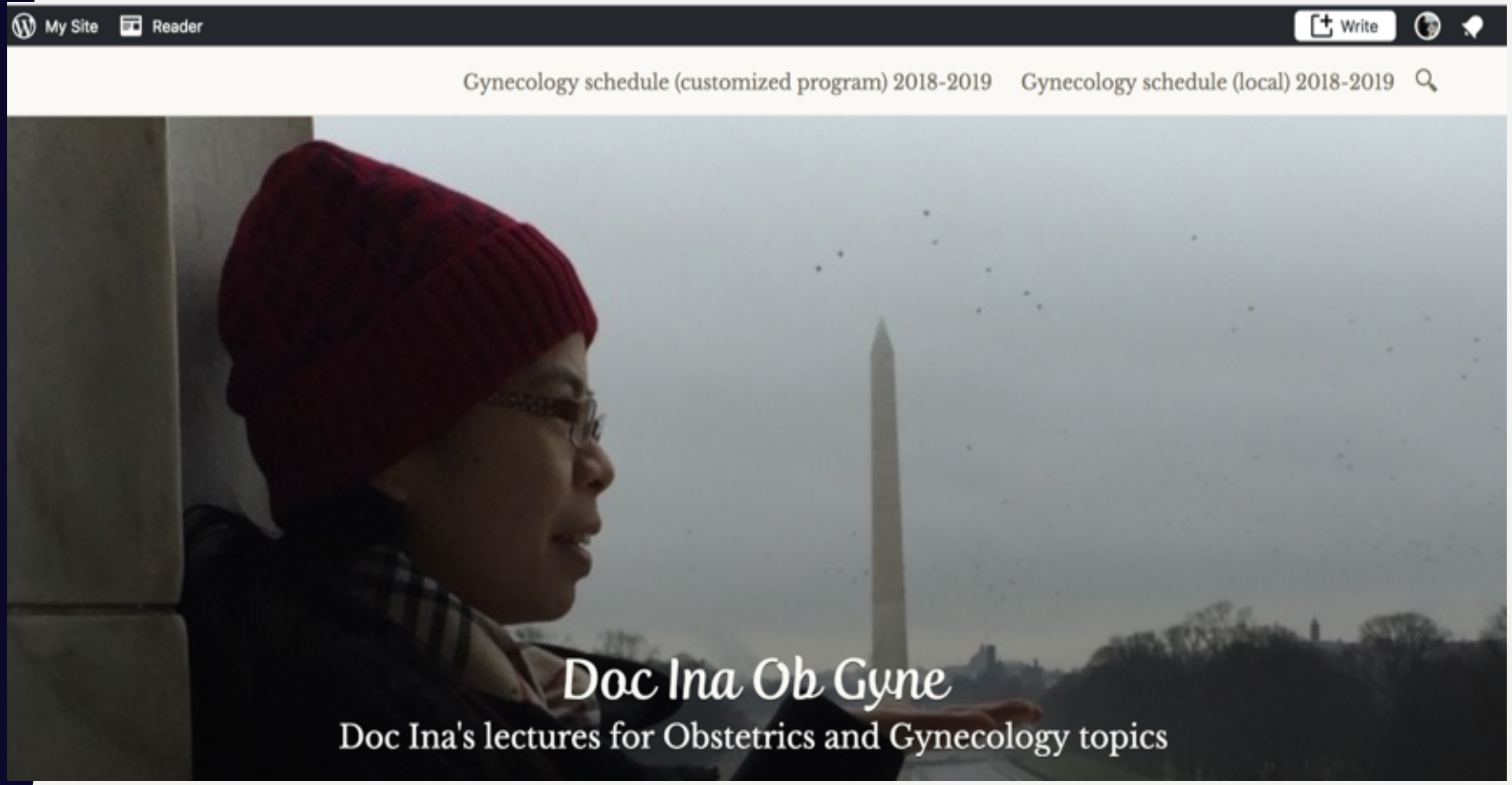
RENAL AND URINARY TRACT DISORDERS OF PREGNANCY

INA S. IRABON, MD, FPOGS, FPSRM, FPSGE
OBSTETRICS AND GYNECOLOGY
REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY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REFERENCE

- Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds). William's Obstetrics 25th edition; 2018; chapter 53 Renal and urinary tract disorders

OUTLINE

1. Review of pregnancy-induced urinary tract changes
2. Asymptomatic bacteriuria
3. Acute pyelonephritis
4. Nephrolithiasis
5. Glomerular diseases
   - Acute nephritic syndrome
   - Nephrotic syndrome
6. Chronic kidney disease
7. Chronic renal insufficiency
8. Acute kidney injury

PREGNANCY-INDUCED URINARY TRACT CHANGES

- Kidneys become larger; calyces and ureters dilate (progesterone- induced relaxation of the muscularis)
- marked dilatation is apparent beginning in midpregnancy because of more distal ureteral compression, especially on the right side
- There is also vesicoureteral reflux during pregnancy.
- Because of these physiological changes, the risk of upper urinary infection rises.
  - Also, imaging studies done to evaluate urinary tract obstruction may occasionally be erroneously interpreted.

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PREGNANCY-INDUCED URINARY TRACT CHANGES

- Glomeruli are larger, although cell numbers do not grow
- Pregnancy-induced intrarenal vasodilatation develops, and both afferent and efferent resistances decline.
  - This leads to greater effective renal plasma flow and glomerular filtration

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ASYMPTOMATIC BACTERIURIA

- persistent, actively multiplying bacteria within the urinary tract in asymptmatic women.
- The American Academy of Pediatrics and the American College of Obstetricians and Gynecologists (2017), as well as the U.S. Preventive Services Task Force (2008), recommend screening for bacteriuria at the first prenatal visit.
- An initial positive urine culture result done as a part of prenatal care should prompt treatment.
- A clean-voided specimen containing more than 100,000 organisms/mL is diagnostic.
- It may be prudent to treat when lower concentrations are identified, because pyelonephritis develops in some women despite colony counts of only 20,000 to 50,000 organisms/mL
- Most studies indicate that if asymptomatic bacteriuria is not treated, approximately 25 % of infected women will develop symptomatic infection during pregnancy

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TREATMENT OF ASYMPTOMATIC BACTERIURIA

Single-dose treatment

- Amoxicillin, 3 g
- Ampicillin, 2 g
- Cephalosporin, 2 g
- Nitrofurantoin, 200 mg
- Trimethoprim-sulfamethoxazole, 320/1600 mg

3-day course

- Amoxicillin, 500 mg three times daily
- Ampicillin, 250 mg four times daily
- Cephalosporin, 250 mg four times daily
- Ciprofloxacin, 250 mg twice daily
- Levofloxacin, 250 or 500 mg daily
- Nitrofurantoin, 50 to 100 mg four times daily or 100 mg twice daily
- Trimethoprim-sulfamethoxazole, 160/800 mg twice daily

Other

- Nitrofurantoin, 100 mg four times daily for 10 days
- Nitrofurantoin, 100 mg twice daily for 5 to 7 days
- Nitrofurantoin, 100 mg at bedtime for 10 days

Treatment failures

- Nitrofurantoin, 100 mg four times daily for 21 days

Suppression for bacterial persistence or recurrence

- Nitrofurantoin, 100 mg at bedtime for pregnancy remainder

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ASYMPTOMATIC BACTERIURIA

- Recurrent bacteriuria: nitrofurantoin 100 mg orally at bedtime for 21 days
- For women with persistent or frequent bacteriuria recurrences:
  - suppressive therapy for the remainder of pregnancy can be given.
  - nitrofurantoin, 100 mg orally at bedtime (this drug may rarely cause an acute pulmonary reaction that dissipates on its withdrawal)

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ACUTE PYELONEPHRITIS

- unilateral and right-sided in more than half of cases, and it is bilateral in a fourth.
- Fever and shaking chills, aching pain in one or both lumbar regions.
- Tenderness usually can be elicited by percussion in one or both costovertebral angles.
- The differential diagnosis includes, among others, labor, chorioamnionitis, adnexal torsion, appendicitis, placental abruption, or infarcted leiomyoma.
- Etiology: E. coli (70-80%), Klebsiella pneumoniae (3-5%), Enterobacter or Proteus spp (3-5%), Grp B Strep or S aureus (10%)

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ACUTE PYELONEPHRITIS

- Intravenous hydration to ensure adequate urinary output is the cornerstone of treatment.
- Antimicrobials are begun promptly but they may initially worsen endotoxemia from bacterial lysis.
- Surveillance for worsening sepsis syndrome includes serial monitoring of urinary output, blood pressure, pulse, temperature, and oxygen saturation.
- High fevers are lowered with a cooling blanket and acetaminophen / paracetamol (important in early pregnancy because of possible teratogenic effects from hyperthermia)
- Antimicrobial therapy usually is empirical:
  - ampicillin plus gentamicin
  - cefazolin or ceftriaxone
  - extended-spectrum antibiotic

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ACUTE PYELONEPHRITIS

TABLE 53-2. Management of the Pregnant Woman with Acute Pyelonephritis

Hospitalize patient
Obtain urine and possibly blood cultures
Evaluate hemogram, serum creatinine, and electrolytes
Monitor vital signs frequently, including urinary output—consider indwelling catheter
Establish urinary output ≥50 mL/hr with intravenous crystalloid solution
Administer intravenous antimicrobial therapy (see text)
Obtain chest radiograph if there is dyspnea or tachypnea
Repeat hematology and chemistry studies in 48 hours
Change to oral antimicrobials when afebrile
Discharge when afebrile 24 hours, consider antimicrobial therapy for 7 to 10 days
Repeat urine culture 1 to 2 weeks after antimicrobial therapy completed

Modified from Lucas, 1994; Sheffield, 2005.

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NEPHROLITHIASIS

- Although calcium oxalate stones in young nonpregnant women are most common, most stones in pregnancy—65 to 75 percent—are calcium phosphate or hydroxyapatite
- Pregnant women may have fewer symptoms with stone passage because of physiologic urinary tract dilatation during pregnancy. → > 90 percent of pregnant women with symptomatic nephrolithiasis present with pain.
- Gross hematuria is less common than in affected nonpregnant women
- Sonography is usually selected to visualize stones, but many are not detected because hydronephrosis may obscure findings
- Transabdominal color Doppler sonography to detect presence or absence of ureteral "jets" of urine into the bladder may exclude obstruction

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NEPHROLITHIASIS: TREATMENT

- Intravenous hydration and analgesics are given.
- Urinary obstruction with concomitant infection is an emergency—"pus under pressure"
- Approximately 65 to 80 percent of symptomatic women will improve with conservative therapy, and the stone usually passes spontaneously
- Others require an invasive procedure such as ureteral stenting, ureteroscopy, percutaneous nephrostomy, transurethral laser lithotripsy, or basket extraction
- Extracorporeal shock wave lithotripsy is contraindicated in pregnancy

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GLOMERULAR DISEASES

- Lewis and Neilson (2015) group glomerular injuries into six syndromes based on clinical patterns

TABLE 53-3. Patterns of Clinical Glomerulonephritis

Acute Nephritic Syndromes: poststreptococcal, infective endocarditis, SLE, antiglomerular basement membrane disease, IgA nephropathy (Berger disease), ANCA vasculitis, Henoch-Schönlein purpura, cryoglobulinemia, membranoproliferative and mesangioproliferative glomerulonephritis
Pulmonary-Renal Syndromes: Goodpasture, ANCA vasculitis, Henoch-Schönlein purpura, cryoglobulinemia
Nephrotic Syndromes: minimal change disease, focal segmental glomerulosclerosis, membranous glomerulonephritis, diabetes, amyloidosis, others
Basement Membrane Syndromes: anti-GBM disease, others
Glomerular Vascular Syndromes: atherosclerosis, chronic hypertension, sickle-cell disease, thrombotic microangiopathies, antiphospholipid antibody syndrome, ANCA vasculitis, others
Infectious Disease-Associated Syndromes: poststreptococcal, infective endocarditis, HIV, HBV, HCV, syphilis, others

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GLOMERULAR DISEASES:

ACUTE NEPHRITIC SYNDROMES

- clinical presentation usually includes hypertension, hematuria, red-cell casts, pyuria, and proteinuria.
- Varying degrees of renal insufficiency and salt and water retention result in edema, hypertension, and circulatory congestion
- The prognosis and treatment of nephritic syndromes depends on their etiology
  - Some recede spontaneously or with treatment.
- In some patients, rapidly progressive glomerulonephritis leads to end-stage renal failure, whereas in others, chronic glomerulonephritis develops with slowly progressive renal disease.

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GLOMERULAR DISEASES:
ACUTE NEPHRITIC SYNDROMES

- Lupus nephritis identified before pregnancy has a 50-percent chance of flaring during pregnancy
- IgA nephropathy, also known as **Berger disease**, is the *most common form of acute glomerulonephritis worldwide*
- The isolated form occurs sporadically, and it may be related to **Henoch-Schönlein purpura** as the systemic form
- Isolated nephritis may be due to anti-glomerular basement membrane (anti-GBM) antibodies.
- These may also involve the lungs to manifest as a pulmonary-renal syndrome with alveolar hemorrhage, which is termed **Goodpasture syndrome**

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GLOMERULAR DISEASES:
ACUTE NEPHRITIC SYNDROMES

Pregnancy

- Acute nephritic syndromes during pregnancy can be difficult to differentiate from severe preeclampsia or eclampsia
- In some of these cases, renal biopsy is sometimes needed to determine etiology and direct management
- Whatever the underlying etiology, acute glomerulonephritis has profound effects on pregnancy outcome.
  - The most frequent lesions on biopsy were membranous glomerulonephritis, IgA glomerulonephritis, and diffuse mesangial glomerulonephritis.
  - the worst perinatal outcomes are expected in women with impaired renal function, early or severe hypertension, and nephrotic-range proteinuria.
- pregnancy outcome was related to the degree of renal insufficiency and hypertension.

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GLOMERULAR DISEASES:

NEPHROTIC SYNDROME

- Heavy proteinuria is the hallmark of the nephrotic syndromes.
  - result from several primary and secondary kidney disorders that cause immunological or toxin-mediated injury with glomerular capillary wall breakdown to allow excessive filtration of plasma proteins.
  - characterized by hypoalbuminemia, hypercholesterolemia, and edema.
  - There frequently is hypertension, albumin nephrotoxicity, renal insufficiency
- frequent causes of the nephrotic syndrome are: minimal change disease (10–15 percent), focal segmental glomerulosclerosis (35 percent), membranous glomerulonephritis (30 percent), and diabetic nephropathy.
- In most cases, renal biopsy will disclose microscopic abnormalities that may help direct treatment

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GLOMERULAR DISEASES:

NEPHROTIC SYNDROME

- Normal amounts of dietary protein of high biological value are encouraged.
- The incidence of thromboembolism is increased and varies with the severity of hypertension, proteinuria, and renal insufficiency
- May develop arterial and venous thromboses, renal vein thrombosis
- The value of prophylactic anticoagulation is unclear.
- Some cases of nephrosis from primary glomerular disease respond to glucocorticosteroids and other immunosuppressants or cytotoxic drug therapy.
- In most of those cases caused by infection or drugs, proteinuria recedes when the underlying cause is corrected.

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GLOMERULAR DISEASES:
NEPHROTIC SYNDROME

Pregnancy

- Maternal and perinatal outcomes in women with the nephrotic syndromes depend on its underlying cause and severity.
  - Some women with nephrotic-range proteinuria will have a rise in daily protein excretion as pregnancy progresses
- Management of edema during pregnancy can be particularly challenging as it is intensified by normally increasing hydrostatic pressure in the lower extremities.
- massive vulvar edema may develop.
- up to half of these women have chronic hypertension that may require treatment.
- preeclampsia is common and often develops early in pregnancy.

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GLOMERULAR DISEASES:
NEPHROTIC SYNDROME

Pregnancy

- Most women with nephrotic syndromes who do not have severe hypertension or renal insufficiency will have successful pregnancy outcomes.
- Conversely, if there is renal insufficiency, moderate to severe hypertension, or both, the prognosis is much worse.
- serum creatinine level >1.4 mg/dL and 24-hour protein excretion >1 g/d are associated with the shortest renal survival times following pregnancy

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CHRONIC KIDNEY DISEASE

- pathophysiological process that can progress to end-stage renal disease.
- The National Kidney Foundation describes six stages of chronic kidney disease defined by decreasing GFR:
  - stage 0 — GFR >90 mL/min/1.73 m^2 → stage 5 — GFR <15 mL/min/1.73 m^2.
  - Those that most frequently lead to end-stage disease requiring dialysis and kidney transplantation include the ff:

    diabetes -35%; hypertension -25%; glomerulonephritis -20 %; and polycystic kidney disease - 15%
- To counsel regarding fertility and pregnancy outcome, the degree of renal functional impairment and of associated hypertension are assessed.
- A general prognosis can be estimated by considering women with chronic renal disease in arbitrary categories of renal function:
  - normal or mild impairment—defined as a serum creatinine <1.5 mg/dL;
  - moderate impairment —defined as a serum creatinine 1.5 to 3.0 mg/dL;
  - severe renal insufficiency— defined as a serum creatinine >3.0 mg/dL.

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CHRONIC KIDNEY DISEASE

Pregnancy and Chronic Renal Disease

- Most women have relatively mild renal insufficiency, and its severity along with any underlying hypertension is prognostic of pregnancy outcome.
- Renal disease with comorbidities secondary to a systemic disorder (eg,diabetes or systemic lupus erythematosus) portends a worse prognosis
- For all women with chronic renal disease, the incidences of hypertension and preeclampsia, preterm and growth-restricted newborns, and other problems are very high.

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CHRONIC KIDNEY DISEASE

Pregnancy and Chronic Renal Disease

- Loss of renal tissue is associated with compensatory intrarenal vasodilation and hypertrophy of the surviving nephrons.
  - The resultant hyperperfusion and hyperfiltration eventually damage surviving nephrons to cause nephrosclerosis and worsening renal function.
  - With mild renal insufficiency, pregnancy causes greater augmentation of renal plasma flow and GFR
  - With progressively declining renal function, there is little, augmented renal plasma flow.
- Importantly, severe chronic renal insufficiency curtails normal pregnancy-induced hypervolemia.
  - Blood volume expansion during pregnancy is related to disease severity and correlates inversely with serum creatinine concentration.
  - With severe renal insufficiency, however, volume expansion averages only 25 percent, which is similar to that seen with hemoconcentration from eclampsia.
  - In addition, these women have variable degrees of chronic anemia due to intrinsic renal disease.

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CHRONIC RENAL INSUFFICIENCY

- In women with chronic kidney disease who also have renal insufficiency, adverse outcomes are generally directly related to the degree of renal impairment.
- Frequent monitoring of blood pressure is paramount,
- serum creatinine levels, protein/creatinine ratio, and 24-hour protein excretion are important.
- Bacteriuria is treated to decrease the risk of pyelonephritis and further nephron loss.
- Protein-rich diets are recommended
- In some women with anemia → may give recombinant erythropoietin (hypertension is a common side effect)
- Serial sonography is performed to follow fetal growth.

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CHRONIC RENAL INSUFFICIENCY

Long-Term Effects

- In some women, pregnancy may accelerate chronic renal disease progression by increasing hyperfiltration and glomerular pressure to worsen nephrosclerosis
- Chronic proteinuria is also a marker for subsequent development of renal failure.

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CHRONIC RENAL INSUFFICIENCY

Dialysis During Pregnancy

- Dialysis during pregnancy is recommend when **serum creatinine levels are between 5 and 7 mg/dL.**
  - Because it is imperative to avoid abrupt volume changes that cause hypotension, dialysis frequency may be extended to five to six times weekly
- Important to replace substances that are lost through dialysis:
  - Multivitamin doses are doubled, and calcium and iron salts are provided along with sufficient dietary protein and calories.
  - Chronic anemia is treated with erythropoietin.
  - To meet pregnancy changes, extra calcium is added to the dialysate along with less bicarbonate.
- Maternal complications are common and include severe hypertension, placental abruption, heart failure, and sepsis.
  - high incidences of maternal hypertension and anemia, preterm and growth-restricted infants, stillbirths, and hydramnios.

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ACUTE KIDNEY INJURY

- Previously termed acute renal failure, acute kidney injury (AKI) is now used to describe suddenly impaired kidney function with retention of nitrogenous and other waste products normally excreted by the kidneys
- acute renal ischemia is still often associated with severe preeclampsia and hemorrhage
  - contributory are HELLP (hemolysis, elevated liver enzymes, low platelet levels) syndrome, placental abruption, septicemia
  - AKI is also common in women with acute fatty liver of pregnancy

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ACUTE KIDNEY INJURY

Diagnosis and Management

- In most women, AKI develops postpartum, thus management is usually not complicated by fetal considerations.
- An abrupt rise in serum creatinine level is most often due to renal ischemia.
- Oliguria is an important sign.
  - severe hypovolemia from massive hemorrhage is common, and preexistent renal ischemia from preeclampsia is often comorbid.
- When azotemia is evident and severe oliguria persists, some form of renal replacement treatment is indicated
  - Hemofiltration or dialysis is initiated before marked deterioration occurs.
  - medication doses are adjusted: magnesium sulfate, iodinated contrast agents, aminoglycosides, and nonsteroidal antiinflammatory drugs (NSAIDs)
  - Early dialysis appears to reduce the maternal mortality rate
  - With time, renal function usually returns to normal or near normal.

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ACUTE KIDNEY INJURY

Prevention

- AKI in obstetrics is most often due to acute blood loss, especially that associated with preeclampsia. Thus, it may often be prevented by the following means:
    1. Prompt and vigorous volume replacement with crystalloid solutions and blood in instances of massive hemorrhage, such as in placental abruption, placenta previa, uterine rupture, and postpartum uterine atony
    2. Delivery or termination of pregnancies complicated by severe preeclampsia or eclampsia, and careful blood transfusion if loss is more than average.
    3. Close observation for early signs of sepsis syndrome and shock in women with pyelonephritis, septic abortion, chorioamnionitis, or sepsis from other pelvic infections.
    4. Avoidance of loop diuretics to treat oliguria before ensuring that blood volume and cardiac output are adequate for renal perfusion.
    5. Judicious use of vasoconstrictor drugs to treat hypotension, and only after it has been determined that pathological vasodilatation is the cause.

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Thank you!

youtube channel: Ina Irabon

www.wordpress.com: Doc Ina OB Gyne