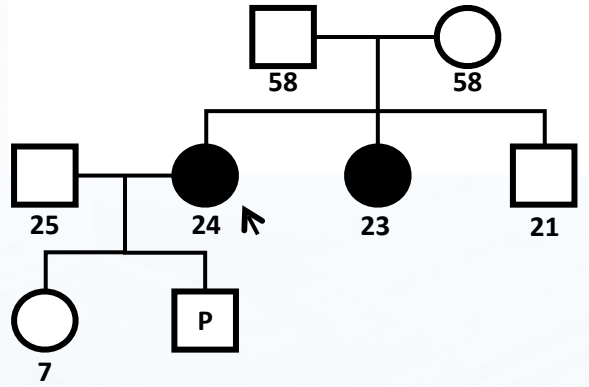
A 24-year-old woman with pregnancy

Known case rickets (diagnosed at 2 years old)

- Documented hypocalcemia, hypophosphatemia, elevated PTH, 25(OH)D level = 27 ng/mL



Now she is 28 weeks pregnant.

PE: Height 140 cm, knock knees, others: unremarkable

Current medication with poor adherence to treatment

- Calcitriol (0.25 mg) 1x2 po pc
- $CaCO_3$ (1250 mg) 1x3 po pc
- Vitamin D_2 (20,000iu) 1 cap/week

Lab at GA 28 weeks		
Ca / CCa	8.4/9.2	mg/dL
PO_4	1.6	mg/dL
Albumin	3.07	g/dL
PTH	193.4	pg/mL
ALP	418	IU/L
25(OH)D	31.2	ng/mL

1. **What is the cause of rickets?**
2. **What is the appropriate management for calcium and phosphate supplementation?**

1. What is the cause of rickets?
2. What is the appropriate management for calcium and phosphate supplementation?

Laboratory characteristics of rickets

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Type	Calcium	Phosphorus	Alkaline phosphatase	PTH	25 (OH)D	1,25 (OH)2D
Calcipenic rickets						
Vitamin D deficiency	↓ or N	N or ↓	↑	↑	↓	variable
VDDR IA	↓ or N	N or ↓	↑	↑	N or ↑	↓ or N
VDDR IB	↓ or N	N or ↓	↑	↑	↓	N or ↓
VDDR II	↓ or N	N or ↓	↑	↑	N	↑
Phosphopenic rickets						
Nutritional phosphate deficiency	N	↓	↑	N or ↑	N	N or ↓
X-linked hypophosphatemic rickets	N	↓	↑	N or ↑	N	N or ↓
AD hypophosphatemic rickets	N	↓	↑	N or ↑	N	N or ↓
AR hypophosphatemic rickets	N	↓	↑	N or ↑	N	N or ↓
Hereditary hypophosphatemic rickets with hypercalciuria	N	↓	↑	N or ↑	N	↑

Genetic Causes of Rickets J Clin Res Pediatr Endocrinol 2017;9(Suppl 2):88-105

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Genetic Causes of Rickets J Clin Res Pediatr Endocrinol 2017;9(Suppl 2):88-105

Adaptive processes during pregnancy and lactation

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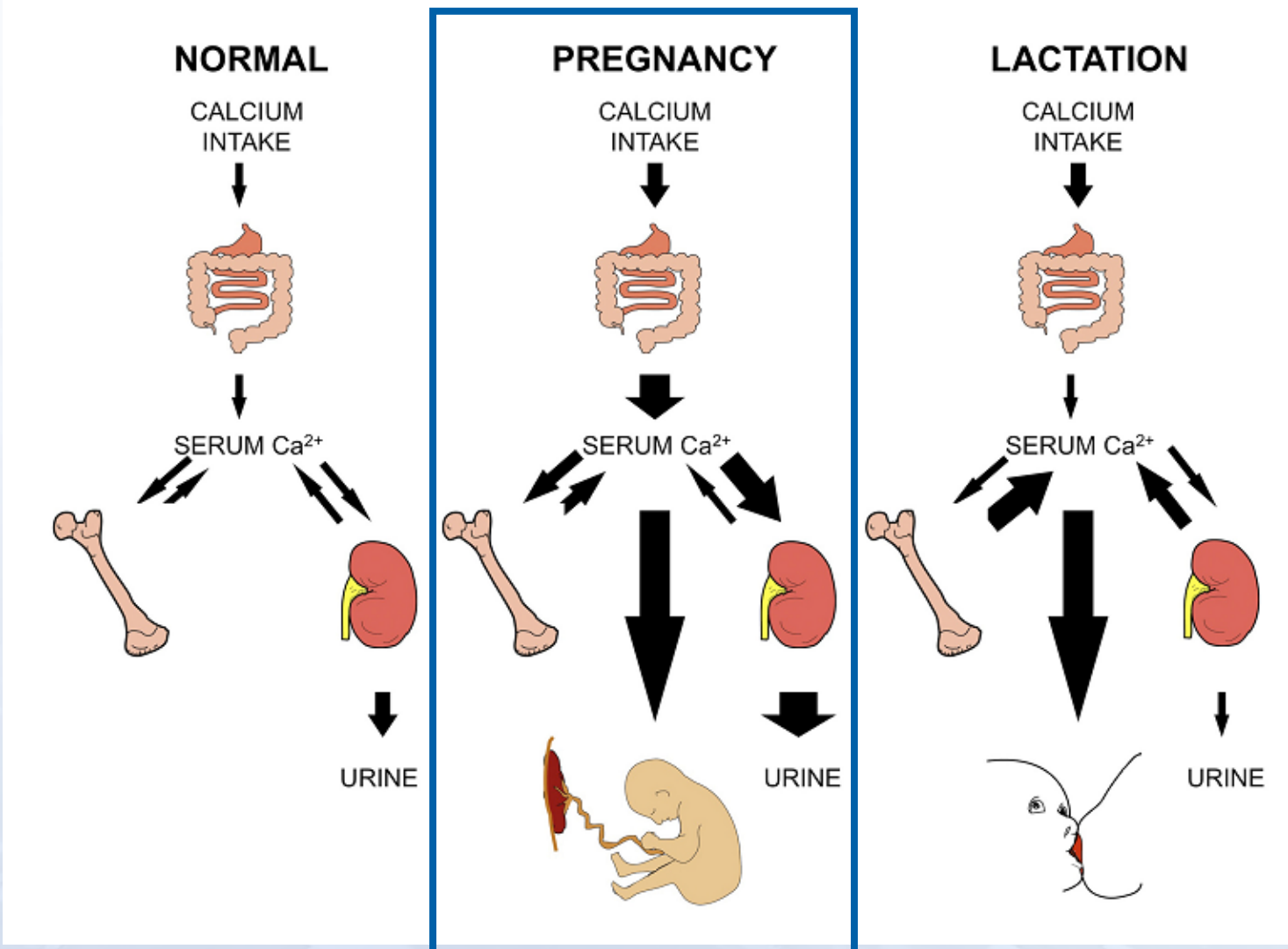

Kovacs CS. Physiol Rev96: 449–547, 2016

Calcium and Phosphate management In Rickets during Pregnancy and Lactation

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Vitamin D dependent rickets

	Gene / protein	Treatment	During pregnancy	During lactation
VDDR 1A	CYP27B1 1-alpha hydroxylase	- Alfacalcidol, calcitrol - Calcium	- 2/3 Increased 1.5-2X - 1/3 Unchange dose of calcitriol	Continue with Prepregnancy dose
VDDR 1B	CYP2R1 25-hydroxylase	- 25-OH vitamin D, calcitriol - Calcium		
VDDR 2A	VDR Vitamin D receptor	- High dose calcitriol - Calcium	Need to increase dose of calcitriol	
VDDR 2B	HNRNPC Heterogenous nuclear ribonucleoprotein C			

Calcium and calcitriol or alfacalcidol should be adjusted to maintain normal ionized or total calcium

Kovacs CS. Physiol Rev96: 449–547, 2016
Edouardet al. J Clin Endocrinol Metab, January 2011, 96(1):82– 89

Pregnancy in woman with VDDR1A (CYP27B1 mutation)

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Short- and Long-Term Outcome of Patients with Pseudo-Vitamin D Deficiency Rickets Treated with Calcitriol

T. Edouard, N. Alos, G. Chabot, P. Roughley, F. H. Glorieux, and F. Rauch

Genetics Unit (T.E., P.R., F.H.G., F.R.), Shriners Hospital for Children, Montréal, Québec, Canada H3G 1A6; and Endocrinology Service (T.E., N.A., G.C.), Centre Hospitalier Universitaire-Ste-Justine, Montréal, Québec, Canada H3T 1C5

- 9 women with 19 pregnancies
- During pregnancy, calcitriol dose were adjusted (every 4 weeks) to maintain normocalcemia
- **12/19 need 50-100% increase dose of calcitriol**
- After delivery, continued at prepregnancy dose
- All these pregnancies were without complications
- All newborns were normocalcemia at birth

Patient	Fœtus gender	Disease pregnancy	Calcitriol increase (%)	Delivery	Gestational age (weeks)	Birth length (cm)	Birth weight (kg)
23	G	-	50	CS (failed trial of labor)	41	50	4.2
	F	-	0	CS (fever)	40	50	3.2
24	F	-	100	CS (narrow pelvis)	40	50	3.2
	G	-	50	VD	40	55	3.4
25	F	-	0	VD	41	50	4.2
	F	Bleeding first trimester	0	CS (failed trial of labor)	39	51.5	3.7
28	F	-	50	VD	40	55	3.8
	F	-	25	VD	40	50	4.0
	G	-	0	CS (placenta praevia)	34	ND	2.2
29	F	-	50	CS (failed trial of labor)	41	50	3.2
	G	-	50	CS (failed trial of labor)	40	53	2.2
	F	-	50	CS (prior cesarean delivery)	38	50	3.2
30	F	-	100	VD	40	53	3.2
	G	-	100	VD	40	50	3.4
31	M	-	100	CS (narrow pelvis)	40	46.5	2.7
32	F	-	0	VD	40	ND	3.0
	M	-	100	VD	40	53	4.0
36	F	-	0	CS (narrow pelvis)	40	48	2.6
	G	-	0	CS (narrow pelvis)	39	51	2.9

CS: cesarean section, VD: vaginal delivery, ND: non documented

Edouardet al. J Clin Endocrinol Metab, January 2011, 96(1):82– 89

Calcium and Phosphate management In Rickets during Pregnancy and Lactation

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Phosphopenic rickets

	Treatment		During pregnancy	During lactation
FGF23-related	Phosphate supplement	0–2000 mg/day in 2 divided doses	2000 mg/day in 2 divided doses	
	Active vitamin D (alfacalcidol)	0–1.5 µg/day in 1 dose	1–1.5 µg/day in 1 dose	
FGF23-independent	Phosphate supplement	0–2000 mg/day in 2 divided doses	2000 mg/day in 2 divided doses	
	Active vitamin D (alfacalcidol)	**Contraindication** (risk for worsening of hypercalciuria)		

Lancet Diabetes Endocrinol. 2020 Feb;8(2):163-174
Therapeutic management of hypophosphatemic rickets from infancy to adulthood Endocr Connect 2014; 3: R13–30.

Genetic Analysis

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Compound heterozygous CYP27B1 mutation