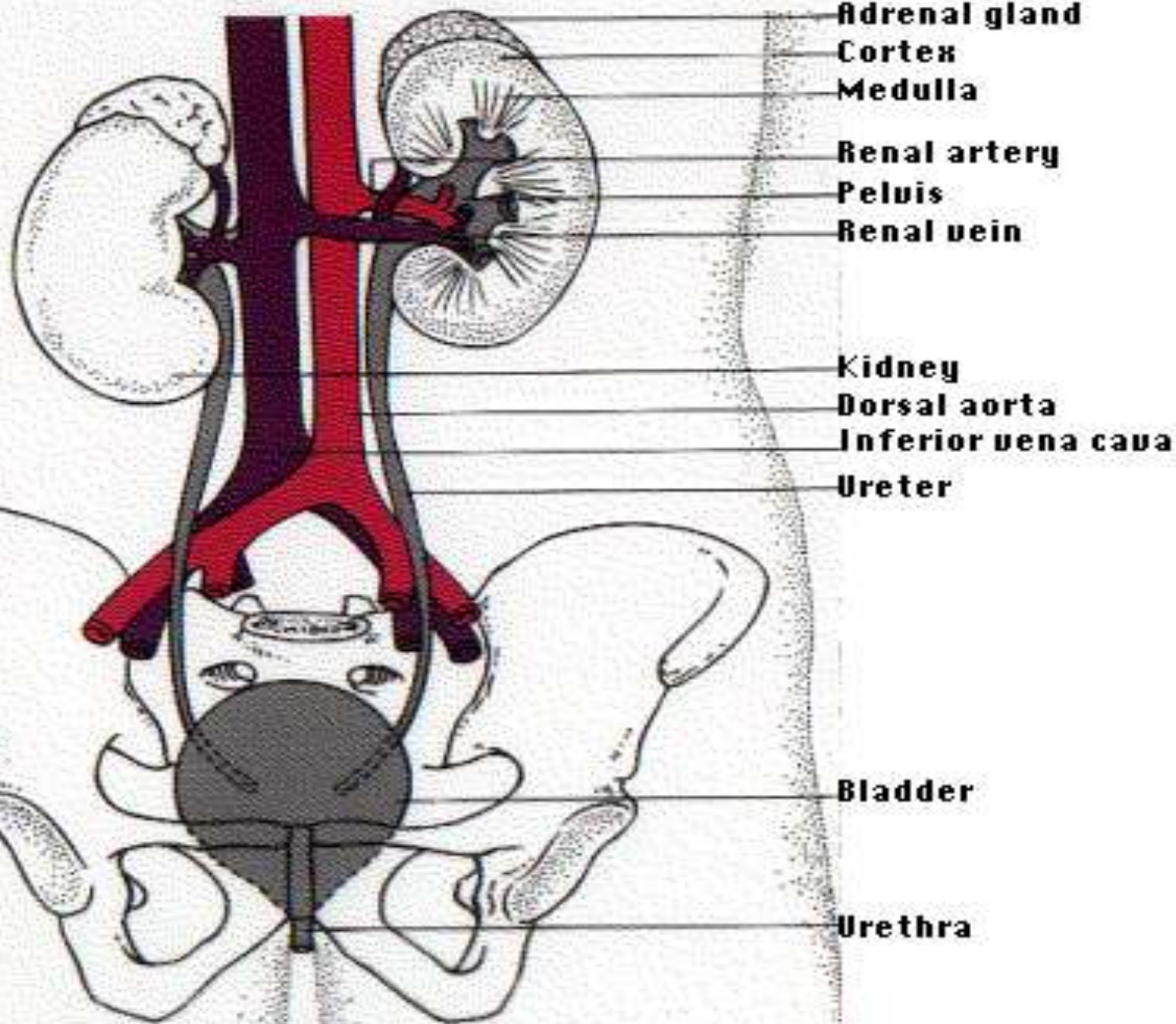
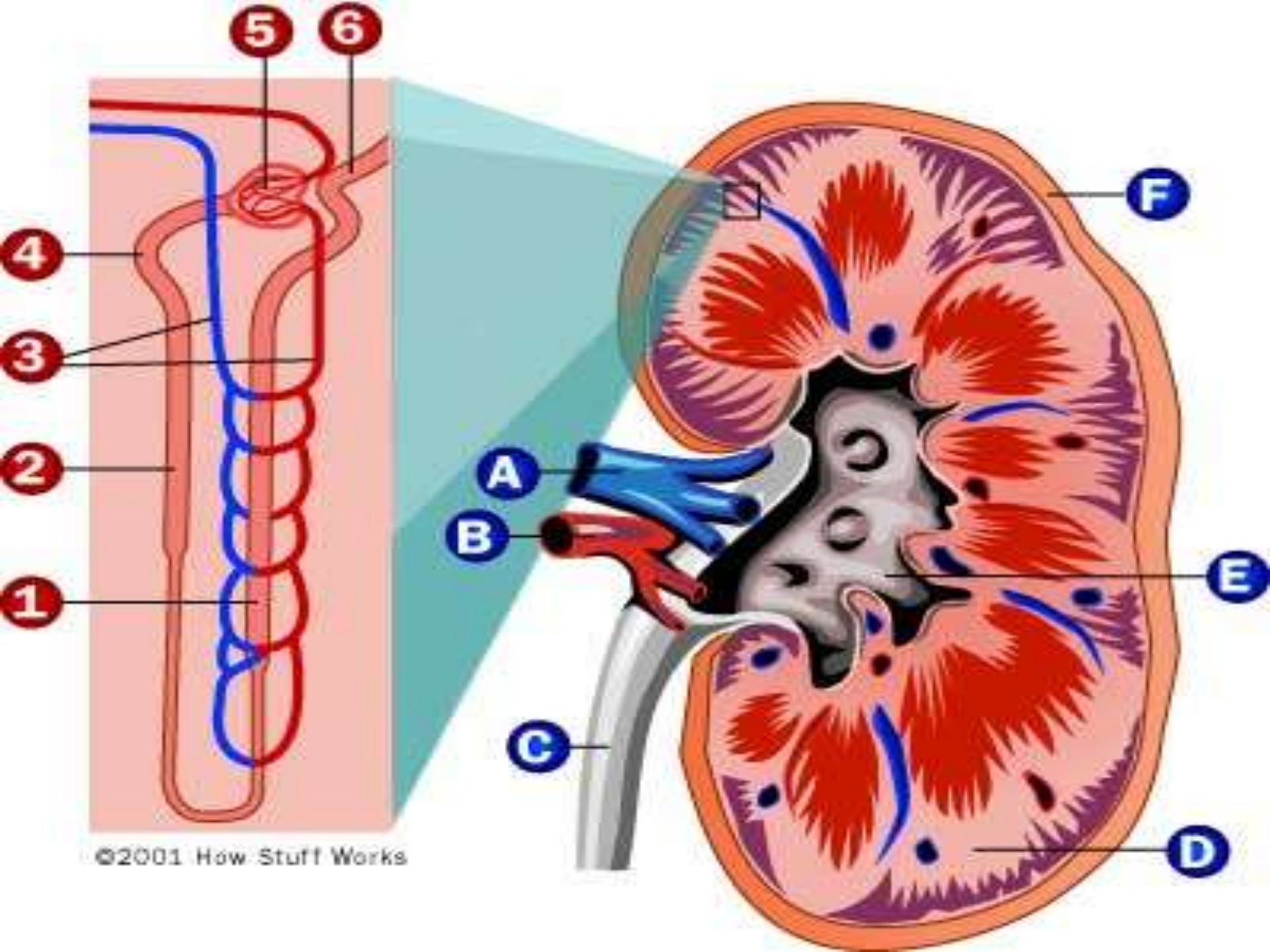


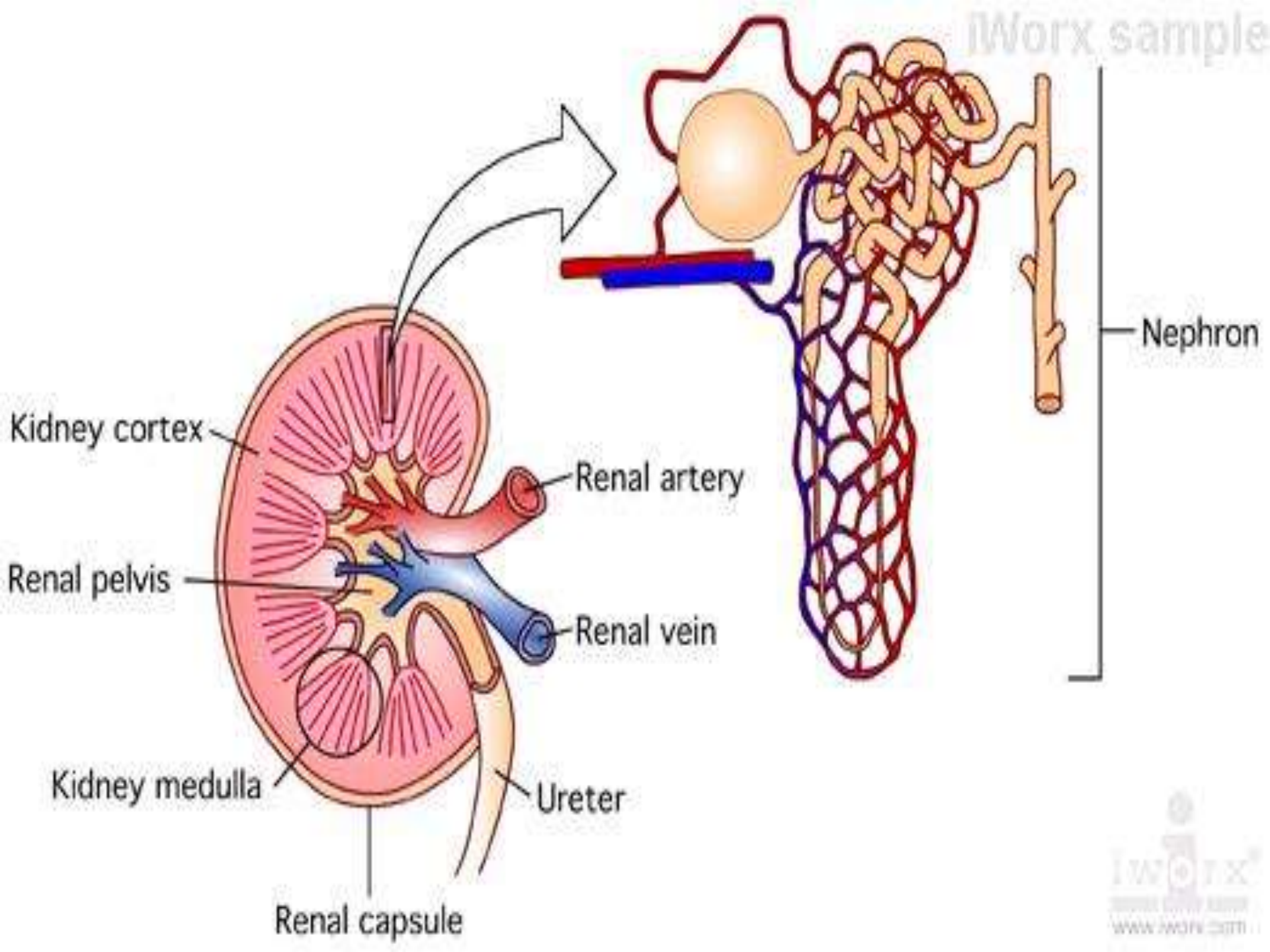
# Kidney & reproductive toxicology

Solmaz Arshi, M.D.  
Occupational Medicine  
Sleep Medicine Fellowship



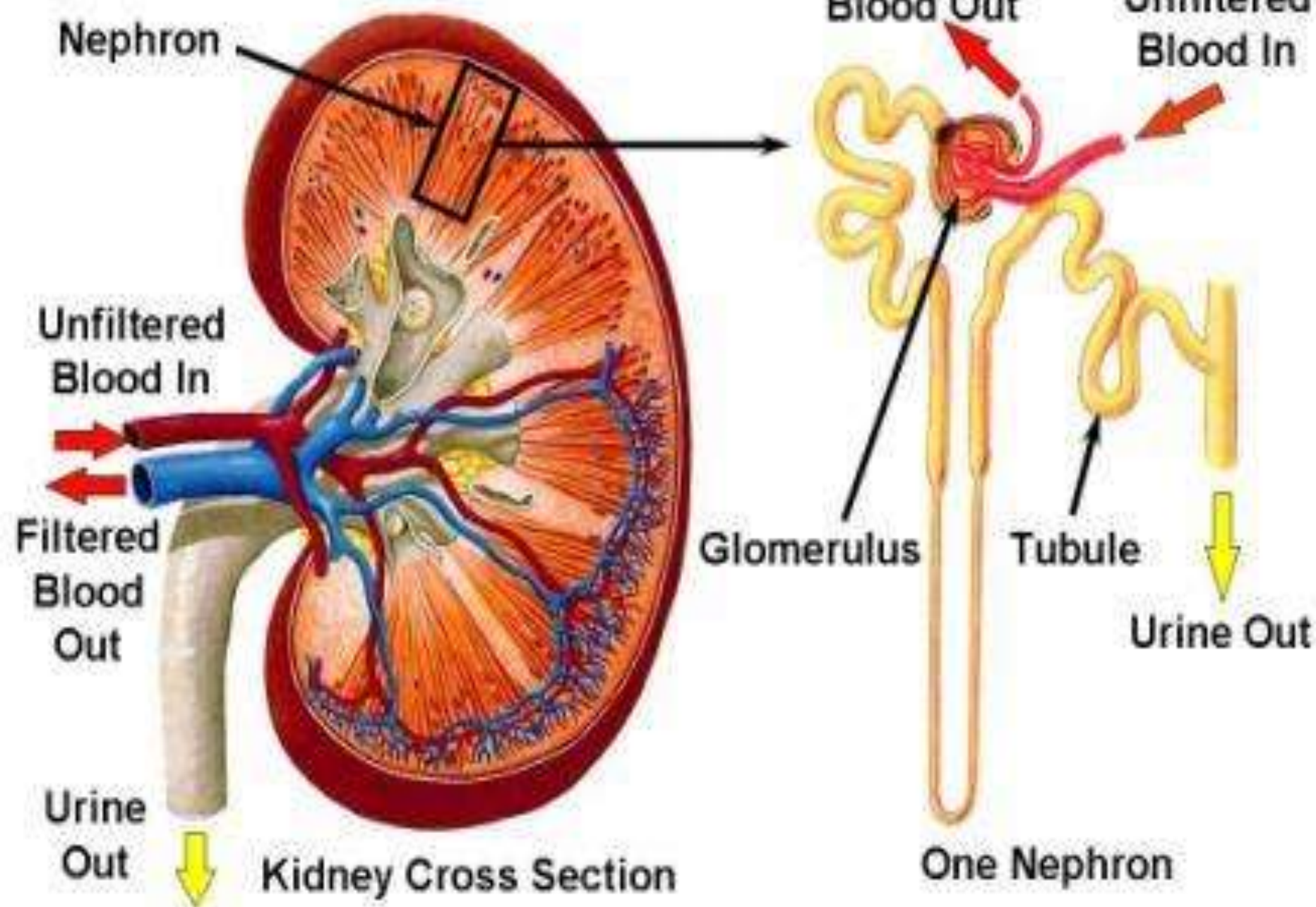




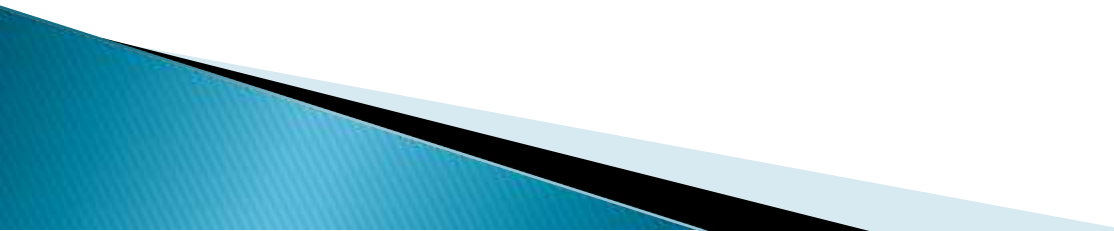




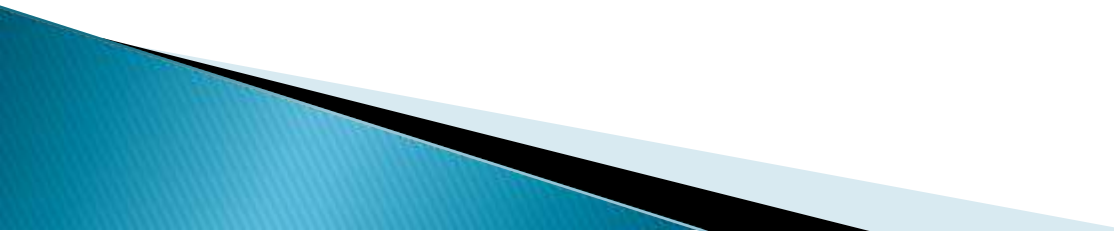
# Parts of the Nephron



# Introduction

- ▶ The kidneys provide a major route of the excretion of toxins
  - ▶ Risk of urinary tract injury from exogenous chemical is theoretically high
  - ▶ Clinical recognition of occupational renal disease is difficult
- 

# Introduction

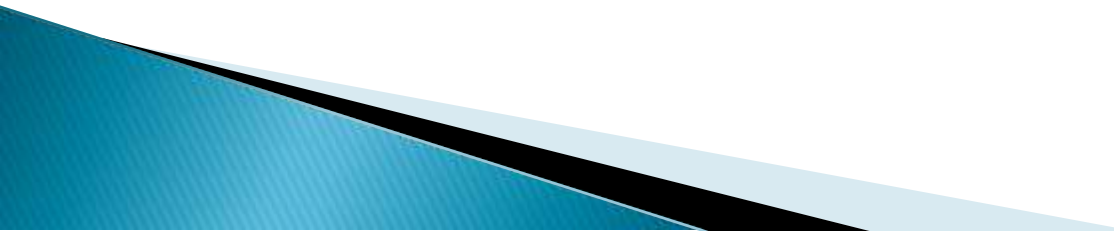
- ▶ Clinicians may have a low index of suspicion for chemical causes of renal disease
  - ▶ It may be difficult to prove chemical causation for renal injury
  - ▶ No specific lab test
  - ▶ No specific treatment
- 

# Cadmium (acute tubular injury)

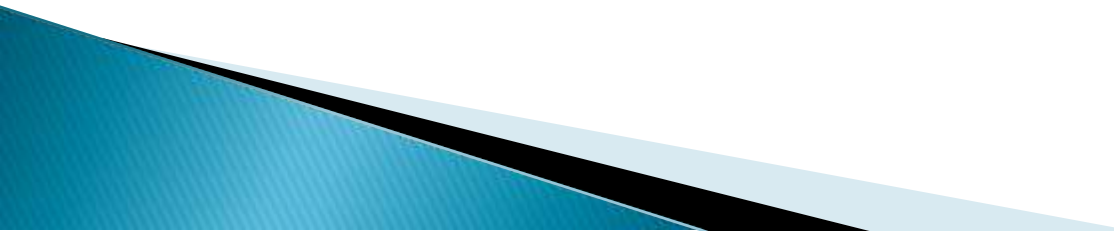
- ▶ Exposure: inhalation of fumes(welding or burning of cadmium-containing metals)
- ▶ Renal effect: proteinuria, acute cortical or tubular necrosis, renal failure
- ▶ Treatment: should be supportive (use of chelating agent BAL is *contraindicated*) EDTA, DMPS, DMSA is not used.



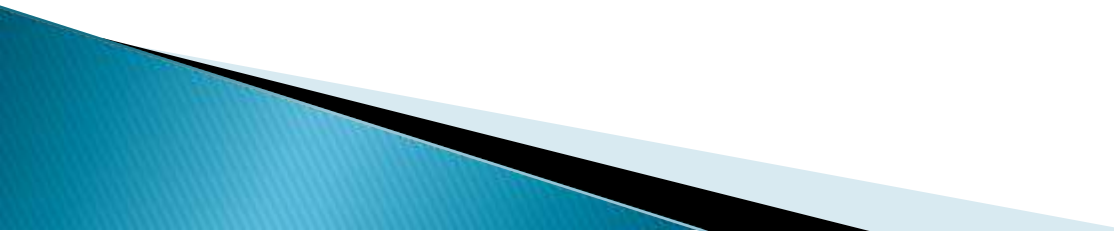
## Cadmium (Chronic tubulointerstitial nephropathy )

- ▶ The *kidney* is the *primary* target organ for cadmium toxicity
  - ▶ Chronic low level of exposure → 50% of body burden (renal cortex bound to metallothionin)
  - ▶ Urine cadmium → indicator of the cumulative body burden
  - ▶ Half-life in the body: >10 years
- 

## Cadmium (Chronic tubulointerstitial nephropathy )

- ▶ The most common manifestation is deficiencies of proximal tubular reabsorption
  - ▶ Tubular proteinuria is the first sign, and glucosuria, phosphaturia, aminoaciduria may occur
  - ▶ HMW proteinuria may occur, not clinically significant
- 

## Cadmium (Chronic tubulointerstitial nephropathy )

- ▶ High risk of renal tubular dysfunction associated with urinary cadmium concentration  $> 10 \mu\text{g/g}$  creatinin
  - ▶ Nephrotoxic effects of cadmium can be irreversible and can progress after cessation
  - ▶ Urine measurement of LMWP have proved effective in monitoring cadmium-exposed worker
- 



# Cadmium (Chronic tubulointerstitial nephropathy )

- ▶ Renal pathology:
  - Frank kidney contraction
  - Tubular atrophy and dilation
  - Interstitial fibrosis
  - Relative sparing of glomeruli

## Cadmium (Chronic tubulointerstitial nephropathy )

- ▶ Treatment: no established beyond removal from exposure

# Lead (acute tubular injury)

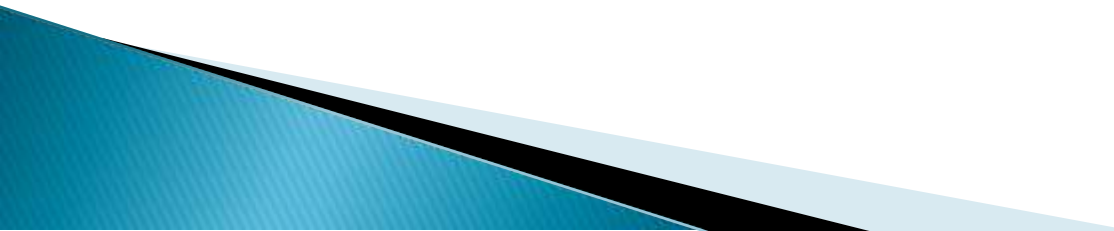
- ▶ Renal effect: proximal tubule reabsorptive defect (Fanconi syndrome associated with *fructosuria* & *citraturia*), RTA.
- ▶ Pathology:
  - Proximal tube: non-specific cytomegaly, mitochondrial morphologic change, *inclusion body*.
  - Glomeruli: unaffected or minimal change



# Lead (acute tubular injury)

- ▶ Inclusion bodies of acute lead poisoning of acute lead nephropathy resolve during and after treatment and exposure cessation
- ▶ Treatment:
  - Replacement of electrolyte & bicarbonate
  - Chelating therapy (EDTA) with or without nephropathy

## Lead (chronic tubulointerstitial nephropathy )

- ▶ Exposure: occupational & environmental
  - ▶ Chronic renal failure, end stage renal disease were identified in chronic occupational lead exposure
  - ▶ High blood lead level  $>60 \mu\text{g/dl}$  and elevated serum creatinine in lead exposed worker
- 

## Lead (Chronic tubulointerstitial nephropathy )

- ▶ Clinical tests not been valuable in assessing lead-exposed workers, increase in NAG in urine
- ▶ Treatment: elimination of further exposure



# Mercury (acute tubular injury)

- ▶ Exposure:(nature & form)
  - Elemental form is rarely produce renal injury
  - Organic form (metabolic transformation to inorganic compound)
  - Inorganic form ( $\text{Hg}_2\text{Cl}_2$ ,  $\text{HgCl}_2$ )

# Mercury (acute tubular injury)

- ▶ Renal effect: acute proximal tubular necrosis
- ▶ Severe poisoning: oliguric renal failure→ polyuria→ resolution of renal impairment
- ▶ Residual renal dysfunction is common:
  - Interstitial nephritis
  - Dystrophic calcification of the renal tubes
  - End-stage renal disease

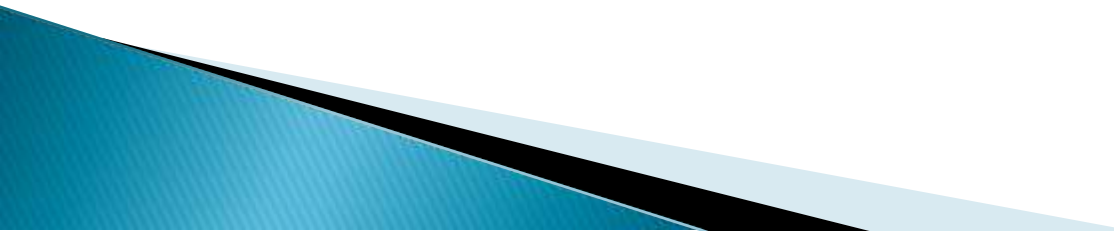
# Mercury (acute tubular injury)

- ▶ Treatment:
  - Chelating agent: DMPS ,DMSA
  - Hemodialysis in combination with chelation therapy

# Mercury (chronic tubulointerstitial nephropathy )

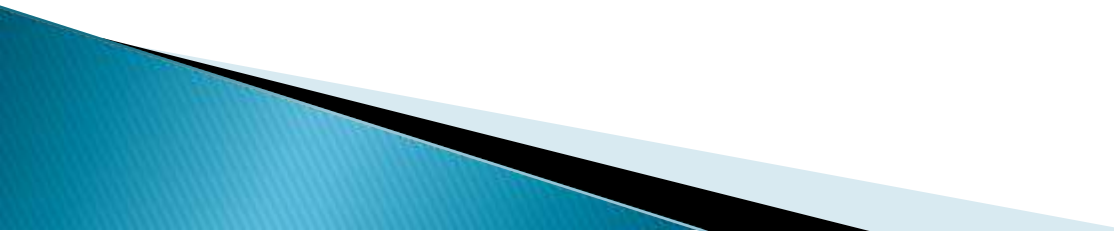
- ▶ Exposure: mercuric salts
- ▶ Effect : proximal tubular dysfunction
- ▶ Increased urinary excretion of certain lysosomal enzymes, NAG

# Mercury (Chronic glomerulonephropathy)

- Exposure: elemental & inorganic mercury
  - Renal effect:
    - Proteinuria
    - Nephrotic syndrome
  - Pathology:
    - Membranous GN
    - Deposition of immune complex in BM
    - Normal
    - Other immunofluorescent pattern
- 

# Reproductive Toxicity

## ▶ REPRODUCTIVE FUNCTION

- Women Who Are Pregnant
  - Women of Child Bearing Age
  - Men
- 



# Reproductive Toxicity

Difficulty in studying repro toxicity in women

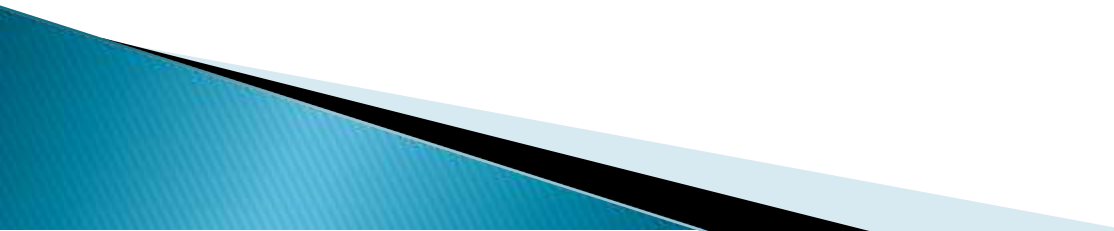
- nature of the female cycle
- relative frequency spontaneous abortions
- common occurrence of birth defects in general population



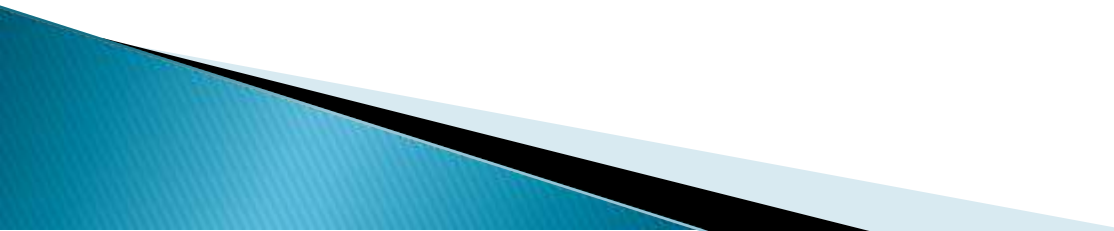
# Male Reproductive Function

- ▶ Normal
  - 70–80 days for spermatogenesis
  - 20–350 million sperm/day
  - 50–100 million sperm/ml
- ▶ Fertility Criteria
- ▶ >20 million sperm/ml
- ▶ >40% motile
- ▶ >70% normal morphology

# Reproductive Function “Norms”

- ▶ Azospermai: 1 / 100
  - ▶ Low Birthweight (2.5kg): 7 / 100
  - ▶ Failure to conception : 10–15 / 100
  - ▶ Spontaneous ab 10–20 / 100
  - ▶ Chromosomal abnormalities 30–40 / 100
- 

# Reproductive Function “Norms”

- ▶ Stillbirths: 2–4/100
  - ▶ Birth Defects: 2–3/100
  - ▶ Chromosomal abnormalities: 0.2/100
  - ▶ Severe retardation: 0.4/100
- 

## *Adverse Male Reproductive Effects of Selected Agent*

<b>Agent</b>	<b>Out come</b>	<b>Strength</b>
<b>Alcohol</b>	<b>azoospermia</b>	<b>+</b>
<b>Boron</b>	<b>oligospermia</b>	<b>+</b>
<b>chloroprene</b>	<b>asthenospermia</b>	<b>++</b>
<b>Lead</b>	<b>Oligospermia</b>	<b>++</b>
<b>Mercury</b>	<b>Decrease libido</b>	<b>+</b>
<b>Microwave</b>	<b>oligospermia</b>	<b>+</b>
<b>Excessive heat</b>	<b>oligospermia</b>	<b>+</b>
<b>Ion-radiation</b>	<b>oligospermia</b>	<b>++</b>

# *Adverse Female Reproductive\_* *Effects of Selected Agent*

<b>Agent</b>	<b>Out come</b>	<b>Strength</b>
<b>Arsenic</b>	<b>SAB-LBW</b>	<b>+</b>
<b>Carbon monoxide</b>	<b>SAB- menstrual dis</b>	<b>+</b>
<b>Mercury</b>	<b>SAB- LBW CNS malformation</b>	<b>++</b>
<b>Lead</b>	<b>SAB-infertility</b>	<b>++</b>
<b>Organic solvent</b>	<b>SAB- menstrual dis</b>	<b>+/?</b>
<b>VDT</b>	<b>SAB - BDs</b>	<b>--</b>
<b>Physical stress</b>	<b>Preterm LBW-SAB-</b>	<b>+/?</b>





*THANKS*