby at the hospital [NICU] and spend time there every day.—36-*year-old, did not attend visit*

Obviously things are harder [after the baby]. I'm just tired . . . because I'm burnt out, frustrated, you know? [I]t's tiring to figure ou where . . . all the resources are, and try to get to a more stabl better situation.—30-*year-old, did not attend visit*

[T]rying to get showers in and get food in is an issue right no [I]f those factors hadn't been met I probably would have cal and said, "I need to reschedule.—37-*year-old, attended visit*

[I]f my husband wasn't able to take off work, then I would pr have to delay [the appointment] until he could. [T]here's no I would've come in here by myself.—33-*year-old, attended visi*

J Women's Health 2011

I checked my [blood sugars] with my regular machine at home. Every day it was good. After pregnancy, one week [later] I checked [and] everything is good.—27-*year-old, did not attend visit*

I was nervous [to come]. Just the whole unknowing, 'cause once you know, then it's, Okay, now what do you do?—33-*year-old, attended visit*

I have my theories about why people aren't coming for their follow up appointments. Whenever I would come here, there would be a different doctor that I would see. . . . I think the continuity of care is very poor here.—36-*year-old, attended visit*

[I] have to come back again, because I had breakfast . . . I didn't know I had to have to be fasting when they do the tests.—32-*year-old, attended visit*

Postpartum Diabetes Screening

Adherence rate and the performance of fasting plasma glucose versus oral glucose tolerance test

SARAH KWONG, MD
REBECCA S. MITCHELL, MD
PETER A. SENIOR, MBBS, PHD
CONSTANCE L. CHIK, MD, PHD

DCare 2009

- 1006 femmes enceintes
- Dépistage postpartum
  - Entre S6 et M6
  - Par HGPO 75g
  - ***Avec rappel téléphonique à M6***
- 48% fait
  - Moins si parité élévée
  - Plus (2/3) si insulinoTTT
- 14 DT2 (72% non détectables sur G à jeun)

Gestational diabetes: risk of recurrence in subsequent pregnancies

Darios Getahun, MD, MPH; Michael J. Fassett, MD; Steven J. Jacobsen, MD, PhD

Recurrence risk of gestational diabetes in subsequent pregnancies based on gestational diabetes histories

		Subsequent birth			
First birth	Second birth	Total births, n	GDM, %	Unadjusted OR (95% CI)	[a]Adjusted OR (95% CI)
First 2 pregnancies (n = 65,132)					
No GDM	–	62,601	4.2	1.00 (Reference)	1.00 (Reference)
GDM	–	2531	41.3	16.1 (14.7–17.9)	13.2 (12.0–14.6)

Risque à la 2ème grossesse après DG: 41%
Risque à la 3ème grossesse après 2 DG: 57%

Réduire le DG à la prochaine grossesse ?

Rates and Risk Factors for Recurrence of Gestational Diabetes

STEPHANIE MACNEILL, MSC[1] B. ANTHONY ARMSON, MD, FRCS (C)[2]

DCare 2001

Table 2—*Predictive factors for recurrence of GDM from the multivariate model*

Variable	Recurrence of GDM *n* (%)	Adjusted RR (95% CI)*
Prepregnancy weight (subsequent pregnancy)		
<120 lb	22 (26.5)	1.0
120–149 lb	62 (30.1)	1.1 (0.7–1.6)
150–189 lb	56 (35.4)	1.2 (0.8–1.9)
≥190 lb	57 (50.4)	1.7 (1.2–2.6)

Réductions des récurrences rapportées avec:

-contrôle poids entre grossesses ***(Pole, Can J Public Health 1999)***

-perte de poids si obésité: BMI -2 = risque -74% ***(Ehrlich, Obstet Gyn 2011)***

-low fat intake entre grossesses ***(Moses, DCare 1997)***

Primary Prevention of Gestational Diabetes Mellitus and Large-for-Gestational-Age Newborns by Lifestyle Counseling: A Cluster-Randomized Controlled Trial

Riitta Luoto[1,2*], Tarja I. Kinnunen[3], Minna Aittasalo[1], Päivi Kolu[1], Jani Raitanen[1,3], Katriina Ojala[1], Kirsi Mansikkamäki[1], Satu Lamberg[3], Tommi Vasankari[1,2], Tanja Komulainen[1], Sirkku Tulokas[4]

- N =400 femmes enceintes à risque de DG
- HGPO à 10±2SA normale

Conseil hygiéno-diététique

Coaché (aux 5 visites anténatales)

Suivi:

+de fibres + de PUFat

-de SatFat - de Saccharose

Baisse MET moindre

Contrôle

PLOSMed 2011

Autant de DG

Variables	8–12 wk Gestation			26–28 wk Gestation		
	Mean ± SD		*p*-Value	Mean ± SD		*p*-Value
	Intervention Group (*n* = 219)	Usual Care Group (*n* = 180)	Difference between Groups[a]	Intervention Group (*n* = 219)	Usual Care Group (*n* = 180)	Difference between Groups[a]
Glucose levels in 2-h OGTT (mg/l)						
Fasting (0)	4.90 ± 0.22	4.89 ± 0.26	0.68	4.74 ± 0.33	4.77 ± 0.32	0.44
1 h	6.43 ± 1.55	6.18 ± 1.37	0.09	7.70 ± 1.74	7.47 ± 1.77	0.23
2 h	5.41 ± 1.07	5.25 ± 0.94	0.12	5.92 ± 1.21	5.87 ± 1.19	0.99
Insulin	11.55 ± 5.92	11.22 ± 5.69	0.70	13.37 ± 6.48	12.31 ± 6.25	0.10
HOMA-IR[b]	1.47 ± 0.72	1.46 ± 0.69	0.86	1.69 ± 0.80	1.57 ± 0.77	0.13

Moins de macrosomies

developed GDM (absolute effect size 1.36, 95% confidence interval [CI] 0.71–2.62, $p = 0.36$). Neonatal birthweight was lower in the intervention than in the usual care group (absolute effect size −133 g, 95% CI −231 to −35, $p = 0.008$) as was proportion of large-for-gestational-age (LGA) newborns (26/216, 12.1% versus 34/179, 19.7%, $p = 0.042$). Women in the

Le suivi nutritionnel après grossesse ne concerne pas que la femme

High Prevalence of Type 2 Diabetes and Pre-Diabetes in Adult Offspring of Women With Gestational Diabetes Mellitus or Type 1 Diabetes

The role of intrauterine hyperglycemia

Clausen, DCare 2008

DT2 et prédiabètes à 22±4 ans chez les enfants de:

- **mère « background »: 4%**
- **mère DT1: 11%**
- **mère à risque de DG: 12%**
- **mère DG: 21%**

Conclusions

- **OUI**, un suivi nutritionnel peut être intéressant après DG, pour:
  - -la femme, ses enfants
  - -sa prochaine grossesse
- Mais ça ne sera pas facile.