Test of Renal Function

Objectives

At the end of the lecture the student should be able to;

List the renal function test

Explain the biochemical basis of renal function tests

Interpretation of the results of RFT in various disorders

Major Renal function Tests

Urine analysis

Estimation of GFR

Tests for Tubular function

Serum Markers for renal functions

Urinalysis (Physical & Chemical analysis)

Physical characteristics

- **Volume -**

  Oliguria , Anuria , Polyuria

- **Appearance -**

  Colour Turbidity

- **Odor -**

- **Specific gravity -**

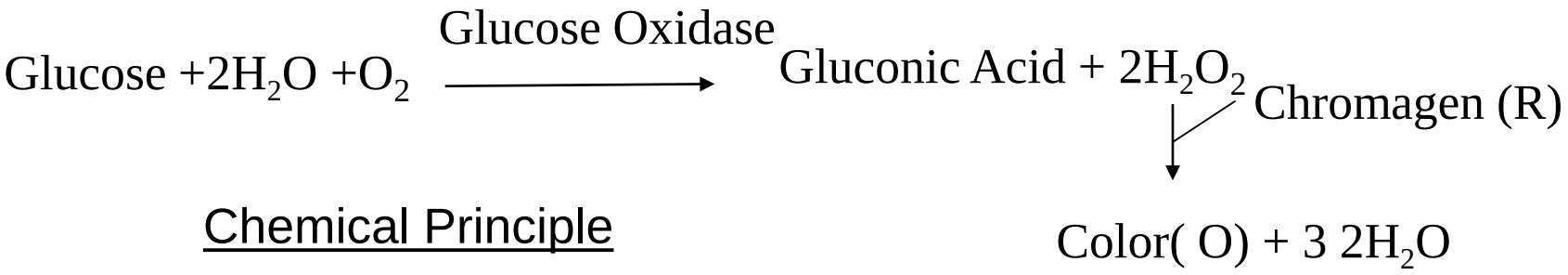
- **pH -**

Chemical Analysis

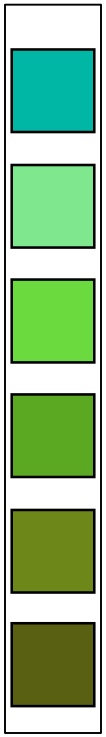
Urine Dipstick

- Glucose
- Bilirubin
- Ketones
- Specific Gravity
- Blood
- pH
- Protein
- Urobilinogen
- Nitrite
- Leukocyte Esterase

Glucose



Chemical Principle



Negative

Trace (100 mg/dL)

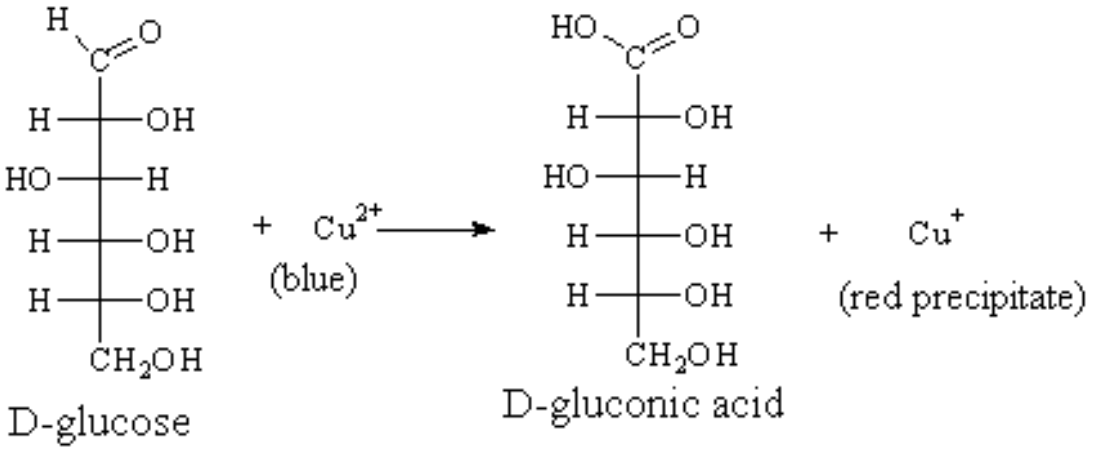
+ (250 mg/dL)

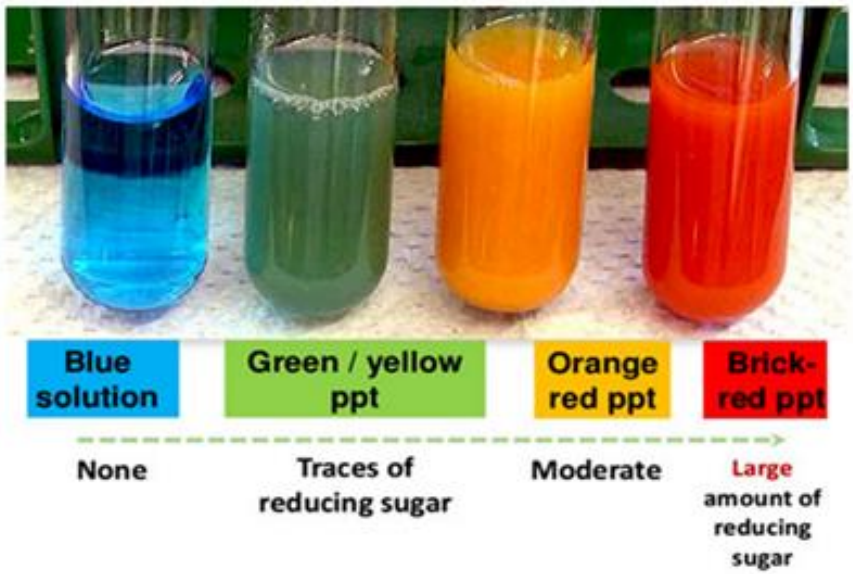
++ (500 mg/dL)

+++ (1000 mg/dL)

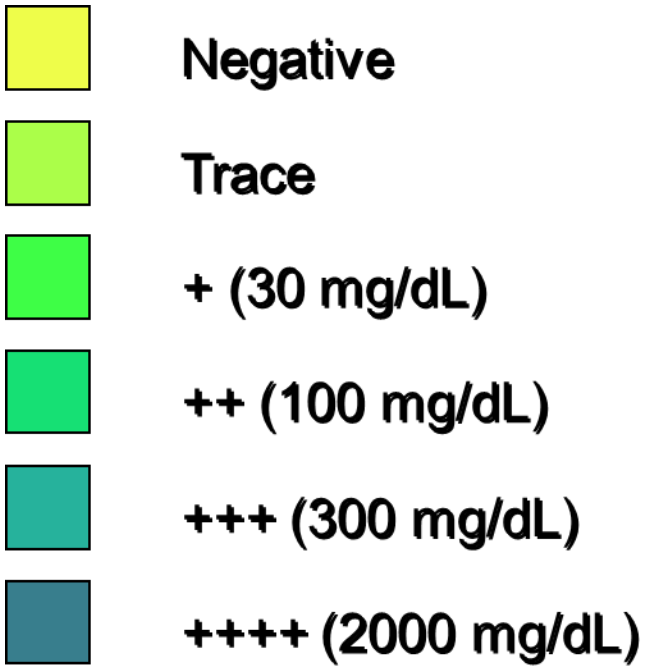
++++ (2000+ mg/dL)

BENADICTS TEST





Protein
Renal Function Test



Causes

- Functional
- Renal

Tests for protein

Protein analysis is carried out to

- ❖ Establish the of diagnosis renal disease
- ❖ Define the nature of the renal disease
- ❖ Define the degree of renal dysfunction
- ❖ Monitor response to treatment

Protein in 24 hr urine collection

Spot sample (1st void sample is the best)

Urinary Protein/Creatinine ratio(PCR)

Albumin/creatinine ratio (ACR)

Assessment of Glomerular function

Serum markers

Measurement of filtration rate

Serum Markers

Creatinine

Urea

Uric acid

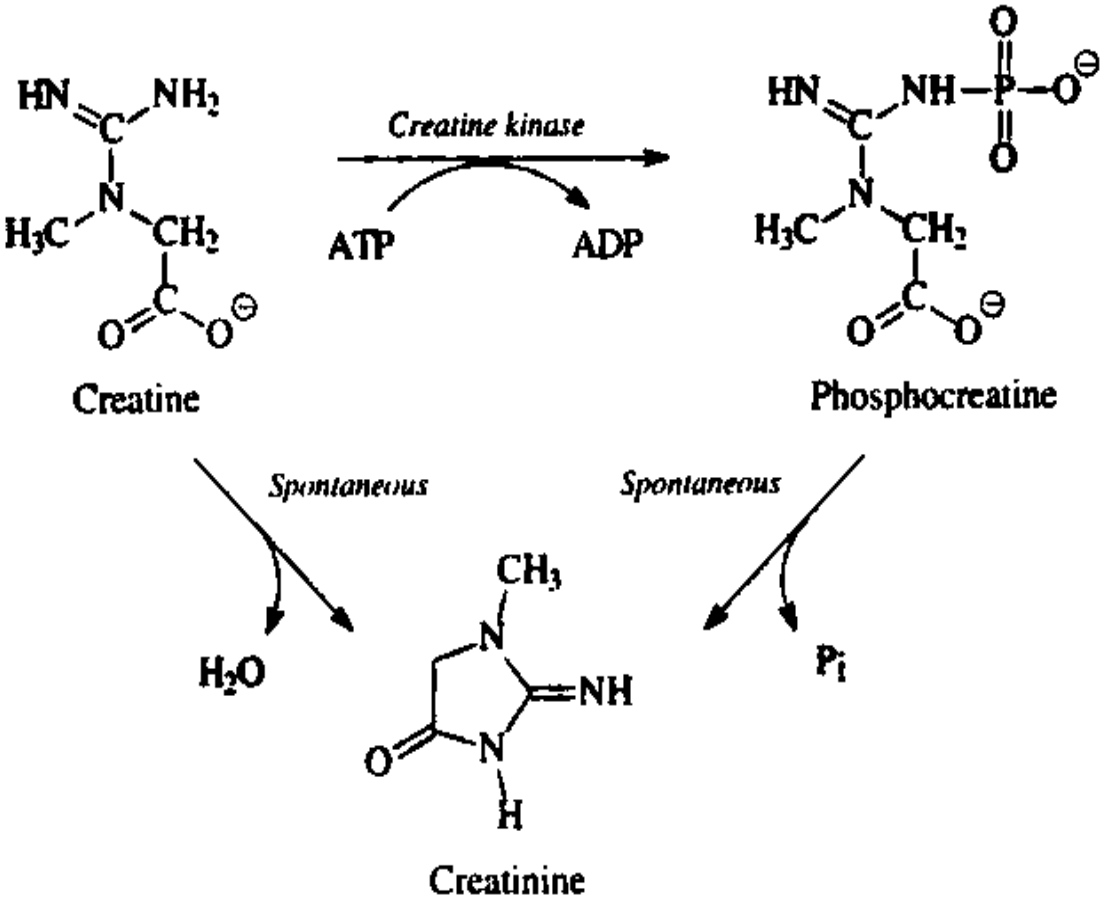
β2 microglobulin

Creatinine

- Creatinine is the end product of creatine catabolism.
- 98% of the body creatine is present in the muscles where it functions as store of high energy in the form of creatine phosphate.

Creatinine

1 to 2% of muscle creatine spontaneously converts to creatinine daily and released into body fluids at a constant rate.

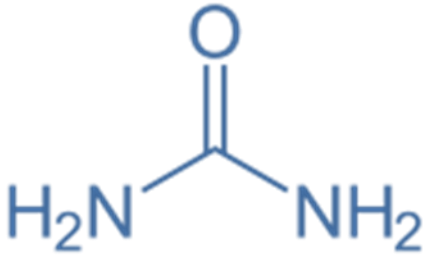


Plasma creatinine concentration is inversely related to the GFR

Normal plasma creatinine does not necessarily imply normal renal function

GFR can decrease by 50% before plasma creatinine concentration rises beyond the normal range

Urea



Urea ???

Urea is filtered freely by the glomeruli

- But ? Reabsorbed (GFR underestimated)

- Blood urea level is sensitive but not specific indicator for renal dysfunction

Increased

Renal
Post renal (obstruction)

Pre (non) renal

High protein intake, increased protein catabolism, starvation, heart failure, dehydration, Some medicines.

Decreased -low protein intake, liver disease. Over hydration

Its level is elevated in last stages of renal failure after 50% of renal function is lost.

Uric acid

- Is the end product of purine metabolism and excreted in urine.
- Purine in body comes from food and break down of body cells.
- Elevated level of uric acid in blood is one of the markers of kidney dysfunction.

High blood uric acid occurs in:

- Renal failure (due to decreased excretion in urine)

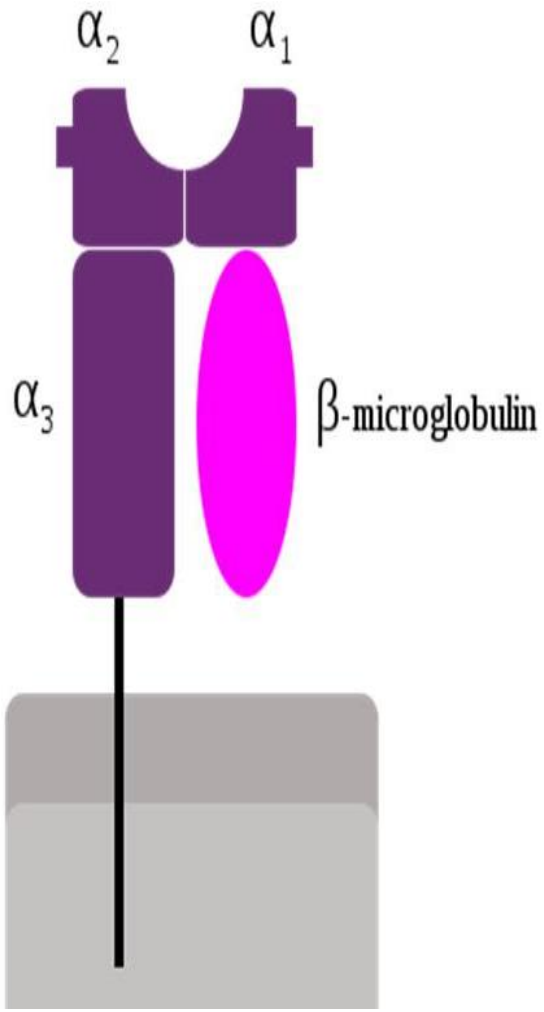
- Leukemia (increased turnover of cells)
- Alcoholism
- Gout

Low blood uric acid occurs in:

- Renal disease that decrease renal tubular re-absorption

- Liver diseases (cirrhosis)
- Some drugs

β Microglobulin



Beta-2 microglobulin (B2M) is a protein that is found on the surface of nucleated cells and functions as part of the human immune system .

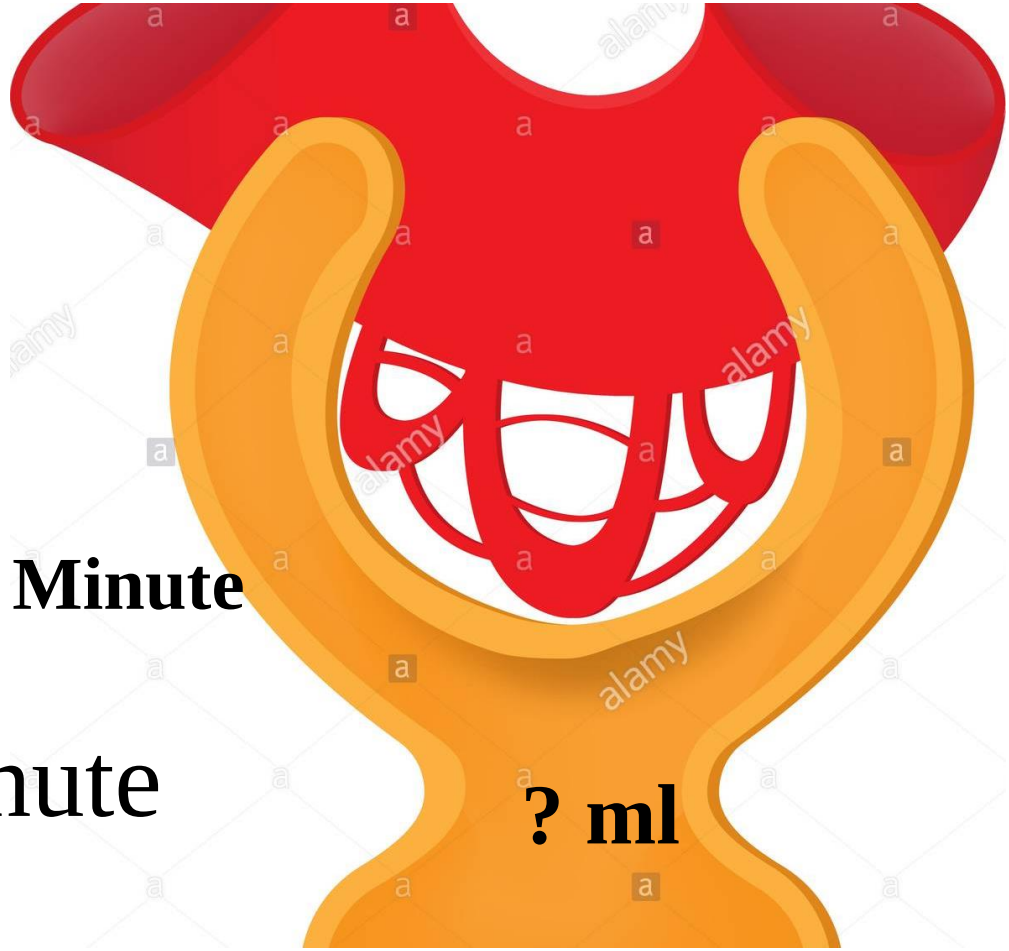
Constantly shed in to the ECF ,Filtered and 99% reabsorb by PCT

Increased shedding in increased cell Turnover. Normally, only small amounts are present in the urine.

Damaged renal tubules – increased excretion. So serum levels decrease

Measurement of GFR (Estimation)

Amount of substance filtered in a given time



PV=UV

V= UV/P in a minute

= Filtration rate

Clearance test

Accurate measurement of GFR substance that is:

- Freely filtered at glomeruli.
- Neither reabsorbed nor secreted by tubules.
- Its concentration in plasma needs to remains constant throughout the period of urine collection.
- Better if the substance is present endogenously.
- Easily measured.

Creatinine meets most of these criteria.

Creatine Clearance

GFR can be estimated by measuring the urinary excretion of a substance that is

Clearance is defined as the (hypothetical) quantity of blood or plasma completely cleared of a substance per unit of time**. (ml/minute)**

$$GFR = \frac{UxV}{P}$$

U= Concentration in urine mg/dl

V= Volume of urine (ml)pass in a minute

P= Concentration in plasma mg/dl

Volume of urine is measured 24 hr and calculate the minute volume

Other substances use in clearance test

Inulin

Gold standard

No secretion or absorption in the tubules

But need to infuse in to blood

Not use in clinical practice

Cystatin –C

Urea

Problems CC

Creatinine **clearance is approximately little greater than the** Normal Clearance

-As it is actively secrete by tubular cells in very small amounts

-So creatinine clearance overestimates actual GFR

-The difference is not significant when GFR is normal

But when the **GFR is very low** (less 10 ml/min),

it is significant

Estimation of GFR

As indicated above, the creatinine clearance is measured by using a 24-hour urine collection,

but this does introduce the potential for errors in terms of completion of the collection.

An alternative and convenient method

calculated creatinine clearance using parameters such as serum creatinine level, sex, age, and weight of the subject.

Estimated GFR (eGFR)

MDRD (Modification of Diet in Renal Disease)

creatinine in mg/dl (MDRD4)

GFR (mL/min/1.73 m^2) =

$175 \times (S_{cr})^{-1.154} \times (Age)^{-0.203} \times$ (0.742 if female) $\times$ (1.212 if African American)

Used to stage CKD (not in normal person)

CDK-EPI

(Chronic Kidney Disease Epidemiology Collaboration)

Sex	Serum creatinine level (μmol/L) (mg/dL)	Equation
Female	≤62 (≤0.7)	$GFR = 144\ (Scr/0.7)^{-0.329} \times (0.993)^{age}$
	>62 (>0.7)	$GFR = 144\ (Scr/0.7)^{-1.209} \times (0.993)^{age}$
Male	≤80 (≤0.9)	$GFR = 141\ (Scr/0.9)^{-0.411} \times (0.993)^{age}$
	>80 (>0.9)	$GFR = 141\ (Scr/0.9)^{-1.209} \times (0.993)^{age}$

Depend on ,Age , sex, race

Better for screening

Renal tubular function tests

Compared with the GFR as an assessment of glomerular function, there are no easily performed tests which measure tubular function in quantitative manner

Investigation of tubular function:

1. Urine specific gravity and osmolality
2. Day & night urine volume
3. Serum electrolytes
4. Concentration test
5. Dilution test

Tests for tubular function

Specific gravity of urine – Normal 1.015-1.025

• • Incase of proteinuria S.G. elevated.

• Earliest manifestation of renal disease may be difficulty in concentrating the urine.

• ↓ Sp.gr.— excessive water intake, ch.nephritis, Diabetes Insipidus

• ↑Sp.gr.— diabetes mellitus, nephrosis, Ch.Renal failure.

Other tests

Concentration test :

- Bladder is emptied in the morning specimen discarded.
- Second specimen after one hour collected and specific gravity measured.
- Sp.gr. >1.022

Adequate renal function.

Dilution test :

- Patients not allowed to drink after mid night.
- Bladder emptied at 7 am
- Water load 1200 ml over next 30 min.
- Hourly urine sample collected for next 4 hrs. Volume, Sp.gr. measured.
- Normal person will excrete all the water load with in 4 hours.
- Sp.gr. of at least on sample should fall to 1.003.

Diseases of the Kidney

Glomerular
AGN

Urinary analysis
Oliguria
Hematuria
Proteinuria
hyaline and granular casts

RBC casts

- decreased GFR,

Serum
- elevated blood urea nitrogen (BUN)
- elevated creatinine,

Glomerular
Nephrotic Syndrome

Massive proteinuria –
Hypoproteinemia – Hypercholesterolemia.
Hypoalbuminemia
↑ high MW proteins
↓ low MW proteins

False hyponatremia
Hypocalcemia

Urea, creatinine
GFR.

Tubular disease
Renal Tubular Acidosis

Decreases

- GFR
- urinary concentrating ability
- metabolic acid excretion

- leukocyte casts in the urine
- inappropriate control of sodium balance.

Diseases of the kidney

Acute renal failure:

Rapid loss of renal functions which is reversible. (CRF is irreversible with slow loss of renal functions)

Causes:

1- Prerenal: (decreased renal perfusion)

due to shock – hge – hypotension – HF ……..

Lab investigations:

Urea – creatinine – UA – K – Na – Mg – Phosphate – Ca – sec.

In acute RF, kidney excrete small vol. of concentrated urine with low Na conc.

2- Renal causes:

Nephrotoxic drugs (Cyclosporine – NSAID)

Kidney diseases (GN-acute tubular necrosis)

Systemic diseases (SLE-rheum. Arthritis)

Lab. Inv.:

as prerenal but with: urine Na > 40 mmol/L

urine osmolality <400

3- Post renal causes:

Obstruction to urine pathway (stone – tumor – prostatic)

Lab. Inv.:

As pre-renal.

Chronic renal failure:

(Irreversible – slowly progressing)

↑ urea, creatinine, K, phosphate, Mg

↓ creatinine clearance, Na, Ca, calcitriol, proteins, pH

Fixed Sp. G. – Polyurea.

Renal Stones

Supersaturation of urine with solutes

Solubility is affected by urine pH, volume and total excretion

Those factors can often be modified with medications and diet

Risk Factors

-Male sex

-Obesity

-Family History

-H/o stone disease (1/2 will have recurrence)

-Dietary factors

-Lower fluid intake, higher animal protein, higher Vitamin C

Signs/Symptoms

Typical symptoms

1.Sudden onset

Unilateral colicky flank pain radiating to groin (localization of pain evolves as stone migrates)

2.Often with nausea/vomiting

3.Hematuria (microscopic or gross)

Differential Diagnosis

Differential for flank pain with hematuria

-UTI

-Renal Cell Carcinoma

-Ectopic pregnancy

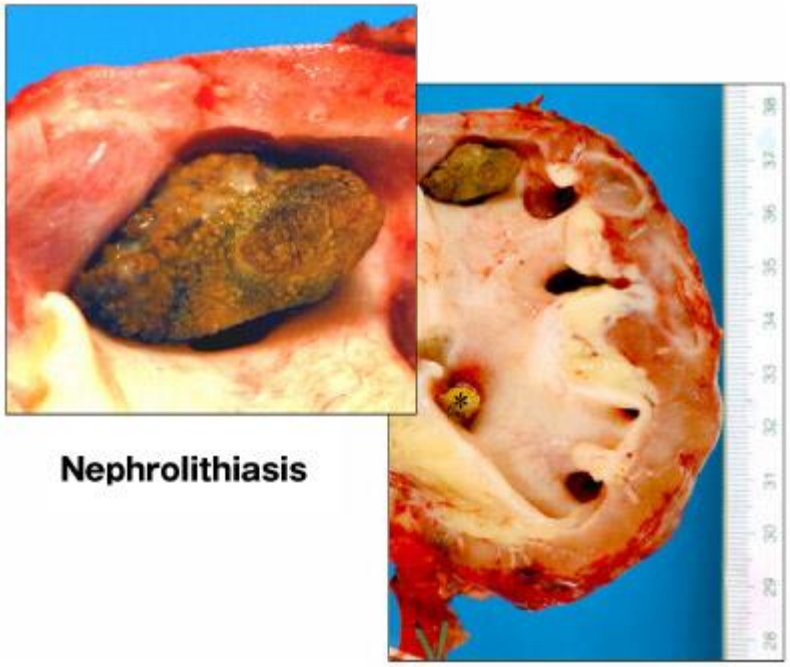
-Dissecting Aortic artery , with renal artery involvement

Types of Stones

In order of prevalence

- Calcium Oxalate
- Calcium Phosphate
- Uric Acid
- Cysteine

Urinary Stones



Nephrolithiasis