ॐ ***Indications of Dialysis***

(after failure of medical Rx) include:-

1. **Anuria or oliguria** (after insertion of Folly's catheter).
2. **Hypervolemia** with evidence of hypertension and/or pulm edema.
3. **Hyperkalemia**, if persistent.
4. **Metabolic acidosis**, if severe

. 5. **Uremia** if > 100-150 mg/dl (with or without uremic symptoms).

6. **Hypocalcemic** tetany.
7. **Neurologic** symptoms e.g. seizures, coma.
8. **Inability** to provide adequate nutritional intake

. ॐ ***Dialysis can be done by 3 methods:-*** 1. Peritoneal dialysis. 2. Intermittent hemodialysis. 3. Continuous renal replacement therapy. ***Note:*** *Peritoneal dialysis is done with either solution A (standard), B (for hypervolemia), or C (for hyperkalemia), see text for more details*

CHRONIC RENAL FAILURE (Chronic Kidney Disease) *Chronic Kidney Disease is defined by either* ***structural or functional abnormalities of the kidney*** *(e.g. composition of the blood or urine, imaging tests, or kidney biopsy)* ***or GFR < 60*** *ml/min/1.73 m2; both are*

for ***≥ 3 mo.***

In addition to the major role of kidney in ***water & electrolyte hemostasis****, it has endocrine role by secretion of* ***Erythropoitin & vit D*** *metabolism.* ***Et.*** *Chronic renal diseases are either due to congenital, acquired, inherited, or metabolic disorders. In* ***Children < 5 yr,*** *it most commonly due to congenital abnormalities e.g. renal hypoplasia, dysplasia, and/or obstructive uropathy, cong nephrotic syndrome, prune belly syndrome, focal segmental*

glomerulosclerosis, polycystic kidney disease, renal vein thrombosis, or

HUS. In ***Children > 5 yr*** *is most commonly due to acquired diseases e.g. various forms of glomerulonephritis, inherited disorders e.g. familial*

juvenile nephronophthisis, Alport syndrome, or metabolic disorders e.g. cystinosis, hyperoxaluria. ***Path.*** *Stages of Chronic Kidney Disease according to GFR (ml/min/1.73 m2): Stage 1: GFR* ***> 90****, Stage 2: GFR* ***90-60****, Stage 3: GFR* ***60-30****, Stage 4: GFR* ***30-15****, Stage 5: GFR* ***< 15 or on dialysis****.*

GFR can be calculated by the following equation:- GFR (ml/min/1.73 m2) = $k \times \frac{\text{Height(cm)}}{\text{serum Creatinine(mg/dl)}}$

Where ***k*** *=* ***0.33*** *for LBW infants < 1 yr,* ***0.44*** *for term infants < 1 yr,* ***0.55***

for children and adolescent females, and ***0.70*** *for adolescent males.* ***Note:*** *Inulin clearance is the gold standard for determination of GFR, but it is not easy to perform.* ***C.M.*** *It depends on the cause of CRF, but in general it includes:-* ***Hx.*** *Headache, fatigue, lethargy, anorexia, vomiting, polydipsia, polyuria, and growth failure..*

Ex. Pallor and earthy color appearance; patients with long-standing untreated CKD may have short stature, bony abnormalities of renal osteodystrophy, & peripheral neuropathy. **Cx & Rx**: Management of CRF requires **multidisciplinary** services & the

goals of Rx are to **replace** absent/diminished renal functions & to **slow**

its progression. ***Fluid & Electrolytes therapy***; electrolyte disturbances are the same as those in ARF (except Na). **Hyperkalemia** causes include: ↓ GFR, excessive dietary potassium intake, severe acidosis, or hyporeninemic hypoaldosteronism. **Rx** by restriction of dietary potassium intake, administration of oral

alkalinizing agents +/_ Kayexalate. **Hyperphosphatemia** can be treated by restriction of dietary phosphorus intake e.g. formulas contain reduced amount of phosphate (Similac PM 60/40) for infants.

 Metabolic acidosis causes include: ↓ net acid excretion, ↓ bicarbonate reabsorption & ↓ ammonia synthesis. **Rx** by oral sodium bicarbonate (or

citrate) to maintain serum bicarbonate >22 mEq/L. **Sodium concentration** is depends on the type of CRF. Some causes e.g. glomerulonephritis are associated with **sodium retention** → edema, hypertension & HF; therefore, they need salt restriction & diuretics, whereas fluid restriction is rarely needed until development of ESRD. Others diseases like renal dysplasia may be associated with polyuria &

significant urinary **sodium losses**; therefore, they may need sodium supplementation with high volume, low caloric density feedings. ***Nutrition***; Provide the recommended dietary allowance of **caloric**

intake for age. Protein restriction is generally **not recommended** for children (although there is risk of progression of CRF) because of adverse effects on growth and development; thus intake should be **2.5 g/kg/24 hr** and should consist of **high biologic value** e.g. eggs and

milk, followed by meat, fish, and fowl that metabolized primarily to

usable amino acids rather than to nitrogenous wastes. **Water-soluble vitamins** should be routinely supplied, zinc and iron are added only if deficiencies occur, whereas fat-soluble vitamins (except vit. D) are usually not required. If oral intake cannot be

maintained, consider NG tube feeding.

 Anemia causes include: ↓ **erythropoietin** production, deficiency of iron, folate & B12, ↓ RBC survival, & bleeding tendency. **Rx** (only when Hb **<10** g/dl) by Erythropoietin (rHuEPO) **50–150 mg/kg/dose SC** 1-3 times weekly (with **iron** supplementation). The aim is to ↑ Hb between **12-13** g/dl. Darbopoeitin alfa is a longer-acting agent administered at dose 0.45 µg/kg/wk or can be given monthly.

SE of Erythropoietin are iron deficiency, hypertension, seizures,

thrombosis, & pure red cell aplasia. Causes of failure of Rx by Erythropoietin; iron deficiency, vitamin B12 or folate deficiency, occult blood loss, chronic infection/inflammatory state, and BM fibrosis related to secondary hyperparathyroidism. ***Growth***; causes of short stature include: Inadequate caloric intake,

Renal osteodystrophy, Metabolic acidosis, Anemia, & GH resistance.

These patient have ↑ GH level, but ↓ ILGF-1 & ILGF-BP. However, they usually respond to exogenous **GH** (rHuGH) in dose **0.05 mg/kg/day SC**

for patients with height < -2 SD until: reach 50th percentile for

midparental height, achieve final adult height, or undergo renal

transplantation. ***Renal Osteodystrophy*** causes include: ↓ renal production of 1, 25-vit.D,

Hyperphosphatemia, Hypocalcemia, & Secondary hyperparathyroidism. **C.M.** are the same as those of rickets, the radiographic finding are called *Osteitis fibrosa cystica*.

Rx is by restrict phosphorus intake with phosphate binders e.g. calcium carbonate (or acetate) or by non–calcium-based binders (when there is

hypercalcemia).

Vit D is the cornerstone of Rx; if serum level of 1,25-dihydroxy-vitamin

D is low & PTH is high, give **1,25-vitD** e.g. Calcitriol 0.01–0.05 µg/kg/day or newer agents e.g. Paricalcitol or Doxercalciferol. ***Note:*** *Maintain calcium/phosphorus product (Ca × PO4) <55 to minimize the risk of tissue deposition of calcium phosphorus salts.* ***Adynamic (low-turnover) Bone Disease*** can cause **osteomalacia** due

to oversuppression of PTH by excessive intake of Ca salt & vit D. ***Hypertension*** causes include: volume overload and/or excessive renin

production related to glomerular disease. **Rx** by **salt restriction** & antihypertensives e.g. **Hydrochlorothiazide** 1

mg/kg/day bid (for stage 1, 2 & 3) or **Furosemide** 1–2 mg/kg/dose bid

or tid (for stage 4); other antihypertensives can be used when hypertension is severe. **ACE Inhibitors** or Angiotensin II blockers can

also be used to ↓ proteinuria that associated with CRF & hypertension. ***Infection*** causes include: Impaired cellular immune functions &

Indwelling dialysis catheters. Patient should **receive all standard**

immunizations including live vaccines, except during Rx with immunosuppressives. ***Neurologic symptoms*** e.g. fatigue, poor concentration, headache, drowsiness, memory loss, seizures, & peripheral neuropathy are mainly due to uremia & hypertension. ***Gastrointestinal symptoms*** e.g. feeding intolerance & abdominal pain

are mainly due to GERD & ↓ GIT motility. ***Pericarditis/CMP*** due to uremia, hypertension, & hypervolemia. ***Bleeding tendency*** due to platelets dysfunction by uremia. ***Hyperlipidemia*** due to ↓ lipoprotein lipase activity. ***Glucose intolerance*** due to insulin resistance. ***Drug toxicity***; Nephrotoxic drugs should be avoided & drugs that are mainly excreted by the kidney should either ↓ dose or ↑ interval

between doses or both. ***Factors that initiate or aggravate glomerular destruction are:***

Hyperfiltration Injury, Hypertension, Proteinuria, Hyperphosphatemia,

Hyperlipidemia, Infection, & Dehydration. Therefore, factors that can

slow the progression of Chronic Kidney Disease include:- 1. Optimal control of **hypertension to <75th** percentile. 2. Use of **ACE Inhibitors** or Angiotensin II blockers for **proteinuria**.

3. Avoid **hyperphosphatemia** & maintain Ca/Pi product **<55**.

4. Aggressive Rx of **infection** & **dehydration**.

5. Correction of **anemia** & **hyperlipidemia**.

6. **Avoidance** of NSAI agents, cigarette smoking, & obesity.

End-Stage Renal Disease ESRD represents the state in which patient's renal dysfunction has progressed to the point at which **homeostasis and survival can no**

longer be sustained with native kidney function and maximal medical Rx unless by renal replacement therapy, i.e. dialysis or renal

transplantation. ॐ **Indications for long-term dialysis** in patient with CRF are similar to those of ARF e.g. refractory fluid overload, electrolyte imbalance, acidosis, uremic symptoms; and growth failure. ॐ **Dialysis** in CRF can be done either by:- ***Daily Peritoneal dialysis***; it easy & can be done at home, it also

suitable for infants. ***Hemodialysis***; it require vascular access by A-V shunt or fistula, it only done in hospital at 3 sessions/wk.

HEMOLYTIC-UREMIC SYNDROME HUS is a **common** cause of community-acquired ARF in young children. It is characterized by the ***triad* of microangiopathic hemolytic anemia, thrombocytopenia, and renal insufficiency**.

Et. HUS can be classified according to etiology as follows:- ▯ **Infection-induced** is the most common cause of HUS; it include: Verotoxin-producing *Escherichia coli* (most common, especially 057:H7 type), Shiga toxin-producing *Shigella dysentereriae* type 1 (common),

Neuraminidase-producing *Streptococcus pneumoniae* (rare), and HIV (rare). ▯ **Genetic (Atypical) HUS** include: von Willebrand factor-cleaving protease (ADAMTS 13) deficiency, Complement factor H (or I) deficiency/mutation, Membrane cofactor protein (MCP) mutations,

Thrombo-modulin mutations, Vitamin B12 metabolism defects, Familial AR & AD of undefined etiology, and sporadic, recurrent, undefined etiology without diarrhea prodrome. ▯ **Other diseases associated with microvascular injury** include: SLE, Antiphospholipid antibody syndrome, Following BM transplantation,

Malignant hypertension, Primary glomerulopathy, and HELLP syndrome. ▯ **Medication-induced** include: some immunosuppressant & cytotoxic

medications, some antiplatelet agents, and quinine. **Path. Microvascular injury** with endothelial cell damage is

characteristic of **all** forms of HUS. In each form of HUS, capillary and

arteriolar endothelial injury in the kidney particularly in glomeruli, leads to localized thrombosis causing a direct decrease in GFR. Progressive platelet aggregation in the areas of microvascular injury results in

consumptive thrombocytopenia. Microangiopathic hemolytic anemia

results from mechanical damage to red blood cells as they pass through the damaged and thrombotic microvasculature. **C.M.** HUS is most common in preschool and school-aged children. In HUS caused by **exotoxin-producing *E. coli***, onset of HUS occurs a **few days**

(as few as 3 days) up to **3 wk** after onset of gastroenteritis with fever,

vomiting, abdominal pain, and diarrhea which is often bloody, but not necessarily, especially early in the illness. Following the prodromal illness, a **sudden onset of pallor, irritability, weakness, and lethargy** herald the onset of HUS. **Oliguria** can be present in early stages but may be masked by ongoing diarrhea. Thus, patients can present with HUS either with significant dehydration or

volume overload. Patients can develop petechiae, but significant or severe bleeding is rare despite very low platelet counts. Patients with **pneumococcus-associated HUS** usually are ill with pneumonia and empyema when they develop HUS. In **genetic forms** of

HUS, onset can be insidious when triggered by a variety of illnesses e.g. mild, nonspecific gastroenteritis or RTI. **Inv.**

 CBP shows **microangiopathic hemolytic anemia** with schistocytes, burr cells, and helmet cells. Coombs test is **negative**, with the exception of pneumococci-induced HUS, where it is usually positive. **Thrombocytopenia** is an invariable finding in the acute phase, but can return to normal in the late stage of disease. **Leukocytosis** is present. PT & PTT are usually **normal**.

 RFT: Renal insufficiency can vary from mild **elevations in serum BUN and creatinine** to ARF. **GUE** typically shows **microscopic hematuria**

and low-grade **proteinuria**. Renal biopsy is rarely indicated because it carry a significant risks during active phase of the disease & the Dx can be made on the above criteria. The etiology of HUS is often clear with the presence of a diarrheal

prodrome. The presence or absence of toxigenic, enteropathic organisms on stool culture has little role in making the Dx because only a minority of patients infected with these organisms develops HUS, and

the organisms that cause HUS may be rapidly cleared during the illness, therefore **stool culture may be negative**.

 If no hx of diarrheal prodrome or pneumococcal infection, then **evaluation for the genetic forms of HUS** should be considered,

because these patients are at risk for recurrence, have a severe prognosis, and can require different therapies.

D.Dx. Thrombotic Thrombocytopenic Purpura (TTP) also is characterized by the same features of HUS (some investigators consider

HUS and TTP to be part of a continuum of disease); however TTP may have a more gradual onset than HUS with more CNS involvement and

fever as well as only a few cases follow the "diarrhea prodrome". **Other causes** of ARF associated with a microangiopathic hemolytic

anemia and thrombocytopenia include: SLE, malignant hypertension, and

bilateral renal vein thrombosis. **Cx.** HUS can be relatively mild or can progress to a severe, and even fatal, multisystem disease. Leukocytosis and severe prodromal enteritis herald a severe course, but no presenting features reliably predict the severity of HUS in any given patient. The combination of rapidly developing renal failure and severe hemolysis can result in **life-threatening hyperkalemia**.

 Volume overload, hypertension, and severe anemia can all develop soon after onset and together can precipitate **heart failure**.

 Direct **cardiac** involvement is rare, but pericarditis, myocardial dysfunction, or arrhythmias can occur. The majority of patients with HUS have some but mild **CNS involvement** e.g. irritability, lethargy, and nonspecific encephalopathy. Severe CNS involvement occurs in ≤20% e.g. seizures & significant encephalopathy due to focal ischemia secondary to microvascular CNS thrombosis. **Intestinal Cxs** can be protean including severe inflammatory colitis, ischemic enteritis, bowel perforation, intussusception, and pancreatitis. **Rx.** The primary approach that has substantially improved acute

outcome in HUS is the early recognition of disease, monitoring for

potential complications, and meticulous supportive care which includes:- **Careful management of fluid and electrolytes** e.g. correction of volume deficit, control of hypertension, and early institution of **dialysis** if the patient becomes anuric or significantly oliguric. **Red cell transfusions** are usually required because hemolysis can be

brisk and recurrent until the active phase of the disease has resolved. In **pneumococci-associated HUS**, it is recommended that any administered **red cells should be washed before transfusion** to

remove residual plasma, because endogenous IgM directed against the revealed T antigen can play a pathogenic role. **Platelets generally should not be administered**, regardless of platelet count because they are almost immediately consumed by the active

coagulation and can theoretically worsen the clinical course. Anticoagulants, antiplatelets, and fibrinolytic therapy are **contraindicated** because they increase the risk of serious hemorrhage. **Antibiotic therapy** to clear the toxigenic organisms can result in

increased toxin release, potentially exacerbating the disease, and

therefore is **not recommended**, but prompt treatment of any underlying **pneumococcal** infection is important. **Plasma therapy** can be of substantial benefit to patients with identified

deficits of ADAMTS 13 or factor H. It may also be considered in patients with other **genetic forms** of HUS e.g. Familial undefined etiology or

sporadic but recurrent HUS. **Eculizumab** (anti-C5 antibody) that inhibits complement activation is a

novel therapy for **atypical familial HUS**.

Pg. The **mortality rate** for diarrhea-associated HUS after careful

supportive care has declined to **<5%.** Half of the patients require dialysis

support during the acute phase of the disease. Most recover renal

function completely, but of surviving patients, 5% remain dependent on dialysis, and up to 20-30% are left with some level of chronic renal insufficiency, these patients require careful **follow-up**.

The prognosis for HUS that not associated with diarrhea is more severe. Pneumococci-associated HUS causes increased patient morbidity, with mortality reported ≈20%. The familial, genetic forms of HUS can be insidiously progressive or relapsing diseases and have a poor prognosis.