NEUROHORMONAL ACTIVATION: RENAL EFFECTS
- Decreases renal blood flow
- Decreases GFR
- Increase Na reabsorption
- Chronically: Causes intraglomerular HTN
- Proteinuria
- Glomerulosclerosis
- Tubulointerstitial fibrosis

These changes lead to further neurohormonal activation, potentiating both the cardiac and renal dysfunction.

CHF: THE MURDEROUS MARRIAGE OF HEART AND KIDNEYS
1) The kidney: ↘ source of neurohormonal toxins in CHF
2) The heart: ↘ cardiac output and ↑ systemic vascular resistance results in ↘ renal perfusion
3) The kidney: ↘ renal perfusion associated with ↘ GFR and ↘ renal excretion of sodium and water
4) The heart: ↑ intravascular volume and ↑ neurohormonal toxins accelerates ventricular remodeling and decreases cardiac output and renal perfusion
5) Re-enter the cycle.

NEUROHORMONAL ACTIVATION ALSO IMPAIRS RENAL FUNCTION, A CRITICAL COMPONENT IN THE COMPENSATION OF CHF, LEADING TO THE: ‘CARDIORENAAL SYNDROME’

Case Presentation
- 63-YO-Male presents to ER with worsening SOB, chest heaviness, and ↑ LE edema
- He states he was at a wedding over the weekend and ate more then he is used to and gained 7 pounds
Case Study: Cardio-Renal Syndrome

- **PMH:**
  - CKD due to diabetic/ischemic nephropathy
    - Baseline SCr 2.8 mg/dL (eGFR 24)
    - Nephrotic syndrome / protein=4 – 5 grams/day (Diabetic Nephropathy)
  - IDDM Type 2 for 10 years
  - Hypertension
  - CAD (CABG X 3)
  - Gout
  - Anemia of CKD

**Medications (Allergies: NKDA)**
- Furosemide 80 mg po qd
- Lisinopril 40 mg po qd
- Amlodipine 10 mg po qd
- Metoprolol 25 mg po bid
- Zolpidem 10 mg po qd
- Insulin
- Aspirin 325 mg po qd
- Pantoprazole 40 mg po qd
- Allopurinol 100 mg po qd
- Gabapentin 100 mg po tid

**Social / Family History**
- Retired school teacher
- Smoker – ½ pack per day for 20 years
- Notable for strong family history of diabetes, HTN and CKD

**Physical Examination**
- General: Visibly short of breath
- VS: BP 168/86, HR 80, Afebrile, O2 Sat 87 %
- Neck: 2 + JVD
- Resp: Marked use of accessory muscles, coarse rales posterior ½ way up chest
- Heart: RRR with systolic ejection murmur
- Extremities: 3 + pitting edema to mid shin
**Laboratory Data**
- Na 131  
- K 5.6  
- Cl 110  
- HgB 10.1  
- Urinalysis: 3 + protein, no WBC or RBC  
- CXR: + moderate interstitial edema

**Hospital Course Day 1**
- In ED IV furosemide 120 mg IV and NTG Drip  
- Admitted to monitored bed  
- Chronic oral diuretic changed to torsemide 100 mg po tid  
- Initial urine output 800 cc / 2 hours  
- Then, urine output fell to 20 – 30 cc/hour, and SCr $\uparrow$ 4.2  
- All other meds continued except for metoprolol, which was d/c by Cardiology

**Hospital Course Day 2**
- Nephrology consult: worsening renal function/oliguria  
- Torsemide held initially  
- Nephrology d/c lisinopril, amlodipine, NTG IV, and started nesiritide infusion  
- Urine output $\uparrow$ to 100 cc/hour, and 6 hours later SCr 4.4  
- Torsemide restarted 100 mg po bid and urine output $\uparrow$ to 160 cc/hour

**Hospital Course Day 3**
- SCr $\downarrow$ to 3.5  
- K = 4.8  
- Diuresed approximately 3 kg and urine output continued at 100 – 130 cc/hr  
- Nesiritide continued

**Hospital Course Day 4**
- SCr returns to baseline 2.8  
- CXR marked improvement: no interstitial edema  
- Nesiritide discontinued
Low dose lisinopril restarted and started on carvedilol at 3.125 mg BID, with plans to increase dose to 6.25 mg BID at 1st clinic visit in 2 weeks post-D/C

- Discharged home

Key Points
- Cardio-renal syndrome and diuretic resistance
- Look for high risk patients and consider holding ACE-I / ARB’s during acute decompensated CHF (temporarily held in this case due to transient hyperkalemia)
- Treatment with nesiritide resulted in
- Decrease in CHF symptoms
- Decrease in loop diuretic dose
- Do not forget to restart ACE-I / ARB and Beta Blocker once patient is compensated prior to discharge
- Titrate these drugs to the appropriate dosage as an outpatient

NESIRITIDE IN CARDIO-RENAI SYNDROME
- Preliminary evidence suggests that Nesiritide is beneficial in ADHF, but conclusive data on its renal effects are lacking
- Ongoing clinical trials will provide more data on the management of these patients.

CARDIO-RENAI SYNDROME TREATMENT
- No real evidence based data from large CHF trial
- Treatment primarily empirical
- RAAS inhibitors cornerstone in Tx of CHF with LV systolic dysfunction
  - Also prevents progression of CKD in Diab. Nephropathy/CKD
- Problem is ↑ Scr with continued use of ACE I/ARB
  - These meds commonly avoided for fear of this
  - Rise in Scr with ACEI = subgroup with greatest benefit from this Tx.
  - (Arch Intern Med. 2000;160:685–693)
  - Discontinuation of ACEI with renal dysfunction identified a group with significant ↑ risk of mortality (57 % over 8.5 months) (J Am Coll Cardiol. 2003;41:2029–2035)
- Try to continue All-antagonists despite ↑ Scr as long as renal dysfunction does not continuously deteriorate or develop severe ↑ K
  - Use ARB in patients with intolerance to ACE I
SUMMARY

• Cardiorenal syndrome is common and should be anticipated in high risk patients
• Early use of vasodilators (nesiritide) shown to reduce filling pressures, improve symptoms and reduce diuretic needs in decompensated CHF
• Aggressive diuretic therapy can lead to diuretic resistance and worsening creatinine and GFR
• Neurohormonal modulation (ACE-I, ARB’s. Beta Blockers, and Aldosterone inhibitors are important to reduce long term mortality.