UREA

→ It is nonprotein nitrogenous compound
→ It is produced by catabolism of protein & nucleic acids by urea cycle in liver

* Excretion :-
→ 90% of urea excreted through the kidney
→ 10% are lost through gastrointestinal tract & skin
→ Urea is neither actively secreted nor reabsorbed by tubules & freely filtered
→ But 40 to 70% of highly diffusible urea moves passively out of renal tubule & into interstitium → ultimately reenters plasma
→ Back diffusion of urea depends on urinary flow rate

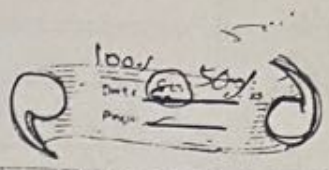
↓

High flow rate = less urea diffusion
Occurs in pregnancy.

→ In kidney d/se, urea is accumulated in Blood

↓

↑ conc. in Blood → k/a "azotemia"



→ Urea clearance generally underestimates GFR. due to back diffusion passively
→ Creatinine measurement is much better than urea for kidney d/s e.

* C/S :-

→ Numerous extrarenal factors influence the circulating urea concentration & limits its value as a test of kidney function.

eg:- Plasma Urea conc. is ↑ By high protein diet, ↑ protein catabolism, reabsorp^{n} of Blood protein after g.i.t haemorrhage, ↑ & cortisol, dehydration, ↓ renal perfusion.

→ In obstructive post renal conditions like Malignancy, nephrolithiasis
↓
Both cr. & urea ↑ed.
↓
In this condi^{n} urea is more ↑ed than cr because of ↑ed back diffusion.

→ S. urea/s.cre. ratio can be used to discriminate prerenal or postrenal causes of azotemia.
↓
(N) is 12 to 20 mg/dl

Urea/creat ratio

- **lowes ration** → denotes Acute tubular necrosis, low protein intake, severe liver dse, starvation. → In ↓ S. urea is ↓ed S. creat is (N).
- **↑ Ratio** → previously described causes → ↓ causes ↑ in S.urea & (N) S. Cr. (Pre-renal Cause)
- **High ratio** → Post renal causes → Both urea & creat ↑ → But urea much more ↑ than Cr.

→ Urea clearance is a poor indicator of GFR
↓
Blood Urea concentration is not constant, &
↓
Various nonrenal factors like diet & activity on urea cycle affects urea concentration

* Blood Urea Nitrogen :—
→ It is calculated from Blood urea.
→ 60 gm of urea contains 28 gm of Nitrogen.
→ Urea mass = 0.467 X Urea Nitrogen
→ Or Urea Nitrogen = 0.467 X Urea Mass
→ Urea conc. = 2.14 X Urea Nitrogen
mass

Analytical method :-

(1) Enzymatic method :- Reference method:

Urea + $2H_2O$ $\xrightarrow{\text{urease}}$ $2NH_4^+$ + CO_3^{-2}

NH_4^+ + α-oxoglutarate $\xrightarrow[\text{NADH + H}^+ \rightarrow \text{NAD}^+]{\text{glutamate dehydrogenase}}$ glutamate + H_2O

NH4 can be measured By Berthelot reaction

→ ↓ in absorbance resulting from glutamate dehydrogenase reaction is monitored at 340 nm

(2) Coupled enzyme Assay :-

Urea + $2H_2O$ $\xrightarrow{\text{Urease}}$ $2NH_4^+$ + CO_3^{-2}

NH_4^+ + glutamate $\xrightarrow[\text{ATP} \rightarrow \text{ADP}]{\text{glutamine synthase}}$ Glutamin + ADP

ADP + PEP $\xrightarrow[\text{Pyruvate kinase}]{}$ ATP + pyruvate

pyruvate + O_2 $\xrightarrow[\text{Pyruvate Oxidase}]{}$ Acetate + H_2O_2

H_2O_2 + phenol + 4-Amino phenazol $\xrightarrow{\text{Peroxidase}}$ quinoamine

↓

Measured spectrophotometrically

(3) Dry chemistry :-

↓

Urease enzyme incorporated into the strip.

④ Conductorimetric method :-

↓

Sample & Urease containing reagent are incubated in a conductivity cell

↓

with ther rate of change of conductivity due to formation of NH_4^+ HCO_3^-

⑤ Potentiometric method :-

↓

Ammonium ion selective electrode is employed & Urease is immbolized on a membrane.

↓

So convession of urea to NH_4^+ is measured or detected By Ammonium sensitive electrode.

⑥ * Newer approaches :-

① IDMS

② Luminometric → Suitable for in vivo monitoring studies using microdialysis technique.

* Refrence Interval :-

Male :

Female :

→ S. Ure slightly lower in children & preg.

→ Slightly wigher in male than female.