

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

Proteinuria in Pregnancy

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Changes in GFR during pregnancy

- ▶ Glomerular filtration rate (GFR) and renal blood flow rise markedly during pregnancy, resulting in a physiologic fall in the serum creatinine concentration.
- ▶ A serum creatinine of 1.0 mg/dL in a pregnant woman probably reflects significant renal insufficiency

CHANGES IN THE URINARY TRACT COLLECTING SYSTEM: THEIR RELEVANCE TO TIMED URINE COLLECTIONS

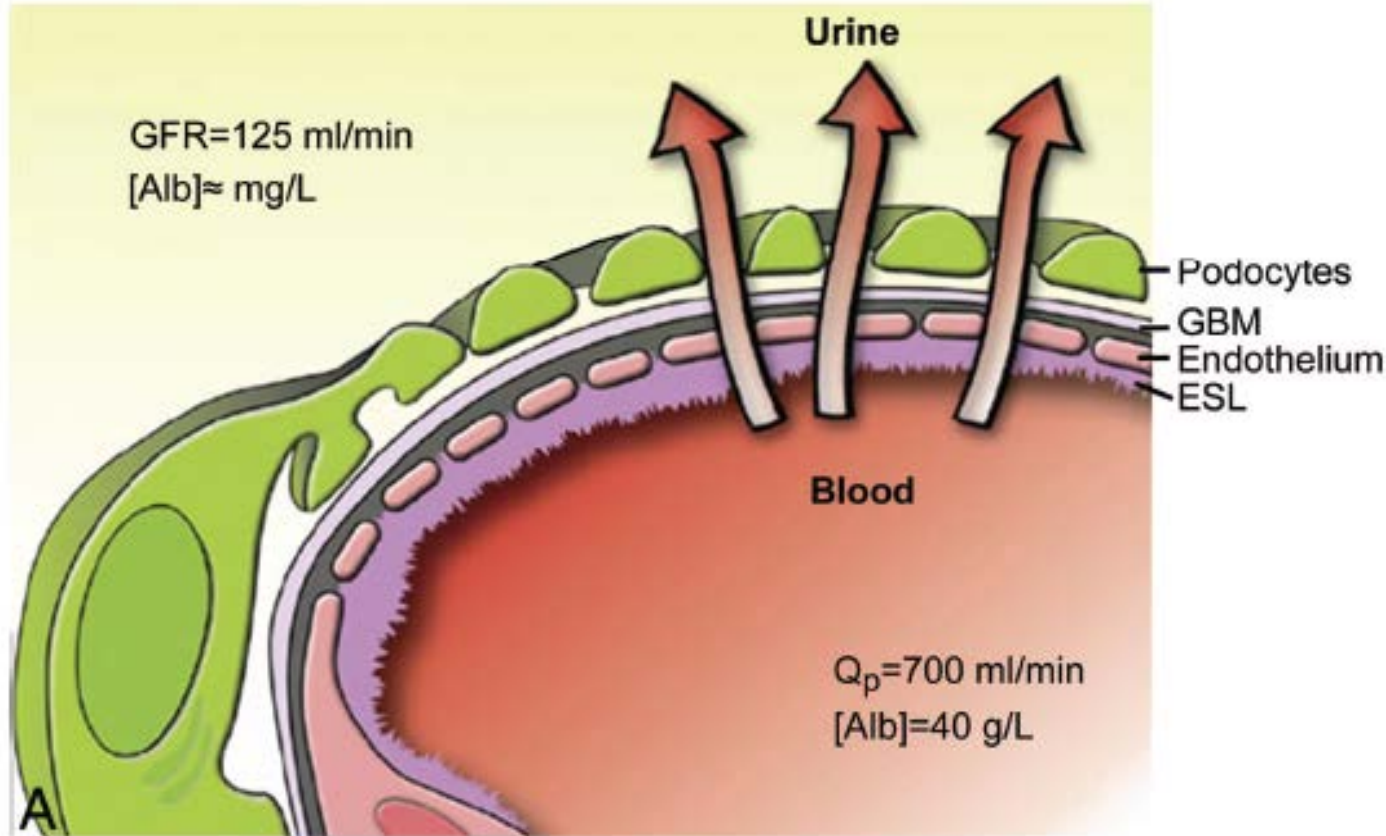
- ▶ There are marked changes in the urinary collecting system during pregnancy. Calyces, renal pelvises, and ureters dilate, accompanied by hypertrophy of ureteral smooth muscle and hyperplasia of its connective tissue.
- ▶ The dilatation, often greatest on the right, may be present as early as the first trimester and is observed in greater than 90% of gravidas at term.

- ▶ the dilated urinary tract may contain large volumes of urine that can introduce substantial collection errors especially **in hydropenic patients**.
- ▶ The errors are both of retention (hundreds of milliliters remaining in dilated tract) and timing (**the remaining urine may have been formed hours before**).
- ▶ Thus it is not surprising that the number of 24-hour urine collections considered incomplete during studies of pregnant women approach 50% and are more than double those in studies of nonpregnant populations.
- ▶ . The 24-hour urine creatinine excretion should be between 15 and 20 mg/kg body weight, calculated using pre-pregnancy weight.

CHANGES IN THE URINARY TRACT COLLECTING SYSTEM: THEIR RELEVANCE TO TIMED URINE COLLECTIONS

- ▶ The best way to avoid both retention and timing errors is
 - ▶ to have the patient hydrated
 - ▶ and positioned in lateral recumbency (the definitive nonobstructive posture) for 45 minutes or 1 hour before starting (ie, the discard),
 - ▶ and again before completing the collection.

THE RENAL HANDLING OF PROTEINS

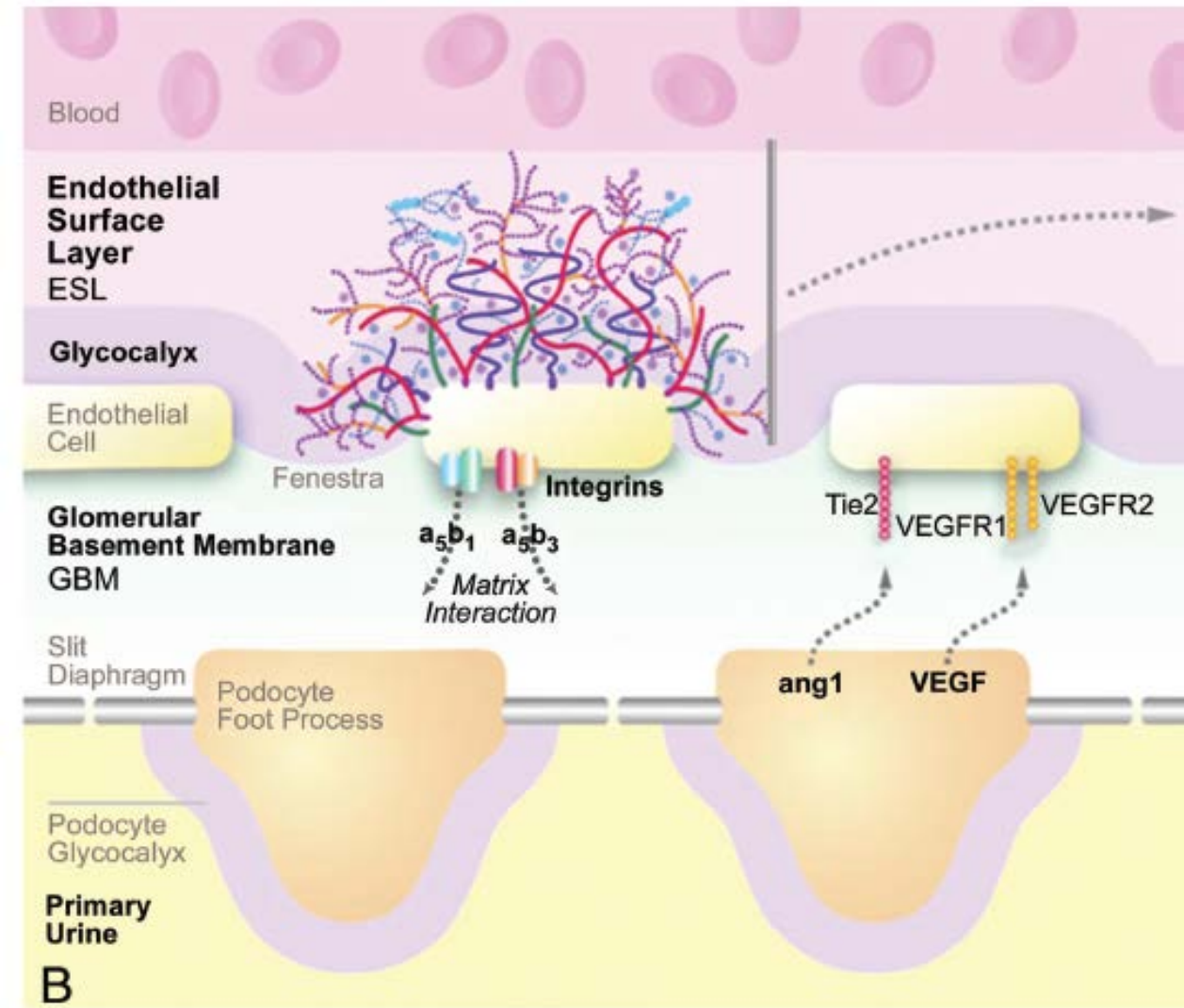


The theoretical amount of albumin filtered in a nonpregnant woman.

In gestation, where glomerular filtration rate increases 50% and circulating albumin decreases only 25% (from 4 to 3 g/100 mL),

the amount filtered would be greater.

THE RENAL HANDLING OF PROTEINS



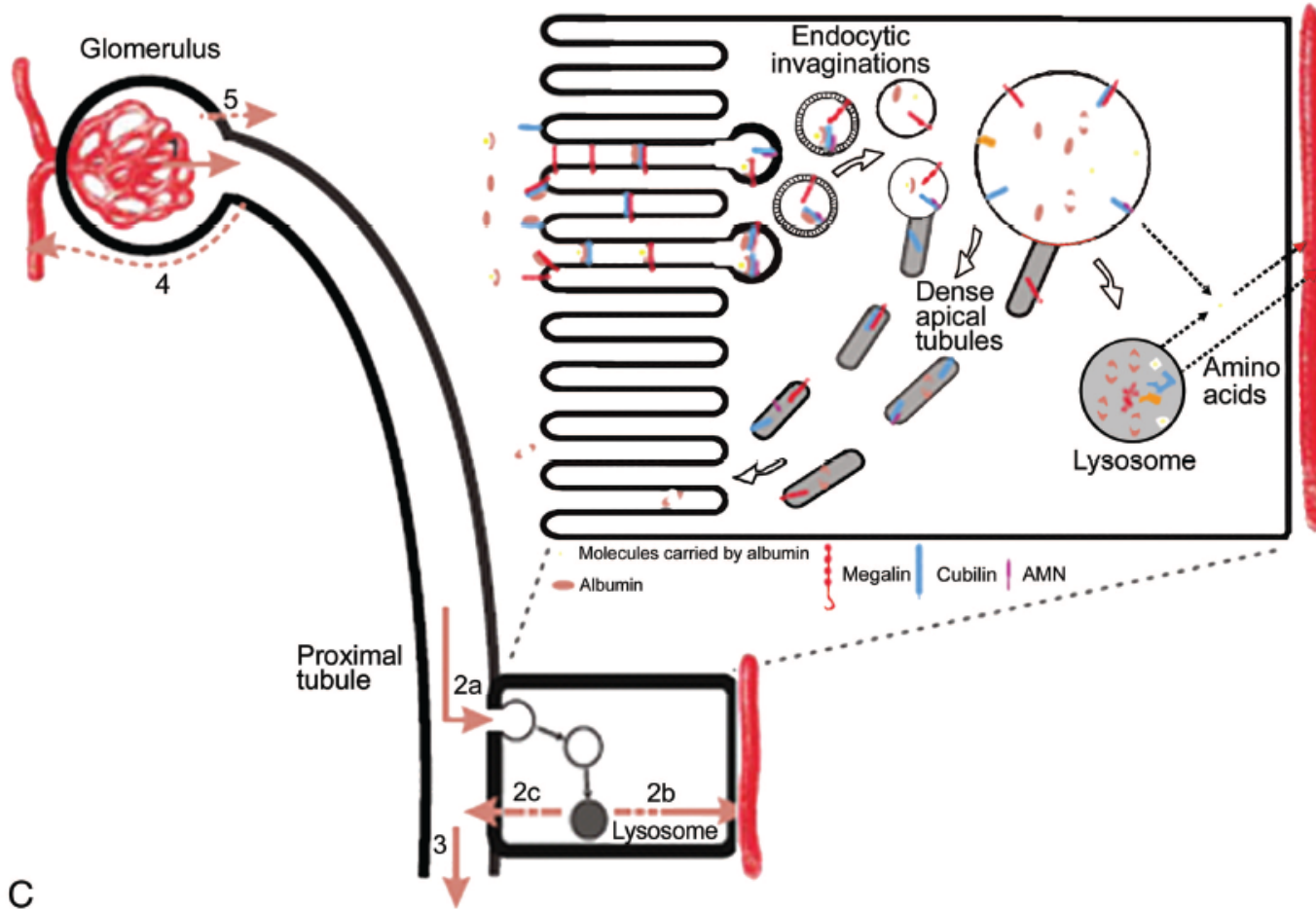
The barriers to filtration, including endothelium, basement membrane, and podocytes.

In this respect the very high circulating levels of sFlt-1 in women with preeclampsia maybe an important cause of their excessive proteinuria.

This is because soluble fms-like tyrosine kinase 1 inactivates vascular endothelial growth factor function in podocytes and is responsible for the characteristic lesion, glomerular endotheliosis.

Not shown are extrinsic barriers to filtration including molecular size, charge, and configuration

THE RENAL HANDLING OF PROTEINS



The fate of the filtered proteins.

There is considerable reabsorption of **albumin** (gram quantities filtered, less than 30 mg/day excreted).

Also virtually all the **low molecular proteins** (ie, less than 25 kDa) are freely filtered but almost completely catabolized within the proximal tubule mainly via receptor mediated endocytosis and lysosomal degradation.

THE RENAL HANDLING OF PROTEINS

- ▶ The cutoff after which urinary protein excretion is considered excessive in **nonpregnant** populations is usually cited as **150 mg/day**, although both lower and higher values have been suggested.
- ▶ In **pregnancy** these cutoff values usually double, the most frequent value being **300 mg/day**.

PROTEIN EXCRETION DURING PREGNANCY

- ▶ Clinicians currently use three approaches to determine whether their pregnant patient is excreting excessive amounts of protein.
- ▶ One is qualitative, the classic dipstick;
- ▶ the second quantitative, the so-called “gold standard” 24-hour collection;
- ▶ and the third is the protein/creatinine or albumin/creatinine ratios on a single voided urine.

- ▶ Evaluation of a fresh midstream urine specimen obtained as a clean voided specimen before pelvic examination minimizes the chance of contamination from vaginal secretions.



Urine dipstick

- ▶ Urine dipstick to screen for proteinuria is associated with frequent **false-positive and false-negative** results, especially when the urine is particularly **concentrated or dilute**, respectively.
- ▶ It is most predictive of abnormal 24-hour proteinuria if +2 or greater.
- ▶ Positive urine dipsticks should be followed-up with a quantitative test.

protein/creatinine or albumin/creatinine ratios

- ▶ ●The urinary protein-to-creatinine (PC) ratio (mg protein/mg creatinine) is an accurate, convenient, and relatively rapid method to quantify proteinuria in pregnancy.
- ▶ A urine PC ratio less than 0.15 mg/mg may be considered normal (predictive of less than 300 mg protein in a 24-hour collection) and values above 0.7 mg/mg are very likely to indicate significant proteinuria (more than 300 mg protein in a 24-hour collection).
- ▶ Ratios between 0.15 and 0.7 mg/mg should be further evaluated by 24-hour urine collection.
- ▶ If a 24 hour urine collection is not obtained, a protein:creatinine ratio of 0.26 mg/mg (30 mg/mmol) in a random urine sample is suggested as the threshold for significant proteinuria.

24-hour collection

- ▶ The 24-hour collection is begun at the usual time the patient awakens. At that time, the first void is discarded and the exact time noted. Subsequently, all urine voids are collected with the last void timed to finish the collection at exactly the same time the next morning.
- ▶ Although generally considered the "gold standard" for diagnosis of proteinuria in both preeclampsia and renal disease, the 24-hour urine protein excretion in pregnant women is frequently inaccurate due to undercollection or overcollection

Differential Diagnosis

- ▶ It is most commonly associated with
 1. Urinary tract **infections** in pregnancy
 2. **Longstanding renal disease**,
 3. But is related to **pre-eclampsia** after 20 weeks gestation in the presence of hypertension

Differential Diagnosis

- ▶ In pregnant ladies with renal disease the main aim is to have delivery at term but patients with preeclampsia quite often develop progressive disease which ends up in the need for iatrogenic delivery.
- ▶ In situations when it is difficult to distinguish preeclampsia from pre-existing renal disease, it is pertinent to assume a working diagnosis of preeclampsia because of its potential for rapid development of serious maternal and foetal complications.

Differential Diagnosis

- ▶ The gestational age at which proteinuria is first documented is important in establishing the likelihood of preeclampsia versus other renal disease.
- ▶ Proteinuria documented prior to pregnancy or in early pregnancy (before 20 weeks of gestation) suggests preexisting renal disease.
- ▶ In late pregnancy, the presence of hypertension or other signs/symptoms of severe preeclampsia (eg, thrombocytopenia, elevated liver transaminases), if present, also helps to distinguish preeclampsia from underlying renal disease.

Preeclampsia

- ▶ Preeclampsia is a multisystem disease that manifests as hypertension and proteinuria in pregnancy.
- ▶ It is peculiar to pregnancy, of placental origin and is only cured by delivery.
- ▶ Preeclampsia affects nulliparous women and is less common in multiparous women unless additional risk factors are present.
- ▶ Regarding pathophysiology, blood vessel endothelial cell damage plus an exaggerated maternal inflammatory response leads to:

Preeclampsia

- ▶ 1. Increase vascular permeability causing oedema and proteinuria
- ▶ 2. Vasoconstriction causing hypertension, eclampsia (reduced cerebral perfusion) and liver damage
- ▶ 3. Reduced placental blood flow causing intrauterine growth restriction
- ▶ 4. Clotting abnormality.

- ▶ Proteinuria is one of the cardinal features of preeclampsia, a common and potentially severe complication of pregnancy.
- ▶ However, two important points should be noted.
 - ▶ First, the **severity of proteinuria** is only weakly associated with adverse maternal and neonatal outcomes, and should not be used to guide management.
 - ▶ Second, although part of the formal diagnostic criteria of preeclampsia, **proteinuria may be absent**.

Investigations

- ▶ If urinalysis is positive for proteinuria,
- ▶ infection is excluded by **urine cultures** .
- ▶ and the protein is quantified by either **24 hour urine collection** or protein creatinine ratio on a single sample.

- ▶ More than 30mg/n-mol on protein creatinine ratio or > 0.3g/24 hour on urine collection represents significant proteinuria.

- ▶ **Blood pressure** and urine is checked at every antenatal appointment.
- ▶ Investigations in preeclampsia also include **monitoring blood tests**, ultrasounds, umbilical artery Doppler scans and cardiotocography

Renal biopsy

- ▶ Renal biopsy is best left until the post-partum period unless unexplained rapidly progressive loss of renal function is occurring.

Nephrotic Syndrome

- ▶ For women with nephrotic syndrome, discomfort from severe leg edema can be managed with sodium restriction (1.5 g, approximately 60 mEq), bedrest, and leg elevation.
- ▶ Prophylactic anticoagulation is reasonable in pregnant women with nephrotic syndrome and severe hypoalbuminemia (serum albumin <2.0 mg/dL, or <2.8 mg/dL in membranous nephropathy), especially if another risk factor (eg, bedrest) is present.
- ▶ Bile acid sequestrants and fibrates can be safely used in pregnancy to treat severe hyperlipidemia due to nephrotic syndrome; statins should be avoided.

Case 1

- ▶ A 19 years old woman G2P0 A1 who is in 28 weeks of Gestational Age has referred for 600mg/day Proteinuria
- ▶ Blood pressure: 120/80
- ▶ Heparin ?
- ▶ U/C : 100,000 for Ecoli
- ▶ She has treated with Cefixime and proteinuria disappeared.

Case 2

- ▶ 29 years old Diabetic woman with 29 weeks gestational Age has referred for 2.5g/d proteinuria and Serum Cr=1.9 mg/dL.
- ▶ Her blood pressure is 120/85 in two visits. Diltiazem has prescribed for her Proteinuria and Alarm Signs was educated. Heparin?
- ▶ On 32 weeks gestation her blood pressure raised to 160/100 so she admitted in our hospital.
- ▶ She has taken corticosteroids for fetal lung maturation on 33 weeks and after that the fetal heart rate has diminished while blood sugar of mother was 500mg/dL.
- ▶ Delivery has done and the neonate transferred to NICU .

Case 3

- ▶ A 48 years Old woman with TS and history of bilateral Angiomyolipoma and CKD and proteinuria