Case 1

- A 35 year old woman is admitted with left flank pain and fever for the last 2 days. Physical examination showed a toxic appearing thin woman. Vital signs showed a blood pressure of 100/68 mmHg, pulse 110, and respiratory rate of 24. Right sided costovertebral tenderness was present. An ultrasound of the abdomen showed normal sized kidneys and no evidence of hydronephrosis. Renal function and serum electrolytes on admission were normal. Right sided pyelonephritis was diagnosed. The patient was treated with intravenous ticarcillin/clavulanate, gentamicin, and tetracycline and the patient’s clinical condition gradually improved over the next several days. After a two week course of parenteral antibiotics she was discharged on no medications.
Case 1-continued

• One week after discharge the patient presented with the complaint of weakness, and paresthesias. Physical examination showed downbeat nystagmus and carpal pedal spasm could be elicited. An ECG showed prominent U waves and Q-T prolongation

Case 1-Laboratory studies

• Creatinine 0.9 mg/dl, BUN 14 mg/dl
• Serum electrolytes (mEq/l)
  – Na⁺ 139
  – K⁺ 2.3
  – Cl⁻ 92
  – HCO₃⁻ 34
• Urine electrolytes (mEq/l)
  – Na⁺ 110
  – K⁺ 35
  – Cl⁻ 106
• Serum Mg²⁺ 0.9 mg/dl
• Urine Ca²⁺/creatinine (mg/mg) 0.53 (normal <0.14)
• Plasma renin activity 2.4 ng/ml/hr (normal 0.8-2.5), aldosterone 235 ng/dl (normal 35-240)
Which One of the following is the Most likely cause of the electrolyte abnormalities?

1. Complication of ticarcillin/clavulanate
2. Surreptitious diuretic use
3. Tetracycline nephrotoxicity
4. Aminoglycoside nephrotoxicity
5. Gitelman syndrome

Renal K⁺ Handling in Setting of a Non-reabsorbed Anion (Ticarcillin)
Which One of the following is the Most likely cause of the electrolyte abnormalities?

• Complication of ticarcillin/clavulanate
  – Urine electrolytes are inconsistent
  – Hypomagnesemia and hypercalciuria are not features
  – Uncommon due to volume resuscitation

Which One of the following is the Most likely cause of the electrolyte abnormalities?

1. Complication of ticarcillin/clavulanate
2. Surreptitious diuretic use
3. Tetracycline nephrotoxicity
4. Aminoglycoside nephrotoxicity
5. Gitelman syndrome
Tetracycline Entry and Effects on Proximal Tubular Cells

Which One of the following is the most likely cause of the electrolyte abnormalities?

1. Complication of ticarcillin/clavulanate
2. Surreptitious diuretic use
3. Tetracycline nephrotoxicity
4. Aminoglycoside nephrotoxicity
5. Gitelman syndrome
Thiazide Diuretic or Gitelman Syndrome

- ↑ Distal Na⁺
- ↑ Aldosterone
- ↓ EABV

Loop Diuretic or Bartter Syndrome

- ↑ Distal Na⁺
- ↑ Aldosterone
- ↓ EABV

- ↑ Na⁺↑ Mg²⁺
- ↑ K⁺↑ Osm
- ↑ Cl⁻↓ Ca²⁺

- ↑ Na⁺↑ Mg²⁺
- ↑ K⁺↑ Osm
- ↑ Cl⁻↑ Ca²⁺

- Na⁺
- K⁺
- (+)
- Mg²⁺
- Ca²⁺

- ↓ EABV

- PC
- IC
- HCO₃⁻
Remote Use of Thiazide or Loop Diuretics

Which One of the following is the most likely cause of the electrolyte abnormalities?

1. Complication of ticarcillin/clavulanate
2. Surreptitious diuretic use
3. Tetracycline nephrotoxicity
4. Aminoglycoside nephrotoxicity
5. Gitelman syndrome
Acquired Bartter-Like Syndrome Associated with Gentamicin Administration

- 4 patients with gentamicin induced Bartter-like syndrome*
- Hypokalemic alkalosis with hypomagnesemia, hypermagnesuria, hypocalcemia, hypercalciuria, normal BP
- Total dose of gentamicin 1.2-1.6 gm
- Abnormalities resolve 2-6 wks after d/c of drug


Gentamicin-induced Bartter-like Syndrome Due to Activation of Basolateral Ca++ Sensing Receptor

Gentamicin is a divalent cation

Nystagmus and Hypomagnesemia

• Downbeat nystagmus can be a manifestation of hypomagnesemia

Arch Neurol 38:650-2, 1981
Neurology 51:1478-80, 1998

Conclusion

• Aminoglycosides can cause a reversible Bartter-like syndrome characterized by hypokalemia and metabolic alkalosis in the setting of normal blood pressure.
• Interaction and stimulation of the basolateral Ca^{++} sensing receptor may be involved in the genesis of this disorder
Case 2 Presentation

• A 54-year-old women is referred for treatment of diabetic nephropathy, PE: BP 148/96 mmHg

• Labs (mEq/l) Na 140, K 4.8, Cl 106, HCO₃ 22, creatinine 1.6 mg/dL, glucose 148 mg/dL

• 24 hour urine: 3.8 gm/24h, eGFR 38 ml/min

• An ARB is prescribed, 2 wks later BP 136/86 mmHg, serum creatinine 2.2 mg/dL
Which of the following would be the most appropriate next step in the management of this patient?

- Schedule a routine follow up appointment in 3 months
- Immediately discontinue the ARB
- Recheck labs in 1-2 weeks and if the serum creatinine remains increased discontinue the ARB
- Recheck labs in 1-2 weeks and if the serum creatinine remains increased reassure the patient and continue ARB therapy

Myogenic Reflex

↑ Perfusion Pressure
Afferent vasoconstriction

Constant
$P_{GC}$

→ Perfusion Pressure
Afferent vasodilation

Constant
$P_{GC}$
Therapeutic Complications

Effect of BP Control on $P_{GC}$ in Setting of Impaired Renal Autoregulation

![Graph showing intraglomerular pressure versus systemic pressure, with pressure-passive and resistant segments.]


MAP and GFR After IV Clonidine in Subjects With and Without Nephropathy

![Bar chart showing reduction in MABP and GFR for Type 1, Type 2, Non-DM, Type 1, Type 2, Non-DM subjects with nephropathy and normal albuminemia.]

Kidney Intl 56:1517-1523,1999
Case Presentation

• Assume the patient was brought back for follow-up two weeks later and the serum creatinine had increased further to 3.0 mg/dl

Maintenance of GFR with Low Flow or Perfusion Pressure
Therapeutic Complications

ANATOMIC
- Renal artery stenosis

FUNCTIONAL
- ↓ EABV
- NSAIDs, Calcineurin inhibitor
- Sepsis

↑ Afferent tone
↓ Flow
Luminal obstruction

GFR

↑ Afferent tone
↓ Flow
Luminal obstruction

ACEI or ARB

↓ Efferent tone

Renal Dysfunction in Setting of Stringent BP Control

- Patients with CKD may exhibit evidence of renal dysfunction in the setting of stringent BP control
- Changes in renal function typically occur within 2 weeks of therapy initiation and stabilize within a week thereafter
- A 30% increase in the serum creatinine above the baseline value does not warrant discontinuation of therapy. Such changes are functional, reversible in nature, and are reflective of decreases in intraglomerular pressure
- Increases of >30% over baseline or progressive increases in the serum creatinine concentration should prompt a search for RAS, contraction of ECF volume, use of NSAIDS, or infection
Case 3

- A 33 year old black man with sickle cell disease presents with severe back pain typical of sickle cell crisis. His past medical history is pertinent for frequent episodes of hemolytic crisis. The patient was not on diuretic therapy. Physical examination shows an anxious man in mild discomfort with blood pressure of 156/94 mmHg, pulse 98, RR 22. There is scleral icterus. Lung exam show basilar crackles and he has hepatomegaly, and trace peripheral edema.
Case 3-Laboratory studies

- Creatinine 0.6 mg/dl
- Serum electrolytes (mEq/l)
  - Na⁺ 136
  - K⁺ 2.2
  - Cl⁻ 84
  - HCO₃⁻ 29
- Urine electrolytes (mEq/l)
  - Na⁺ 63
  - K⁺ 49
  - Cl⁻ 58
- Plasma renin activity 1.1 ng/ml/hr (normal 3-9), aldosterone 2 ng/dl (normal <10)

Case 3 (cont)

- The patient was treated with exchange transfusion and he was given K⁺ supplements to correct the hypokalemia. Blood pressure at the time of discharge was 118/78 Hg and labs showed a total bilirubin of 8 mg/dl and a K⁺ of 4.1 mmol/l off K⁺ supplements. Five months later the patient was readmitted with a hemolytic crisis. Blood pressure was again noted to be increased at 158/98 mmHg.
- Laboratory examination:
  - total bilirubin of 45 mg/dl
  - serum K⁺ 2.1 mmol/L with TTKG of 12
  - Aldosterone was 2.5 ng/dl.
Which One of the following is the best explanation for the recurrent hypokalemia in this patient?

1. Liddle syndrome
2. Shift of $K^+$ into cells
3. Acquired deficiency of 11β Hydroxy-steroid dehydrogenase II
4. Surreptitious loop diuretic use
5. Glucocorticoid suppressible hyperaldosteronism

Case 3 Summary

• A 33 year old man with sickle cell disease presents with evidence of sickle cell crisis.
• Findings include hypokalemia with increased urinary $K^+$ excretion and hypertension in setting of suppressed renin and aldosterone levels
• The abnormalities resolve as the crisis remits and then redevelop with a second crisis 4 months later
Urinary K⁺ +

<20 mEq/day
Gastrointestinal loss

(R) Renin, (A) Aldosterone

↑ R, ↑ A
Renal artery stenosis
Renin secreting tumors

↑ R, ↑ A
Adrenal adenoma
Bilateral cortical hyperplasia
Glucocorticoid suppressible hyperaldosteronism

↓ R, ↓ A
Cushing’s syndrome
Syndrome of apparent mineralocorticoid excess
Liddle syndrome
Mineralocorticoid receptor mutation

>20 mEq/day
Blood pressure, effective arterial blood volume

Low-Normal

Serum [HCO₃⁻]

↓ Renin, ↓ Aldosterone

Increase or Apparent Increase in Nonaldosterone Mineralocorticoid

• Congenital adrenal hyperplasia
• Cushings syndrome
• Genetic Causes
  – Liddle syndrome
  – Activating mutation of the mineralocorticoid receptor
  – Syndrome of apparent mineralocorticoid excess

Low

Renal tubular acidosis

↓ Urine [Cl⁻]

Non-reabsorbable anion

Low

Diuretics
Mg²⁺ deficiency
Bartter syndrome
Gitelman syndrome

High

Serum [HCO₃⁻]

Low

Urine [Cl⁻]

High
Syndrome of Apparent Mineralocorticoid Excess

- Cortisol circulates at 1000-fold higher concentration than aldosterone
- $11\beta$-OSHDH-2 inactivates cortisol to cortisone CD
- $11\beta$-OSHDH-2 deficiency allows cortisol to activate MR receptor
- Excess cortisol in Cushing syndrome

Syndrome of Apparent Mineralocorticoid Excess

- Deficiency can be genetic or acquired
- Glycyrrhetinic acid (licorice, Asam Boi), flavonoids in grapefruit juice
- Bile acids

Hepatology 30: 623-629, 1999
Bile Acids and 11β-Hydroxysteroid Dehydrogenase Type II

- Chenodeoxycholic acid and deoxycholic acid inhibit 11β-Hydroxysteroid dehydrogenase II and cause cortisol-induced activation of MR receptor
- 11β-Hydroxysteroid dehydrogenase II activity is reduced in patients with cholestasis

J Biol Chem 277:26286-26292, 2002

Mechanism of Salt Retention in Cirrhosis
Salt Retention in CCL₄ Cirrhosis

- Liver cirrhosis induced by CCL₄ in rats
- Rats divided into 2 groups based on degree of Na⁺ retention
  - Group A: Decreased urine Na⁺ vs control
  - Group B: no change in urine Na⁺

Increased Apical Targeting of ENaC and Decreased 11β-HSD Type 2

Immunoperoxidase microscopy of α -ENaC

Immunoperoxidase microscopy of 11-β HSD2
Salt Retention in Rats with Common Bile Duct Ligation-induced Cirrhosis

- Rats with common bile duct ligation studied at 6 and 8 weeks
- At 6 wks: positive Na$^+$ balance and ascites
  - ↑ trafficking of ENaC to apical membrane
  - ↓ expression of 11β-OHD type 2
- At 8 wks: $U_{Na}$ excretion similar to controls
  - ENaC expression decreased

*Kidney Intl 69:89-98, 2006*

Increased Apical Targeting of ENaC and ↓ Expression of 11β-HSD Type 2

*Kidney Intl 69:89-98, 2006*
Conclusion

- The results strongly suggest that the marked increase in apical ENaC subunit targeting combined with diminished abundance of 11 HSD2 in the DCT2, CNT and collecting duct is likely to play key roles for the sodium retention associated with liver cirrhosis.

Kidney Int 69:89-98, 2006

Hypokalemia During Sickle Cell Crisis Apparently Due to Intermittent Mineralocorticoid Excess

Which One of the following is the best explanation for the recurrent hypokalemia in this patient?

- Liddle syndrome
- Shift of K⁺ into cells
- Acquired deficiency of 11β Hydroxy-Steroid dehydrogenase II
- Surreptitious loop diuretic use
- Glucocorticoid suppressible hyperaldosteronism
Case 4 Presentation

- A 54 yo women is referred for CKD stage 3 secondary to diabetic nephropathy, BP 146/88 mmHg
- Medications include naproxen 500 mg bid prescribed by an ER physician secondary to a sprain two weeks earlier and HCTZ 25 mg/d
- Labs (mEq/l) Na⁺ 140, K⁺ 5.4, Cl⁻ 106, HCO₃⁻ 19, creatinine 1.8 mg/dL, glucose 148 mg/dL, urine total protein/creatinine ratio 3.8

Which of the following steps is most appropriate in the management of this patient?

- Note in the chart that an ARB or ACEI should not be used in this patient because of the risk of worsening hyperkalemia
- Start high dose ARB therapy since these agents do not cause ↑ K⁺
- Discontinue the NSAID and recheck K⁺ in 1 week
- Discontinue the HCTZ and begin furosemide 20 mg once daily
Management of Hyperkalemia in the setting of Renin-Angiotensin System Blockade

- Low K⁺ diet (70 mEq/d)

Excess Intake

- Usually in setting of impaired renal excretion
- Salt substitutes
- Large amounts of juice
  - coconut juice (44.3 mmol/l)
  - orange juice: (51 yo man with K⁺ of 9, drank 2.5 l daily, 1125 mEq/d for 3 wks)
  - Noni juice
- River bed clay (100 mEq per 100 gm clay)
- Burnt match heads (cautopyreiphagia)
- Bananas: 15 yo with K⁺ 6.1 ingesting 20/d
Management of Hyperkalemia in the setting of Renin-Angiotensin System Blockade

- Low K⁺ diet (70 mEq/d)
- Discontinue other meds that interfere in K⁺ excretion

![Diagram of Renin-Angiotensin System Blockade and Hyperkalemia Management](image-url)

Primary Decrease in Mineralocorticoid Activity

![Diagram showing the primary decrease in mineralocorticoid activity](image-url)

Primary Decrease in Mineralocorticoid Activity

Primary Decrease in Mineralocorticoid Activity

Management of Hyperkalemia in the setting of Renin-Angiotensin System Blockade

- Low K⁺ diet (70 mEq/d)
- Discontinue other meds that interfere in K⁺ excretion
- Effective diuretic therapy: loop diuretics when estimated GFR <30ml/min (use furosemide twice daily)
- NaHCO₃ tablets (650-mg tablet, 8 mEq)
- Decrease dose of ACEI or ARB

Efficacy and Safety of Benazepril for Advanced CKD

- 422 patients with CKD not due to DM enrolled in a double blind randomized study:
  - Gp 1: n = 104 with SCr of 1.5-3.0 mg/dl treated with benazepril 20 mg/d
  - 215 patients with SCr of 3.0-5.0 mg/dl
    - Gp 2: n = 112 treated with benazepril 20 mg/d
    - Gp 3: n = 112 conventional therapy
  - Mean f/u 3.4 years
Efficacy and Safety of Benazepril for Advanced CKD

Primary Composite End Point: Doubling of SCr, ESRD, Death

Change in BP and Proteinuria

Group 1, benazepril
Group 2, benazepril
Group 2, placebo

No. at Risk
Group 1, benazepril 192
Group 2, benazepril 107
Group 2, placebo 108

Group 1, benazepril 102
Group 2, benazepril 107
Group 2, placebo 108

Management of Hyperkalemia in the setting of Renin-Angiotensin System Blockade

- Low K⁺ diet (70 mEq/d)
- Discontinue other meds that interfere in K⁺ excretion
- Effective diuretic therapy
- NaHCO₃ tablets (650-mg tablet, 8 mEq)
- Decrease dose of ACEI or ARB
- Binding resins
Case 5

• A 33 year old man with known chronic kidney disease is admitted with increasing dyspnea. He has had several admissions over the last 6 months for chest pain and severe hypertension which developed in association with smoking crack cocaine. In addition to using crack cocaine, over the last 2 days he started using intranasal cocaine after obtaining the drug from a new source.
Case 5 (continued)

• One day prior to admission he noticed the gradual onset of increasing shortness of breath later accompanied by development of a bluish discoloration of his lips. Past medical history is significant for stage 4 CKD secondary to poorly controlled hypertension. Physical examination shows BP 180/110 mmHg, pulse 104, and respiratory rate 22 breaths per minute. His lips and nail beds are a dark grayish-brown color. The lungs are clear to auscultation. The remainder of the exam is normal.

Laboratory Data

• Creatinine 4.8 mg/dL, BUN 55 mg/dl (unchanged from one month ago)
• Serum electrolytes (all in mEq/L)
  – Na⁺ 142
  – K⁺ 4.8
  – Cl⁻ 92
  – HCO₃ 25
• Arterial blood gas (room air)
  – pH 7.47
  – pCO₂ 28 mmHg
  – pO₂ 110 mmHg
• Pulse oximetry on room air: 88%
Which ONE of the following BEST describes the acid-base status of the patient?

1. Respiratory alkalosis and anion gap metabolic acidosis
2. Anion gap metabolic acidosis and metabolic alkalosis
3. Anion gap metabolic acidosis, metabolic alkalosis, respiratory acidosis
4. Anion gap metabolic acidosis, metabolic alkalosis, respiratory alkalosis
5. Metabolic alkalosis and respiratory acidosis

Which ONE of the following adulterants is MOST likely to be contained in the cocaine?

1. Levamisole
2. Benzocaine
3. “Bath salts” (methyleneoxypyrovalerone)
4. Methamphetamine
5. Phenacetin
Case 5: Summary

- 33 yo man with chronic kidney disease is an active user of crack cocaine
- Recently starts using intranasal cocaine obtained from a different source
- Presents with one day of increasing shortness of breath

- What is the acid-base disturbance on admission?

Case 5

- Anion gap metabolic acidosis
- Metabolic alkalosis
- Respiratory alkalosis

<table>
<thead>
<tr>
<th>142</th>
<th>92</th>
<th>55</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.8</td>
<td>25</td>
<td>4.8</td>
</tr>
</tbody>
</table>

pH = 7.47
pCO₂ 27

Anion gap = 25
Which ONE of the following BEST describes the acid-base status of the patient?

1. Respiratory alkalosis and anion gap metabolic acidosis
2. Anion gap metabolic acidosis and metabolic alkalosis
3. Anion gap metabolic acidosis, metabolic alkalosis, respiratory acidosis
4. Anion gap metabolic acidosis, metabolic alkalosis, respiratory alkalosis
5. Metabolic alkalosis and respiratory acidosis

Acid Base Disturbances with Cocaine Use

- Lactic acidosis
  - Seizures
  - Malignant hyperthermia
  - Rhabdomyolysis
- Respiratory alkalosis
- Metabolic alkalosis

Crack Cocaine-Induced Metabolic Alkalosis

- Cocaine HCl vaporizes at a temperature close to where it burns
- Cocaine base vaporizes at much lower temperature and is suitable for inhalation
- Alkali is added to Coc HCL
  \[ \text{Coc-H}^+\text{Cl}^- + \text{NaHCO}_3 \rightarrow \text{Coc} + \text{H}_2\text{O} + \text{CO}_2 + \text{NaCl} \]
- Additional base may be added to increase weight and street value
- CKD is a risk factor


Case 5: Summary

- 33 yo man with chronic kidney disease is an active user of crack cocaine
- Recently starts using intranasal cocaine obtained from a different source
- Presents with one day of increasing shortness of breath

- What is the acid-base disturbance on admission?
Case 5

- Anion gap metabolic acidosis
- Metabolic alkalosis
- Respiratory alkalosis

\[ \begin{array}{c|c|c}
\text{Na}^- & \text{Cl}^- & \text{HCO}_3^- \\
142 & 92 & 55 \\
4.8 & 25 & 4.8 \\
\end{array} \]

pH = 7.47
pCO\textsubscript{2} = 27
Anion gap = 25

Which ONE of the following BEST describes the acid-base status of the patient?

1. Respiratory alkalosis and anion gap metabolic acidosis
2. Anion gap metabolic acidosis and metabolic alkalosis
3. Anion gap metabolic acidosis, metabolic alkalosis, respiratory acidosis
4. Anion gap metabolic acidosis, metabolic alkalosis, respiratory alkalosis
5. Metabolic alkalosis and respiratory acidosis
Acid Base Disturbances with Cocaine Use

- Lactic acidosis
  - Seizures
  - Malignant hyperthermia
  - Rhabdomyolysis
- Respiratory alkalosis
- Metabolic alkalosis


Crack Cocaine-Induced Metabolic Alkalosis

- Cocaine HCl vaporizes at a temperature close to where it burns
- Cocaine base vaporizes at much lower temperature and is suitable for inhalation
- Alkali is added to Coc HCL
  - $\text{Coc-H}^+\text{Cl}^- + \text{NaHCO}_3 \rightarrow \text{Coc} + \text{H}_2\text{O} + \text{CO}_2 + \text{NaCl}$
- Additional base may be added to increase weight and street value
- CKD is a risk factor

Case 5: Summary

• Following use of intranasal cocaine obtained from a different source, he begins to complain of increasing dyspnea
• Lips and nail beds are noted to be a grey-brownish color

pH = 7.47  
pCO₂ 27 mmHg  
pO₂ 110 mmHg (room air)  
O₂ sat = 88% by pulse oximeter

Which ONE of the following adulterants is MOST likely to be contained in the cocaine?

1. Levamisole
2. Benzocaine
3. Bath salts (methylenedioxy.pyrovalerone)
4. Methamphetamine
5. Phenacetin
Methemoglobinemia

- Suspect with clinical cyanosis in setting of a normal arterial pO₂ by arterial blood gas
- Arterial blood gas (room air)
  - pH 7.47
  - pCO₂ 28 mmHg
  - pO₂ 110 mmHg
  - Pulse oximetry on room air: 88%
- Symptoms related to impaired oxygen delivery to tissues
Methemoglobinemia

• Congenital
  – Autosomal recessive disorder with deficiency in cytochrome b₅ reductase
  – Cyanotic appearance at birth
• Acquired
  – Dapsone, bezocaine, and lidocaine common
  – Clinically suspected by the presence of clinical "cyanosis" in the presence of a normal arterial pO₂ (PaO₂) by arterial blood gases

Methemoglobinemia

• Normal [MetHb] 1-2%
• Reduced tissue O₂ delivery
  – MetHb unable to bind O₂ thus reducing O₂ carrying capacity
  – MetHb alters unaffected Hb leading to increased O₂ affinity
• Leads to respiratory alkalosis
• If severe: lactic acidosis
Correlation of MetHb Fraction and Signs and Symptoms

<table>
<thead>
<tr>
<th>Fraction MetHb (%)</th>
<th>Signs and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-15</td>
<td>None to slate gray cutaneous coloration</td>
</tr>
<tr>
<td>15-30</td>
<td>Cyanosis, chocolate brown blood</td>
</tr>
<tr>
<td>30-50</td>
<td>Dyspnea, headache, fatigue, syncope, weakness</td>
</tr>
<tr>
<td>50-70</td>
<td>Tachypnea, lactic acidosis, seizures, CNS depression, coma</td>
</tr>
<tr>
<td>&gt;70</td>
<td>Severe hypoxic symptoms, death</td>
</tr>
</tbody>
</table>

Methemoglobinemia

- Pulse oximetry is inaccurate (86%)
- Assumes only 2 varieties of Hb are present: oxyhemoglobin and deoxyhemoglobin
- Co-oximetry is accurate because absorptive characteristics of several Hb species can be detected to include MetHb
Methylene Blue Treatment of MetHb

Hexose monophosphate shunt

Glucose → Glucose-6-phosphate → 6-Phosphogluconolactone

NADP+ → NADPH → NADPH-MetHb Reductase

Methylene blue → Leukomethylene blue → MetHb → Hb

Cocaine-Induced Methemoglobinemia

• Secondary to adulterant
• Benzocaine commonly used as it shares numbing properties typically associated with cocaine (useful to artificially increase the weight of the powder being sold)

British J Clin Pharm 72:18-26, 2011
Resuscitation 81:138-139, 2010
Which ONE of the following adulterants is MOST likely to be contained in the cocaine?

1. Levamisole
2. Benzocaine
3. Bath salts (methylenedioxypyrovalerone)
4. Methamphetamine
5. Phenacetin

---

**Levamisole**

- An antihelminthic agent used in veterinary medicine
- Used illicitly as a cocaine adulterant
  - Bulking agent
  - Speculated to enhance euphoric effect
- Complicated by bone marrow suppression and ANCA-positive vasculopathy

Levamisole

54 yo woman with known cocaine use presents with 2 day history of painful rash over face. Labs showed neutropenia and positive tests for p-ANCA and c-ANCA

Bath Salts

- The term usually refers to the primary ingredient 3,4-methylenedioxyxyrovalerone
- CNS stimulant with hallucinogenic effects
- Administered by mouth, nasal insufflation, smoking, IV or IM
- Extreme sympathetic stimulation:
  - tachycardia, hypertension, arrhythmias, seizures, stroke
- Recurrent AKI and rhabdomyolysis
Methamphetamine

- Highly addictive drug that acts as a stimulant for the central nervous system
  - Hypertension, arrhythmias, hallucinations and violent behavior
- “Meth Mouth” poor oral hygiene, xerostomia, rampant caries, and excessive tooth wear.

Phenacetin

- Sometimes used as a cutting agent to adulterate cocaine

Drug Test Anal 3:89-96, 2011