Disclosures

- Nothing to disclose

Learning Objectives for Pharmacists

- Describe general principles of intranasal drug delivery using the MAD device
- Discuss indications and literature to support intranasal administration of medications using the MAD device
- Explain administration techniques for intranasal administration of medication using the MAD device
- Review example protocols for the administration of intranasal medications using the MAD device

Learning Objectives for Technicians

- Review the advantages of intranasal medication administration with the MAD device
- Identify medications that are commonly administered via the intranasal route using the MAD device
- Discuss clinical pearls for administering medications using the MAD device

Patient Case Scenarios

<table>
<thead>
<tr>
<th>Patient</th>
<th>Scenario</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 year old male in severe pain</td>
<td>Presents to ED with obvious left arm deformity, Patient is screaming, Will not let the RN touch him to start an IV</td>
</tr>
<tr>
<td>3 year old female with h/o seizure</td>
<td>EMS called for grand mal seizure, duration 10 minutes, Unable to establish IV access</td>
</tr>
<tr>
<td>40 year old unconscious male</td>
<td>Presents to ED with slow respirations, pinpoint pupils, cool dusky skin with obvious track marks bilaterally, Unable to establish IV access</td>
</tr>
</tbody>
</table>

Routes of Medication Administration

- Intravenous
- Oral
- Intramuscular
- Subcutaneous
- Topical
- Rectal

Intranasal
Advantages of IN administration

- Easy, convenient
- Non-invasive
- Needleless
- Painless
- Favorable tolerability profile
- Rapid onset of clinical effect

IN Drug Absorption

- Physiological factors of nasal mucosa
- Properties of formulation
- Drug characteristics

Nasal Cavity: Why IN delivery?

- Respiratory region
  - Large mucosal surface area
  - Rich vascular bed of highly permeable capillaries
- Olfactory region
  - "Nose-brain pathway"
- Avoids 1st pass metabolism

Drug and Formulation Characteristics

- Lipophilic
- Low molecular weight
- pH
- Concentration
- Volume

Delivery Characteristics

- Nasal mucosal
  - Use of vasoconstrictors
  - Bloody nose, nasal congestion, mucous discharge
  - Destruction of nasal mucosa
- Delivery system
  - Large surface area = higher bioavailability
  - Atomized devices

Mucosal Atomization Device (MAD)

**LMA® MAD NASAL™ Device Specifications**

<table>
<thead>
<tr>
<th>Specification</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical Particle Size</td>
<td>30-100 microns</td>
</tr>
<tr>
<td>System Dead Space</td>
<td>0.13 mL MAD100 and MAD140, 0.07 mL MAD300</td>
</tr>
<tr>
<td><em>round to 0.1 mL for clinical purposes and accuracy of dosing</em></td>
<td></td>
</tr>
<tr>
<td>Tip Diameter</td>
<td>0.17 inches (4.3 mm)</td>
</tr>
<tr>
<td>Applicator Length (MAD300)</td>
<td>1.65 inches (4.2 cm)</td>
</tr>
</tbody>
</table>

*www.lmana.com LMA MAD NASAL Accessed March 31, 2015*
Places in Therapy

- Acute pain
- Seizures
- Opioid reversal
- Sedation
- Hypoglycemia
- Epistaxis

IN Fentanyl Drug Characteristics

- Opioid analgesic
- Lipophilic
- Potent
- Rapidly absorbed through nasal mucosa
- Bioavailability: 55-89%
  - Peak effect: ~6-10 minutes
  - Short acting: 30-60 minutes

IN Fentanyl Concentrations

- Objectives
- Compare IN fentanyl vs. IV morphine for treatment of pediatric orthopedic fractures

- Methods
- Randomized, double blind, placebo controlled trial
- Pediatric patients aged 7-15 years with clinically deformed closed long-bone fracture
- IV morphine or IN fentanyl

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Initial dose IN fentanyl</th>
<th>Initial dose IV morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-30</td>
<td>30 mcg</td>
<td>2 mg</td>
</tr>
<tr>
<td>31-40</td>
<td>45 mcg</td>
<td>3 mg</td>
</tr>
<tr>
<td>41-50</td>
<td>60 mcg</td>
<td>4 mg</td>
</tr>
</tbody>
</table>

- Pain scores rated with 100-mm visual analog scale at 0, 5, 10, 20, and 30 minutes


- Mean Doses: IN fentanyl 1.7 mcg/kg  IV morphine: 0.11 mg/kg

Pain Scales

- Verbal Pain Intensity Scale
- Visual Analogue Scale
- 0-10 Numeric Pain Intensity Scale
- “FACES” Scale


- Mean pain scores (by visual analog scale) over time

- n=34 subjects IV morphine
- n=33 subjects IN fentanyl

• Results
  ◦ No difference in pain scores for IV morphine and IN fentanyl at all time points
  ◦ No serious adverse effects

• Conclusions
  ◦ IN fentanyl is effective as IV morphine for treating pain associated with long bone fractures

Borland, et al 2008

• Objectives
  ◦ Compare time to analgesia with IN fentanyl and IV morphine
  ◦ Rate of IV access for analgesia alone

• Methods
  ◦ Retrospective chart review
  ◦ Tertiary pediatric ED after implementation of IN fentanyl protocol

Additional Studies for IN Fentanyl

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient Population</th>
<th>Intervention</th>
<th>Results/Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rickard, et al 2007</td>
<td>Prehospital analgesia</td>
<td>IN fentanyl 180 mcg vs. IV morphine 2.5-5mg</td>
<td>n=227</td>
</tr>
<tr>
<td></td>
<td>Adult patients aged 18-65 years presenting with severe pain</td>
<td>Primary outcome: change in pain score using verbal rating 10-point scale</td>
<td>No statistically significant difference between IN fentanyl and IV morphine from baseline to destination</td>
</tr>
<tr>
<td>Finn, et al 2010</td>
<td>Pediatric ED patients aged 1-16 years presenting with severe pain</td>
<td>IN fentanyl 1.5 mcg/kg</td>
<td>n=81</td>
</tr>
<tr>
<td></td>
<td>IN fentanyl 1.5 mcg/kg</td>
<td>Primary outcome: change in pain score using 100-mm visual analog scale</td>
<td>IN fentanyl resulted in substantial reductions in pain scores</td>
</tr>
<tr>
<td>Saunders, et al 2010</td>
<td>Pediatric ED patients aged 3-18 years presenting with painful orthopedic injuries</td>
<td>IN fentanyl 2 mcg/kg single dose</td>
<td>n=81</td>
</tr>
<tr>
<td></td>
<td>IN fentanyl 2 mcg/kg single dose</td>
<td>Primary outcome: change in pain score using 100-mm/visual analog scale or Wong Baker Faces Scale</td>
<td>IN fentanyl resulted in a statistically significant reduction in pain scales</td>
</tr>
</tbody>
</table>

IN Fentanyl for Pain Management

**Systematic Review**

3 important points:
- IN fentanyl is as efficacious as IV/IM/PO morphine or IV fentanyl
- No difference in adverse effects
- Decreases time to analgesia administration and pain relief

Seizure Control

• 15% of all pediatric EMS calls in the US
• Prolonged or recurrent seizure activity can cause significant morbidity and mortality

1st line treatment:
- IV lorazepam

Alternatives:
- PR or IV diazepam
- IM or IN midazolam
IN Midazolam Drug Characteristics

• Quick acting benzodiazepine
• Water soluble
  ◦ Lipophilic at physiologically pH allowing it to cross nose-brain barrier
• pH 3.5
• Bioavailability: 50-83%
  ◦ Rapid onset: peak effect ~10 minutes
  ◦ Short acting: 30-60 minutes

IN Midazolam Concentrations

Fisgin, et al 2002

• Objective
  ◦ Compared safety and efficacy of IN midazolam vs. PR diazepam

• Methods
  ◦ Odd days: diazepam PR 0.3 mg/kg
  ◦ Even days: midazolam IN 0.2 mg/kg
  ◦ HR, RR, BP obtained at 5, 10 minutes after drug administration
  ◦ ED physician categorized seizure

Results (n=45)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PR Diazepam n(%)</th>
<th>IN midazolam n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>11 (50)</td>
<td>15 (65.2)</td>
</tr>
<tr>
<td>Male</td>
<td>11 (50)</td>
<td>8 (34.8)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-24 months</td>
<td>16 (72.7)</td>
<td>12 (52.1)</td>
</tr>
<tr>
<td>25 months-7 years</td>
<td>4 (18.1)</td>
<td>7 (30.4)</td>
</tr>
<tr>
<td>&gt; 7 years</td>
<td>2 (9)</td>
<td>4 (17.3)</td>
</tr>
<tr>
<td>Fever</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Febrile</td>
<td>5 (22.7)</td>
<td>5 (21.7)</td>
</tr>
<tr>
<td>Non-febrile</td>
<td>17 (77.3)</td>
<td>18 (78.3)</td>
</tr>
</tbody>
</table>

• IN midazolam effective in 87% of seizures
• PR diazepam 60%

Fisgin, et al 2002

• Conclusions
  ◦ IN midazolam is more effective for controlling seizures than PR diazepam
  ◦ IN midazolam will be “very useful” in the emergency setting

Holsti, et al 2007

• Objective
  ◦ Compare IN midazolam vs. PR diazepam for treatment of pediatric seizure in EMS setting

• Methods
  ◦ Retrospective review
  ◦ Patients < 18 years old, had a seizure in the presence of an EMS provider, received PR diazepam or IN midazolam in the pre-hospital setting
**Holsti, et al 2007**

<table>
<thead>
<tr>
<th>IN Midazolam</th>
<th>PR Diazepam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preparation</td>
<td>Apply oxygen; suction nose if there are secretions</td>
</tr>
<tr>
<td>Indication</td>
<td>Seizure &gt; 5 minutes</td>
</tr>
<tr>
<td>Dose</td>
<td>0.2 mg/kg</td>
</tr>
<tr>
<td>Maximum dose</td>
<td>10 mg</td>
</tr>
<tr>
<td>Repeat dose</td>
<td>0.2 mg/kg, 5 minutes after 1st dose</td>
</tr>
</tbody>
</table>

**Indication**
- Seizure > 5 minutes
- Dose: 0.2 mg/kg
- Route: IN; divided into each nare using MAD®

**Maximum dose**
- IN midazolam: 10 mg
- PR diazepam: 20 mg

**Repeat dose**
- IN midazolam: 0.25 mg/kg if seizure persists
- PR diazepam: 0.3-0.5 mg/kg

**Results:**
- 39 patients in IN midazolam group vs. 18 in PR diazepam
- IN midazolam: 19 minutes less seizure activity
  - 11 minutes vs. 30 minutes
- PR diazepam: more likely to...
  - Re-seize (OR 8.4)
  - Need intubation (OR 12.2)
  - Require hospitalization (OR 29.3)
  - Require ICU admission (OR 53.5)

**Conclusions:**
- IN midazolam controlled seizures better than PR diazepam in the prehospital setting and resulted in fewer complications

**Additional Studies for IN Midazolam**

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient Population</th>
<th>Intervention</th>
<th>Results/Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lahat, et al 2000</td>
<td>Pediatric patients aged 6 months to 5 years with prolonged (at least 10 minutes) febrile seizures</td>
<td>IN midazolam (0.2 mg/kg) vs. IV diazepam (0.3 mg/kg)</td>
<td>n=53 patients; IN midazolam effective in 88.5% vs. 92.3% in IV diazepam group; Overall time from arrival to cessation of seizures was shorter with IN midazolam (6.1 min vs. 8 min; p&lt;0.1)</td>
</tr>
<tr>
<td>Bhattacharyya, et al 2006</td>
<td>Pediatric patients aged 3 months to 12 years presenting with a seizure to ED</td>
<td>IN midazolam (0.2 mg/kg) vs. PR diazepam (0.3 mg/kg)</td>
<td>n=46 patients (188 episodes); 96.7% of seizures were controlled with IN midazolam at 10 minutes compared to 89.5% with PR diazepam</td>
</tr>
<tr>
<td>Harbord, et al 2004</td>
<td>Pediatric patients aged 4-18 years with at least 1 generalized tonic-clonic seizures in community settings</td>
<td>IN midazolam (0.2-0.3 mg/kg)</td>
<td>n=122 patients (45 episodes); 89% of seizures controlled with IN midazolam; 90% of caregivers reported no difficulty in administering</td>
</tr>
</tbody>
</table>

**IN Midazolam Considerations**

- **Home use**
  - Education for caregivers
  - Better social acceptance

- **Cost**
  - Rectal diazepam 20 mg: brand $289.59/pack and generic $232.09/pack
  - Midazolam (5 mg/ml): $0.86 per vial
  - MAD®300 Nasal Mucosal Atomization device: $2.98 per atomizer

**IN Naloxone**

- **Opioid Antagonist**

- **Pharmacokinetic studies:**
  - Human data lacking
  - Animal studies:
    - 100% bioavailability in rats
    - Onset of action: 3 minutes

**Drug Overdose**

- Drug overdose was the leading cause of injury death in the United States in 2012
- 43,982 deaths reported in 2013
  - Approximately half of those deaths were related to prescription medications
  - Majority involved opioid analgesics
  - Also observed an increase in heroin overdoses

**IN Naloxone**

- **Opioid Antagonist**

- **Pharmacokinetic studies:**
  - Human data lacking
  - Animal studies:
    - 100% bioavailability in rats
    - Onset of action: 3 minutes
Barton, et al 2002

- **Objective**
  - Assess effectiveness and safety of IN naloxone administered by EMS providers for possible opioid overdoses

- **Methods**
  - All patients aged 14 and older
  - Diagnosis of "altered mental status," "found down," or "suspected opioid overdose"
  - 2 mg IN naloxone
  - IV naloxone used for rescue

**Results**
- 52 patients included in study
- 43 patients defined as IN naloxone responder
- Median time to response was 3 minutes following IN administration
- 9 patients reported to only respond to IV naloxone

**Conclusion**
- Potential use of IN naloxone in EMS practice

Kelly, et al 2005

- **Objective**
  - Determine the effectiveness of IN naloxone vs. IM naloxone for treatment of respiratory depression due to suspected opiate overdose in the prehospital setting

- **Methods**
  - Prospective, randomized, unblinded study of suspected overdose patients
  - 2 mg IN naloxone or 2 mg IM naloxone
  - Primary outcome: response time to regain a respiratory rate > 10 breaths/minute

**Results**
- 155 patients (81 IN naloxone; 71 IV naloxone)
- IM group more likely to have > 10 spontaneous breaths/min compared to the IN group (82% vs. 63%, p=0.017)
- No statistically significant difference between needing rescue naloxone (13% in IM vs. 26% in IN, p=0.06)

**Conclusions**
- IN naloxone is effective in treating opiate-induced respiratory depression, but not as effective as IM naloxone
- IN delivery of naloxone reduce risk of needlestick injury to EMS providers

****Take Home Naloxone Programs****

- **Saved by the Nose: Bystander-Administered Intranasal Naloxone Hydrochloride for Opioid Overdose**
  - Mayra Deo-Simkina, MPN, Alexander Y. Marks, MD, MS, Andy Epstein, RN, MPH, and Peter Meyer, MD, MPH

Patient Case Scenarios

- **10 year old male in severe pain**
  - Presents to ED with obvious left arm deformity
  - Patient is screaming
  - Will not let the RN touch him

- **3 year old female with h/o seizure**
  - EMS called for grand mal seizure, duration 15 minutes
  - Unable to establish IV access

- **40 year old unconscious male**
  - Presents to ED with slow respirations, pinpoint pupils, cool dusky skin with obvious track marks bilaterally
  - Unable to establish IV access
Example IN Fentanyl Protocol

• Indications:
  ▫ Adult and pediatric minor painful injuries or procedures
  ▫ Orthopedic trauma not requiring an IV (or prior to starting an IV)
  ▫ Burn dressing changes
  ▫ Re-packing wounds such as abscesses
  ▫ Any time an IM shot for pain control is considered

• Dose:
  ▫ IN Fentanyl: 2-3 mcg/kg
  ▫ May repeat half the initial dose at ~10 minutes intervals until desired effect is achieved

IN Fentanyl Dosing Table

<table>
<thead>
<tr>
<th>Patient Weight (kg)</th>
<th>Fentanyl dose (2 mcg/kg)</th>
<th>Fentanyl volume (dose + dead space)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-5 kg</td>
<td>10 mcg</td>
<td>0.3 ml (0.2 ml + 0.1 ml)</td>
</tr>
<tr>
<td>6-10 kg</td>
<td>20 mcg</td>
<td>0.5 ml (0.4 ml + 0.1 ml)</td>
</tr>
<tr>
<td>11-15 kg</td>
<td>30 mcg</td>
<td>0.7 ml (0.6 ml + 0.1 ml)</td>
</tr>
<tr>
<td>16-20 kg</td>
<td>40 mcg</td>
<td>0.9 ml (0.8 ml + 0.1 ml)</td>
</tr>
<tr>
<td>21-25 kg</td>
<td>50 mcg</td>
<td>1.1 ml (1 ml + 0.1 ml)</td>
</tr>
<tr>
<td>26-30 kg</td>
<td>60 mcg</td>
<td>1.3 ml (1.2 ml + 0.1 ml)</td>
</tr>
<tr>
<td>31-35 kg</td>
<td>70 mcg</td>
<td>1.5 ml (1.4 ml + 0.1 ml)</td>
</tr>
<tr>
<td>36-40 kg</td>
<td>80 mcg</td>
<td>1.7 ml (1.6 ml + 0.1 ml)</td>
</tr>
<tr>
<td>41-45 kg</td>
<td>90 mcg</td>
<td>1.9 ml (1.8 ml + 0.1 ml)</td>
</tr>
<tr>
<td>46-50 kg</td>
<td>100 mcg</td>
<td>2.1 ml (2 ml + 0.1 ml)</td>
</tr>
<tr>
<td>51-55 kg</td>
<td>110 mcg</td>
<td>2.3 ml* (2.2 ml + 0.1 ml)</td>
</tr>
</tbody>
</table>

*Volumes in this range should be divided in half and administered 10 minutes apart

IN Fentanyl Administration

• Materials Needed:
  ▫ 1 ml or 3 ml syringe*
  ▫ Blunt and/or filter needle to draw up medication
  ▫ Mucosal atomization device
  ▫ Medication of appropriate concentration

• Aspirate the proper dose/volume of medication (Remember to account for dead space)

*exception: naloxone (use prefilled 2mg/2ml syringe)

IN Fentanyl Administration

• Attach atomizer tip via Luer lock mechanism and twist into place
• Use the free hand to hold the crown of the head stable, place the tip of the atomizer snugly against the nostril aiming slightly up and outward
• Briskly compress the syringe plunger to deliver half of the medication into the nostril
• Move to other nostril and repeat

Patient Case Scenarios

10 year old male in severe pain
  ▪ Presents to ED with obvious left arm deformity
  ▪ Patient is screaming
  ▪ Will not let the RN touch him

3 year old female with h/o seizure
  ▪ EMS called for grand mal seizure, duration 15 minutes
  ▪ Unable to establish IV access

40 year old unconscious male
  ▪ Presents to ED with slow respirations, pinpoint pupils, cool dusky skin with obvious track marks bilaterally
  ▪ Unable to establish IV access

Example IN Midazolam Protocol

• Indication:
  ▪ Treatment of seizures when IV access is unavailable

• Dose
  ▫ IN midazolam: 0.2 mg/kg
  ▫ Use table to determine proper volume
  ▫ Concentration: 5 mg/ml
  ▫ If seizures persist after treating:
    ▪ Consider repeating ½ dose of midazolam either intranasally, intramuscularly or intravenously
    ▪ Secure airway if necessary
### IN Midazolam Dosing Table

**Midazolam concentration 5 mg/ml**

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Midazolam dose (~0.2 mg/kg)</th>
<th>Midazolam volume (dose + dead space)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-5 kg</td>
<td>1 mg</td>
<td>0.3 ml (0.2 ml + 0.1 ml)</td>
</tr>
<tr>
<td>6-10 kg</td>
<td>2 mg</td>
<td>0.5 ml (0.4 ml + 0.1 ml)</td>
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<td>21-25 kg</td>
<td>5 mg</td>
<td>1.1 ml (1 ml + 0.1 ml)</td>
</tr>
<tr>
<td>26-30 kg</td>
<td>6 mg</td>
<td>1.3 ml (1.2 ml + 0.1 ml)</td>
</tr>
<tr>
<td>31-35 kg</td>
<td>7 mg</td>
<td>1.5 ml (1.4 ml + 0.1 ml)</td>
</tr>
<tr>
<td>36-40 kg</td>
<td>8 mg</td>
<td>1.7 ml (1.6 ml + 0.1 ml)</td>
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<td>41-45 kg</td>
<td>9 mg</td>
<td>1.9 ml (1.8 ml + 0.1 ml)</td>
</tr>
<tr>
<td>46-50 kg</td>
<td>10 mg</td>
<td>2.1 ml (2 ml + 0.1 ml)</td>
</tr>
<tr>
<td>&gt; 50 kg</td>
<td>10 mg</td>
<td>2.1 ml (2 ml + 0.1 ml)</td>
</tr>
</tbody>
</table>

### Patient Case Scenarios

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  - Presents to ED with obvious left arm deformity
  - Patient is screaming
  - Will not let the RN touch him

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  - EMS called for grand mal seizure, duration 15 minutes
  - Unable to establish IV access

- **40 year old unconscious male**
  - Presents to ED with slow respirations, pinpoint pupils, cool dusky skin with obvious track marks bilaterally
  - Unable to establish IV access

### Example IN Naloxone Protocol

- **Indication**
  - Suspected opiate overdose when IV access is unavailable

- **Dose**
  - IN naloxone: 2mg
  - Concentration: 2mg/2ml
  - If no arousal occurs after 5 minutes, consider repeat dose of IV or IN naloxone
  - Secure airway if necessary

### Clinical Pearls

- Minimize volume and maximize concentration
  - Ideal volume: 1/3 to 1/4 ml per nostril
  - Maximum volume: 1 ml per nostril
  - Use concentrated formulations when available

- Maximize total mucosal absorptive surface area
  - Use both nostrils to double the absorptive area
  - Atomize the medication (rather than drip it in) to increase surface area

- Beware of abnormal mucosal characteristics
  - Mucous, blood and vasoconstrictors reduce absorption
  - Suction nostrils or consider alternate drug deliver method in these situations

### Additional medications...

- IN dexmedetomidine
- IN ketoralac
- IN glucagon
- IN ketamine
- IN lidocaine
- IN sufentanil

### Summary

- IN drug delivery is convenient and easy
- Can provide an alternative for rapid drug administration
- Be aware of the limitations and characteristics needed for optimal absorption
- Education and protocols are important to ensure appropriate administration
- Nasal drug delivery cannot completely replace the need for injections
- Additional studies are needed
What concentration of midazolam should be used for IN administration?

A. 1 mg/mL  
B. 2 mg/mL  
C. 5 mg/mL

A 4 yo male with an obvious left distal arm deformity. Patient is in severe pain with no IV access. The patient is screaming and crying with thick mucous coming out of his nose. Is this patient an appropriate candidate for IN fentanyl?

A. No, just take the patient to X-ray without any medication  
B. No, the patient has thick mucous that will prevent absorption  
C. Yes, if the patient’s nasal cavity is cleared by suction before administration  
D. Yes, the patient has no IV access and mucous does not affect absorption

What extra volume must be drawn up to account for dead space in the MAD 300 device?

A. 0.1 mL  
B. 0.3 mL  
C. 0.5 mL  
D. 1 mL

• Slides: 48, 49

• Slides: 11, 52

What extra volume must be drawn up to account for dead space in the MAD 300 device?

A. 0.1 mL  
B. 0.3 mL  
C. 0.5 mL  
D. 1 mL

• Slides: 12, 44