**Acetaminophen (Paracetamol) Overdose**

**Policy**:  
Iranian Hospital has policy to provide immediate and proper clinical care for patients referring to Emergency Department (ED) with Acetaminophen overdose.

**Introduction**:  
Acetaminophen is not only metabolized through glucuronidation and sulfation to nontoxic metabolites but also, in small part, to N-acetyl-pbenzoquinoneimine (NAPQI), a hepatotoxic metabolite at a cellular level. This latter metabolic pathway is used to a greater extent in the overdose setting when physiologic stores of sulfhydryl donors are depleted, thereby limiting the nontoxic means for acetaminophen metabolism. N-Acetylcysteine (NAC) has been shown to limit hepatotoxicity in Acetaminophen-toxic patients by several mechanisms. First, NAC serves as a sulfhydryl group donor, allowing continued nontoxic metabolism; second, NAC can serve to conjugate NAPQI into a nontoxic metabolite; and finally, NAC has been shown to blunt the hepatocellular toxicity of NAPQI.

So it is of crucial importance to start treatment in acetaminophen overdose patients as soon as possible (when it is indicated) to decrease hepatotoxicity and prevent later morbidity and mortality caused by that.

**Definitions**

**Hepatotoxicity**: is defined as any increase in aspartate aminotransferase (AST) concentrations above normal limit.

**Severe Hepatotoxicity**: as an AST greater than 1,000 IU/L.
Hepatic failure: as hepatotoxicity with hepatic encephalopathy.

Acute Acetaminophen Overdose: A single acute poisoning at a known time who were no more than 24 hours post-ingestion of Acetaminophen.

Chronic Acetaminophen Overdose: A suspected or known acetaminophen overdose, including repeated supra-therapeutic ingestions.

Scope:
All Physicians including general and specialized involving in patient care including diagnosis and treatment planning in all Iranian Hospital inpatients and outpatients facilities are responsible to study and follow this policy and procedure properly in treating acetaminophen overdose patients.

Procedure:
1. Admit any patient referring with history of Acute Acetaminophen overdose or Chronic Acetaminophen overdose suspicious of Hepatotoxicity.

2. Always think about other complications and Co-diagnosis; don’t ignore diagnosis or treatment of other medical conditions that patient might suffer.


4. In case of Acute Acetaminophen overdose verify exact timing of ingestion. If more than 4 hours and less than 24 hours passed ingestion request serum Acetaminophen level.

5. In case of acute Acetaminophen overdose as soon as Acetaminophen serum level reported by laboratory plot it’s level in Rumack-Matthew Nomogram (Appendix CEm2- I & II).

6. The Rumack-Matthew nomogram allows for risk stratification for hepatotoxicity of patients who present with a single known time of an Acetaminophen overdose within 24 hours of ingestion (Acute Acetaminophen Overdose).
7. Spot the Acetaminophen serum level in Rumack-Matthew nomogram form (S6-5) and add it to patient file.

8. If the Acetaminophen level is in Possible or Probable hepatotoxicity range in Nomogram start NAC infusion immediately as it’s protocol (Appendix CEm2-III).

9. The golden time for treatment by NAC is first 8-10 Hour after ingestion of Acetaminophen. So quick action is necessary.

10. If the Acetaminophen level is in no hepatotoxic level do not start NAC and follow the patient general condition.

11. In chronic Acetaminophen overdose which hepatotoxicity is possible request for AST/ALT levels. (Appendix CEm2 – II)

12. As AST / ALT levels reported administer NAC to patients who have hepatotoxicity (Based on above definitions) thought to be due to Acetaminophen and have a suspected or known Acetaminophen overdose, including repeated supra-therapeutic ingestions.

13. Administer NAC to patients with hepatic failure (Based on above definitions) thought to be due to acetaminophen.

14. The finding of normal serum AST / ALT levels in the ED does not always exclude the risk of Acetaminophen toxicity developing during the next several hours. In suspicious cases follow the patient under observation and repeat AST / ALT levels request in 12 hours of first normal result. In case of any increase in AST / ALT levels administer NAC immediately.

15. Follow and observe other medical issues of patient seriously and do not ignore them.

16. After first 24 Hour administration of NAC either in acute or chronic overdoses check AST/ALT again. In case of increase in AST/ALT levels continue treatment. Check AST/ALT every 12 Hour and stop treatment as soon as decrease in them.

17. Continue treatment of NAC maximum up to three cycles (72 Hours).

18. Before administration of NAC read side effect profile in details and be prepared for handling them (Appendix CEm2-IV).
Acetaminophen (Paracetamol) Overdose

Appendix CEm2 – I

ACETAMINOPHEN TOXICITY RECORD

TOXICITY ASSESSMENT

Date and approximate time of ingestion: 

Quantity ingested (estimated mg) mg

Lab Test 

Serum Acetaminophen 

Serum AST/ALT 

ADMINISTRATION OF NAC 

1st NAC cycle 2nd NAC cycle 3rd NAC cycle 

Date/Time 

NAC

Nurse Stamp & Signature 

Physician Stamp & Signature 

S6-5
Acetaminophen (Paracetamol) Overdose

Appendix CEm2 – III

NAC ADMINISTRATION PROTOCOL

150 mg/kg in 200 ml DW 5% - in one hour

50 mg/kg in 500 ml DW 5% - in 4 hours

50 mg/kg in 500 ml DW 5% - in 8 hours

50 mg/kg in 500 ml DW 5% - in 8 hours

Check Serum Level AST/ALT

Decreasing → Increasing

Follow-up Routine Care → Repeat Another NAC Cycle

Check Serum Level AST/ALT Every 12 Hours

Acceptable Number of Repetitions: Maximum 3 Cycles of NAC
N-Acetyl –L-Cysteine (NAC)

Drug Information

Medication Safety Issues

Sound-alike/look-alike issues:

- Acetylcysteine may be confused with acetylcholine
- Mucomyst® may be confused with Mucinex®

Pronunciation

- (a se teel SIS teen)

U.S. Brand Names

- Acetadote®

Index Terms

- N-Acetyl-L-cysteine
- N-Acetylcysteine
- Acetylcysteine Sodium
- Mercapturic Acid
- Mucomyst
- NAC

Canadian Brand Names
Acetaminophen (Paracetamol) Overdose

- Acetylcysteine Solution
- Mucomyst®
- Parvolex®

Pharmacologic Category

- Antidote
- Mucolytic Agent

Pharmacologic Category Synonyms

- Expectorant, Mucolytic

Use: Labeled Indications

Antidote for acute acetaminophen (APAP) poisoning; repeated supratherapeutic ingestion (RSTI) of APAP; adjunctive mucolytic therapy in patients with abnormal or viscid mucous secretions in acute and chronic bronchopulmonary diseases; pulmonary complications of surgery and cystic fibrosis; diagnostic bronchial studies

Use: Unlabeled/Investigational

Prevention of contrast-induced renal dysfunction (oral, I.V.); distal intestinal obstruction syndrome (DIOS, previously referred to as meconium ileus equivalent)

Pregnancy Risk Factor

B

Pregnancy Considerations

Based on limited reports using acetylcysteine to treat acetaminophen poisoning in pregnant women, acetylcysteine has been shown to cross the placenta and may provide protective levels in the fetus.

Lactation
Excretion in breast milk unknown/use caution

**Contraindications**

Hypersensitivity to acetylcysteine or any component of the formulation

**Warnings/Precautions**

*Concerns related to adverse effects:*

- Anaphylactoid reactions: Acute flushing and erythema have been reported; usually occurs within 30-60 minutes and may resolve spontaneously. Serious anaphylactoid reactions have also been reported and are more commonly associated with I.V. administration. When used for APAP poisoning, the incidence is reduced when the initial loading dose is administered over 60 minutes. Acetylcysteine infusion may be interrupted until treatment of allergic symptoms is initiated; the infusion can then be carefully restarted. Treatment for anaphylactoid reactions should be immediately available. Use caution in patients with asthma or history of bronchospasm as these patients may be at increased risk. Conversely, patients with high APAP levels (>150 mg/dL) may be at a reduced risk for anaphylactoid reactions (Pakravan, 2008; Waring, 2008).

*Disease-related concerns:*

- Acute APAP poisoning: Appropriate use: Acetylcysteine is indicated in patients with a serum APAP level that indicates they are at "possible" risk or greater for hepatotoxicity when plotted on the Rumack-Matthew nomogram. There are several situations where the nomogram is of limited use. Serum acetaminophen levels obtained <4 hours postingestion are not interpretable; patients presenting late may have undetectable serum concentrations, despite having received a toxic dose. The nomogram is less predictive of hepatic injury following an acute overdose with an extended release APAP product or in patients who have coingested APAP with an agent known to delay gastric emptying. The nomogram also does not take into account patients who may be at higher risk of APAP toxicity (eg,
alcoholics, malnourished patients). Nevertheless, acetylcysteine should be administered to any patient with signs of hepatotoxicity, even if the serum APAP level is low or undetectable. Patients who present >24 hours after an acute ingestion or patients who present following an acute ingestion at an unknown time may be candidates for acetylcysteine therapy; consultation with a poison control center or clinical toxicologist is highly recommended.

- Repeated supratherapeutic ingestion (RSTI) of APAP: Appropriate use: The Rumack-Matthew nomogram is not designed to be used following RSTIs. In general, an accurate past medical history, including a comprehensive APAP ingestion history, in conjunction with AST concentrations and serum APAP levels, may give the clinician insight as to the patient's risk of APAP toxicity. Some experts recommend that acetylcysteine be administered to any patient with "higher than expected" serum APAP levels or serum APAP level >10 mcg/mL, even in the absence of hepatic injury; others recommend treatment for patients with laboratory evidence and/or signs and symptoms of hepatotoxicity (Hendrickson, 2006; Jones, 2000). Consultation with a poison control center or a clinical toxicologist is highly recommended.

**Dosage form specific issues:**

- Inhalation: Since increased bronchial secretions may develop after inhalation, percussion, postural drainage, and suctioning should follow. If bronchospasm occurs, administer a bronchodilator; discontinue acetylcysteine if bronchospasm progresses.

**Adverse Reactions**

- **Inhalation:** Frequency not defined.
- Central nervous system: Drowsiness, chills, fever
- Gastrointestinal: Vomiting, nausea, stomatitis
- Local: Irritation, stickiness on face following nebulization
- Respiratory: Bronchospasm, rhinorrhea, hemoptysis
Acetaminophen (Paracetamol) Overdose

- Miscellaneous: Acquired sensitization (rare), clamminess, unpleasant odor during administration

**Intravenous:**

- >10%: Miscellaneous: Anaphylactoid reaction (8% to 18%; shorter infusion periods [eg, <60 minutes] associated with increased incidence)
- 1% to 10%:
  - Cardiovascular: Flushing (1% to 8%), tachycardia (1% to 4%), edema (1% to 2%)
  - Dermatologic: Urticaria (6% to 8%), rash (2% to 4%), pruritus (1% to 4%)
  - Gastrointestinal: Vomiting (2% to 10%), nausea (1% to 6%)
  - Respiratory: Pharyngitis (?1%), rhinorrhea (?1%), rhonchi (?1%), throat tightness (?1%)
- <1%, postmarketing, and/or case reports (limited to important or life-threatening): Anaphylaxis, bronchospasm, chest tightness, cough, dyspnea, hypotension, respiratory distress, stridor, wheezing

**Drug Interactions**

There are no known significant interactions.

**Storage**

- Solution for injection (Acetadote®): Store unopened vials at room temperature, 20°C to 25°C (68°F to 77°F). Following reconstitution with D5W, solution is stable for 24 hours at room temperature. A color change may occur in opened vials (light purple) and does not affect the safety or efficacy.
- Solution for inhalation: Store unopened vials at room temperature; once opened, store under refrigeration and use within 96 hours. A color change may occur in opened vials (light purple) and does not affect the safety or efficacy.
Reconstitution

- Solution for injection (Acetadote®):
  - Loading dose: Dilute 150 mg/kg in D₅W 200 mL.
  - Second dose: Dilute 50 mg/kg in D₅W 500 mL.
  - Third dose: Dilute 100 mg/kg in D₅W 1000 mL.

Note: To avoid fluid overload in patients <40 kg and those requiring fluid restriction, decrease volume of D₅W proportionally (see table in dosing section). Discard unused portion.

- Solution for inhalation: The 20% solution may be diluted with sodium chloride or sterile water; the 10% solution may be used undiluted.
- Intravenous administration of solution for inhalation (unlabeled route): Using D₅W, dilute acetylcysteine 20% oral solution to a 3% solution.

Compatibility

- Inhalation: Incompatible with rubber and metals (particularly iron, copper, and nickel); do not mix with ampicillin, tetracycline, oxytetracycline, erythromycin.
- Intravenous: Compatible with D₅W, 1/2NS, SWFI. Incompatible with rubber, metals (particularly iron, copper, and nickel), cefepime, and ceftazidime.

Mechanism of Action

Exerts mucolytic action through its free sulphydryl group which opens up the disulfide bonds in the mucoproteins thus lowering mucous viscosity.

In patients with APAP toxicity, acetylcysteine acts as a hepatoprotective agent by restoring hepatic glutathione, serving as a glutathione substitute, and enhancing the nontoxic sulfate conjugation of APAP.
The presumed mechanism in preventing contrast-induced nephropathy is its ability to scavenge oxygen-derived free radicals and improve endothelium-dependent vasodilation.

**Pharmacodynamics/Kinetics**

- Onset of action: Inhalation: 5-10 minutes
- Duration: Inhalation: >1 hour
- Distribution: 0.47 L/kg
- Protein binding: 83%
- Half-life elimination: Reduced acetylcysteine: 2 hours
- Total acetylcysteine: Adults: 5.6 hours; Newborns: 11 hours
- Time to peak, plasma: Oral: 1-2 hours
- Excretion: Urine

**Dosage**

Acetaminophen poisoning: **Note:** Only the 72-hour oral and 21-hour I.V. regimens are FDA-approved. Ideally, in patients with an acute APAP ingestion, treatment should begin within 8 hours of ingestion. In patients who present following RSTI and treatment is deemed appropriate, acetylcysteine should be initiated immediately.

**Children and Adults:**

Oral: **Note:** Consultation with a poison control center or clinical toxicologist is highly recommended when considering the discontinuation of oral acetylcysteine prior to the conclusion of a full 18-dose course of therapy.

- 72-hour regimen: Consists of 18 doses; total dose delivered: 1330 mg/kg
- Loading dose: 140 mg/kg
- Maintenance dose: 70 mg/kg every 4 hours; repeat dose if emesis occurs within 1 hour of administration
I.V. (Acetadote®):

- 21-hour regimen: Consists of 3 doses; total dose delivered: 300 mg/kg
- Loading dose: 150 mg/kg infused over 60 minutes
- Second dose: 50 mg/kg infused over 4 hours
- Third dose: 100 mg/kg infused over 16 hours

**Note:** The fluid volume should be reduced in patients weighing <40 kg according to the following table:

**Acetadote® Dosing / Fluid Volume Guidelines for Patients <40 kg Body Weight (kg)**

<table>
<thead>
<tr>
<th>Loading Dose (mL)</th>
<th>Second Dose (mL)</th>
<th>Third Dose (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>150</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

*Acetadote® (mL) D₃W (mL) Acetadote® (mL) D₃W (mL) Acetadote® (mL) D₃W (mL)*

<table>
<thead>
<tr>
<th>22.5</th>
<th>100</th>
<th>7.5</th>
<th>250</th>
<th>15</th>
<th>500</th>
</tr>
</thead>
<tbody>
<tr>
<td>18.75</td>
<td>100</td>
<td>6.25</td>
<td>250</td>
<td>12.5</td>
<td>500</td>
</tr>
<tr>
<td>140</td>
<td>10</td>
<td>280</td>
<td>15</td>
<td>11.25</td>
<td>45</td>
</tr>
<tr>
<td>3.75</td>
<td>105</td>
<td>7.5</td>
<td>210</td>
<td>10</td>
<td>7.5</td>
</tr>
<tr>
<td>22.5</td>
<td>16</td>
<td>5</td>
<td>20</td>
<td>5</td>
<td>140</td>
</tr>
</tbody>
</table>

Table has been converted to the following text. **Acetadote® Dosing / Fluid Volume Guidelines for Patients <40 kg Body weight 30 kg:** Loading dose (150 mg/kg over 1 hour): Acetadote® 22.5 mL in D₃W 100 mL Second dose (50 mg/kg over 4 hours): Acetadote® 7.5 mL in D₃W 250 mL Third dose (100 mg/kg over 16 hours): Acetadote® 15 mL in D₃W 500 mL Body weight 25 kg: Loading dose (150 mg/kg over 1 hour): Acetadote® 18.75 mL in D₃W 100 mL Second dose (50 mg/kg over 4 hours): Acetadote® 6.25 mL in D₃W 250 mL Third dose (100 mg/kg over 16 hours): Acetadote® 12.5 mL in D₃W 500 mL Body weight 20 kg: Loading dose (150 mg/kg over 1 hour): Acetadote® 15 mL in D₃W 60 mL Second dose (50 mg/kg over 4 hours): Acetadote® 5 mL in D₃W 140 mL Third dose (100 mg/kg over 16 hours): Acetadote® 10 mL in D₃W 280 mL Body weight 15 kg: Loading dose (150 mg/kg over 1 hour): Acetadote® 11.25 mL in D₃W 45 mL Second dose (50 mg/kg over 4 hours): Acetadote® 3.75 mL in D₃W 105 mL Third dose (100 mg/kg over 16 hours): Acetadote® 7.5 mL in D₃W 210 mL Body weight 10 kg: Loading dose (150 mg/kg over 1 hour): Acetadote® 7.5 mL in D₃W 30 mL Second dose (50 mg/kg over 4 hours): Acetadote® 2.5 mL in D₃W 70 mL Third dose (100 mg/kg over 16 hours): Acetadote® 5 mL in D₃W 140 mL

**Adjuvant therapy in respiratory conditions:** **Note:** Patients should receive an aerosolized bronchodilator 10-15 minutes prior to acetylcysteine.
Acetaminophen (Paracetamol) Overdose

Inhalation, nebulization (face mask, mouth piece, tracheostomy): Acetylcysteine 10% and 20% solution (dilute 20% solution with sodium chloride or sterile water for inhalation); 10% solution may be used undiluted

Infants: 1-2 mL of 20% solution or 2-4 mL of 10% solution until nebulized given 3-4 times/day

Children and Adults: 3-5 mL of 20% solution or 6-10 mL of 10% solution until nebulized given 3-4 times/day; dosing range: 1-10 mL of 20% solution or 2-20 mL of 10% solution every 2-6 hours

Inhalation, nebulization (tent, croupette): Children and Adults: Dose must be individualized; may require up to 300 mL solution/treatment

Direct instillation: Adults:

Into tracheostomy: 1-2 mL of 10% to 20% solution every 1-4 hours

Through percutaneous intratracheal catheter: 1-2 mL of 20% or 2-4 mL of 10% solution every 1-4 hours via syringe attached to catheter

Diagnostic bronchogram: Nebulization or intratracheal: Adults: 1-2 mL of 20% solution or 2-4 mL of 10% solution administered 2-3 times prior to procedure

Prevention of contrast-induced nephropathy (CIN) (unlabeled use): Adults: Oral: 600-1200 mg twice daily for 2 days (beginning the day before the procedure); may be given as powder in capsules (some centers use solution, diluted in cola beverage or juice)

Prevention of CIN in acute MI patients requiring emergent cardiac catheterization (unlabeled use): Adults: I.V.: 1200 mg over 5-10 minutes prior to cardiac catheterization, followed by 1200 mg orally twice daily for 48 hours

**Administration: Oral**
Acetaminophen (Paracetamol) Overdose

Treatment of APAP poisoning, administer orally as a 5% solution. Dilute the 20% solution 1:3 with a cola, orange juice, or other soft drink. Use within 1 hour of preparation. Unpleasant odor becomes less noticeable as treatment progresses. If patient vomits within 1 hour of dose, readminister. (Note: It is helpful to put acetylcysteine on ice, in a cup with a cover, and drink through a straw; alternatively, administer via an NG tube).

Administration: I.V.

Acetadote®:

Acetaminophen poisoning:

- Loading dose: Dilute in D₅W 200 mL; administer over 60 minutes.
- Second dose: Dilute in D₅W 500 mL; administer over 4 hours.
- Third dose: Dilute in D₅W 1000 mL; administer over 16 hours.

Note: To avoid fluid overload in patients <40 kg and those requiring fluid restriction, decrease volume of D₅W proportionally (see table in dosing section). Discard unused portion.

If the commercial I.V. form is unavailable, the solution for inhalation has been used; each dose should be infused through a 0.2 micron Millipore filter (in-line) over 60 minutes (Yip, 1998); intravenous administration of the solution for inhalation is not USP 797-compliant.

Prevention of CIN in acute MI patients requiring emergent cardiac catheterization (unlabeled use): Administer 1200 mg I.V. push over 5-10 minutes prior to contrast administration.

Administration: Inhalation

Acetylcysteine is incompatible with tetracyclines, erythromycin, amphotericin B, iodized oil, chymotrypsin, trypsin, and hydrogen peroxide. Administer separately.
Intermittent aerosol treatments are commonly given when patient arises, before meals, and just before retiring at bedtime.

**Monitoring Parameters**

Acetaminophen poisoning: Monitor patient for the development of anaphylaxis or anaphylactoid reactions; monitor serum APAP levels, AST, ALT, bilirubin, PT, INR, serum creatinine, BUN, serum glucose, hemoglobin, hematocrit, and electrolytes. Assess patient for nausea, vomiting, and skin rash following oral administration. Reassess LFTs for possible hepatotoxicity every 4-6 hours.

Acute ingestion: Obtain the first APAP level 4 hours postingestion (or as soon as possible thereafter); plot on the Rumack-Matthew nomogram. In patients who have ingested an extended release formulation of APAP or have coingested an agent known to delay gastric emptying, obtain a repeat serum APAP measurement 4-6 hours following the first measurement if the original level (taken at 4-8 hours postingestion) when plotted on the Rumack-Matthew nomogram indicated that treatment was not necessary.

**Patient Education**

Pulmonary treatment: Prepare solution (may dilute with sterile water to reduce concentrate from impeding nebulizer) and use as directed. Clear airway by coughing deeply before using aerosol. Wash face and face mask after treatment to remove any residual. You may experience drowsiness (use caution when driving or engaging in tasks requiring alertness), nausea, or vomiting (small, frequent meals may help). Report persistent chills or fever, adverse change in respiratory status, palpitations, or extreme anxiety or nervousness. **Breast-feeding precaution:** Inform prescriber if you are breast-feeding.

**Anesthesia and Critical Care Concerns/Other Considerations**

Clinical Pearls/Comments: Intravenous acetylcysteine may be indicated over oral formulation in treatment of acetaminophen overdose for a restricted number of indications (oral cannot be tolerated, coingested toxin requires ongoing gastrointestinal decontamination, gastrointestinal tract nonfunctional, late
presentation of acetaminophen overdose, neonatal toxicity from maternal overdose) (Yip, 1998). A commercially manufactured intravenous product is now available in the United States. If this formulation is unavailable, the product normally administered by inhalation can be administered intravenously. The inhalation preparation is sterile, but not labeled “pyrogen free.”

Evidence-Based Information:

**Adverse events related to administration:** A retrospective case series was performed to determine adverse events associated with intravenous acetylcysteine. Adverse reactions occurred in four (~5%) cases. Flushing, pruritus, and phlebitis were reported; one was labeled as an “anaphylactic” reaction (Yip, 1998).

Another retrospective case series evaluated patients who received intravenous acetylcysteine and the literature to develop management guideline for anaphylactoid reactions (Bailey, 1998). Their recommendations for treatment of nonlife-threatening allergic reactions include administering diphenhydramine (1 mg/kg I.V.; maximum dose: 50 mg) and reassessing the need for intravenous acetylcysteine. If the acetylcysteine infusion was stopped initially and symptoms resolved, consider restarting infusion 1 hour after diphenhydramine's administration. Anaphylactoid reactions have also been reported with the commercial I.V. formulation. Monitor closely for allergic reactions. Be prepared to handle anaphylactoid reaction if it occurs.

**Cardiovascular Considerations**

**Contrast-Induced Nephropathy (CIN): Oral:** Although study results vary, acetylcysteine may be beneficial in prevention of CIN in patients undergoing cardiac catheterization (Curhan, 2003). Tepel (2000) and his group originally randomized 83 patients with chronic renal insufficiency to oral acetylcysteine (600 mg twice daily) and intravenous saline 0.45% or placebo and intravenous saline 0.45%. All patients were having a CT scan with iopromide contrast. Patients receiving acetylcysteine had a significant reduction in serum creatinine 48 hours after the procedure. Conversely, patients in the placebo arm had significant increase in serum creatinine.
A recent randomized, placebo-controlled trial in 200 Chinese patients with stable mild-to-moderate renal insufficiency also evaluated acetylcysteine in prevention of CIN (Kay, 2003). Patients were undergoing elective coronary angiography and/or intervention, and had serum creatinine concentrations >1.2 mg/dL or Clcr <60 mL/minute (estimated and measured). A low-osmolality nonionic contrast agent was used. All patients received saline 0.9% I.V. at 1 mL/kg/hour for 12 hours before and for 6 hours after contrast exposure. Three doses of acetylcysteine (600 mg twice daily) or matching placebo were given before and one dose after dye exposure. Contrast nephropathy developed more frequently in the control group (12%) than in the acetylcysteine group (4%). The average length of hospitalization was 0.5 days shorter in the acetylcysteine group. No adverse events related to acetylcysteine were reported.

However, these results differed from those in another prospective, randomized trial (Allaqaband, 2002) that compared the efficacy of acetylcysteine (600 mg twice daily for 48 hours) plus saline 0.45% versus fenoldopam (0.1 mcg/kg/minute) plus saline 0.45% versus saline 0.45% alone (at 1 mL/kg/hour for 12 hours before procedure, during procedure, and 12 hours afterwards) in preventing CIN. Patients were high-risk (serum creatinine >1.6 mg/dL or Clcr <60 mL/minute) and undergoing cardiovascular procedures using low-osmolality nonionic contrast. Authors concluded that there was no benefit in either oral acetylcysteine or fenoldopam over saline in preventing CIN.

Marenzi, et al (2006) showed that acetylcysteine’s effect may be dose dependent. Patients with acute MI requiring emergent cardiac catheterization for possible PCI received either high dose acetylcysteine (1200 mg I.V. bolus followed by 1200 mg administered orally twice daily for 48 hours), a low dose regimen (600 mg I.V. bolus followed by 600 mg administered orally twice daily for 48 hours) or placebo. The group that received the high dose regimen developed CIN (defined as an increase in serum creatinine concentration of >25% from baseline within 72 hour) less often than the low dose group (p<0.001). All patients received saline 0.9% NaCl at 1 mL/kg/hour (0.5 mL/kg/hour for cases of overt heart failure) for 12 hours.

Briguori, et al (2007) evaluated three prophylactic regimens (normal saline and acetylcysteine (NAC); sodium bicarbonate and NAC; normal saline, ascorbic acid and NAC) in 326 patients with chronic kidney disease (serum creatinine >2 mg/dL)
undergoing coronary and/or peripheral procedures with iodixanol. Saline was given I.V. at 1 mL/kg/hour (0.5 mL/kg/hour for LVEF <40%) for 12 hours before and 12 hours after contrast administration. Sodium bicarbonate administration was similar to that in the Merten trial. The oral NAC dose was 1200 mg twice daily given the day before and the day of contrast administration (4 doses total). The ascorbic acid dose was given I.V. as 3 g 2 hours before the procedure followed by 2 g the night of and the morning after the procedure. The amount of contrast administered and the contrast nephropathy risk scores were similar in each group. Contrast induced nephropathy (CIN) occurred in 9.9% (11/111 of patients) of saline/NAC group, 2% (2/108 of patients) of bicarbonate/NAC group and 10.3% (11/107 of patients) in saline/NAC/ascorbic acid group. The bicarbonate/NAC group had significantly fewer episodes of CIN when compared to saline/NAC group in this patient population.

Parameters used to define CIN varied among studies.

**Contrast-Induced Nephropathy (CIN): I.V.:** Several studies have evaluated intravenous acetylcysteine in the prevention of CIN. Three different dosing regimens were used. The initial study (Baker, 2003) randomized patients with stable renal function undergoing cardiac catheterization to intravenous acetylcysteine 150 mg/kg over 30 minutes followed by 50 mg/kg over 4 hours or placebo. The study was stopped when an interim analysis indicated borderline statistical significance (p=0.045). Hydration volumes were different between the groups as well. The mean serum creatinine level in the active treatment group was lower after administration when compared to baseline. Acetylcysteine may have a direct affect on creatinine levels.

Another trial (Webb, 2004) studied 500 mg of intravenous acetylcysteine administered immediately before cardiac catheterization. No significant difference was seen between acetylcysteine and placebo.

Rashid (2004) randomized patients with peripheral vascular disease to 1 g acetylcysteine in 500 mL of normal saline 6-12 hours before and after the procedure. No significant differences were seen in renal function.

Marenzi, et al (2006) evaluated the use of an initial I.V. push dose (high and low dose) of acetylcysteine prior to cardiac catheterization in acute MI patients followed
by an oral regimen (high and low dose) compared to placebo. This trial is described above.

**Note:** Itching, flushing, and rash, as well as more serious allergic reactions, may occur with intravenous acetylcysteine.

**Dental Health: Effects on Dental Treatment**

Key adverse event(s) related to dental treatment: Stomatitis, drowsiness, fever, vomiting, nausea, bronchospasm, rhinorrhea, hemoptysis, and dizziness

**Dental Health: Vasoconstrictor/Local Anesthetic Precautions**

No information available to require special precautions

**Mental Health: Effects on Mental Status**

May cause drowsiness

**Mental Health: Effects on Psychiatric Treatment**

Sedative effects may be potentiated by psychotropic agents

**Nursing: Physical Assessment/Monitoring**

Instruct patient on appropriate use, adverse effects to report, and interventions to reduce side effects. Monitor pulmonary function and response to therapy. If giving I.V., monitor for possible anaphylactoid reactions and be prepared to treat appropriately if needed.

**Dosage Forms**

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.
Acetaminophen (Paracetamol) Overdose

Acetadote®: 20% (30 mL) [200 mg/mL; contains disodium edetate]

Solution, inhalation/oral: 10% (4 mL, 10 mL, 30 mL) [100 mg/mL]; 20% (4 mL, 10 mL, 30 mL) [200 mg/mL]