Renal disease in pregnancy

Thursday morning teaching
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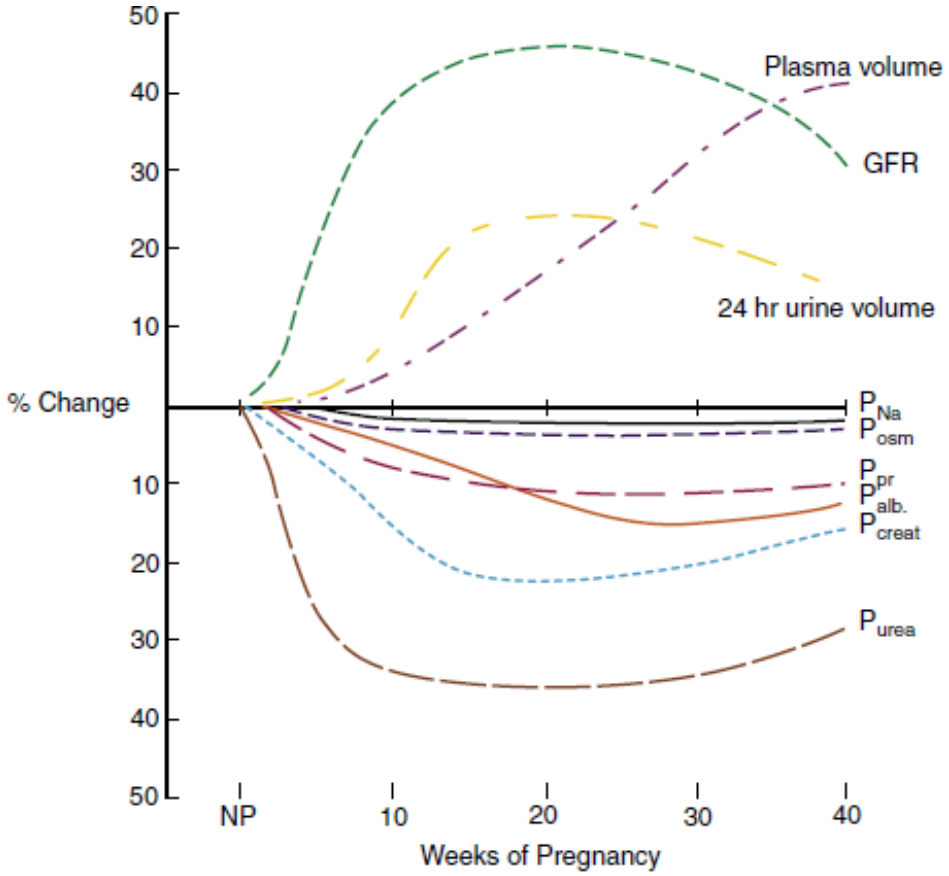
Nephrology Changes during Pregnancy



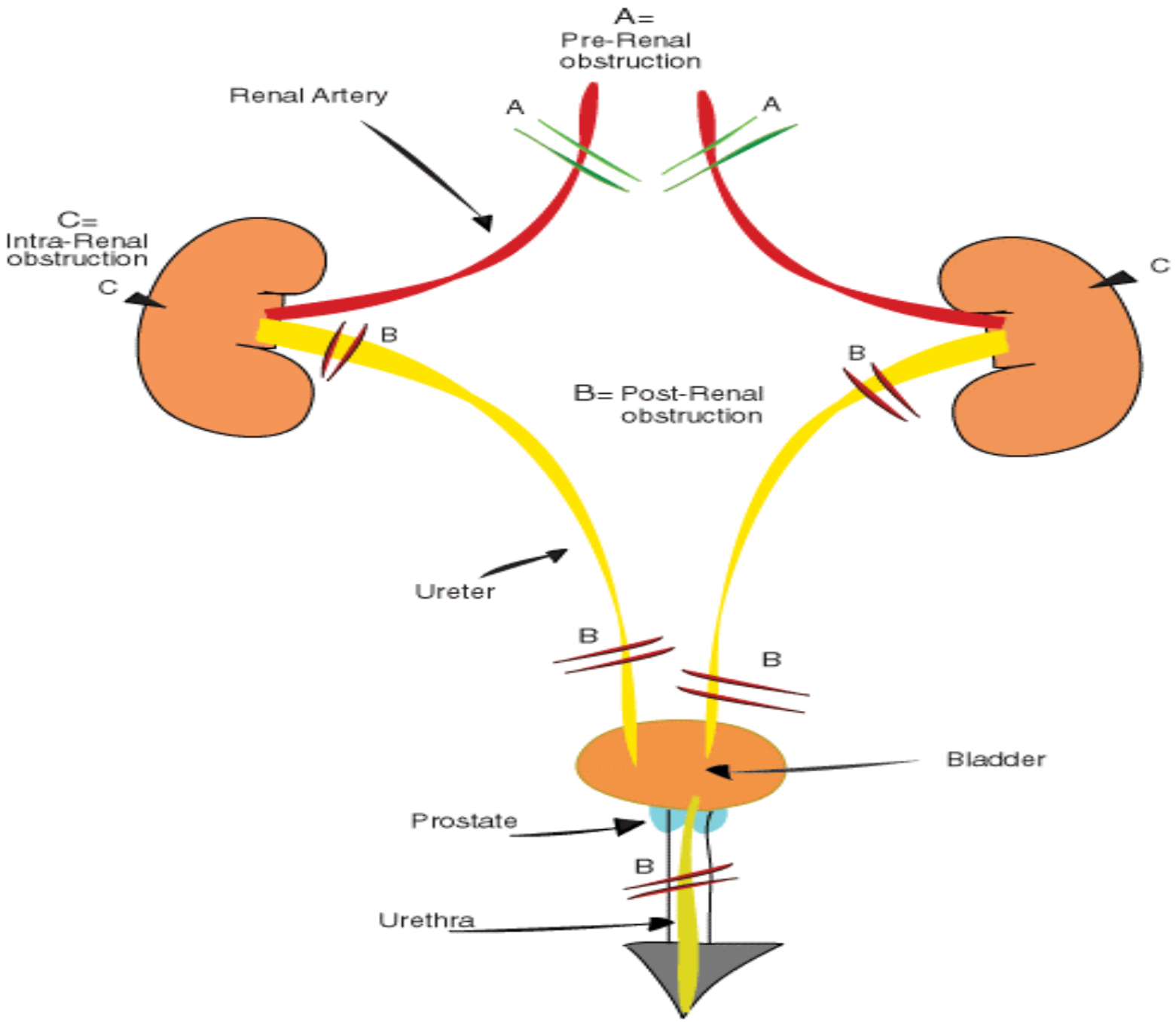
Physiologic changes induced in pregnancy. Increments and decrements in various parameters are shown in percentage terms with reference to the nonpregnant baseline. *GFR,* Glomerular filtration rate; *NP,* nonpregnant; P_{alb}, plasma albumin; P_{creat}, plasma creatinine; P_{Na}, plasma sodium; P_{osm}, plasma osmolality; P_{pr}, plasma proteins; P_{urea}, plasma urea. (From Davison JM: The kidney in pregnancy: a review, *J Royal Soc Med* 76:485-500, 1983.)

Normal laboratory values in pregnancy/non-pregnancy

	Pre-pregnancy	First trimester	Second trimester	Third trimester
Urea (mmol/L)	2.5–7.5	2.8–4.2	2.5–4.1	2.4–3.8
Creatinine (μmol/L)	65–101	52–68	44–65	55–73
Creatinine clearance (mL/min)	70–140	140–162	139–169	119–139
Na (mmol/L)	135–145	130–140	130–140	130–140
K (mmol/L)	3.5–5.0	3.3–4.1	3.3–4.1	3.3–4.1

Adapted from Nelson Piercy (2010).

AKI During Pregnancy


A=
Pre-Renal
obstruction
Renal Artery
A
A
C=
Intra-Renal
obstruction
C
C
B
B
B= Post-Renal
obstruction
Ureter
B
B
Bladder
Prostate
B
Urethra

AKI – KDIGO staging

AKI stage	Serum Creatinine criteria	Urine output criteria
1	SCr increase ≥ 26 µmol/L within 48hrs or SCr increase ≥ 1.5-2 X reference SCr within 1 week	< 0.5 mL/kg/hr for 6 consecutive hrs
2	SCr increase ≥ 2-3 X	< 0.5 mL/kg/hr for 12 hr
3	SCr increase ≥ 3 X reference SCr within 1 week or SCr increase ≥ 354 µmol/L or initiated on RRT (irrespective of stage at time of initiation)	< 0.3 mL/kg/hr for 24 hr or anuria for 12 hr

Rule of Thumb: At least 50% increase in Creat that occurs within a 7 day period

Baseline serum creatinine within (or presumed to be within) 7 days

Causes of AKI in pregnancy

Pre renal	Renal	Post renal
Hyperemesis gravidarum	Pre-eclampsia	Gravid uterus
Post-partum haemorrhage	HELLP	Papillary necrosis
Placental abruption	Acute fatty liver of pregnancy	Urinary retention
Sepsis	Microangiopathic haemolytic anaemia (TTP/HUS)	Damaged ureters
Heart failure	Acute tubular necrosis	Pelvic haematoma
	Interstitial nephritis	
	Glomerulonephritis	

HELLP = haemolysis elevated liver enzymes and low platelet count; HUS = haemolytic uraemic syndrome; TTP = thrombotic thrombocytopenic purpura.

Adapted from Nelson-Piercy (2010).

Table 50.2 Features of Microangiopathic Syndromes Associated With Pregnancy

Features	HELLP	TTP	HUS	AFLP
Clinical onset	Third trimester	Any time	Postpartum	Third trimester
Unique to pregnancy	Yes	No	No	Yes
Underlying pathophysiology	Defective placentation	ADAMTS 13 deficiency	Mutations in genes regulating complement function	Defective mitochondrial beta-oxidation of fatty acids
Hypertension	Yes	Occasional	Yes	Frequently
Kidney failure	Yes	Yes	Yes	Yes
Thrombocytopenia	Present	Present	Present	Present
Liver function tests	Elevated	Normal	Normal	Elevated
Coagulation studies	Normal to high	High	Normal	Normal
Antithrombin III	Low	Normal	Normal	Low
Management	Delivery	Plasma exchange	Plasma exchange	Delivery

AFLP, Acute fatty liver of pregnancy; *HUS,* hemolytic uremic syndrome; *TTP,* thrombotic thrombocytopenic purpura.

Pegnancy in CKD patients

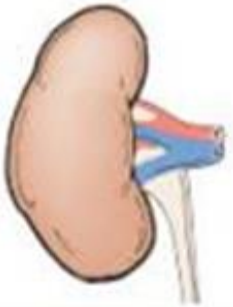
Table 11. Definition of Chronic Kidney Disease

Criteria
1. Kidney damage for ≥3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by *either*: • Pathological abnormalities; or • Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests
2. GFR <60 mL/min/1.73 m^2 for ≥3 months, with or without kidney damage

Methods to estimate GFR are discussed in Guideline 4. Markers of kidney damage are discussed in Guidelines 5–6.

Stages of Chronic Kidney Disease[18]

Description	Stage	GFR (mL/min/1.73 m²)
Kidney damage with normal or high GFR	1	≥ 90
Kidney damage with mild decrease in GFR	2	60-89
Moderate decrease in GFR	3	30-59
Severe decrease in GFR	4	15-29
Kidney failure	5	< 15 (or dialysis)



Chronic renal failure

- Sodium and water balance
  - Hypertension
  - Increased vascular volume
    - Edema
    - Heart failure
- Potassium balance
  - Hyperkalemia
- Elimination of nitrogenous wastes
  - Uremia
    - Pericarditis
    - Skin disorders
    - Gastrointestinal manifestations
    - Neurologic manifestations
    - Sexual dysfunction
  - Coagulopathies
- Erythropoietin production
  - Anemia
- Acid-base balance
  - Acidosis
  - Skeletal buffering
- Activation of vitamin D
  - Hypocalcemia
- Phosphate elimination
  - Hypocalcemia
  - Hyperparathyroidism

Osteodystrophies

Porth C.M. [2004]. *Pathophysiology : Concept of Altered Health States*. [7th ed.]. Lippincott Williams & Wilkins

Problems according to CKD aetiology

Renal disease	Potential problems in pregnancy
Reflux nephropathy	Increased risk of pre-eclampsia/fetal growth restriction Increased risk of urinary tract infection Increased risk of progression of renal disease Possible inheritance by offspring-infant screening recommended
IgA nephropathy	Worse outcomes if heavy proteinuria or severe lesions on biopsy
Diabetic nephropathy	Nephrotic range proteinuria. Continue ACEI/ARB until conception if possible
ADPKD	Risk of cyst infection or haemorrhage Risk of liver cyst growth 1:2 chance of offspring affected
Lupus nephritis	Worse pregnancy outcomes for level of renal function Risk of flare during pregnancy Risk of congenital lupus syndromes
Renal transplant	Worse pregnancy outcomes for level of renal function Second transplant worse outcomes than first Calcineurin inhibitor requirements increase

ACEI = angiotensinogen converting enzyme inhibitor; ADPKD = autosomal dominant polycystic kidney disease; ARB = angiotensin II receptor blocker.

Antenatal Care
Medications
• Start aspirin 75 mg • Continue folic acid • Stop any teratogenic medication
• Treat hypertension—Target blood pressure < 140/90 mmHg, but diastolic > 70 mmHg
• Treat vitamin D deficiency—cholecalciferol and/or 1-alpha-calcidol depending on level of renal impairment
• Thromboprophylaxis if albumin < 20 g/dL and proteinuria > 2 g/24 hours or protein creatinine ratio > 200 mg/mmol –LMWH if serum creatinine < 200 µmol/L –UFH if serum creatinine > 200 µmol/L
Monitoring
• Urine culture, and start antibiotic prophylaxis after one infection
• Haemoglobin—target 10–11 g/dL—use oral or intravenous iron and start/increase erythropoietin as necessary
• Creatinine—monthly then fortnightly after 32 weeks' gestation
• Consider haemodialysis if urea > 20 mmol/L, or problems with hyperkalaemia or acidosis or fluid balance
• Uterine artery dopplers at 22 weeks' gestation, and repeat if notching at 24 weeks • Serial growth scans in women with CKD stage 3–5 or CKD 1 or 2 with hypertension • Monitor tacrolimus or ciclosporin levels every 4 weeks

Management strategy for CKD in pregnancy.

Postnatal Care
• Review blood pressure and fluid balance –Target blood pressure < 140/90 mmHg • Assess for proteinuria at 6 weeks postpartum and revise target blood pressure accordingly: –< 130/80 mg/mmol if protein creatinine ratio >150 mg/mmol –< 140/90 mg/mmol if protein creatinine ratio <150 mg/mmol • Stop aspirin if not required for long-term cardiovascular disease prophylaxis • If taking thromboprophylaxis, continue for 6 weeks postpartum • Reduce tacrolimus or ciclosporin immediately to pre-pregnancy dose and monitor levels • Inform women with lupus regarding risk of flare up to 6 months postpartum • Discuss future contraception

Management strategy for CKD in pregnancy.

Estimated pregnancy outcomes for women with CKD stages 1 and 2

CKD stages 1 and 2	
Approximate pre-pregnancy creatinine µmol/L (non-black)	<100
Approximate pre-pregnancy creatinine µmol/L (black)	<120
Maternal pregnancy outcomes	
Pre-eclampsia/superimposed pre-eclampsia	10–20%
Caesarean section	40–57%
Neonatal outcomes	
Live birth	99–100%
Preterm delivery	30–40%
Small for gestational age	10–25%
Maternal renal outcomes	
Temporary decline in renal function (> 25%)	2%
Permanent decline in renal function (> 25%)	0
Requires replacement therapy	0

Adapted from Williams and Davison (2008) and Piccoli et al. (2010)

Estimated pregnancy outcomes for women with CKD stages 3 and 4

CKD stages 3 and 4		
CKD stage	3	4
Approximate pre-pregnancy creatinine µmol/L (non-black)	100–180	180–300
Approximate pre-pregnancy creatinine µmol/L (black)	120–200	200–400
Maternal pregnancy outcomes		
Pre-eclampsia/superimposed pre-eclampsia	40%	60%
Caesarean section	60–80%	
Neonatal outcomes		
Live birth	95%	90%
Preterm delivery	60%	>90%
Small for gestational age	40%	65%
Maternal renal outcomes		
Temporary decline in renal function (>25%)	40%	70%
Permanent decline in renal function (>25%)	20%	50%
Requires replacement therapy	2%	35%

Adapted from Williams and Davison (2008) and Piccoli et al. (2010).

Estimated pregnancy outcomes for women with CKD stage 5

CKD stage 5	
Maternal pregnancy outcomes	
Pre-eclampsia/superimposed pre-eclampsia	75%
Caesarean section	90–100%
Neonatal outcomes	
Live birth	50–100%
Preterm delivery	>90%
Small for gestational age	>90%
Maternal renal outcomes	
Temporary decline in renal function (>25%)	90–100% if not on dialysis
Permanent decline in renal function (>25%)	90–100% if not on dialysis
Requires replacement therapy	90–100% if not on dialysis

Adapted from Williams and Davison (2008) and Piccoli et al. (2010).

Box 50.3 Management of Pregnant Hemodialysis Patients

Dialysis Dose

At least 20 hours of dialysis/week; goal BUN of <40 mg/dL

Dialysate Composition

Bicarbonate: 25 mEq/L
Calcium: 2.5 to 3.0 mmol/L with weekly Ca and Phos measurement
Sodium: 130 to 135 mEq/L based on serum Na

Diet/Vitamin Supplementation

Double dose of MVI
Folic acid 5 mg/daily
Unrestricted diet
Protein intake: 1.5 to 1.8 g/kg/day

Dry Weight

Assess weekly
Increases by 0.5 kg/week in second and third trimesters

Anemia

Increase in ESA and iron requirements
Target hemoglobin of 10 g/dL

Hypertension

Target postdialysis BP of 140/90 mm Hg

Diagnosis of Preeclampsia

Difficult to diagnose; must rely on worsening BP control
Aspirin 75 mg daily for prophylaxis of preeclampsia

Metabolic Bone Disease

Vitamin D analogs to maintain PTH levels, as in general dialysis patients
Oral phosphorus binders generally not required

State of the Art

- Renal function may decline as a result of pregnancy among patients with renal disease. Increased risk for this decline is conferred by an elevated plasma creatinine concentration (above 1.5 mg/dL or 132 micromol/L) and hypertension.

- Renal biopsy can be performed safely in women with well-controlled blood pressure and normal coagulation indices who are at or before 32 weeks gestation. Biopsy after week 32 is not recommended.

State of the Art

- Renal impairment is associated with both increased risk for adverse maternal outcomes, including gestational hypertension, preeclampsia, eclampsia, and death, and also adverse fetal outcomes, including preterm birth, intrauterine growth restriction, small for gestational age, and still birth.

State of the Art

The reported frequency of conception among women of childbearing age on dialysis ranges from 0.3 to 1.5 percent per year. Aggressive management of the uremic state has increased the number of live births. Supportive measures include the following:

- Intensive dialysis targeting a blood urea nitrogen (BUN) under 50 mg/dL (17 mmol/L) or even under 45 mg/dL (16 mmol/L).
- Target hemoglobin of 10 to 11 g/dL.

State of the Art

•Correction of metabolic acidosis and hypocalcemia.

•Careful uterine and fetal monitoring during hemodialysis, combined with measures to prevent dialysis-induced hypotension

❖ Attention to nutrition and proper weight gain, including a careful weekly physical examination to help detect volume overload unrelated to the pregnancy.

UTI with pregnancy

Question 1

A 30-year-old woman was found to have asymptomatic bacteriuria 18 weeks into her second pregnancy. Coliform bacilli sensitive to trimethoprim, ciprofloxacin and cefalexin were cultured from a midstream urine sample. She had no history of renal disease.

Investigations:

serum creatinine 42 µmol/l (60–110)

Which of the following is not applicable?

A. a first episode of uncomplicated asymptomatic bacteruria in pregnancy should be treated with antibiotics
B. antibiotic prophylaxis is indicated during pregnancy if two or more episodes of bacteriuria occur
C. asymptomatic bacteriuria is associated with preterm delivery
D. asymptomatic bacteriuria should be monitored with follow up urine culture and treatment instituted if symptoms develop
E. bacteriuria is more common during pregnancy

QUESTION 1

- 30 yr old woman, 18 weeks gestation
  - Asymptomatic bacteriuria
  - Coliform sensitive to TMP, CiP, Cefalexin
  - No history of renal disease
  - Creatinine 42

- Which of the following is ***not*** applicable?

- **Answer**

QUESTION 1

- 30 yr old woman, 18 weeks gestation
  - Asymptomatic bacteriuria
  - Coliform sensitive to TMP, CiP, Cefalexin
  - No history of renal disease
  - Creatinine 42

- **Answer – D**
  - **“monitored and treated if symptoms develop”**

QUESTION 1

- Asymptomatic bacteriuria 2-10% pregnancies
- Associated with an increased incidence of
  - Symptomatic UTI
  - Pyelonephritis 30-40% (recurrent 6-8%)
  - Preterm delivery, low birth weight, perinatal mortality

- Treatment leads to a substantial reduction in these risks
  - Follow-up culture 1 week post treatment
  - Monthly thereafter
- UTI Prophylaxis

Question 2

A 19-year-old woman with reflux nephropathy presented at 16 weeks gestation. Vesicoureteric reflux disease had been diagnosed when she was 8 years old and imaging had shown unilateral upper pole scarring. She had no history of hypertension and was on no medication.

Investigations:

serum creatinine 75µmol/L (60-110)

Which of the following statements is false?

A. her child is at risk of inheriting reflux disease and should be offered screening in infancy
B. her risk of developing hypertension during pregnancy or pre-eclampsia is increased
C. monthly urine culture to screen for asymptomatic bacteruria is advisable
D. pregnancy is likely to be associated with significant (>20%) loss of renal function post-partum
E. the likelihood of a successful pregnancy is similar to that of the general population

QUESTION 2

- 19 yr old woman
  - Presented at 16 weeks gestation
  - Known CKD – reflux nephropathy
  - Creatinine 75
  - Normotensive

- Which of the following is ***false***?

  - **Answer**

QUESTION 2

- 19 yr old woman
  - Presented at 16 weeks gestation
  - Known CKD – reflux nephropathy
  - Creatinine 75
  - Normotensive

  - **Answer – D**
  - **“pregnancy is likely to be associated with significant (> 20%) loss of renal function post partum”**

QUESTION 2

Baseline creatinine	<125	125-180	>180
IUGR	25%	40%	65%
Preterm delivery	30%	60%	90%
Pre-eclampsia	22%	40%	60%
Perinatal death	1%	4%	10%
Loss of 25% GFR	2%	40%	70%
Permanent loss of 25% GFR	<1%	20%	50%
ESRD within 1 year	<1%	2%	35%

Williams D, Davison J. Chronic disease in pregnancy. BMJ 2008;336(7637):211-215

QUESTION 2

- Screening for bacteriuria advisable
  - UTI Prophylaxis ?
    - If preceding history or following a single episode

- Screening for VUR in offspring??
  - VUR up to 1% newborns
  - 36% offspring
  - 27% siblings
  - Identical twins – 80%

Nephrotic Syndrome and Proteinuria in Pregnancy

Question 3

A 36-year-old woman at 13 weeks gestation complained to her midwife of swollen legs. On examination her blood pressure was 142/91 mmHg and she had pitting oedema to her knees.

Investigations:

serum sodium	132 µmol/L (137–144)
serum creatinine	48 µmol/L (60-110)
serum albumin	27 g/dL g/L (37–49)
serum alkaline phosphatase	95 U/L (45–105)
serum cholesterol	9.3 mmol/L (<5.2)
dipstick urinalysis	protein +++, blood -, leu -, nit–
urine protein/creatinine ratio	936 mg/mmol (<2.5)

What is the most likely diagnosis?

A. class 5 lupus nephritis
B. haemolytic uraemic syndrome
C. inferior vena cava thrombosis
D. minimal change nephropathy
E. pre-eclampsia

QUESTION 3

- 36 year old woman
  - 13 weeks pregnant
  - Nephrotic (Alb 27, oedema, PCR 936, Chol 9.3)
  - Creatinine 48
  - Hypertensive
  - No microhaematuria

- What is the most likely diagnosis?

- **Answer**

QUESTION 3

- **Answer – D, “minimal change nephropathy”**
- MCGN most likely given the absence of
  - Haematuria, systemic symptoms
  - At this stage in pregnancy
- Class 5 lupus nephritis
- HUS
  - No clues to this diagnosis and a nephrotic presentation very unusual
- IVC thrombosis
- Pre-eclampsia
  - Exceedingly rare before 20 weeks

QUESTION 3

- Treat the patient not the foetus
  - Biopsy and establish diagnosis
    - If likely to alter management
    - Prone up to 24 weeks
    - Seated up to 32 weeks
  - Aspirin
  - Anti-hypertensives
  - VTE prophylaxis
  - Specific treatment - risks of nephrotic syndrome and treatment
  - LBW, pre-term, fetal loss, VTE, infection

Features	Lupus nephritis	Pre-eclampsia
Haematuria/red cell casts	Present	Absent
Anti-DNA antibodies	Raised	Normal
Complement C3 and C4	Low	Normal or raised
Liver function tests	Normal	Normal or raised
Hypertension	Present	Present and rising
Proteinuria	Present	Present
Oedema	Present	Present
Low platelets	Present	Present
Rising creatinine	Present	Present

Question 5

Which statement about nephrotic syndrome and pregnancy is true?

A. most cases of nephrotic syndrome in pregnancy are secondary to pre-eclampsia
B. renal biopsy is contraindicated in pregnancy
C. corticosteroids should not be used to treat nephrotic syndrome in pregnancy
D. relapses of steroid-responsive minimal change nephropathy in pregnancy do not affect fetal outcomes
E. thromboprophylaxis in pregnancy patients with nephrotic syndrome should be commenced in the puerperium

QUESTION 5

- What statement about nephrotic syndrome and pregnancy is true?

- **Answer**

QUESTION 5

- What statement about nephrotic syndrome and pregnancy is true?

- **Answer – A**
  - **“most cases of nephrotic syndrome in pregnancy are secondary to pre-eclampsia”**

Pregnancy in renal transplant

Question 4

A 35-year-old woman with IgA nephropathy was seen at her first transplant annual review after receiving a pre-emptive 1-0-0 mismatch kidney from her sister. Apart from delayed graft function she had an uncomplicated first year.

serum creatinine 110 µmol/l (60-110)

A routine surveillance transplant biopsy at 10 months showed no significant abnormality. She was taking lisinopril 10mg od, amlodipine 5mg od. tacrolimus 4mg bd, mycophenolate mofetil 1g bd, and prednisolone 5mg od.
During the consultation she stated that she may be pregnant. A test performed in clinic was positive and an ultrasound scan confirmed a viable 6 week fetus. On examination her blood pressure was 137/83 mmHg.

What changes should be made to her treatment regimen?

A. continue amlodipine, mycophenolate and prednisolone. Stop tacrolimus and lisinopril. Start azathioprine.
B. continue amlodipine, tacrolimus and mycophenolate. Stop lisinopril and prednisolone. Start bendroflumethiazide.
C. continue amlodipine, tacrolimus and prednisolone. Stop lisinopril and mycophenolate. Start azathioprine and aspirin.
D. continue all current treatment without change until the end of pregnancy.
E. increase prednisolone to 10mg od. Stop lisinopril, amlodipine, tacrolimus and mycophenolate. Start aspirin and sirolimus.

QUESTION 4

- 35 year old woman, ERF secondary to IgA
  - LRTx 1 year earlier, 1-0-0 mismatch, DGF
  - Creatinine 110 (eGFR 52-63), hypertensive
  - Unplanned pregnancy (6/40)
  - Current drugs
    - Tac, Pred, MMF
    - Lisinopril, amlodipine

- What changes should be made to her treatment regimen?
- **Answer**

QUESTION 4

- **Answer – C**
  - **“continue amlodipine, tacrolimus and prednisolone. Stop lisinopril and mycophenolate. Start azathioprine and aspirin”**

QUESTION 4

“Safe”	“Not safe”
Prednisolone (< 7.5mg/d) Azathioprine (< 2mg/kg) Tacrolimus Cyclosporin	Mycophenolate Sirolimus
Nifedipine (+probably amlodipine) Methyldopa Labetalol Hydralazine	ACE inhibitors ARBs Diuretics Most beta-blockers Spironolactone

QUESTION 4

- Unplanned
  - What does she want?
  - Potential teratogenic effects of MMF and lisinopril
  - Pregnancy outcomes quite good
    - >90% chance of success after 1st trimester
    - Spontaneous abortion 13%
    - PET 30%
    - IUGR 25% and preterm delivery 50%
    - Risk of decreased renal function
  - Drug levels

Table 50.1 Antihypertensive Medications in Pregnancy

Medication	Daily Dose	Side Effects/ Comments	Safety Label
Methyldopa	500 to 3000 mg in divided doses	First-line agent	Category B
Labetalol	200 to 1200 mg in divided doses	Widely used; efficacy and safety similar to methyldopa	Category B
Other beta blockers	Variable	IUGR and fetal bradycardia	Category C/D
Calcium channel blockers	Variable	Relatively safe	Category C
Diuretics	Variable	May cause diminished volume expansion	Category B/C
Clonidine	0.1 to 0.8 mg in divided doses	Limited data	Category C
Hydralazine	30 to 200 mg in divided doses	Widely used; not effective as a single agent	Category C
Minoxidil	2.5 to 10 mg in divided doses	Limited data	Category C
Spironolactone	Variable	Feminization of male fetus in animal studies; limited human data	Category C
Alpha blockers	Variable	Limited data	Category B/C
ACE inhibitors	Contraindicated	Renal dysplasia	Category D
ARBs	Contraindicated	Neonatal anuric renal failure	Category D

Category B: Animal studies show no fetal risk, but human data lacking.
Category C: Animal studies show fetal risk, but human data lacking.
Category D: Positive evidence of human fetal risk.
ACE, Angiotensin converting enzyme; *ARB,* angiotensin receptor blocker; *IUGR,* intrauterine growth retardation.

Common pharmacological agent used to treat hypertension in pregnancy and the post-partum period

Agent	Dose	Side effects	Comments
Antenatal			
Labetalol	100 mg bd–500 mg tds		Avoid in asthma
Methyldopa	250 mg bd–1 g tds	Lethargy Depression	Documented safety profile 7-year follow-up of off-spring
Nifedipine slow release	10 mg–40 mg bd	Headache Flushing Swollen lower limbs	Tocolytic Synergistic interaction with magnesium sulphate
Hydralazine	25 mg bd–75 mg tds	Headache Flushing Tachycardia	
Amlodipine	5–10 mg od	Swollen lower limbs	
Doxazosin	1 mg od–8 mg bd		
ACEIs and angiotensin receptor blockers	CONTRAINDICATED	Congenital cardiac and CNS anomalies Fetopathy Oligohydramnios Fetal growth restriction Neonatal renal failure	
Postnatal			
Enalapril	5–20 mg bd		Safe in breastfeeding
Nifedipine SR	10–40 mg bd		Safe in breastfeeding
Amlodipine	5–10 mg od		Safe in breastfeeding
Atenolol	25–50 mg od		Safe in breastfeeding

Adapted from NICE (2011) and Palma-Reis et al. (2013).

Table 50.3 Immunosuppressive Medications in Pregnancy*

Medication	Safety Label	Comments	Dosing Adjustments
Cyclosporine/tacrolimus	Category C	Increased incidence of maternal diabetes, hypertension, and preeclampsia	Higher doses required due to increased metabolism
Sirolimus	Category X	Contraindicated	Stopped 6 weeks before conception
Mycophenolic acid	Category X	Contraindicated	Stopped 12 weeks before conception
Azathioprine	Category D	Widely used despite being category D; low birth weights and leukopenia reported in newborns	No dosing adjustments required
Cyclophosphamide	Category D	Increased risk for congenital anomalies and childhood cancer	Used with caution
Rituximab	Category C	Limited human data; crosses placenta; B cell lymphocytopenia reported	Limited data

Category C: Animal studies show fetal risk, but human data lacking.
Category D: Positive evidence of human fetal risk.
Category X: Positive evidence of human fetal risk, and risks clearly outweigh potential benefits.
*Breastfeeding not recommended with any of the medications in this table.

Question 6

A 22-year-old woman attended for outpatient review and requested advice about family planning. She had end-stage renal failure secondary to renal dysplasia, and had undergone pre-emptive transplantation 6 months previously. She had gained 6 kg in weight since her transplant and had not had any infections or episodes of rejection. Her current treatment comprised low-dose prednisolone, and tacrolimus titrated against trough levels.

Examination was normal. Her blood pressure was 142/78 mmHg.

serum urea 7.8 mmol/L (2.5–7.0)

serum creatinine 116 μmol/L (60–110)

urinary protein:creatinine ratio 28 mg/mmol (<30)

What is the most appropriate advice?

A attempt to conceive without delay

B avoid pregnancy because of risks to the fetus

C delay conception for 6 months

D introduce antihypertensive therapy before conception

E substitute mycophenolate for tacrolimus before conception

Answer :
C delay conception for 6 months

State of the Art

- Fertility improves after renal transplantation. However, pregnancy and live birth rates are far lower in female transplant recipients than in the general population.

- Pregnancy has little or no effect on renal function in the transplant patient, provided baseline renal function is close to normal.

State of the Art

- Women are advised to wait at least **one year** after living-related-donor transplantation and **two years** after deceased transplantation to avoid complications arising from immunotherapy and rejection. The renal allograft should be functioning well, with a stable serum creatinine level <1.5 mg/dL (132 micromol/L) and urinary protein excretion <500 mg/day.

- Immunosuppressive regimens may need to be adjusted prior to attempting to conceive. Mycophenolate mofetil and sirolimus are contraindicated in pregnancy. Women should change from mycophenolate mofetil to azathioprine and from sirolimus to tacrolimus or cyclosporine if there are no contraindications to the switch.

State of the Art

- Patients with renal disease should be monitored jointly by a nephrologist and by an obstetrician familiar with the effects of renal disease on pregnancy. General principles of management include:
- increased frequency of prenatal visits,
- early detection and treatment of asymptomatic bacteriuria,
- serial monitoring of maternal renal function and for the treatment of hypertension,
- monitoring for the development of preeclampsia,
- and fetal surveillance with ultrasound and fetal heart rate.
- Preterm intervention may be necessitated by deteriorating renal function, severe preeclampsia, fetal growth restriction, or nonreassuring fetal testing.

Thank you.