

# **Nephrotoxicity**

**Presented**

**By**

**Dr / Said Said Elshama**

**Professor of Forensic Medicine and Clinical Toxicology**

**Medical Education (DHPE)**

**College of Medicine - Taif & Suez Canal University**



# Learning objectives

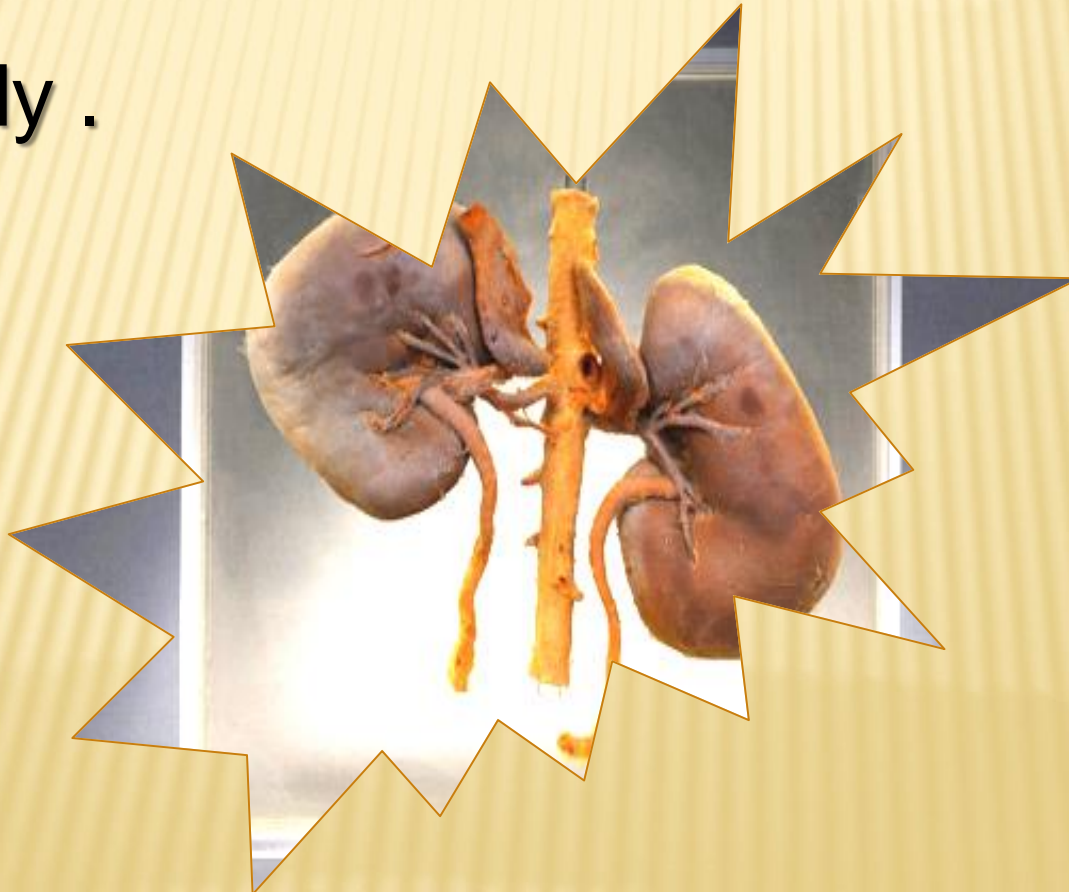
---

- ✘ Nephrotoxicity definition .
- ✘ Mechanisms of nephrotoxicity.
- ✘ Drugs induced nephrotoxicity.
- ✘ Clinical picture of nephrotoxicity.
- ✘ Management of nephrotoxicity.



# Definition

- ✘ Disturbance or harmful effect on the kidney.
- ✘ By introducing drugs or toxic substances into the body .



**intraglomerular  
hemodynamic**

**acute tubular cell  
necrosis**

# **Mechanisms of nephrotoxicity**

**Inflammation**

**Rhabdomyolysis**

**Crystal  
nephropathy**

**Thrombotic  
microangiopathy**

# Intra-glomerular pressure

**GFR**

Urine output

Prostaglandin Mediated  
vasodilatation of afferent  
arterioles (NSAID, cyclosporine)

Angiotensin 11- Mediated  
vasoconstriction of efferent  
arterioles (ACE inhibitors)

**Concentrating glomerular  
filtrate**

**Reabsorbing  
glomerular filtrate**



**Renal tubular cells  
Acute tubular cell necrosis  
Aminoglycosides  
Cisplatin**

# inflammation

1. Glomerulonephritis
2. Acute interstitial nephritis (Non-dose dependent)
3. Chronic interstitial nephritis (Chronic drug use with high dose)
  - Immune reaction without classic symptoms of hypersensitivity “fever, rash, eosinophilia”
  - Ex. Acetaminophen, aspirin, NSAID, vancomycin, antiviral and rifampicin,

# Crystal nephropathy

Ex . Acyclovir, ciprofloxacin

Concentration  
of drug

Volume  
depletion

Urinary pH

Renal insufficiency

# Rhabdomyolysis

Ex. Cocaine heroin , amphetamine

Direct toxicity

Tubular  
obstruction

Alteration in GFR

**Immune mediated  
reaction**

**Direct endothelial  
toxicity**



# **Thrombotic Microangiopathy**

Antiplatelets(cyclosporine)

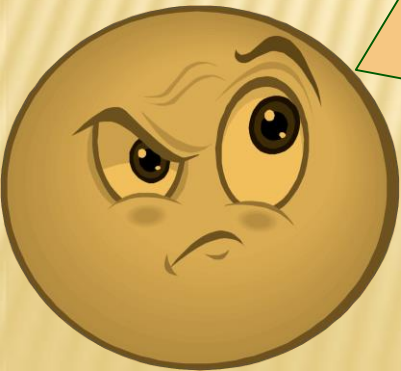
# Causes of nephrotoxicity

1. **Antibiotics**
2. **Analgesics**
3. **Heavy metals**
4. **Contrast agents**
5. **Anti cancer**
6. **Solvents**
7. **Herbicides and pesticides**
8. **Overproduction of uric acid**



# Risk Factors

1. **Age**
2. **Underlying kidney disease**
3. **Severe dehydration**
4. **Prolonged exposure to toxic agents**
5. **heart failure**
6. **Sepsis**
7. **Renal insufficiency (GFR is less than 60 ml/m)**
8. **Overproduction uric acid disease**
9. **Intravascular volume depletion**



# Factors affecting susceptibility of kidney to toxicants

**1**

**High renal  
blood flow**

**2**

**Concentration  
of chemicals**

**3**

**Re-absorption and  
secretion of  
chemicals**

**4**

**Activation pro-toxicants  
to reactive**

# Common nephrotoxic drugs

---

Non steroidal anti - inflammatory

Aspirin- ibuprofen

Aminogycosides

Gentamycin

Antibiotics

Vancomycin

Antiviral

Acyclovir

# Clinical picture

1. Excess urea in the blood (azotemia)
2. Anemia
3. Acidosis
4. Over hydration
5. Hypertension
6. Hematuria
7. Pyuria
8. Oliguria
9. Seizures
10. Coma



# DIAGNOSIS

History taking

Examination

Investigations

Urine analysis

Renal functions tests



# Management

**Diagnosis**  
History  
Examination  
Investigation

**Treatment**

**Prevention**

# TREATMENT

---

- ✘ **Stop the drug**
- ✘ **Remove the toxin**
  1. Diuretics
  2. Chelation
  3. Hemodialysis
  4. Hemoperfusion

# PREVENTION

---

- ✘ Adjust dose
- ✘ Assess renal function
- ✘ Avoid nephrotoxic combinations
- ✘ Correct risk factors
- ✘ Ensure adequate hydration
- ✘ Use non-nephrotoxic drugs

# QUESTIONS

---

## Mechanism of gentamycin nephrotoxicity is

1. intraglomerular hemodynamic
2. acute tubular cell necrosis
3. Inflammation
4. Thrombotic microangiopathy
5. Crystal nephropathy



# QUESTIONS

✘ **If patient has tobramycin nephrotoxicity, the first step of treatment is to:-**

1. Give excess fluid
2. Slow the infusion rate
3. Stop the medication
4. Add antidote



# QUESTIONS

✘ **Antiprostaglandin activity of nephrotoxic drugs due to**

1. Vasodilatation of efferent arterioles
2. Vasodilatation of afferent arterioles
3. Vasoconstriction of afferent arterioles
4. Vasoconstriction of efferent arterioles



***Thank you***

***Thank you***



***Thank you***

***Thank you***