# Neurological and Skin complications in End stage renal failure on hemodialysis

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## Nervous System Disorders in Renal Failure:

- **Central nervous system:** ESRD and underlying disease itself and secondary to hemodialysis.
- **Peripheral nervous system:** ESRD and underlying disease itself and secondary to hemodialysis

## Central nervous system

- 1. uremic encephalopathy
- 2. dialysis disequilibrium syndrome
- 3. hypertensive encephalopathy
- 4. dialysis dementia
- 5. intracranial hemorrhage
- 6. cerebral ischemia and infarction
- 7. electrolytes imbalance
- 8. others

## Uremic encephalopathy

- **Clinical features:** flapping tremor, lethargy, psychosis, disorientation, confusion, delirium, stupor and coma.
- **Causes:** unknown
- Accumulation of metabolites and, perhaps, imbalance in excitatory and inhibitory neurotransmitters are possible etiologies
- PTH and abnormal calcium as possible important contributing factors
Uremic encephalopathy

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<thead>
<tr>
<th>Parameter</th>
<th>Before Hemodialysis</th>
<th>After Hemodialysis</th>
<th>p value</th>
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<tbody>
<tr>
<td>Systolic blood pressure</td>
<td>161±15</td>
<td>155±29</td>
<td>0.48</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>84±14</td>
<td>78±12</td>
<td>0.06</td>
</tr>
<tr>
<td>Plasma osmolality</td>
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<td>31±2</td>
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<tr>
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<tr>
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</tr>
<tr>
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<td>12±5</td>
<td>0.01</td>
</tr>
<tr>
<td>Blood pH</td>
<td>7.32±0.07</td>
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EEG in uremic encephalopathy

absence of a dominant alpha rhythm and diffuse slowing with mixed theta- and delta-frequency signal

VGH-KS Studies

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Cerebral edema

Severe azotemia in end-stage renal disease leads to interstitial brain edema reflected as increased Dapp.

Brain edema seems not restricted in the occipital lobe.
uremic encephalopathy

- Diagnosis: first exclusion other diagnosis
- Azotemia and The EEG background in uremic encephalopathy demonstrates bilateral, frontal-predominant slow activity, which may include diphasic and triphasic waves
- Treatment: dialysis
- Poor response; think another diagnosis

disequilibrium syndrome

Definition: is a set of systemic and neurological symptoms often associated with characteristic EEG findings that occur during or soon after dialysis (the diagnosis should be one of the exclusion)

disequilibrium syndrome

Clinical symptoms:
Early findings: dizziness, headache, nausea, disorientation, restlessness, blurred vision and asterixis
Severely affected patients: confusion, coma, seizure
Differential diagnosis disequilibrium syndrome

- **Intracranial bleeding**
  - subdural, subarachnoid, intracranial
- **Metabolic disorders**
  - hyperosmolar states, hypercalcemia, hypoglycemia, hyponatremia
- **Cerebral infarction**
- **Hypotension**
  - excessive ultrafiltration, cardiac arrhythmia, myocardial infarction, anaphylaxis
- **Aluminum intoxication** (subacute)
- **Underlying disease**

Management:

- **Severe disequilibrium:** seizure, obtundation or coma
  - Early terminate hemodialysis
  - The differential diagnosis of severe disequilibrium syndrome should be considered
  - Keep airway
  - Intravenous mannitol

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1. Reverse urea effect theory
   - **JASN** 1995:1000-1006
2. Cerebral intracellular acidosis
   - **J Clin Invest** 1977:306-311
3. Idiogenic osmole theory
   - **Am J Physiol** 1935:543-548
Disequilibrium syndrome

Dialysis and serum osmolarity change

Dialysis and urea clearance

**disequilibrium syndrome (Risk factors)**

- Patients with certain pre-existing neurological conditions: intracranial lesion—head trauma, stroke, brain tumor, subdural hematoma or metabolic encephalopathy (hyponatremia, hepatic encephalopathy, malignant hypertension)
- Pediatric patients, older adults, patients new to hemodialysis, patients with severe azotemia, abnormal weight gains and severe metabolic acidosis

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**How to prevention disequilibrium syndrome**

**identification risk factors and slow urea removal**

1. Shortened dialysis time (<3 hours), decreased dialysis blood flow rates (150-200 ml/min) and a small surface area dialyzer
2. Infusion of glycerol, mannitol during dialysis,
3. Bicarbonate dialysis

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**Example**

- Case 1: A 44-year-old woman was admitted to our hospital because of general weakness, nausea, vomiting and obtundation for 3 days. She has a history of chronic glomerulonephritis with chronic renal failure for 20 years. She has used some herb drugs since one month ago. The serum levels of blood urine nitrogen were 230 mg/dl, creatinine was 24 mg/dl, sodium was 125 meq/L, and K was 5.6 meq/L and blood gas PH was 7.24. Sonogram revealed bilateral atrophy kidney. What is your dialysis plan? After dialysis, she became stupor. What is your next diagnostic plan?
How to perform dialysis in patients with acute brain injury?

### Cerebral perfusion pressure

- Monitor cerebral perfusion pressure > 60 mmHg
- High sodium dialysis (Na>140 meq/L)
- Short term dialysis (2-3 hours); mannitol; QB 150-200 cc/min; bicarbonate 35 to 30 meq/L
- Continuous renal replacement therapy

### Brain edema control in patients with acute brain injury
**dialysis dementia**  
(Aluminum intoxication)

- Clinical manifestation:  
  dysarthria, apraxia, slurring of speech, personality change, myoclonus, seizure and dementia  
- Clinical hint: unexplained hypercalcemia, neurological symptoms and low serum PTH should lead to consideration of aluminum toxicity

**Aluminum intoxication**

- EEG in dialysis encephalopathy.

**Aluminum intoxication**

- Diagnosis:  
  EEG loss of alpha rhythm and multifocal bursts of slow and delta waves, often accompanied by spikes  
  serum aluminum level of 50 ug/L: a reliable index response to aluminum chelator  
- Treatment: Deferroxime  
  prevention aluminum containing drugs monitor dialysate aluminum level

**Hypertensive encephalopathy**

- Clinical presentation: high blood pressure, cortical blindness  
- Treatment: control blood pressure as soon as possible: capoten, trandate, sodium nitroprusside
Electrolyte imbalance and acidosis change related metabolic encephalopathy

- Calcium imbalance: hypercalcemia
- Clinical presentation: drowsy, stupor, myoclonus, coma, seizure
- Cause: vitamin D and calcium drugs
- Treatment: low calcium dialysis

Electrolyte imbalance and acidosis change related metabolic encephalopathy

- K imbalance: hyperkalemia or hypokalemia
- Symptoms: ECG change and shock; CNS symptoms secondary to CV conditions
- Cause: GI bleeding, food
- Treatment: Low K dialysis or supply potassium

Electrolyte imbalance and acidosis change related metabolic encephalopathy

- Sodium imbalance: hyponatremia
- Clinical presentation: nausea, headache, drowsiness, convulsion and coma
- Treatment: correction of chronic hyponatremia should be kept at a rate less than 10 mmol/L in any 24-hour period.
- Central Pontine Myelinolysis occur with a rapid rate of correction after the treatment of chronic hyponatremia.

Osmotic Demyelination Syndrome

- spastic quadriaparesis and pseudobulbar palsy, and mental disorders ranging from mild confusion to coma
Subdural hematoma
Clinical presentation: headache, nausea, vomiting, and hemiplegia etc
Onset: acute onset after accident during 72 hours or chronic onset after accident at least 3 weeks

Infective endocarditis
Unexplained fever, seizure or new onset heart murmur or vascular access infection

Henoch-Schonlein purpura and cerebral vasculitis

Central nervous system involvement in systemic lupus erythematosus
Other cause of encephalopathy

- Drug overdosage: Penicillin, Tineam, cephalosporin, H2 blockers, acetazolamide, bacrofen, amantadine, Star fruit, quinolone
- Cerebral vascular disease, hypoglycemia, sepsis, CNS infection, Wernicke’s encephalopathy, hypertensive encephalopathy

Peripheral nervous system

- polyneuropathy
  1. Uremic
  2. Diabetic
  3. Other systemic diseases-vasculitis
- mononeuropathy
  1. Carpal tunnel syndrome
  2. Ischemic monomelic neuropathy
  3. Compression neuropathy

uremic polyneuropathy

- a distal symmetrical, mixed motor and sensory polyneuropathy.
- Clinical symptoms present with sensation of burning foot, crowling, prickling and pruritus. The loss of deep tendon reflex, particularly in the knee and ankle
uremic polyneuropathy

- muscle cramps: quinidine, clonazepam
- Restless leg syndrome: involuntary movement of lower limb because of sensation of crawling, pruritus over feet and relieve by movement of legs respond to benzodiazipam and levodopa/carbidopa, particularly clonazepam.
- Autoneuropathy can cause intradialysis hypotension and impotency
- Diagnosis: typical clinical symptoms and by exclusion of other possible disorders
- Treatment: adequate dialysis

polyneuropathy

- Diabetic
  Clinical presentation: overt autonomic dysfunction, cranial nerve palsy and compressive neuropathy
  Not response to dialysis
- Other systemic diseases-vasculitis

uremic mononeuropathy

carpal tunnel syndrome:
burning, tingling and numbness sensation especially in median nerve territory.

uremic mononeuropathy

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Carpal tunnel syndrome

- Diagnosis: median nerve denervation NCV/EMG
- Cause: beta-2 microglobulin deposition plays a major role
- Treatment: prevention beta2-microglobulin deposition
  1. Peritoneal dialysis and high flux dialysis
  2. Splinting the affected wrist in a neutral resting position, especially at night and during dialysis
  3. Decompression surgery

Ischemic monomelic neuropathy

- Arteriovenous fistula over proximal upper arm induce severe ischemia especially the last hour of dialysis
- Treatment: close the fistula

Compressive neuropathy

- Most possibly involved region
  - Ulnar nerve at elbow region
  - Peroneal nerve at the fistula head

Cutaneous Manifestations in Renal Failure

- Nail
- Skin
Nail manifestations in Renal Failure

Half-and-half nails
(azotemic onychopathy)

Beau’s lines

A.D.A.M. Inc

Splinter hemorrhage

Associated with trauma or
Infective endocarditis
especially during fever and
new onset of heart murmur
or seizure

Kyrle’s disease

Renal disease and DM

Treatment: steroid, Vitamin A, Clindamycin, renal transplantation

Eczema
Fungus infection

Herpes zoster

Scabies infection

Other important skin disorder: calciphylaxis
Skin Disorders in Renal Failure: 
(pruritus)

- pruritus varies reportedly from 50% to 90%
- mast cell activation C fiber nerve terminals that transmit the itching sensation to the central nervous system

Itching mechanism:
- dry skin, maybe the results of ischemic atrophy of sweat gland
- hyperparathyroidism, high calcium phosphate metabolism and hypervitaminosis
- Uremia toxin
- interleukin-2, interleukin-6 etc
- Vitamin A, aluminum overload, bile acid, opioid peptide etc

"Uremic pruritus": A misnomer

- a. Pruritus not present in all uremic patients
- b. Not observed in acute renal failure despite the existence of uremia
- c. Clinical severity not correlate well with the biochemical levels of "uremic toxins"

"Uremic pruritus": A misnomer

- d. No significant relief even with adequate clearance of uremic "toxins" using high-flux dialyzers
- e. Non-uremic conditions such as advanced age, diabetes mellitus, iron deficiency anemia and intrahepatic cholestasis coupled with hepatitis B and C virus infections prevalent among patients on long-term HD
Exclude scabies; allergy; urticaria; contact dermatitis; occult malignancies; and skin infections (Tinea), herpes zoster.

Assessment of calcium and phosphorus metabolism and dialysis efficacy.

Emollients, skin-moisturizing creams:
- Capsaicin
- Topical steroid
- Tacrolimus
- Ultraviolet (UV) B irradiation
- Anti-histamine
- Oral charcoal
- Cholestyramine
- Ondansetron
- Nicergoline
- Thalidomide, gabapentin, naltrexone
- Acupuncture

Check Aluminum renal transplantation.

Thank you for your attention.