SCHOOL OF MEDICINE AND HEALTH SCIENCES
DIVISON OF BASIC MEDICAL SCIENCES
DISCIPLINE OF BIOCHEMISTRY AND MOLECULAR BIOLOGY

PBL SEMINAR: RENAL FAILURE: OLIGURIA AND ANURIA – An Overview

What are some of the major functions of the kidneys?
Some of the major functions of the Kidneys include:

- Regulation of Water (Fluid),
- Regulation of Electrolyte
- Regulation of Acid-Base Balance
- Excretion of products of Protein and Nucleic Acid metabolism – such as Urea, Creatinine, Creatine, Uric Acid, Sulfate, Phosphate, etc.
- Kidneys are also Endocrine Organs, producing a number of Hormones, and are under the control of other hormones

How can the functional state of the kidneys be assessed?

- To answer this question check your seminar on Renal function for details

RENAL FAULURE:

- Renal failure is the cessation of kidney function
- Acute Renal Failure (ARF) is when the kidneys suddenly fail to carryout major functions, this can occur over a period of hours or days.
- ARF is usually reversible and normal Renal Function can be regained.
- Chronic Renal Failure (CRF) develops over months or years and leads eventually to End Stage Renal Failure (ESRF).
- CRF usually cause irreversible damage to the kidneys.
- ARF can arise from a variety of problems affecting the kidneys and/or their circulation.
- ARF usually presents as a sudden deterioration of Renal function indicated by rapidly rising:
    - Serum urea concentration and
    - Serum creatinine concentrations.

- Severely ill patients may develop ARF thus monitoring of kidney function is important in these groups of patients.
- Usually in the first 24 hours of ARF: Serum and Urine tests for Renal function might not reveal any abnormality.
- If the Urine Output of the patient falls to less than 400ml in 24 hours, the patient is said to be **Oliguric (Oliguria)**.
- Some patients may have Normal Urine Output, with reduced Glomerular Filtration and Tubular Dysfunction (this is referred as **Non-Oliguric ARF**)
- Some patient may not pass any urine, such patients are said to be **Anuric (Anuria)**.

What are the different phases of ARF?
The different phases are:

- Oliguric Phases, Diuretic Phase and Recovery Phase

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OLIGURIC PHASE - in brief:

- When the urine output falls to less than 400 ml in 24 hours, the patient is said to be Oliguric.
- Some patients may not pass any urine, such patients are said to be Anuric
- Some patients may have normal urine flow, low GFR, when tubular dysfunction predominates (Non-Oliguric ARF)
- Oliguria is mainly due to a fall in the GFR
- In Oliguric phase the urine formed usually has Osmolality similar to Plasma and a relatively high Na^+ concentration, since the composition of the small amount of Glomerular Filtrate produced is only slightly altered by the damaged Tubules.
- Plasma Na^+ ion concentration is usually low due to a combination of factors:
    - Intake of water in excess of the amount able to be excreted,
    - Increase in metabolic water from increased tissue catabolism, and
    - A shift of Na^+ ions from ECF to (ICF)

- Plasma K^+ ion concentration, on the other hand, is usually increased due to:
    - Impaired Renal output and
    - Increased tissue catabolism,
        - Aggravated by the shift of K^+ ions out of cells that accompanies the metabolic acidosis which develops due to failure to excrete H^+ ions and to the increased formation of H^+ ions from tissue catabolism

- Retention of: Urea, Creatinine, Phosphate, Sulfate and other waste products occurs
- Rate of increase of urea concentration in plasma depends on the rate of tissue catabolism; this, in turn, depends on the cause of the ARF.

How can the low urinary output in ARF be differentiated from Hypovolaemia?

- To differentiate the low urinary output of suspected ARF from that due to severe circulatory impairment with reduced blood volume the tests in the table below may be helpful.
- Note that none of these tests can be completely relied upon to make the important and urgent distinction between Renal Failure and Hypovolaemia.
- Careful assessment of fluid status of the patient, possibly including measurement of the central venous pressure, is also required.

INVESTIGATION OF LOW URINARY OUTPUT		
Investigation	**Simple Hypovolaemia**	**Acute Renal Failure**
Urine Osmolality	usually > 500mmol/kg	usually < 400mmol/kg
Urine [urea]:Plasma [urea]	usually > 10	usually < 5
Urine [Na^+]	usually < 20mmol/L	Usually > 40mmol/L

What laboratory parameters are used to monitor the Oliguric phase?
For monitoring patients in the Oliguric phase of ARF:

- The following are very important and must be determined at least once daily
  - Plasma Creatinine, Plasma Urea and K^+ ion concentrations are particularly important,

In order to determine fluid and Electrolyte replacement requirement, the following must be regularly assessed:

- Volume of urine and its Electrolyte composition
- Volume and composition of any other measurable sources of fluid loss

DIURETIC PHASE:

- With the onset of the diuretic phase:
  - Urine volume increases,
  - Clearance of Urea, Creatinine and other waste products may not improve to the same extent
- Plasma Urea and Creatinine concentrations may therefore continue to rise, at least at the start of the Diuretic phase.
- Large losses of Electrolytes may occur in urine, this should be monitored and replaced as appropriate.
- Plasma K^+ ion concentration tends to fall as the diuretic phase continues, due to the shift of K^+ ions back into the cells and to marked losses in the urine resulting from impaired conservation of K^+ ions by the still-damaged tubules.
- Usually, Na^+ deficiency occurs also, due to failure of renal conservation.
- Throughout the diuretic phase therefore, it is important to measure:
  - Plasma creatinine, Plasma urea,
  - Na^+ and K^+ concentrations at least once daily, and
  - Monitor the urine flow rate and electrolyte output.

How can Acute Renal Failure be classified?

- ARF is usually caused by problems that affect the kidneys.
- A simplified classification of ARF or uraemia is as follows:
  - **Pre-Renal**:
    - When blood supply to the kidneys is affected, this may be due to vascular obstruction or to reduced perfusion
  - **Renal**:
    - When the problem is within the kidneys (damage kidneys).
    - May be due to a variety of diseases, or the
    - Renal damage may be a consequence of prolonged Pre-renal or Post-renal problems.
  - **Post-renal**:
    - When the urinary drainage of the kidneys is impaired because of an obstruction,
    - May be due to either Renal Stones, Carcinoma of cervix, Prostate, or Bladder.

What are some of the factors that can cause Pre-renal ARF?

- Some of the factors that can precipitate Pre-renal ARF are usually associated with a reduced effective ECF volume and may include some of the following:
    - Decreased plasma volume because of: Blood loss, Burns, Prolonged Vomiting or Diarrhea
    - Diminished Cardiac Output
    - Local factors such as an Occlusion of Renal Artery.

- Pre-renal factors usually lead to decreased renal perfusion and reduction in glomerular filtration rate (GFR).
- Both Arginine Vasopressin (AVP – act to influence water balance) and Aldosterone (affects Na^+ reabsorption in the nephron) are secreted maximally and a small volume of concentrated urine is produced.

What are some of the Biochemical finding in a patient with Pre-renal ARF?
Some of the Biochemical finding in Pre-renal ARF include the following:

- Serum Urea and Creatinine are increased:
    - Urea is increased proportionally more than Creatinine because of its reabsorption by the Tubular cells, particularly at low urine flow-rates.
    - This leads to a relatively higher serum Urea concentration than Creatinine, which is not so reabsorbed.
- Hyperkalaemia due to decreased GFR and Acidosis.
- Metabolic Acidosis due to the inability of the kidney to excrete H^+ ions
- High urine Osmolality.

What are some of the factors that can cause Post-renal ARF?

- Post-renal factors usually cause decreased Renal function, because:
    - Effective Filtration pressure of the Glomeruli is reduced due to the backpressure caused by the blockage.
- Some of the causes of this include the following:
    - Renal Stones,
    - Carcinoma of Cervix, Prostate or Occasionally Bladder.

- Failure to correct the Pre-renal or Post-renal factors in a patient can lead to Intrinsic Renal damage (Acute Tubular Necrosis).
- Patients in the early stages of Acute Tubular Necrosis may have only a modestly increased Serum Urea and Creatinine, which then rises rapidly over a period of days, in contrast to the slow increase over months and years seen in chronic renal failure.
- It may be difficult to decide the reason for a patient's oliguria.
- The biochemical features that distinguish pre-renal ARF from Intrinsic Renal damage are shown below.

Biochemical features in the differential diagnosis of Oliguric patient

Biochemical feature	Pre-renal failure	Intrinsic Renal Damage
Urine sodium	**< 20 mmol/L**	**> 40 mmol/L**
Urine [urea] : Serum [urea]	**> 10:1**	**< 3:1**
Urine/Plasma Osmolality	**> 1.5:1**	**< 1.1:1**

The Bicarbonate buffer system:

- The main buffer in the blood is the Bicarbonate buffer, which is regulated by the enzyme called Carbonic Anhydrase.
- The buffer can be represented as follows:

$$CO_2 + H_2O \leftarrow\!=\!=\!\rightarrow H_2CO_3 \leftarrow\!=\!=\!\rightarrow H^+ + HCO_3^-$$

$$pH = pKa + Log\ \{(PCO_2) / [HCO_3^-]\ \}$$

- This equation shows that the pH (or H^+ ion concentration) in blood varies as the Bicarbonate ion concentration (i.e., $[HCO_3^-]$) and Partial Pressure of CO_2 (i.e., PCO_2) change.

What are the factors that affect the Bicarbonate buffer?

- Factors that can affect the Bicarbonate buffer are as follows:
- The following factors will cause an increase in $[H^+]$ ion, which implies a decrease in pH.
  - Adding H^+ ions,
  - Removing HCO_3^- ion or
  - Increasing PCO_2

The following factors will cause the $[H^+]$ ion to fall, which implies an increase in pH.

- Removing H^+ ions,
- Adding HCO_3^- or
- Lowering PCO_2

What do you understand by "Metabolic" and "Respiratory" Acid – Base disorders?

- **"Metabolic" Acid – Base** disorders are those, which directly cause a change in the Bicarbonate concentration (i.e., $[HCO_3^-]$).
  - **E**xamples include:
    - Loss of Bicarbonate ions from the Extracellular Fluid or
    - Build up of H^+ ions from the Ionization of Ketone bodies.

- "**Respiratory" Acid – Base** disorders are those that directly affect the PCO_2.
  - Impaired Respiratory function causes a build up of CO_2 in blood, whereas, less commonly, Hyperventilation can cause a decrease of PCO_2.

The definitions are as follows:

- Metabolic acidosis – The primary disorder is a decrease in [HCO_3^-]
- Metabolic alkalosis – The primary disorder is an increased [HCO_3^-]
- Respiratory acidosis – The primary disorder is an increased PCO_2
- Respiratory alkalosis – The primary disorder is a decreased PCO_2

What are the compensatory responses for Primary Acid – Base disorders?

- In general the predicted Compensatory response in [HCO_3^-] or PCO_2 when [H^+] changes as a result of Primary Acid – Base disorders are show in the table below:

PRIMARY DISORDER	**COMPENSATORY RESPONES**
↑ PCO_2 (Respiratory acidosis)	↑ HCO_3^-
↓ PCO_2 (Respiratory alkalosis)	↓ HCO_3^-
↓ HCO_3^- (Metabolic acidosis)	↓ PCO_2
↑ HCO_3^- (Metabolic alkalosis)	↑ PCO_2