

Den gravide med diabetes

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Dagsorden

- Fokus på type 1 diabetes
 - Lidt baggrundsfysiologi
 - Generel, og udvalgte detaljer
 - Fokus på blodtryk
 - Lidt om fødslen
 - Langtidseffekter for børnene?
 - Alt primært baseret på danske studier
-

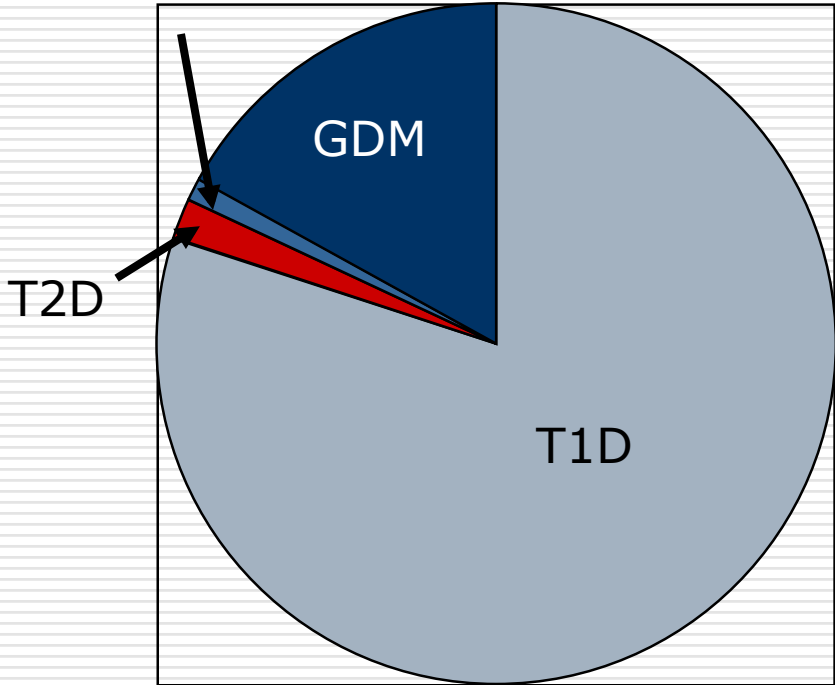
Diabetes og graviditet

- Gestationel diabetes (3-4%)
 - Prægestationel diabetes
 - Type 1 – 250/år
 - Type 2 – 150/år
 - MODY – 10-15/år
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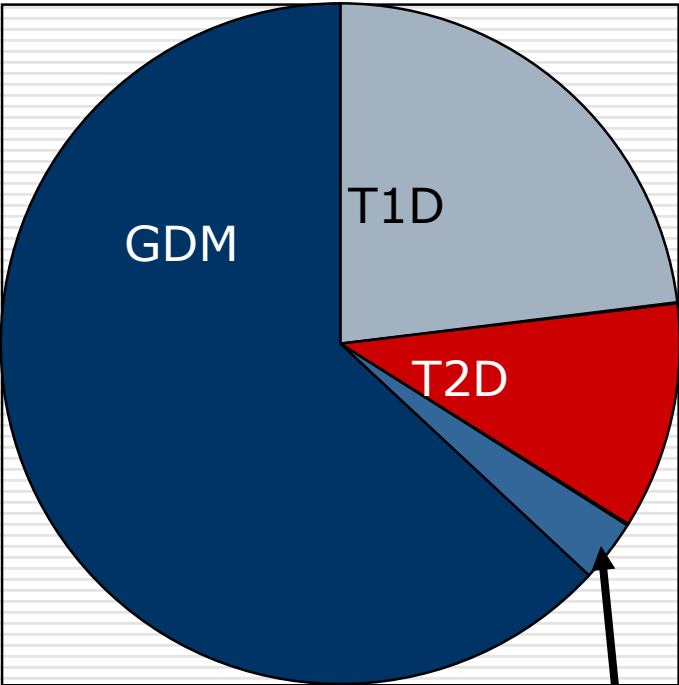
Diabetes and pregnancy

Diabetes types in Copenhagen

Unknown T2D



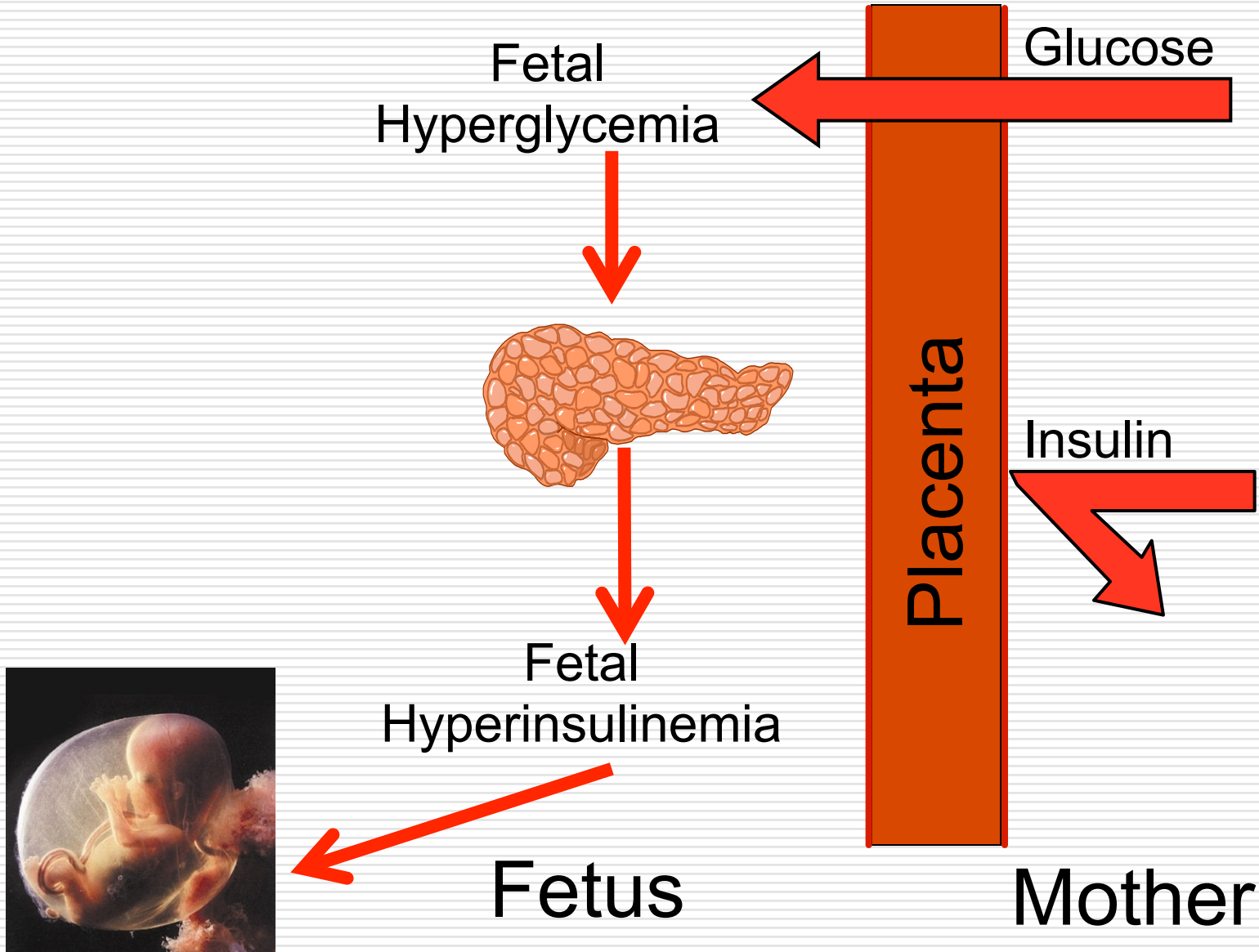
30-50 years ago



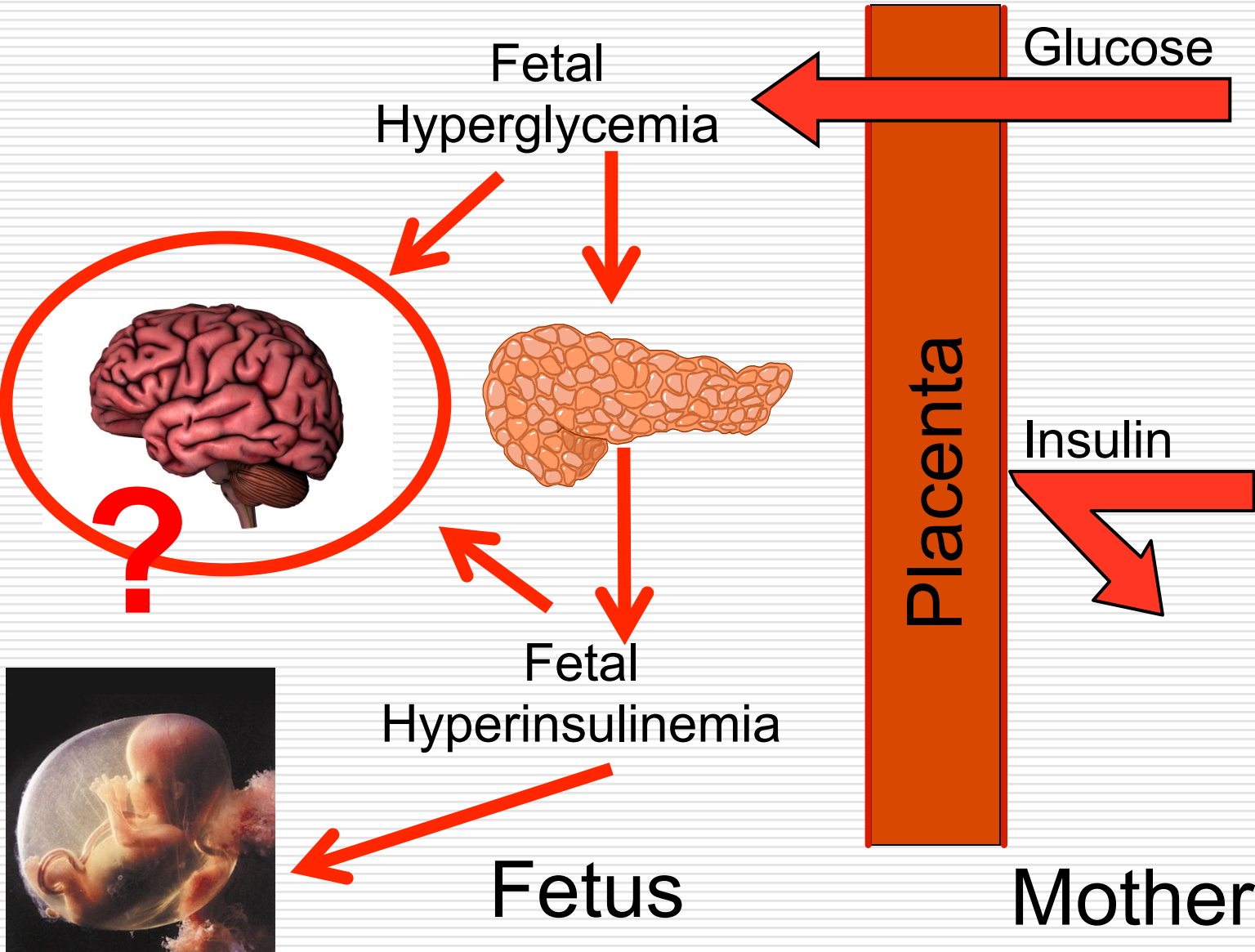
Unknown T2D

This millennium

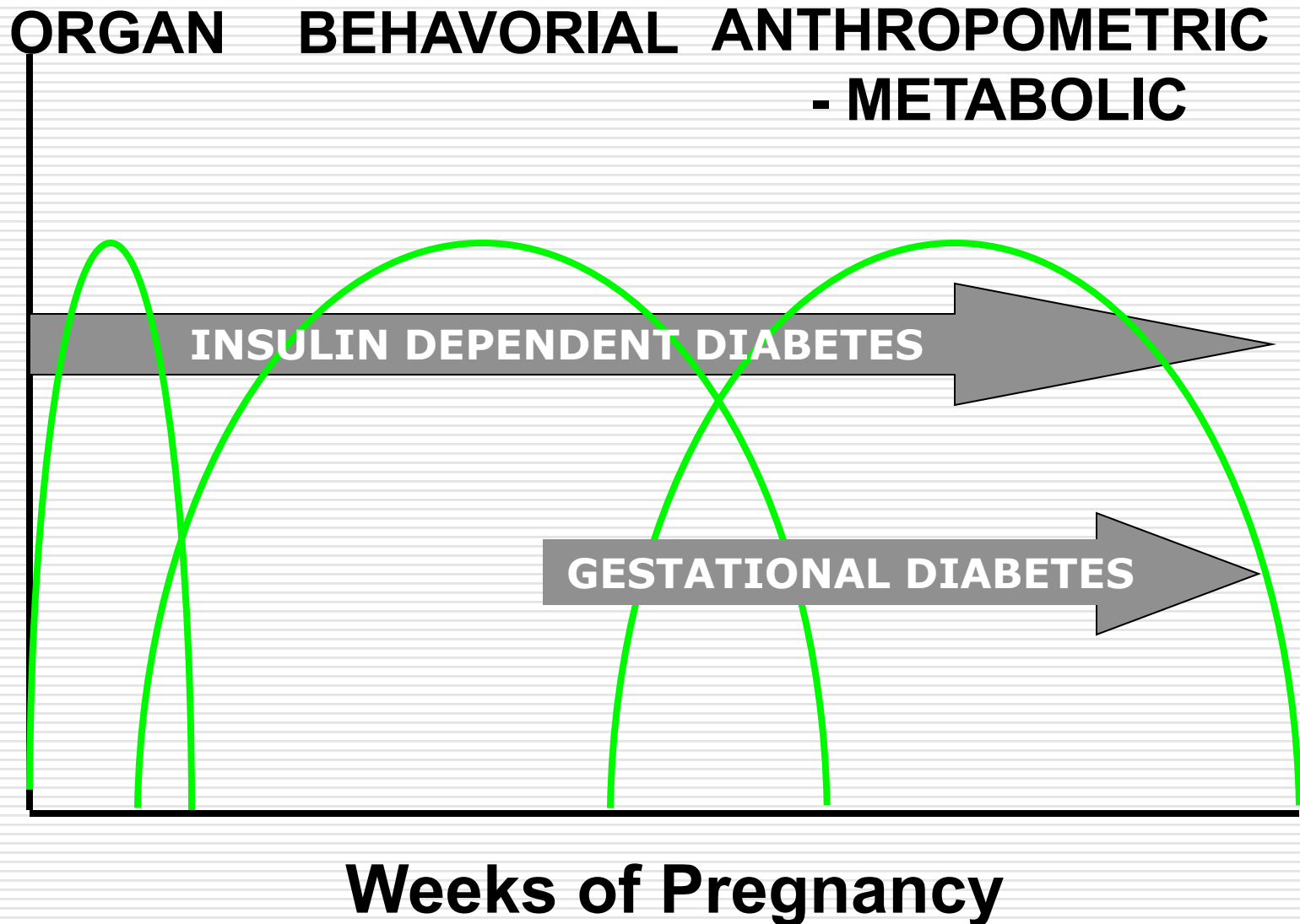
The Pedersen hypothesis



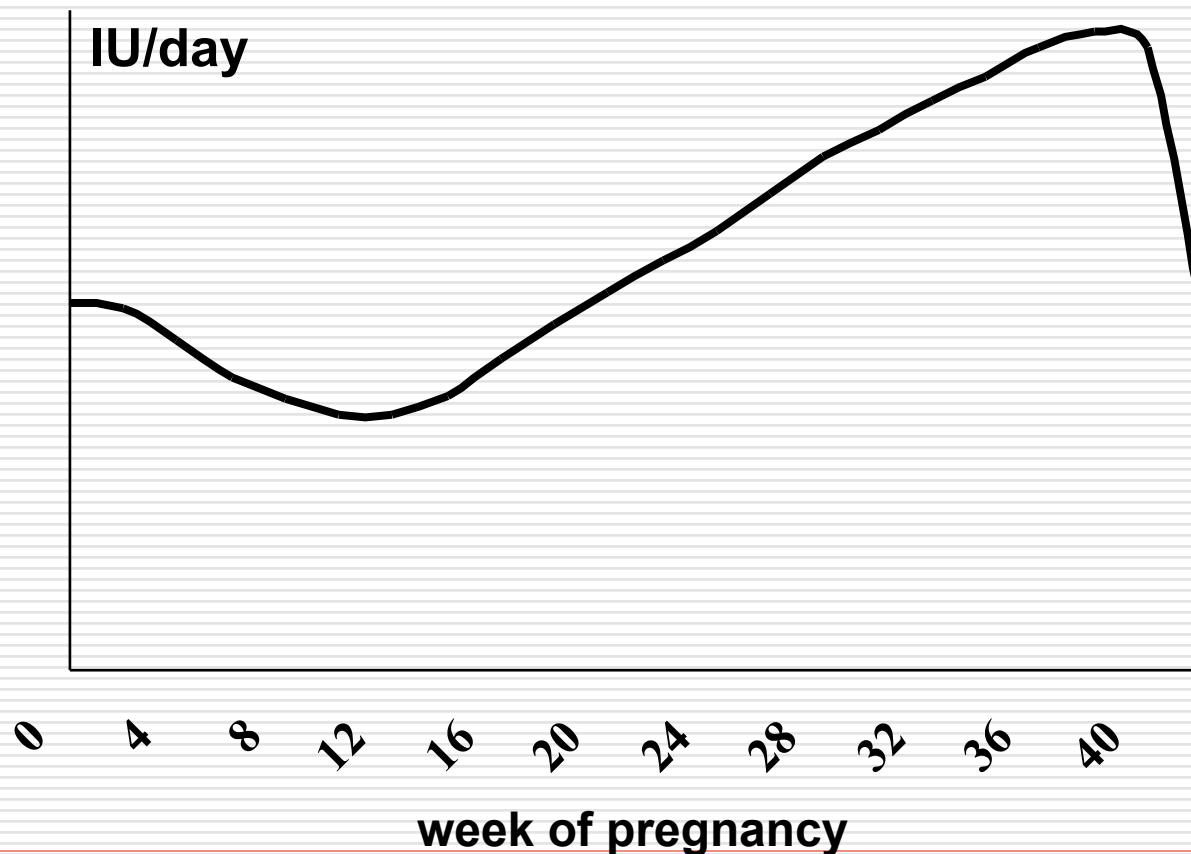
The Pedersen hypothesis



Fuel-mediated teratology



Changes in insulin requirement in diabetic women during pregnancy



Perinatal implications of maternal hyperglycemia



Severe pre-gestational diabetes

- Congenital malformations ↑
- Perinatal mortality ↑
- Prematurity ↑
- Neonatal hypoglycemia ↑
- Shoulder dystocia ↑
- Macrosomia ↑



Mild GDM

Maternal complications Denmark 1993-99 (N=1215)

	Type 1 diabetes	Background population	RR
Preeclampsia	18%	2.6%	6.9 *
Preterm delivery	42%	6%	7.0 *
Caesarean section	56%	13%	4.3 *

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Neonatal complications Denmark 1993-99 (N=1215)

	Type 1 diabetes	Background population	RR
Stillbirth	2.1%	0.45%	4.7 *
Perinatal mortality	3.1%	0.75%	4.1 *
Congenital malformations	5.0%	2.8%	1.7 *

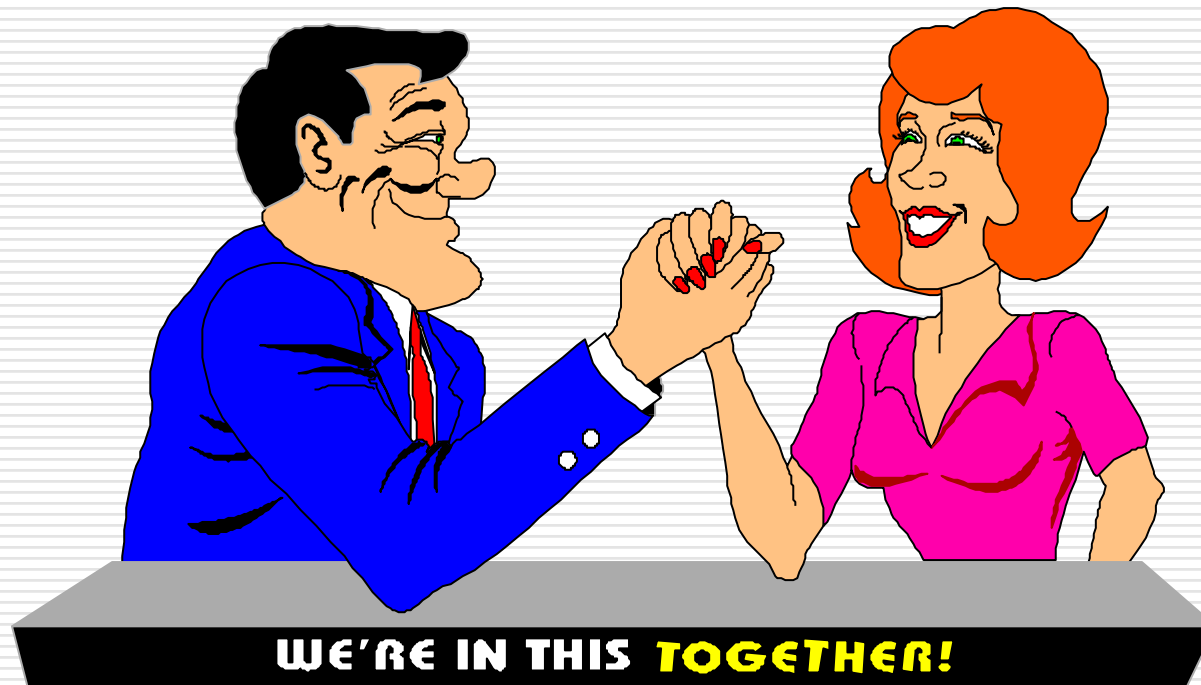
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Planlagt graviditet



Hvordan sikrer den vordende mor sig at graviditeten forløber så godt som muligt – før graviditeten ?

- ❑ God kontakt til diabetesteam
 - ❑ God metabolisk kontrol,
 - HbA1c < 53 mmol/l (7%)
 - ❑ Folinsyretilskud 400 ug per dag
 - ❑ Medicinliste gennemgås:
 - insulin, blodtryksmedicinØjne og nyrer undersøges
-

Hvordan sikrer den vordende mor sig at graviditeten forløber så godt som muligt – under graviditeten ?

- God kontakt til fødested og diabetesteam
 - God metabolisk kontrol,
 - HbA1c < 48/38 mmol/mol (6,5/5,6%)
 - Blodsukkermåling 7 gange dagligt
 - Blodsukker før måltider 4-5,5
 - Blodsukker efter måltider 4-7
 - Hyppige ambulante kontroller (blodtryk m.m.)
 - Insulinføling 2-4 gange ugentligt accepteres
-

Hvordan sikrer den vordende mor sig at graviditeten forløber så godt som muligt – under graviditeten ?

- Fokus på begrænset vægtstigning
 - Brug af insulin analoger
 - Insulinpumper og glukosesensorer?
-

Pump-treatment is it of value in pregnancy?

Theoretically –yes

In practise – may be - no proof



Is intermittent continuous glucose monitoring of value in pregnancy

- Theoretically – Yes

- In practise – may be
 - One randomized trial with effect



Fosterovervågning



Fosterovervågning

- Ultralydsscanning
 - 8, 12, (14), 20, 28, 34, 37 uger
 - Misdannelser, vægt, vand og flow???
- CTG på vid indikation
- Opmærksomhed på dagligt liv fra 28-30 uger
- Insulinbehov

Stillbirth

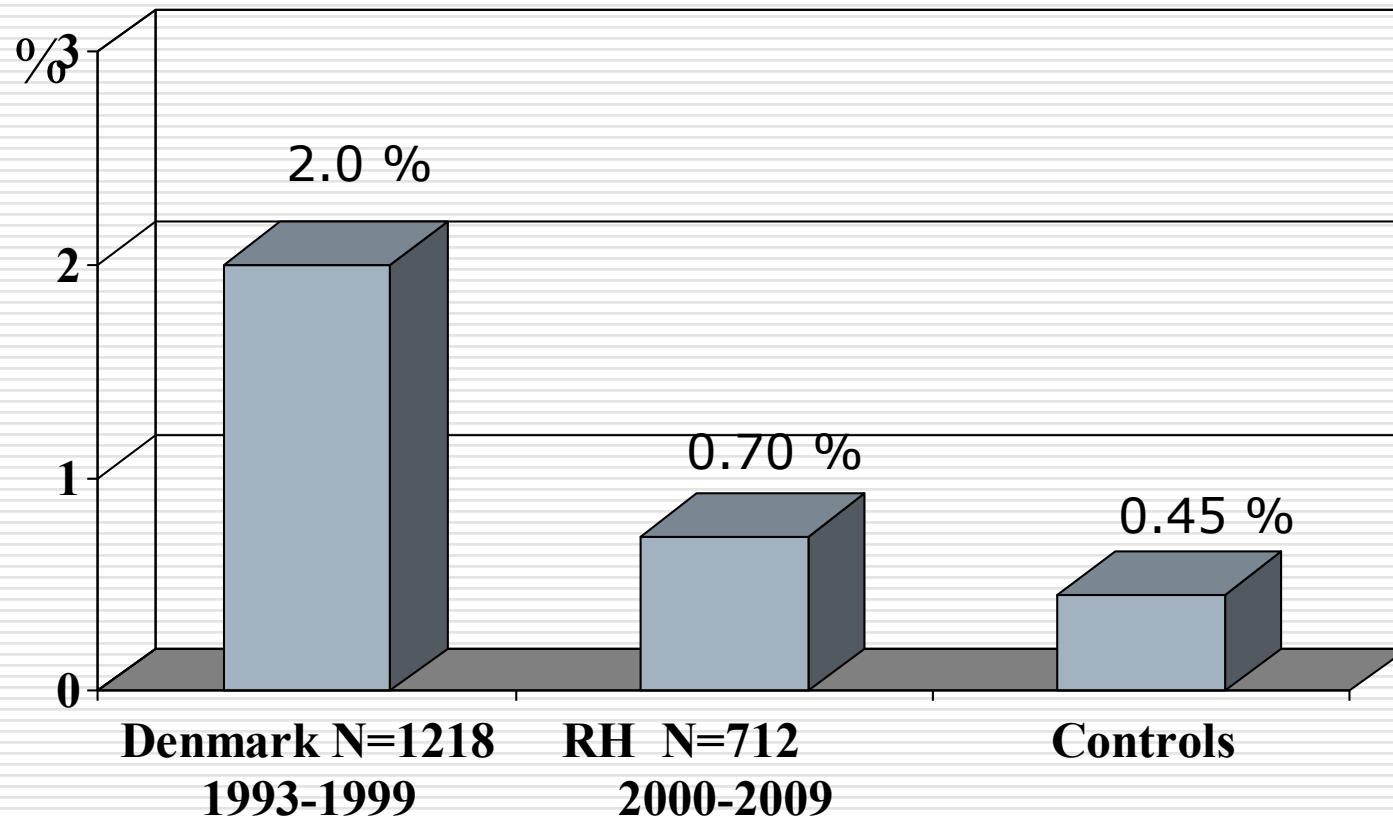
Audit on stillbirth in type 1 diabetic pregnancy in Denmark 1990-2000

- Women experiencing stillbirth were characterized by an increased frequency of
 - suboptimal glycemetic control

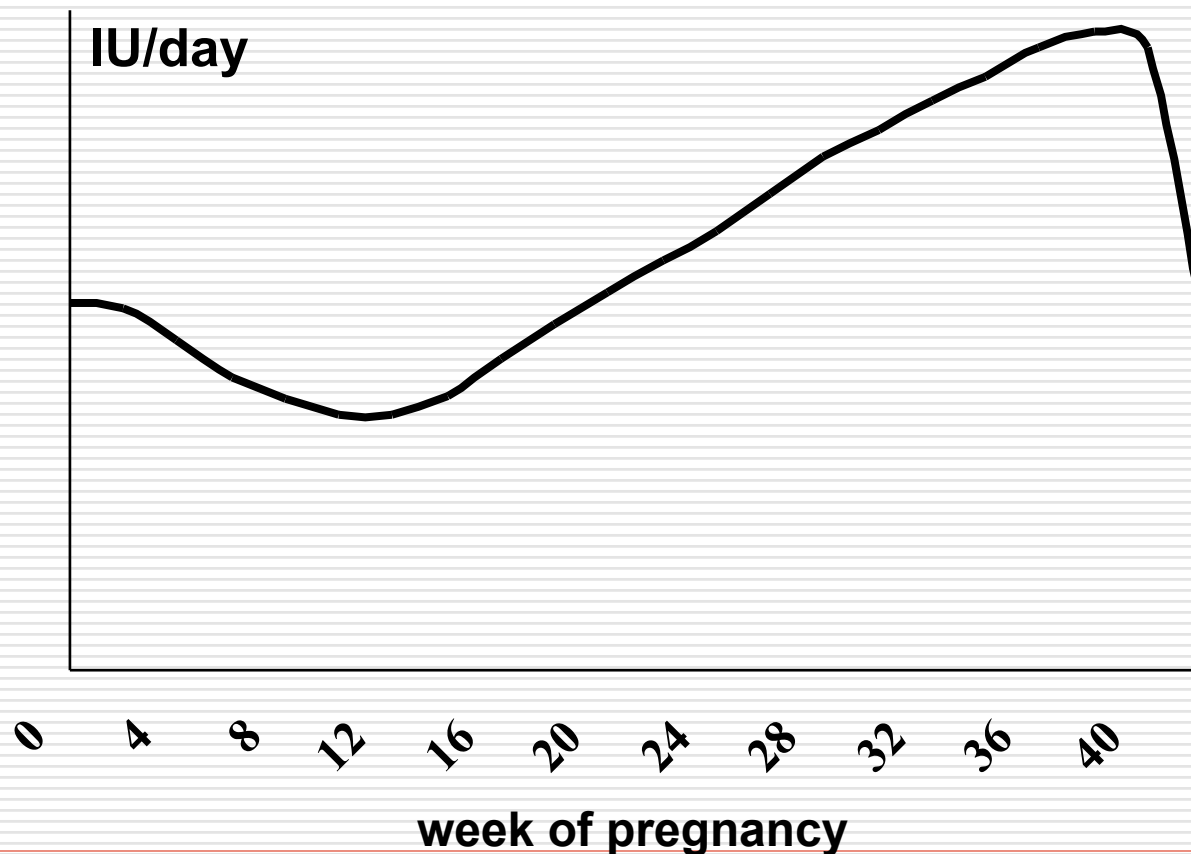
Audit on stillbirth in type 1 diabetic pregnancy in Denmark 1990-2000

- Women experiencing stillbirth were characterized by an increased frequency of
 - suboptimal glycemetic control
 - diabetic nephropathy
 - smoking
 - low social status
 - previous stillbirth

Stillbirth in pregnant women with type 1 diabetes



Changes in insulin requirement in diabetic women during pregnancy



Betydning af hypoglykæmi under svangerskabet

- ❑ Fosteret tåler hypoglykæmi utrolig godt.
- ❑ Hypoglykæmi behandles som vanligt
- ❑ Ved blodsukker mindre end 5-6 før sengetid tilrådes ekstra kulhydrater
- ❑ Næsten hver anden kvinde har mindst et svært insulintilfælde i graviditeten.
- ❑ Risiko for død og trafikuheld

Er det farligt at have syre i urinen under graviditeten ?

- ❑ Sukkersygen kommer lettere ud af balance når man er gravid.
 - ❑ Syre (ketonstoffer) i urinen skal tages alvorligt - fødestedet eller diabetesteamet skal kontaktes.
 - ❑ Syreforgiftning er en alvorlig sag for et foster og skal behandles intensivt.
 - ❑ Mål altid blodsukker og urin ketonstoffer ved "syge" gravide med diabetes
-

Lung maturation - Glucocorticoid treatment

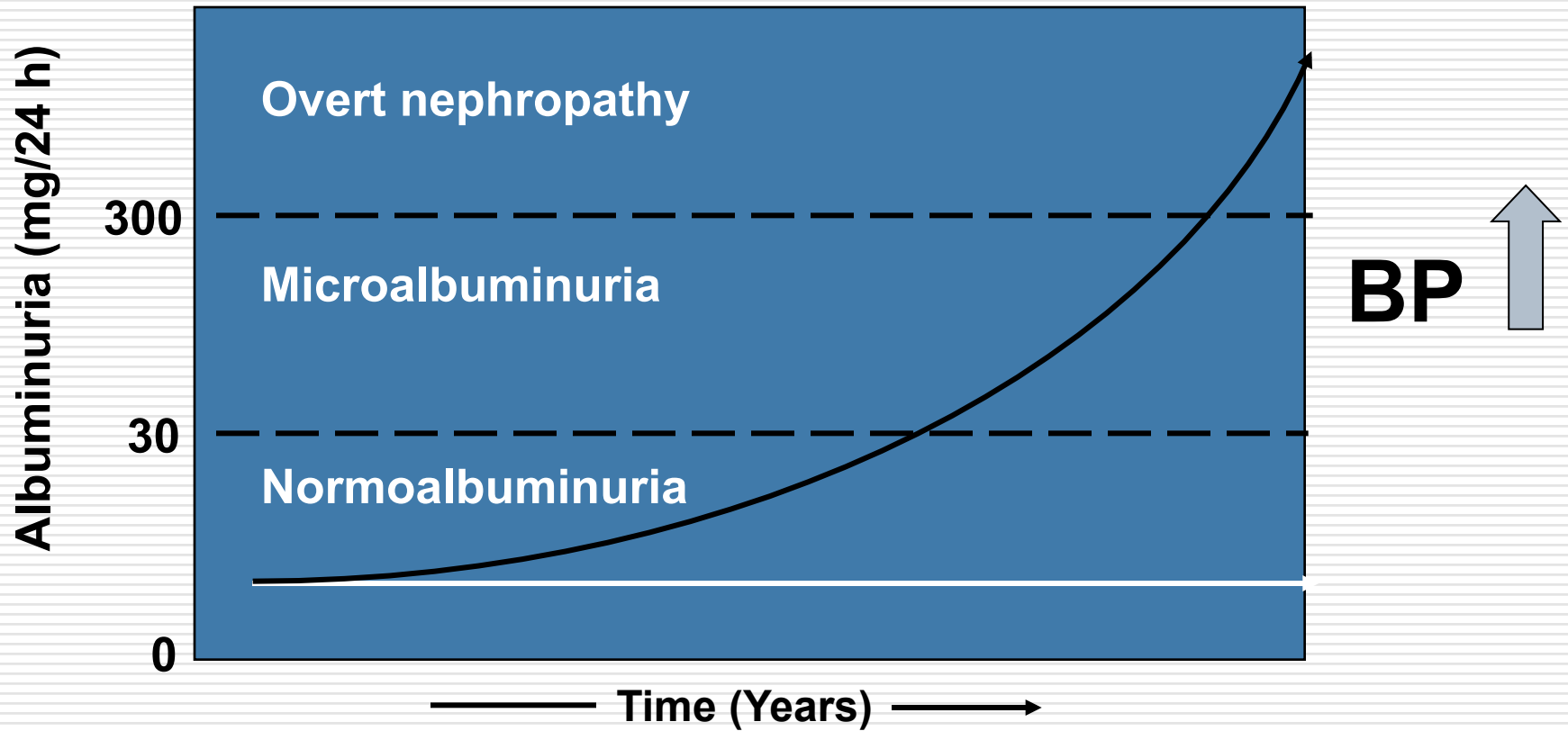
- Usual insulin dose is set to 100%
- Day 1, night insulin dose +25%
- Day 2, all 4 insulin doses +40%
- Day 3, all 4 insulin doses +40%
- Day 4, all 4 insulin doses +20%
- Day 5, all 4 insulin doses +10%

Ved celeston – ring til en ven!

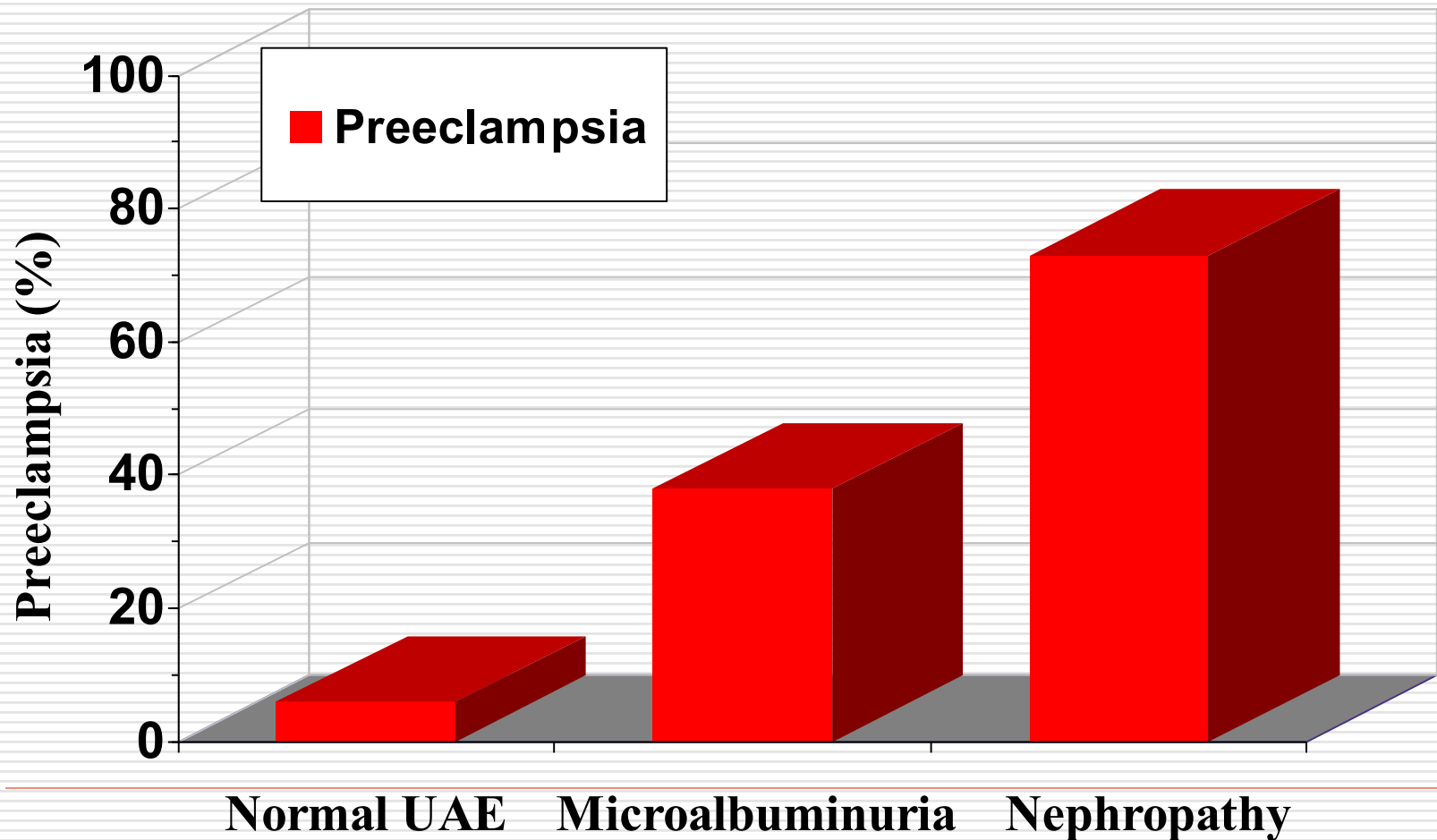
Er æggehvitestof i urinen farligt ?

- Nyresygdom tidligt i graviditeten er af betydning for forløbet af graviditeten.
 - Æggehvitestof i urinen og forhøjet blodtryk senere i graviditeten er tegn på begyndende svangerskabsforgiftning
 - Det kræver tæt kontrol og behandling
 - Fører ofte til for tidlig fødsel
-

Diabetes and microalbuminuria



Preeclampsia in type 1 diabetic pregnancy in relation to urinary albumin excretion



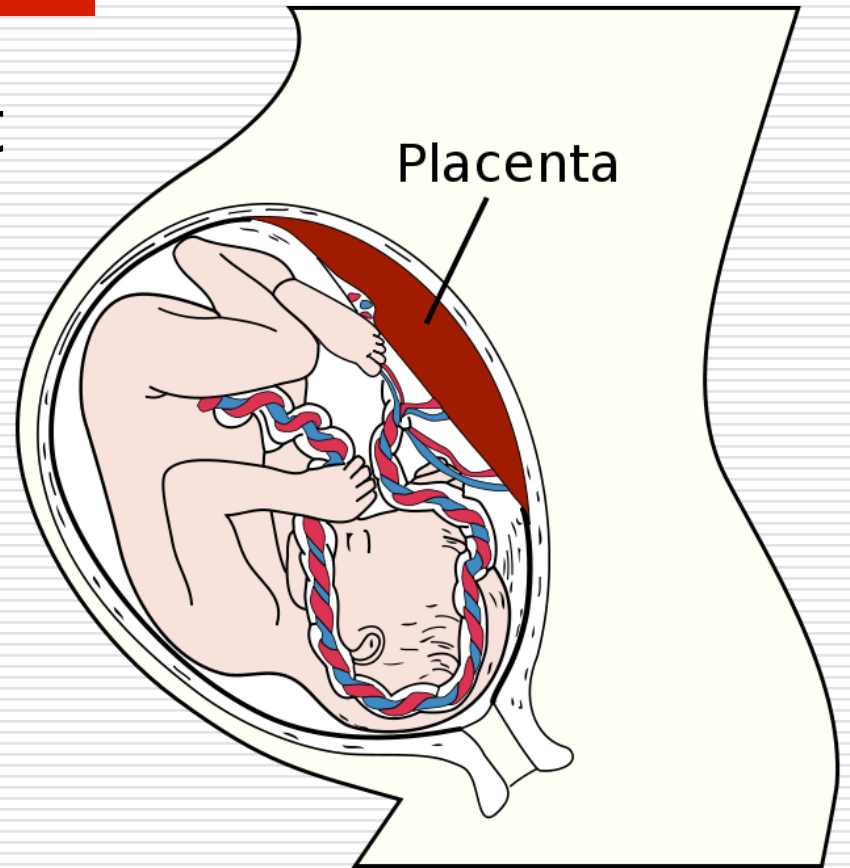
Development of preeclampsia in women with type 1 diabetes is preceded by presence of

- Higher blood pressure
- Increased urinary albumin excretion
- Decreased maximal vasodilatory capacity
- Signs of endothelial dysfunction

- All which theoretically can be modulated by antihypertensive treatment

- Placenta function is often well preserved

Consensus of treatment
of hypertension
in pregnancy when
 $BP \geq 150/100$ mmHg



Antihypertensive drugs used during pregnancy

- Methyldopa
 - Labetalol
 - Calcium antagonists
 - Diuretics
-

Effect of early antihypertensive treatment in pregnant women with microalbuminuria

Cohort- year	1995-99	2000-2003	2004-2006
AH- treatment protocol	BP>140/95 AH-pause		
Methyldopa first choice			
Number	26		
AH- treatment	35%		
AH-treatment onset (week)	29 (20-34)		
HbA1c at 28 wks (%)	6.3		
Preeclampsia (%)	42%		
Delivery < 34 wks	23%		
Delivery < 37 wks	62%		

Effect of early antihypertensive treatment in pregnant women with microalbuminuria

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AH- treatment protocol	BP>140/95 AH-pause	U-alb>2000 BP>140/90 AH-shift	
Methyldopa first choice			
Number	26	20	
AH- treatment	35%	50%	
AH-treatment onset (week)	29 (20-34)	13 (0-34)	
HbA1c at 28 wks (%)	6.3		
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Delivery < 34 wks	23%	0	0
Delivery < 37 wks	62%	40%	20%



Preeclampsia

- ❑ Hypertension in diabetic pregnancy is prevalent
 - ❑ Hypertension is associated with increased risk of preeclampsia and preterm delivery
 - ❑ Early antihypertensive treatment may reduce the risk
 - ❑ Safe drugs must be used and avoid blockers of the renin angiotensin system
-

The Copenhagen recommendations for antihypertensive treatment in diabetic pregnancy

- ❑ BP > 135/85
- ❑ U-albumin > 300 mg/24h
- ❑ If antihypertensive treatment is given prior to pregnancy then shift to drugs approved for use in pregnancy
- ❑ Low dose aspirin
- ❑ Seems safe for the fetus



Should we be even more aggressive or are we treating too many

- White coat hypertension



Delivery

- 0-3 weeks before term after individual judgement
 - Induction of labor
 - medical
 - prostaglandins
 - oxytocin
 - physical
 - rupture of the membranes
 - balloon catheter
 - Elective Cesarean Section
-

Treatment during delivery

- Aim for blood glucose: 4-7 mmol/l
 - Normal insulin and food until regular contractions or rupture of the membranes
 - Hereafter fasting, and infusion of 5% glucose in water, 60 ml/h, plus insulin in reduced doses (25-50%) at regular hours
-

Hvor kommer d

genen og vasker hår og skifter tøj. Det er ikke
som hun havde håbet. Men hun har affundet sig med det og er
endda glad og opstemt. Den lange rejse er endt. Nu står hun
ved porten, og overlægen har selv lovet at føre kniven.

Hun har planlagt alting i mindste detalje. Toilettasken blir
pakket. Overfrakken blir rullet sammen omkring tøflerne. Det
irgrønne strikketøj blir lagt i en plasticpose og ugebladene for-
æret væk – efter at strikkeopskrifterne først er revet ud. Stella
Nova-billedet af Kalle blir pakket ind i papir og lagt ned i lom-
men på den store taske.

En time før morgenmaden blir serveret, får Olivia en ka-
nyle lagt i armen. Der sættes glykosedrop op, som skal løbe
med 20 dråber i minuttet.

NEA TRIER MØRCH



Treatment during delivery

- Close fetal surveillance (CTG, STAN)
 - Be prepared for shoulder dystocia
-

**SHOULDER
DYSTOCIA!**

Skulderdystoci

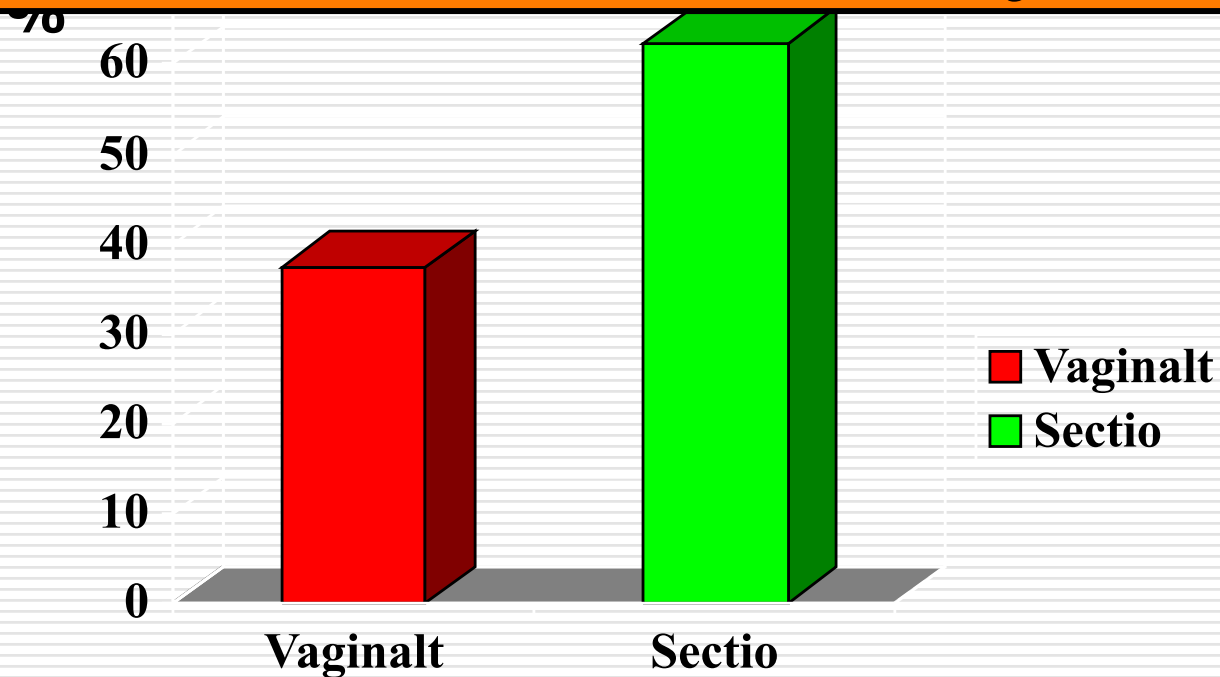


Source: Knoop KJ, Stack LB, Storrow AB, Thurman RJ: *The Atlas of Emergency Medicine, 3rd Edition*: <http://www.accessmedicine.com>

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Fødselsmåde hos gravide med type 1 diabetes – 2004-2006 - RH

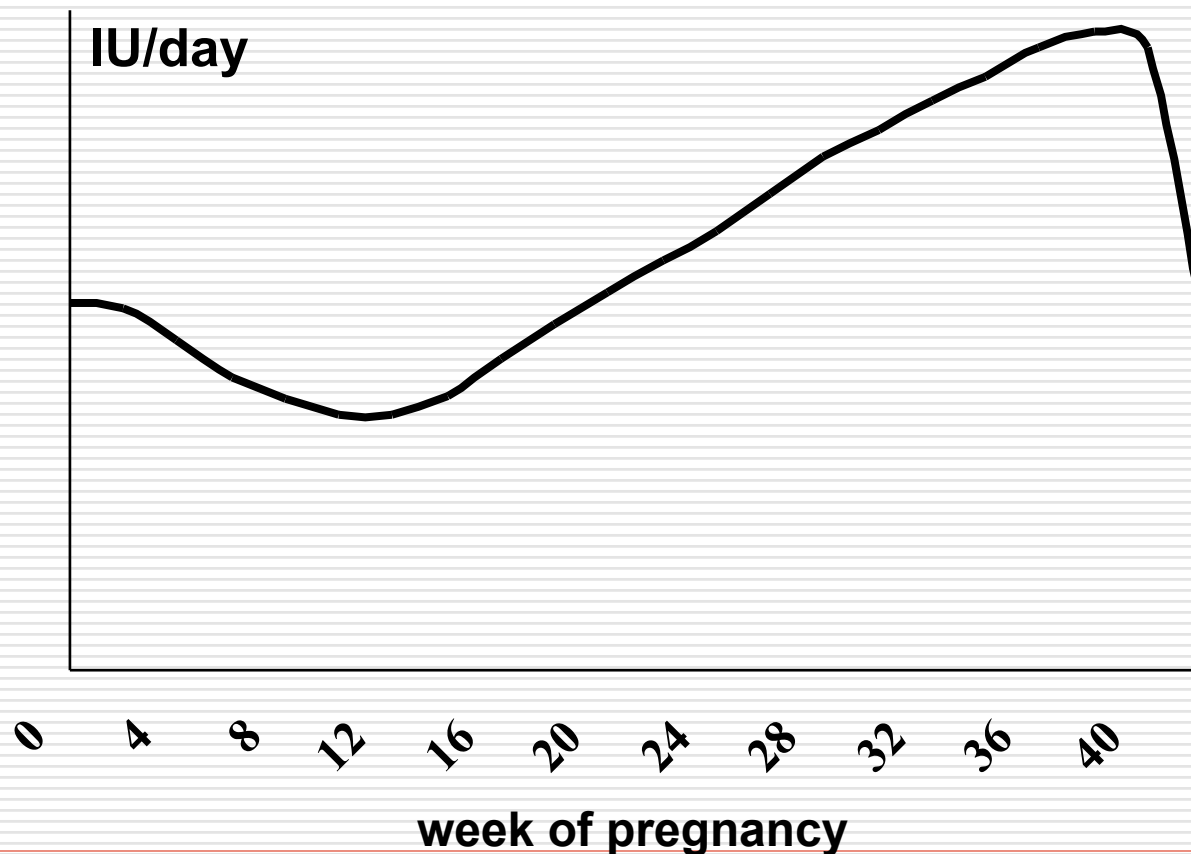
2012-2014 – 45 % føder ved kejsersnit



Et par erfarne jordemødre ved vagtskifte



Changes in insulin requirement in diabetic women during pregnancy



Insulin treatment post partum

- Insulin dose is reduced to around 70% of the prepregnancy dose to avoid hypoglycemia
-

Recent data – 2012-16

Rigshospitalet

	Type 1 DM (n=307)	Type 2 DM (n=187)
HbA1c, last visit, mmol/mol (%)	43±6 (6.1±0.5)	42±7 (6.0±0.6)
Gestational hypertension	9%	6%
Preeclampsia	9%	7%
Preterm delivery	17%	16%
LGA	42%	29%
Cesarean section	44%	43%

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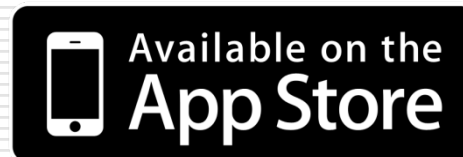
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App on diabetes in pregnancy - free



- ❑ Intended for pregnant women with diabetes and those planning pregnancy
- ❑ Features quick, convenient and easily accessible information
- ❑ Based on the treatment recommendations at the Center for Pregnant Women with Diabetes in Copenhagen



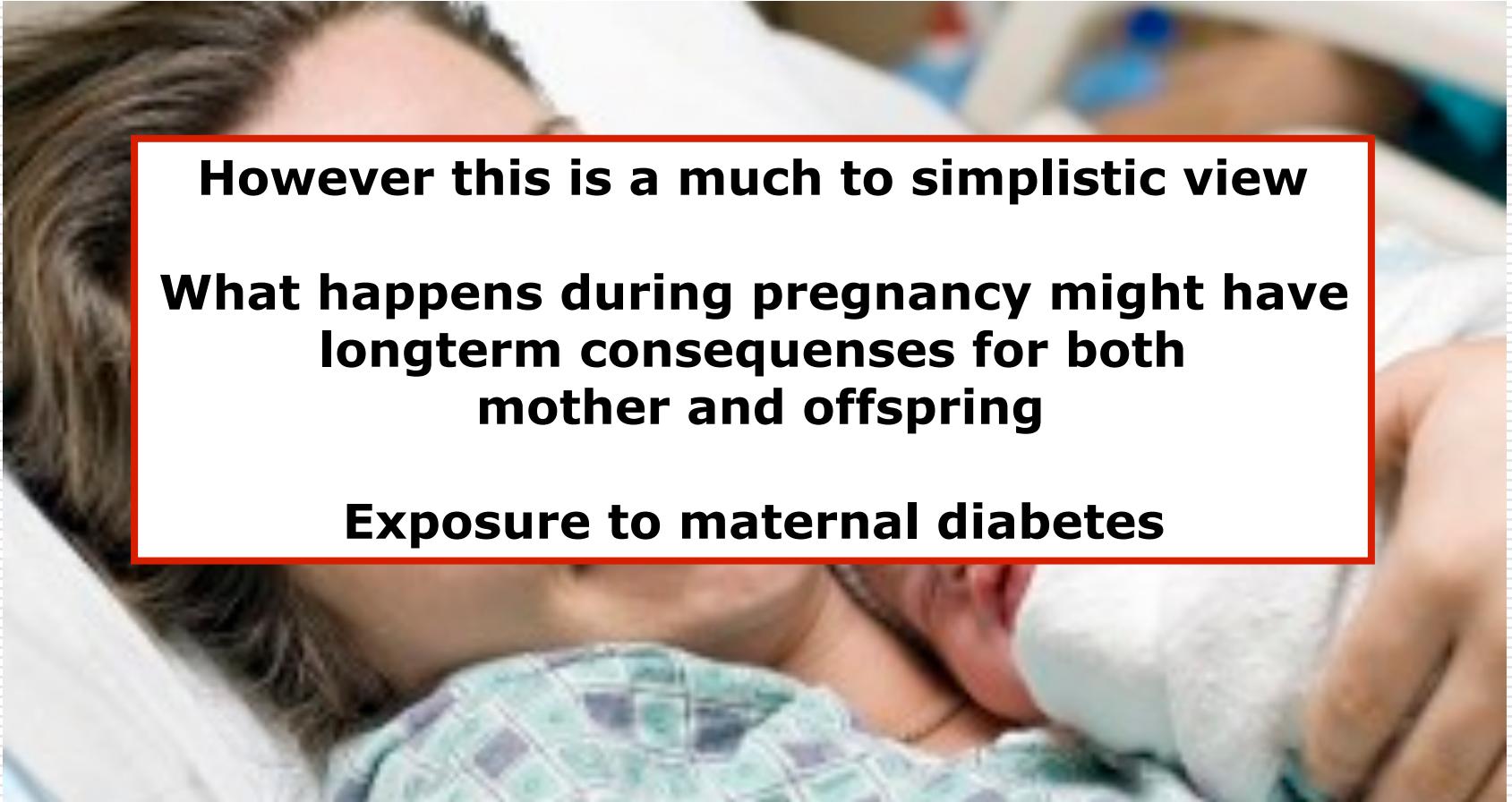
<http://www.pregnantwithdiabetes.com>

The obstetricians dream

However this is a much to simplistic view

**What happens during pregnancy might have
longterm consequences for both
mother and offspring**

Exposure to maternal diabetes



Maternal type 1 diabetes and offspring longterm health

Summary

- Increased risk of type 2 diabetes/pre-diabetes, overweight and the metabolic syndrome

- Lower cognitive scores
 - More learning difficulties in school
 - But similar school grades finishing primary school

- Offspring longterm complications might be prevented by optimal treatment of maternal hyperglycemia – solid evidence is currently lacking

Take home message

- Planlagt graviditet
 - God diabetes- og blodtryksregulation er alt afgørende
 - Tæt obstetrisk kontrol
 - Obs ved Celeston
 - Ring til en ven!
 - Outcome af graviditeterne bedres, men er stadig et stykke fra det normale
-

Tak for opmærksomheden

