“What was thought to be a product for beautification for people with grey hair, it turned out to be a dreadful poison for people with desperation to say goodbye to this society and world”
Hair Dye Poisoning

• Increase in global suicide rates by 60% in 50 years in underdeveloped and developing countries

• Hair dye ingestion an important etiological factor:
  o Easy availability
  o Cost (Super Vasmol 33™ with 4 g PPD/100 ml < 1 $)
  o Purchased without raising suspicion of suicidal intention
  o Perceived as “not bad enough to kill”
  o Availability of information on Internet and mass media

Hair Dye Poisoning

• Extensively used as an oxidizable hair dye

• In Africa, Middle East and Indian subcontinent, mixed with heena which is traditionally applied to do color on hands and feet, and to dye hair:
  o Intensifies color of Henna (Lawsonia alba)
  o Shortens duration of application
Types of Hair Dyes

- Vegetable hair dyes (e.g. Henna)
- Temporary hair dyes (water-soluble)
- Semi-permanent hair dyes
- Permanent hair dyes:
  - Oxidation hair dyes
  - Progressive hair dyes

Progressive Hair Dyes

- Contain lead acetate or bismuth citrate
- Concentration of lead acetate not exceeding 0.6% w/v, calculated as metallic lead
- Change color of hair gradually from light straw color to almost black by reacting with sulfur of hair keratin as well as oxidizing on hair surface
Permanent Hair Dyes

- **Precursor-coupler**: Surfactants, reducing agent, precursors (such as p-phenylenediamine, 2,5-diaminotoluene, paminophenol etc.), couplers (such as resorcinol), in an alkaline soap or base.
  - Surfactants to dissolve precursors & couplers, to assist in spreading dye evenly over hair
  - Alkaline base to facilitate oxidation reaction
  - PPD forms hair color on chemical reaction
  - Preformed dyes to achieve intended shades

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Permanent Hair Dyes

- **Oxidizing base**: An oxidizing agent (e.g. peroxide), stabilizer for the peroxide, and surfactants.
- Precursor-coupler base and oxidizing base formulated separately
- Mixed immediately prior to use
Permanent Hair Dyes

• Cascade of reaction when precursors and peroxide diffuse into hair shaft
• Dye precursors oxidized by \( H_2O_2 \) to \( p \)-benzoquinone diamine; further oxidized to a trimer (Bandrowski's base) which may cause anaphylaxis and mutation
• Rapid reaction of couplers with intermediates resulting colorant molecules; too large to escape

Permanent Hair Dyes

• Available in stone, powder, or liquid forms
• Mortality higher with the stone forms
• Stone Hair Dye cheap and available in 20 grams pack (contains 70-90% PPD)
• ‘Godrej’ Kesh kala, Super Vasmol 33™, Color mate in powder/liquid forms; contain 2-10% PPD
• EU Cosmetic Directive regulates \( PPD \leq 6\% \) in hair dyes
Poisonous Ingredients

• **Permanent Dyes:**
  - PPD
  - Resorcinol
  - Propylene glycol
  - Ethylenediaminetetraacetic acid (EDTA) sodium, others

---

Poisonous Ingredients

• **Resorcinol:**
  - Seizures, lethargy, coma and death
  - Nausea, dyspnea, hypotension, diaphoresis, salivation
  - Methaemoglobinema; Pulmonary edema

• **Propylene glycol:**
  - Anion gap metabolic acidosis; CNS depression; Arrhythmias
  - Renal dysfunction

• **EDTA Sodium:**
  - Hypocalcemia (also due to rhabdomyolysis)
Hair Dye – Real Picture

• Bureau of Indian Standards (BIS):
  o Concentration of PPD in powder form ≤ 30%
  o Concentration of PPD in liquid type ≤ 4%
  o “Warning: not to dye eyebrows and eyelashes”

• Consumer Education and Research Society (CERS):
  o 3/14 did not conform to parameters of total PPD
  o 12/14 did not conform to packing requirements
  o Warning absent in 1/14

---

Hair Dye – Real Picture

Scientific Committee on Consumer Products (Europe):

• PPD is a very strong potential skin sensitizer
• A patch test before each application
• Even if no reaction first time, person can become “sensitized” to PPD over time
• No such warning on many products
Henna – Real Picture

- 25 henna samples from 15 saloons
- 11/25 black henna; 14/25 red henna
- PPD in all the black henna samples (0.38 % and 29.5%)
- PPD in 6 black henna samples higher than permitted concentration of PPD established by the EU
- ↑ risk of sensitization among those using black henna
- **Recommendation**: Addition of PPD to natural henna should be prohibited

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Epidemiology

- PPD poisoning a common health problem in the Middle East, especially Sudan and Morocco
- Also common in India; Rare in the west
- Most reported cases in children, adolescents and adults
- **From Sudan**: 3159 patients reported to suffer from PPD poisoning; among these, 568 (18%) children
- **From Morocco**: 374 cases in adults and children over a 10-year period; 54% in 15-24 years age group

---

Epidemiology

<table>
<thead>
<tr>
<th>Type of Poisoning</th>
<th>Number of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organophosphorus</td>
<td>383</td>
<td>17.2</td>
</tr>
<tr>
<td>Scorpion bite</td>
<td>280</td>
<td>12.5</td>
</tr>
<tr>
<td>Snake Bite</td>
<td>208</td>
<td>9.3</td>
</tr>
<tr>
<td>Overdose</td>
<td>187</td>
<td>8.4</td>
</tr>
<tr>
<td>Unknown pill</td>
<td>173</td>
<td>7.7</td>
</tr>
<tr>
<td>Endosulphan</td>
<td>143</td>
<td>6.42</td>
</tr>
<tr>
<td>Alcohol intoxication</td>
<td>134</td>
<td>6</td>
</tr>
<tr>
<td>Unknown bite</td>
<td>112</td>
<td>5.03</td>
</tr>
<tr>
<td>Rodenticide</td>
<td>71</td>
<td>3.1</td>
</tr>
<tr>
<td>Corrosive substance</td>
<td>65</td>
<td>3</td>
</tr>
<tr>
<td>House hold item</td>
<td>63</td>
<td>2.83</td>
</tr>
<tr>
<td>Hair dye</td>
<td>58</td>
<td>2.6</td>
</tr>
<tr>
<td>Kerosene ingestion</td>
<td>48</td>
<td>2.15</td>
</tr>
<tr>
<td>Nail Polish</td>
<td>31</td>
<td>1.33</td>
</tr>
<tr>
<td>Multitablets</td>
<td>270</td>
<td>12.1</td>
</tr>
</tbody>
</table>


Pathogenesis

• Angioneurotic edema:
  o Bandrowski's base highly allergic, mutagenic and toxic → leads to angioneurotic edema
  o Increased permeability of the blood vessels
  o Asphyxia and respiratory failure

• Rhabdomyolysis:
  o Promotes leakage of calcium ions from smooth ER
  o Continuous contraction and irreversible change in the muscle's structure
Pathogenesis

• **Acute kidney injury:**
  - Rhabdomyolysis; intravascular hemolysis
  - Hypovolemia
  - Direct toxic effect on renal tubules
  - Effect of propylene glycol and resorcinol
  - Bismuth sulfate $\rightarrow$ acute interstitial nephritis

• **Myocarditis:**
  - Direct effect of PPD
  - Rhabdomyolysis of myocardial muscle
  - Hyperkalemia

Clinical Features – Local Application

• Contact with PPD $\rightarrow$ skin irritation, dermatitis, keratoconjunctivitis, swelling & eczema of eyelids, chemosis, lacrimation, permanent blindness and even asthma

• Severe contact dermatitis

Clinical Features – Local Application

- Adverse events in 110/263 volunteers
- 67% reactions within 1 h of using hair dye compared to 33% after 1 h

![Bar chart showing adverse events](chart.png)


Clinical Features – Local Application

- Cross-sectional study on 72 hairdressers in Sudan
- Mean duration of exposure - 6 years (range 1-20 years)
- Renal impairment, hematuria, proteinuria and hypertension in 14%, 41.1%, 26.4% and 19.4%
- PPD content between 10% to 97%
- Interstitial fibrosis suggesting CKD in 6/8 biopsies
- Glomerular involvement in 3/8 renal biopsies

Clinical Features – Local Application

- Risk factors for elevated serum creatinine

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Odds ratio</th>
<th>P-value</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Using pure forms of PPD</td>
<td>5.9</td>
<td>0.02</td>
<td>1.3-27</td>
</tr>
<tr>
<td>Exposure duration to PPD (Years)</td>
<td>1.3</td>
<td>0.01</td>
<td>1.1-1.6</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>0.9</td>
<td>0.1</td>
<td>0.8-1.0</td>
</tr>
</tbody>
</table>

- Risk factors for proteinuria

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Odds ratio</th>
<th>P-value</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Using pure forms of PPD</td>
<td>9.8</td>
<td>0.02</td>
<td>2.4-40</td>
</tr>
<tr>
<td>Exposure duration to PPD (Years)</td>
<td>1.4</td>
<td>0.01</td>
<td>1.1-1.6</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>0.9</td>
<td>0.1</td>
<td>0.8-1.0</td>
</tr>
</tbody>
</table>


Clinical Features - Systemic

- Toxic amount: 2-3 g; Fatal amount: 4-10 g
- Characteristic triad:
  - Early angioedema
  - Rhabdomyolysis with dark urine
  - Acute renal failure
- Others common feature:
  - Myocarditis with cardiac arrhythmias and sudden death
Clinical Features - Systemic

- Early features (within 1-2 hours):
  - Angioedema
  - Myocarditis
- Late features (after 2-6 days):
  - Rhabdomyolysis
  - Myoglobinuria
  - Acute renal failure

---

Clinical Features – Early

- Angioedema:
  - Hard swollen protruding tongue
  - Edematous bull neck
  - Onset within first few minutes to hours
  - Reported in 40-100% of patients
  - Respiratory distress, CNS depression
- Other early features:
  - Numbness and burning of mouth and throat
  - Vomiting
  - Dysphagia
Angioedema


Rhabdomyolysis

- Results in muscular pain, tenderness, weakness
- Affected muscles hard and tense
- Localized or generalized painful swelling of muscles
- Black urine due to myoglobinuria
- Elevated CPK
- Sudden cardiac death due to hyperkalemia
Acute Renal Failure

- Two phases: an oliguric or anuric and a recovery phase
- Proteinuria and hematuria
- May develop despite aggressive hydration, alkanilization and early use of diuretics
- Incidence varies from 25% to 100% (Reddy et al: 81/247 developed AKI)
- May occur as late as 6 days after ingestion


Acute Renal Failure

- A study of 19 patients with AKI (Sudan):
  - Glomerular injury in 94%
  - Interstitial lesions in 84%
  - Tubular lesions in 79%
  - No evidence of vascular injury

Acute Renal Failure

• A study of 30 patients with AKI:
  o High-colored urine in only 3; CK elevated in 6
  o Mean duration of onset of AKI: 3 days
  o 25% cases died
  o Renal biopsies in 15:
    o Acute tubular necrosis in 8
    o Acute interstitial nephritis in 7
    o Glomerular injury in 14


Acute Renal Failure

• 18 rats in 6 groups: one control; five given DD

<table>
<thead>
<tr>
<th>Groups</th>
<th>Glomerular changes</th>
<th>Tubulo-interstitial changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral lethal dose (80 mg/kg) (Killed at 3 h)</td>
<td>Severe glomerular congestion</td>
<td>Extensive intertubular hemorrhages</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Focal areas of tubular necrosis</td>
</tr>
<tr>
<td>Oral sub-lethal dose group (40 mg/kg)</td>
<td>Glomerular congestion</td>
<td>Mild intertubular hemorrhages</td>
</tr>
<tr>
<td>(Killed at 3 days)</td>
<td></td>
<td>Focal areas of tubular necrosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Focal areas of tubular proliferation</td>
</tr>
<tr>
<td>Oral minimal dose group (20 mg/kg)</td>
<td>Mild glomerular congestion and mesangial proliferation</td>
<td>Mild intertubular hemorrhages</td>
</tr>
<tr>
<td>(Killed at 6 days)</td>
<td></td>
<td>Moderate tubular necrosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tubular proliferation and regeneration</td>
</tr>
<tr>
<td>Intraperitoneal lethal dose (37 mg/kg)</td>
<td>Moderate glomerular congestion</td>
<td>Moderate intertubular hemorrhages</td>
</tr>
<tr>
<td>(Killed at 3 hours)</td>
<td></td>
<td>Extensive tubular necrosis with casts</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Focal mononuclear infiltration</td>
</tr>
<tr>
<td>Intraperitoneal sub-dose (18 mg/kg)</td>
<td>Glomerular congestion</td>
<td>Interstitial hemorrhages</td>
</tr>
<tr>
<td>(Killed at 3 days)</td>
<td></td>
<td>Tubular epithelium necrosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tubular epithelial cell proliferation</td>
</tr>
</tbody>
</table>

Cardiac Involvement

- Commonly neglected complication

**Clinical Features:**
- Fatigue, dyspnea, chest pain, palpitations, giddiness, syncope, sudden death
- Hypotension, shock, CHF, arrhythmias

**ECG:**
- Sinus tachycardia
- BBB, intra-ventricular conduction defect
- Atrial and ventricular premature complexes
- Atrial fibrillation; Ventricular tachyarrhythmias
- ST segment elevation/depression; T wave inversion

**Cardiac biomarkers:** Elevated

**Echocardiography:**
- Wall motion abnormality; reduced ejection fraction
## Cardiac Involvement

### Description of cases

<table>
<thead>
<tr>
<th>Description of cases</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases excluded</td>
<td>363</td>
</tr>
<tr>
<td>Brought dead</td>
<td>67</td>
</tr>
<tr>
<td>Died within 5 hours</td>
<td>83</td>
</tr>
<tr>
<td>Mild/No symptoms</td>
<td>167</td>
</tr>
<tr>
<td>Not willing to part</td>
<td>41</td>
</tr>
<tr>
<td>Known cardiac/Renal disease</td>
<td>5</td>
</tr>
<tr>
<td>Cases included in study after PPD ingestion</td>
<td>1595</td>
</tr>
<tr>
<td>Total</td>
<td>1958</td>
</tr>
</tbody>
</table>

Jain PK, et al. A prospective clinical study of myocarditis in cases of acute ingestion of paraphenylenediamine (hair dye) poisoning in northern India. JAPI 2013; 61:633-637

### Symptoms / Signs

<table>
<thead>
<tr>
<th>Symptoms / Signs</th>
<th>No. of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe edema of face and neck</td>
<td>1180</td>
<td>74</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>1148</td>
<td>72</td>
</tr>
<tr>
<td>Chocolate brown color urine</td>
<td>861</td>
<td>54</td>
</tr>
<tr>
<td>Pain/rigidity of limb</td>
<td>765</td>
<td>48</td>
</tr>
<tr>
<td>Respiratory difficulty</td>
<td>366</td>
<td>23</td>
</tr>
<tr>
<td>Sinus Tachycardia</td>
<td>350</td>
<td>22</td>
</tr>
<tr>
<td>Presyncope/syncope</td>
<td>287</td>
<td>18</td>
</tr>
<tr>
<td>Palpitation</td>
<td>255</td>
<td>16</td>
</tr>
<tr>
<td>Chest pain</td>
<td>265</td>
<td>16</td>
</tr>
<tr>
<td>Hypotension</td>
<td>239</td>
<td>15</td>
</tr>
<tr>
<td>Oliguria/Anuria</td>
<td>223</td>
<td>14</td>
</tr>
<tr>
<td>Ventricular tachycardia/fibrillation</td>
<td>22</td>
<td>9</td>
</tr>
<tr>
<td>Convulsion</td>
<td>47</td>
<td>3</td>
</tr>
</tbody>
</table>

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# Cardiac Involvement

<table>
<thead>
<tr>
<th>Form of cardiac complication</th>
<th>Number of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated cardiac biomarkers</td>
<td>138</td>
<td>57.5</td>
</tr>
<tr>
<td>Decreased left ventricular ejection fraction (LVEF&lt;35%)</td>
<td>130</td>
<td>54</td>
</tr>
<tr>
<td>Cardiac dilatation</td>
<td>110</td>
<td>46</td>
</tr>
<tr>
<td>Death due to cardiac causes</td>
<td>69</td>
<td>29</td>
</tr>
<tr>
<td>Ventricular tachycardia/Ventricular fibrillation</td>
<td>22</td>
<td>9</td>
</tr>
</tbody>
</table>

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# Other Features

- Hypocalcemia, tetany
- Hepatotoxicity
- Anaphylaxis
- Myocardial infarction
- Methemoglobinemia
- Convulsions
- Pneumothorax
- Intravascular hemolysis

Diagnosis

- Characteristic triad:
  - Early angioneurotic edema with stridor
  - Rhabdomyolysis with chocolate colored urine
  - Acute renal failure
- Thin layer chromatography on urine to detect PPD

Management

- A quick clinical examination
- Focus on vital parameters
- Guedel’s airway and emergency tracheostomy
- Endotracheal intubation not possible in majority
- Intravenous antihistamines and steroids
## Treatment

<table>
<thead>
<tr>
<th>Intravenous corticosteroid</th>
<th>Duration treatment (Days)</th>
<th>No. of Patients</th>
<th>Disappearance of edema (Days)</th>
<th>No. of Death</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone (300 mg/d)</td>
<td>7</td>
<td>300</td>
<td>8±2</td>
<td>83/300</td>
<td>27.77%</td>
</tr>
<tr>
<td>Methyl prednisolone (1 gm/d)</td>
<td>5</td>
<td>720</td>
<td>4±1</td>
<td>101/720</td>
<td>14.02%</td>
</tr>
</tbody>
</table>

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## Management

- **Induction of emesis:**
  - Contraindicated
- **Gastric lavage:**
  - Role not clear
  - Resorcinol, a phenolic derivative, highly corrosive
  - Whether lavage a friend or foe not clear
  - Most physicians perform a gastric lavage
- **Activated charcoal:**
  - Controversial
Supportive Management

- Maintenance of circulatory volume and pressure
- Continuous cardiac monitoring in ICU
- Vasopressors (IV norepinephrine and/or dopamine)
- For ventricular arrhythmias, amiodarone and defibrillation
- For AKI, dialysis
- Calcium gluconate for hypocalcemia

Management

- Minimize renal injury:
  - Large volume of fluids (up to 8–10 liters/day) to maintain urine output of 250-300 ml/hour
  - IV mannitol
  - IV bicarbonate to alkalinize urine (22.3 – 44.6 mEq TID)
  - Avoid dehydration and anoxia
- Methemoglobinemia:
  - Methylene blue
Management

- Oxygen for hypoxic cases or those with angioedema
- Emergency tracheostomy for marked orofacial swelling
- Gastric lavage with activated charcoal within 1-2 hours of presentation
- Continuous cardiac monitoring
- Intravenous fluids for hypotension; if unresponsive, vasopressors
- Intravenous amiodarone for ventricular tachyarrhythmia
- Intravenous corticosteroids (methylprednisolone)
- Sodium bicarbonate along with diuretics to maintain adequate urine volume
- Chlorpheniramine maleate till orofacial edema subsides
- Calcium gluconate is given to counteract hypocalcaemia
- Hemodialysis or peritoneal dialyses for AKI and hyperkalemia

Experience at AIIMS, New Delhi

- Over the last 15 years, 8 patients with hair dye poisoning
- Suicidal ingestion
- Presenting features:
  - Angioedema (5/8)
  - Rhabdomyolysis (3/8)
  - Acute kidney injury (2/8)
  - Myocarditis (1/8)
- Two patients died
Summary

- It is important that medical fraternity becomes aware of hair dye poisoning as this poison is available quite freely and is used extensively.
- Clinical outcomes rely on early recognition, prompt referral, and aggressive supportive treatment.

Summary

- Immediate ban of the sale of stone hair dye and dyes with high content of PPD
- “FOR DYEING AND NOT FOR DYING”
THANK YOU