Urological problems in pregnancy

Anatomical changes in the urinary tract during pregnancy

- **Increased kidney size**: of approximately 1 cm and 30% more volume capacity. These changes are due to an increase in total renal vascular and interstitial volume.
- **Dilation of the collecting system** (hydronephrosis and hydroureter) occurs in 80% of pregnancies. Is it more common, and usually occurs to a greater degree, on the right hand side, characteristically extending to the pelvic rim. The main causes are:
  - *Mechanical compression*: due to the progressively larger uterus and ovarian venous complex.
  - *Effects of progesterone*: its muscle relaxant effects may explain urinary tract dilation in the early stages of pregnancy when the uterus has not yet reached a significant volume. However, its role is still being debated in the literature.
- **Bladder anatomy**: pressure of the uterus on the bladder dome with the ureters in a higher position compared to non-pregnant women. In the last trimester, both the anterior vaginal wall and the bladder usually descend to the threshold of the vaginal introitus. This process is asymptomatic and reverses after delivery, in which case it requires no special study or treatment.

Renal hemodynamic changes

- **Pregnancy increases renal plasma flow** (RPF) by 40-65% and the **glomerular filtration rate** (GFR) by 50-85% in the first half of pregnancy. There is also a secondary increase in **creatinine clearance**, which oscillates between 100-150 mL/min. This leads to a decrease in serum **creatinine** and **urea** levels, with average values of 0.5 and 9 mg/dL, respectively.
- **Increased renal plasma flow and GFR lead to a decrease in the resistance index** (RI). Thus, in terms of vascularization of the nephron, the increase in RPF does not involve an increase in glomerular hydrostatic pressure since pre- and post-glomerular arteriolar resistance is lower. These mechanisms are probably due to hormonal regulation, especially considering the 20% increase in GFR during the luteal phase of the menstrual cycle in non-pregnant women.

Changes in blood/urine analysis levels

- **Glucose in urine**: an increased GFR may limit the reabsorption of glucose in the proximal renal tubule, giving rise to the physiological glycosuria typical of pregnancy. This determination is therefore not a useful screening tool for glucose intolerance in pregnant women.
- **Acid-base balance**: the buffering capacity of the kidney decreases in pregnancy due to reduced renal reabsorption of **bicarbonate**. This is a compensatory mechanism for the relative respiratory alkalosis caused by the hyperventilation associated with pregnancy.
- **Uric acid**: blood concentrations decrease by 25-35%, with levels around 2-3 mg/dL in the 3rd trimester. This is due to an increase in GFR and a reduction in its tubular reabsorption.
- **Proteinuria**: during pregnancy there is a physiological excretion of proteins in the urine. The upper limit of normal is 300 mg/24 h (20 mg/24 h of albumin). Possible causes include increased GFR and its reduced reabsorption at the tubular level.

Lower urinary tract symptoms

- **Urinary symptoms such as frequency, nocturia, and urgency** in the absence of UTIs are common in pregnancy, increasing as the pregnancy progresses. **Frequency** appears in 76-95% of pregnant women, **nocturia** in 56-72%, and **urgency** in 63-68%. The causes are increased GFR and diuresis, longer periods of time in supine position, increased fluid intake, and the mechanical pressure of the uterus in the pelvis, which reduces bladder capacity.
- **Treatment**: involves limiting inappropriately high fluid intake.
Urinary infections and pregnancy (see chapter on UTI and Pregnancy)

- **Asymptomatic bacteriuria in pregnant women has a similar prevalence** (5-10%) to that in premenopausal women, but with a greater tendency to become symptomatic (1-2%). 20-40% of untreated bacteriuria end in acute pyelonephritis in the 2nd and 3rd trimester. In turn, 3% of these women present with symptomatic bacteriuria (1% pyelonephritis, 2% cystitis).

  - **Pathogeny:**
    - **Risk factors:** older multiparous women, sexual activity, previous UTIs, and vesicoureteral reflux.
    - **Factors related to pregnancy:**
      - Enlarged, hyperemic kidneys with increased glomerular filtration rate.
      - Dilated ureters due to uterine pressure and smooth muscle relaxation.
      - Bladder displaced to a higher, anterior position due to an enlarged uterus along with inadequate emptying.
      - Pregnancy-related immunosuppression.
    - **Microorganisms:** *E. coli, K. pneumoniae, P. mirabilis, and E. faecalis.*
    - **Risk for the fetus:** UTI leads to a higher incidence of premature birth and mortality.

  - **Diagnosis:** urine culture is positive if >10³ cfu/mL in a pregnant woman with symptoms and pyuria. In cases of *asymptomatic bacteriuria,* values >10⁵ cfu/mL in two cultures 24 h apart are considered significant.

  - **Treatment:**
    - **Cystitis and asymptomatic bacteriuria:** short courses of antibiotics lasting 3-5 days. Recommended drugs include *Nitrofurantoin* (contraindicated in labor at term), *penicillin* (Amoxi-clavulanate), *cephalosporins,* *Phosphomycin,* and *Cotrimoxazole* (should be avoided in the 1st and 2nd trimesters and at delivery).
    - **Pyelonephritis:** longer courses of 7-10 days (with iv administration for the first 24-48 h). Recommended drugs include *penicillin, cephalosporins,* and *monobactams.*
    - **Recurrent infections:** antimicrobial prophylaxis until delivery should be considered (nocturnal or postcoital suppressive therapy). Recommended drugs include *Cephalexin,* *Cephadroxil,* and *Nitrofurantoin.*

Urinary retention during pregnancy

- **Incidence:** rare pathology with an incidence of 1/3000-1/8000 pregnancies.
- **Etiology:** usually between the 12th-14th weeks in a retroverted uterus. The main causes are:
  - Narrow pelvis.
  - Myoma uteri.
  - Uterine abnormalities.
  - Action of high doses of progesterone: may promote smooth muscle relaxation, bladder detrusor inactivity, and retention. Its etiological role is controversial.

  - **Treatment:** bladder catheterization and bimanual manipulation of the uterus to an anteverse position with the patient in lithotomy or genu-pectoral position. If the maneuver fails, permanent or clean intermittent catheterization is indicated, lasting 1-2 weeks until the uterus has increased in size and cannot be squeezed into a sacral position.

Urinary incontinence

- **Incidence:** urinary incontinence is a common condition in pregnant women at term, with stress incontinence being more prevalent (34-38%) than urge incontinence (5-20%). Mixed forms are also very common. Its incidence increases as the pregnancy progresses.
- **Treatment:** treatment during pregnancy consists of pelvic floor rehabilitation. If done preventively, it appears to reduce the likelihood of incontinence during pregnancy and the immediate postpartum period.
- **Prognosis:** the presence of urinary stress incontinence in the first pregnancy is a predictor of symptoms of stress incontinence 5 years later. Early treatment before its appearance is thus recommended to reduce the persistence of symptoms.
Renal colic during pregnancy (see chapter on Lithiasis in Pregnancy)

- **Incidence**: similar to that of non-pregnant women. It affects approx. 1/1500 pregnancies, usually appearing in the 2nd or 3rd trimester (80-90%). The composition of the stones differs discretely from that of the rest of the population, with stones comprised of calcium phosphate (70%) being more common than those containing calcium oxalate (30%).

- **Symptoms**: low back pain (most common symptom), hematuria (second most common symptom), frequency, urinary infections and pyuria (especially with struvite stones).

- **Diagnosis**: ultrasound is the diagnostic method of choice. The use of ionizing radiation techniques must be evaluated on a case-by-case basis. MRI, although it produces no irradiation, does not correctly detect lithiasis.

- **Treatment**: the first step is analgesic treatment and fluid therapy. If symptoms persist, placement of a double J catheter or percutaneous nephrostomy may be considered (with a high risk of encrustation due to the hypercalciuria typical of pregnancy). If active intervention is favored, percutaneous nephrolithotomy and uroscopy are good options, but always when performed by expert practitioners and evaluating the risk/benefit ratio. Extracorporeal lithotripsy is contraindicated due to its proven teratogenic effects.

Bladder pain syndrome/Interstitial cystitis in pregnancy

- **Introduction**: BPS/IC is a multifactorial disease. While the contributing factors may be altered during pregnancy, there is no evidence indicating that pregnant women exhibit changes in symptoms.

- **Diagnostic criteria**: the same as those described for non-pregnant women (see chapter on Bladder Pain Syndrome/Interstitial Cystitis).

- **Treatment**:  
  - **Oral**: Hydroxyzine is not a safe drug. The safest drugs for use during pregnancy are Pentosanpolysulphate (only if clearly needed) and Amitriptyline.

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand name®</th>
<th>Oral dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pentosan polysulfate sodium</td>
<td>ELMIRON</td>
<td>1 caps of 100 mg/8 h</td>
<td>tailored</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>TRYPTIZOL</td>
<td>1 tab of 25 mg/12-24 h</td>
<td>tailored</td>
</tr>
</tbody>
</table>

  - **Intravesical**: Heparin is the safest drug as it is unlikely to be absorbed in the bladder and cross the placental barrier. Dimethylsulphoxide acid, lidocaine, and intravesical corticosteroids are contraindicated due to their teratogenic effects.

  - **Neurostimulators**: should not be used during pregnancy. If they are already in place, they should be disabled for the duration of the pregnancy.

Urological tumors in pregnancy

- **Incidence**: urological tumors occur with an incidence of 1/1000 pregnancies.

- **Symptoms**: depending on the type of tumor. The appearance of symptoms such as hematuria, pain, or hypertension, usually attributable to pathologies such as infections, pre-eclampsia, or pyelonephritis, require a urological study to rule out malignancies.

- **Type of tumor**:  
  - **Urethral tumors**: a rare pathology.  
    - **Benign**: the more common type. Include urethral caruncle, prolapse, urethral polyp, granuloma gravidarum, and leiomyoma. Treatment entails surgical excision.  
    - **Malignant**: very rare. Squamous cell, transitional cell, or adenocarcinomas.

  - **Bladder tumors**:  
    - **Incidence**: very rare.  
    - **Symptoms**: the most common symptom is hematuria (81%).  
    - **Diagnosis**: the diagnostic method of choice is flexible cystoscopy under local anesthesia. Bladder ultrasound only diagnoses 52% of tumors.  
    - **Initial treatment**: transurethral resection of the bladder.  
    - **Treatment of low-risk tumors**: can be delayed. Cystoscopy every three months.
- **Treatment of intermediate-risk tumors**: restaging resection at 4-6 weeks. Avoid treatment with Mitomycin, Thiotepa, and Doxorubicin due to their fetal toxicity.
- **Treatment of high-risk tumors**: restaging resection at 4-6 weeks. Induction of labor when fetus has reached maturation and treatment with endovesical BCG.
- **Treatment of muscle-invasive tumors**: given their rarity, there is no clear consensus. If detected in the 1st trimester, pregnancy termination and immediate cystectomy are recommended. In the 2nd and 3rd trimesters, a cesarean section at 28 weeks followed by immediate cystectomy is recommended.

- **Ureteral tumors**:
  - **Incidence**: very rare (2 described cases).

- **Renal cell carcinoma**:
  - **Incidence**: the most frequently diagnosed urological tumor during pregnancy.
  - **Symptoms**: pain, palpable mass, hematuria, and hypertension.
  - **Diagnosis**: ultrasound or MRI.
  - **Treatment**: radical nephrectomy, preferably via laparoscopy.

- **Angiomyolipoma**:
  - **Incidence**: the most common benign tumor during pregnancy. Usually single and unilateral.
  - **Symptoms**: usually asymptomatic. The onset of symptoms is associated with spontaneous rupture (pain, hematuria, and retroperitoneal mass).
  - **Diagnosis**: ultrasound or MRI.
  - **Treatment**: if the tumor is asymptomatic, monitoring is recommended. If symptomatic with bleeding and hemodynamic instability, the best option is angiographic embolization as it conserves the nephrons.

- **Adrenal tumor**:
  - **Pheochromocytoma**: a rare tumor (1/50,000 pregnancies). Usually presents with severe or fluctuating hypertension, headache, palpitations, hyperhidrosis, nausea, vomiting, changes in vision, or congestive heart failure. The diagnostic test of choice is the determination of catecholamines or their metabolites in 24 h urine. The diagnostic imaging test of choice is MRI (bright lesions on T2-weighted images). The treatment of choice is surgical excision. After diagnosis, treatment with α-blockers (Phenoxybenzamine) should be initiated; 1-2 weeks later, β1 blockers (Atenolol) should be added. The timing of surgery depends on gestational age: if detected in the 1st trimester, pregnancy termination and immediate excision of the tumor is recommended. If the patient does not want to terminate the pregnancy, treatment may be delayed until fetal lung maturity, after which a cesarean section and tumor excision can be performed in the same procedure. Currently, laparoscopic resection without terminating the pregnancy appears to be a safe alternative without aftereffects to the fetus despite the CO2 pneumoperitoneum.
  - **Cushing’s syndrome**: very rare. The most common cause is cortical adenoma. Under normal conditions during pregnancy, plasma concentrations of free cortisol and cortisol-binding proteins increases, maintaining a stable diurnal variability. Urinary concentrations of cortisol also increase, with a certain degree of resistance to inhibition by Dexamethasone. The diagnosis is thus made due to the total absence of suppression caused by low doses of Dexamethasone. The imaging test of choice is MRI. Treatment involves suppression with Metyrapone (starting at the 8th week of gestation) until laparoscopic resection is performed prior to delivery.
  - **Hyperaldosteronism**: a rare pathology. Presents with pre-eclampsia and hypokalemia. Treated with Potassium supplements and laparoscopic surgery.
Diagnostic imaging tests during pregnancy

- **Ionizing radiation produces three types of effects:** teratogenic effects and cell death, carcinogenesis, and genetic effects. At high doses (100 mSv), its effects on the fetus include intrauterine growth retardation, stillborn, microcephaly, and mental retardation. However, none of the radiological tests habitually used in urology exceed this level of radiation. The amount of radiation absorbed by the fetus based on the technique used is given below:

<table>
<thead>
<tr>
<th>Radiologic techniques</th>
<th>Fetal dose (mSv)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound</td>
<td>0</td>
</tr>
<tr>
<td>MRI</td>
<td>0</td>
</tr>
<tr>
<td>Chest radiography</td>
<td>0.2</td>
</tr>
<tr>
<td>KUB X-ray</td>
<td>0.5</td>
</tr>
<tr>
<td>Limited IVP</td>
<td>1-2</td>
</tr>
<tr>
<td>Fluoroscopy</td>
<td>15-20/min</td>
</tr>
<tr>
<td>CT scan (abdominopelvic)</td>
<td>20-25</td>
</tr>
</tbody>
</table>

- **Ultrasound:** for urological symptoms, abdominal ultrasound is the initial diagnostic test of choice. Its ability to detect lithiasis during pregnancy is approximately 50%. The measurement of resistance index in hydronephrosis to determine whether the cause is obstructive or not, and the use of transvaginal ultrasound to detect the presence of stones in the distal ureter may increase the sensitivity of ultrasound in the assessment of lithiasis.
- **IVP:** in selected cases in which this diagnostic test is necessary, a limited IVP to three or four plates may be performed (1-2 mSv).
- **CT:** not recommended due to excessive fetal exposure to radiation (20-25 mSv).
- **MRI:** does not expose the fetus to radiation. Highly sensitive in detecting hydronephrosis, determining the level of obstruction, and for studying renal masses, but of limited value in the study of lithiasis.
- **Retrograde pyelography, URS, or catheterization:** these procedures require the use of a radioscope, with high irradiation for the fetus (15-20 mSv/min). Ultrasound is therefore recommended to ensure the correct placement of catheters or to perform URS without radioscopic monitoring.
- **Scintigraphy:** the amount of radiation absorbed by the fetus is small, but depends on the radioisotope used. *Radioactive iodine* is not recommended after the 10th week of pregnancy.

Transplantation and pregnancy

- **Because CRF is associated with sexual dysfunction and infertility,** renal transplantation tends to improve both sexual function and the ability to conceive. In the past few years, the pregnancy rates of women who have received transplants have increased from 2% to 5%.
- **Pregnancies should be planned** when the recipient and transplanted organ are both healthy, with stable renal function and immunosuppression, and no signs of rejection, hypertension, proteinuria, hydronephrosis, or chronic infection. The ideal time is the 1st or 2nd year after implantation since the risk of chronic rejection or deterioration of renal function increases with time.
- **Pregnancy monitoring:** should focus on controlling proteinuria, hypertension, renal function, rejection, and urinary infection (monthly cultures). Pre-eclampsia affects 30% of pregnant transplant recipients.
- **Immunosuppressive treatment:** there are various options:
  - The most common treatment is with *Cyclosporin* with or without *Azathioprine* and corticosteroids. Although all three drugs pass through the placental barrier, they do not seem to have teratogenic effects. Because blood levels of *Cyclosporin* decrease in the 3rd trimester, the dose must be increased accordingly.
  - *Tacrolimus* also seems to be a safe drug during pregnancy.
  - *Micophenolate mofetil* and *rapamycin* (SIROLIMUS®) are teratogenic.
- **Delivery:** although vaginal delivery is neither contraindicated nor does it pose a mechanical risk for the transplanted organ, 50% of deliveries in transplant recipients are by cesarean section, probably due to a high incidence of premature birth (fetal distress, pre-eclampsia, membrane rupture due to laxity secondary to corticosteroid treatment).
- **Newborns:** 20% have a low birth weight; however, the incidence of malformations is similar to that of the general population.
- **Breastfeeding:** not recommended due to the risk of absorption of immunosuppressive agents by the infant.
- **Monitoring:** close follow-up is recommended for the mother during the first three months, with weekly assessment of renal function. Immunizations for the infant should be delayed for 6 months.

**Diagnostic algorithm in pregnancy**