A close-up photograph of a human nose, showing the nostrils and the bridge of the nose. The skin is a light, natural tone. The text is overlaid on the image.

Up the Nose-Intranasal Medication Administration

Blake Byrd, Nationally Registered
Paramedic & Melissa M. Doak,
Nationally Registered Paramedic

Disclosure

- Melissa is a paid contracted employee of Teleflex Corporation
- Teleflex is the marketer of the device
- I receive no financial incentives for teaching today's class

Disclaimer

- As always, just because you learned it here in class, does not mean you should go back to your agency and perform the skill
- You must ALWAYS operate under the direction of your own Operational Medical Director & under the authority and permission of your own EMS agency
- Always follow your local medical protocols

Objectives

- Cover brief A & P of nose
- Cover how to use IN devices (intranasal delivery devices)
- What are common meds used for IN delivery in EMS-Pharmacology Section
- Tips & Tricks
- Where IN is headed in medicine
- Perform the skill in class

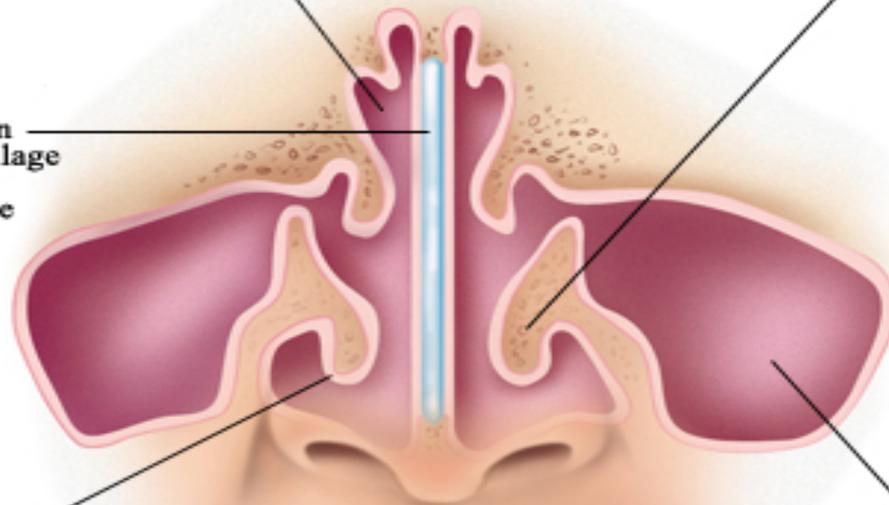


A & P of the Nose

The nasal cavity is a hollow space behind the nose that air flows through.

The septum is a thin "wall" made of cartilage and bone. It divides the inside of the nose into two chambers.

The mucous membrane is thin tissue that lines the nose, sinuses, and throat. It warms and moistens the air you breathe in. It also makes the sticky mucus that helps clean that air of dust and other small particles.



The turbinates on each side of the nose are curved, bony ridges lined with mucous membrane. They warm and moisten the air you breathe in.

The sinuses are hollow, air-filled chambers in the bones around your nose. Mucus from the sinuses drains into the nasal cavity.

Interesting Fact

- Historically, nasal drug delivery systems have received interest since ancient times-it's not new

How the IN medications work

- Highly vascularized nasal mucosa and the olfactory tissue is in direct contact with the central nervous system, this allows drugs to be rapidly transported into the bloodstream & brain with onset of action near that of IV drug administration
- Some drugs will need molecular modification before they can be used IN-current studies ongoing-VERY PROMISING FUTURE ON THE HORIZON

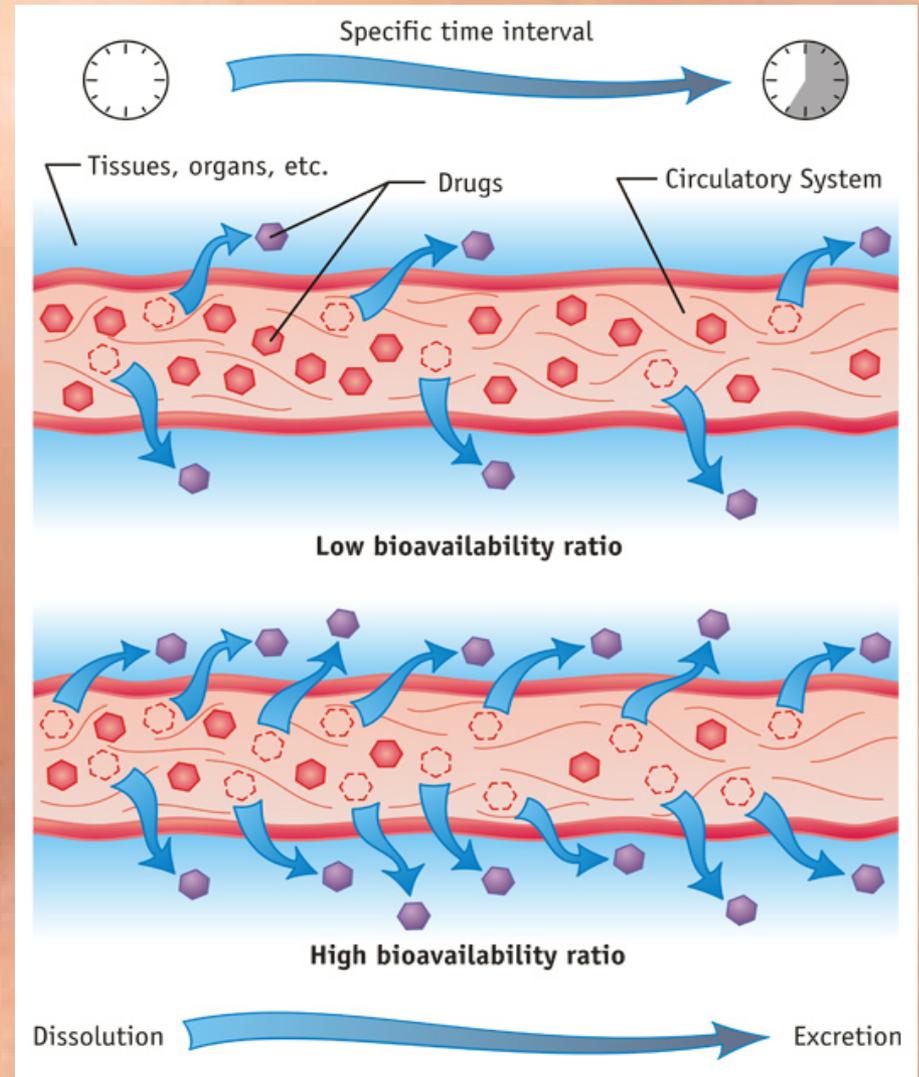
Factors of IN Medication Delivery

- Bioavailability
- First Pass Metabolism
- Nose/Brain Pathway & Blood Brain Barrier
- Lipophilicity



Bioavailability

- How much of the administered medication actually ends up in the blood stream



Bioavailability Factors

- **Factors that affect bioavailability**
- **Characteristics of the drug**
 - Molecular size, complexity and lipophilicity
 - pH of solution
- **Drug concentration/volume of solutions**
- **Properties of the formulation vehicle (absorption enhancers)**

Avoids First Pass Metabolism

First Pass Metabolism:

Nasal: Drug absorbs directly into the veins

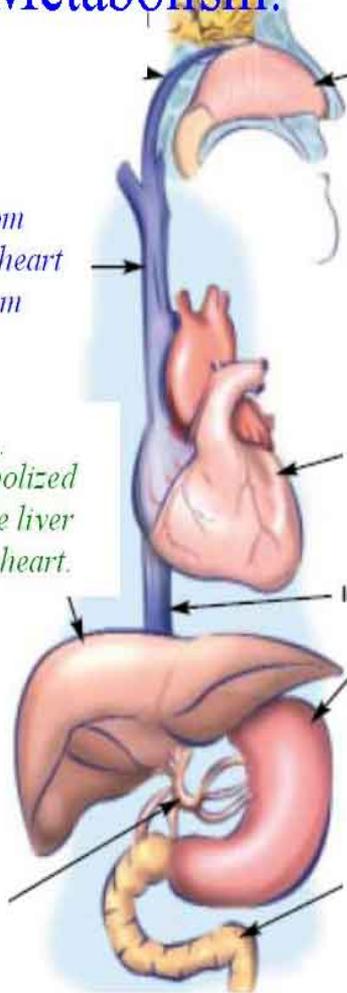
Venous system: transports blood from nose directly to the heart – no liver metabolism

Liver: 90% of oral medication is metabolized and destroyed by the liver before it gets to the heart.

Heart: pumps blood out to entire body – no delay

Portal circulation: All blood from the intestines is taken to the liver for detoxification.

Oral medications: Sit in the stomach for 30-45 minutes



- Molecules absorbed through the gut, including all oral medications enter the “portal circulation” & are transported to the liver
- Liver enzymes then break down most of these drug molecules and only a small fraction enter the body circulation as active drug

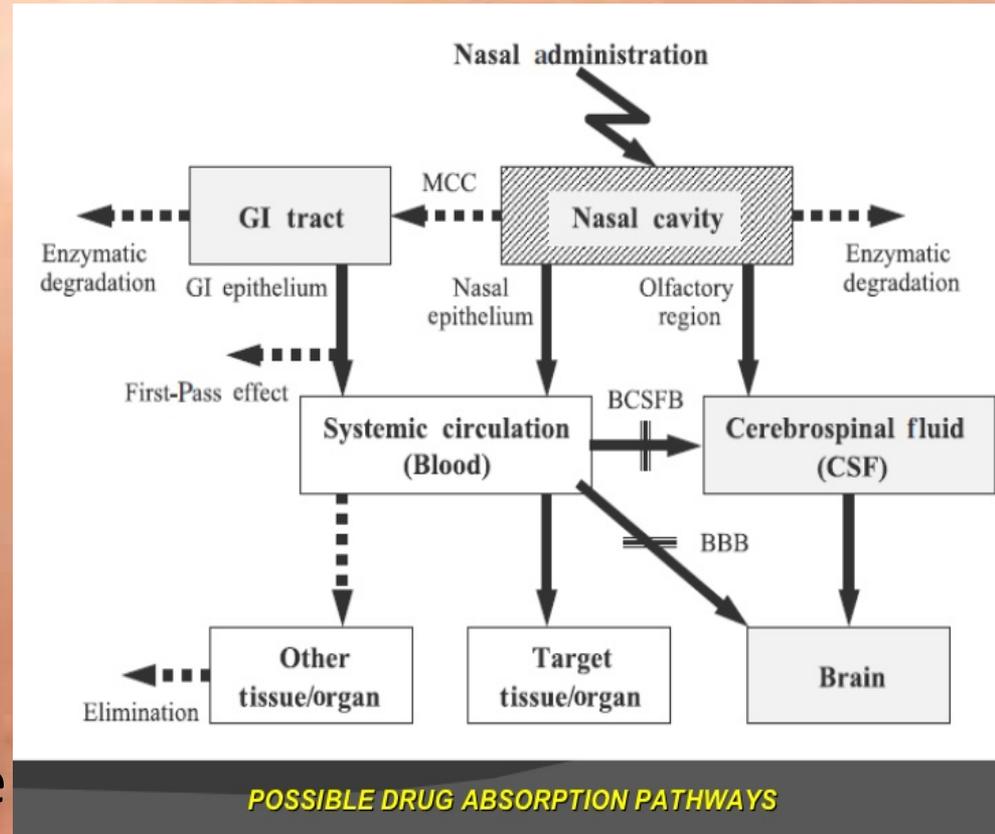
Avoids First Pass Metabolism

- This process is called “First Pass Metabolism”
- Important FACT-
Nasally delivered medications avoid the gut so they do not suffer first pass metabolism



Nose/Brain Pathway

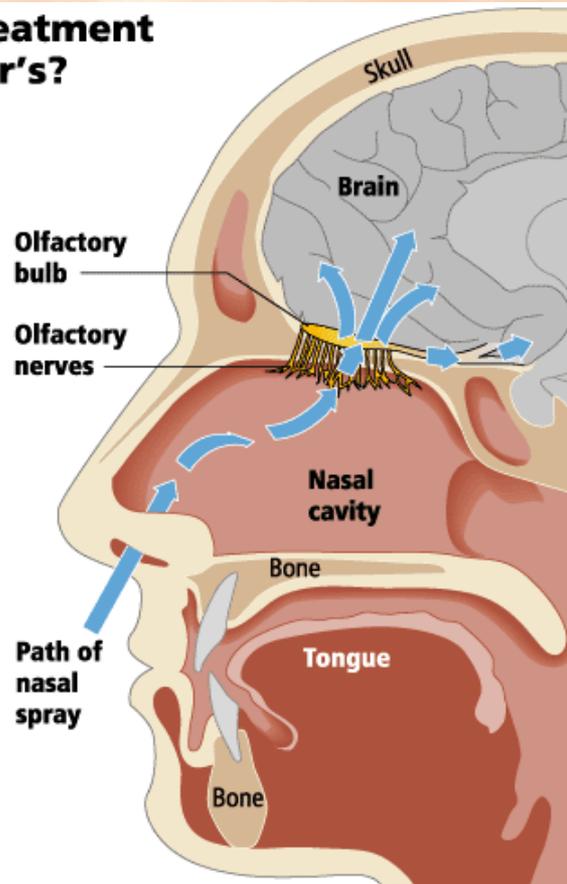
- The olfactory mucosa (smelling area in nose) is in direct contact with the brain and CSF
- Medications absorbed across the olfactory mucosa directly enter the brain
- This area is termed the nose brain pathway and offers a rapid, direct route for drug delivery to the brain



Nose/Brain Pathway & Blood Brain Barrier (BBB)

Intranasal treatment for Alzheimer's?

A discovery by a Regions Hospital researcher may yield a treatment for Alzheimer's disease. It takes advantage of nerves in the upper portion of the nose, which lead to the brain. Drugs can travel along and through these nerves, bypassing the blood-brain barrier that otherwise shields the brain from harmful bacteria or organisms. One of the routes is the olfactory nerves, which are critical for the sense of smell.



Source: Alzheimer's Research Center at Regions Hospital

PIONEER PRESS

- Large molecules do not pass through the BBB easily
- Low lipid (fat) soluble molecules do not penetrate into the brain. However, lipid soluble molecules, such as barbituate drugs, rapidly cross through into the brain
- IN avoids the BBB

Lipophilicity

- “Lipid Loving”
 - Cellular membranes are composed on layers of lipid material
 - Drugs that are lipophilic are easily and rapidly absorbed across the mucous membranes
- There is increasing evidence to suggest that control of physicochemical properties such as lipophilicity, within a defined optimal range, can improve compound quality and the likelihood of therapeutic success
- The role of lipophilicity in drug discovery and design is a critical one.
-
- Lipophilicity is a key physicochemical property that plays a crucial role in determining ADMET (absorption, distribution, metabolism, excretion, and toxicity) properties and the overall suitability of drug candidates.

How the IN Medication Delivery Works

- Rapid onset of pharmacological action (medications work quickly)
- Ease of use by EMS
- Pain-free (virtually or compared with needles) for patients
- No “dirty needlestick” worries since there is no “dirty needle” involved

Comparable bioavailability to intravenous drug delivery

Within a few minutes of delivery, serum levels of some medications delivered intranasally are comparable to injectable levels.⁴

Needle-free drug delivery device

LMA MAD Nasal™ decreases the chances of accidental needlestick injuries both on scene and while managing patients during transport.⁵

Fast onset of action through the nasal mucosa

Utilising low molecular weight lipophilic drugs intranasally ensures that molecules are easily absorbed across the nasal mucosa for comparable efficacy vs IM and oral drug delivery.^{1,6,7}

User-friendly device

LMA MAD Nasal™ is an easy and effective drug delivery device, which enables users to deliver medication directly into the nose from any angle.^{1,3,4,7}

Other Information on How It Works

- In general, medications that consist of small, simple, lipophilic molecules will cross membranes most easily.
- Having a pH near physiologic helps as well.

Other Information on How It Works

- If drug concentration is such that it can be delivered in a reasonable volume to the nose so no runoff into the throat or out the nostril occurs, then more absorption and higher bioavailability is possible. (FINE MIST)
- Ideal volume for one nostril is about 0.25 to 0.3 ml, though some clinicians use as much as 1 ml per nostril and accept runoff and drug loss at this higher volume.

Pearls to Using IN Medication Delivery

- Almost everyone has a nose
- Easy to use
- Few contraindications
- Virtually pain-free
- Easy to train EMS providers how to use
- Many drugs being studied & changed to allow IN delivery
- Rapid to use and competes nicely with IV delivery for time
- Impact your clinical practice!



Pearls to Using IN Medication Delivery

- Can use the device in any position, even standing on their head!
- Eliminates dirty needlestick injury to EMS providers, 100% needlestick injury-free
- Relatively inexpensive to use
- Exceptional application in pediatric medication administration



Benefits of IN Delivery Compared to Other Routes of Administration

Key Benefits	Nasal	Oral	IM	IV	PR	Reference
▶ High serum drug levels	✓	✗	+/-	✓	✗	Wolfe & Macfarlane 2006
▶ Rapid onset of action	✓	✗	+/-	✓	✗	Kerr 2009, Wermeling 2010, Fisgin 2002, Holsti 2007, Wolfe & Macfarlane 2006
▶ Painless	✓	✓	✗	✗	✗	Wolfe & Braude 2010, Massey 2011
▶ Easy to use and administer	✓	✓	+/-	✗	✓	Kerr 2009, Wolfe & Macfarlane 2006, Talon 2009
▶ Low resource utilisation (equipment, additional medication, healthcare professional time)	✓	✓	+/-	✗	✓	Holsti 2007
▶ Reduces needlestick risk	✓	✓	✗	✗	✓	Kerr 2009, Wermeling 2010
▶ Non-invasive	✓	✓	✗	✗	✗	Kerr 2009, Wermeling 2010

Common EMS Medications Used IN

- Fentanyl (Pain Management, Acute Coronary Syndromes, etc.)
- Midazolam/Versed (seizures, sedation, Therapeutic Hypothermia shivering)
- Naloxone/Narcan-Narcotic reversal agent (drug overdose, accidental overdose, obtunded due to pain management meds)
- Glucagon (diabetic with difficult IV access for D50 administration)
- Lorazepam/Ativan (anti-seizure medication, behavioral use, etc.)

Pharmacology

- Locally here in Virginia in the PEMS Region, we use the following medications successfully within our regional protocols for IN Delivery
- Always refer to your local protocols and your agency policies and directions of your own medical director when administering medications

Pharmacology

- Fentanyl-Used for pain management
- Our dose range is 25-100mcg with no more than 1mL given per nostril in a 15 minute period



Pharmacology

- Midazolam/Versed used for seizures, behavioral emergencies, airway management, etc.
- Dosing varies based on adult versus pediatrics and clinical presentation/condition



ADULT DOSAGE:

Airway Management/Post-Advanced Airway:

Midazolam (Versed) 2 mg IN or Slow IV/IO, may repeat as needed - 5 minutes after initial dose up to maximum dose of 5 mg (including any doses administered during intubation)

Cardiac Dysrhythmia Bradycardia/Unstable Bradycardia:

If time and patient condition permits, administer *Midazolam (Versed) 2 mg IN/IM/IV/IO*

Cardiac Dysrhythmia Narrow Complex Tachycardia Unstable Narrow Tachycardia:

For mild sedation, if time and patient condition permits, administer *Midazolam (Versed) 2 mg IN/IM/IV/IO*

Adult Cardiac Dysrhythmia Wide Complex Tachycardia Unstable with a Pulse:

For mild sedation, if time and patient condition permits, administer *Midazolam (Versed) 2 mg IN/IM/IV/IO*

Seizure:

Midazolam (Versed) 2 mg IN followed by 1 mg every 2 min until seizure activity stops up to a total dose of 5 mg

Behavioral Emergencies Combative Patients:

If patient still requires chemical restraint, administer *Midazolam (Versed) 5mg IN/IM or 2.5mg IV/IO*, then restrain patient

Pharmacology

Peninsulas EMS Council, Inc.
Therapeutic Hypothermia



[I]	To help prevent shivering or seizures: <i>Midazolam (Versed) 2 mg IN/IM or slow IV/IO followed by 1 mg every 2 minutes until seizure activity stops up to a total dose of 5 mg</i> <i>or</i> <i>Sublimaze (Fentanyl) 25-100 mcg IN, IM or IV/IO over 2 minutes, initial dose, may repeat 25 mcg every 5 minutes titrated to pain relief up to maximum dose of 100 mcg as long as patient systolic blood pressure is greater than 90 mmHg</i>	[I]
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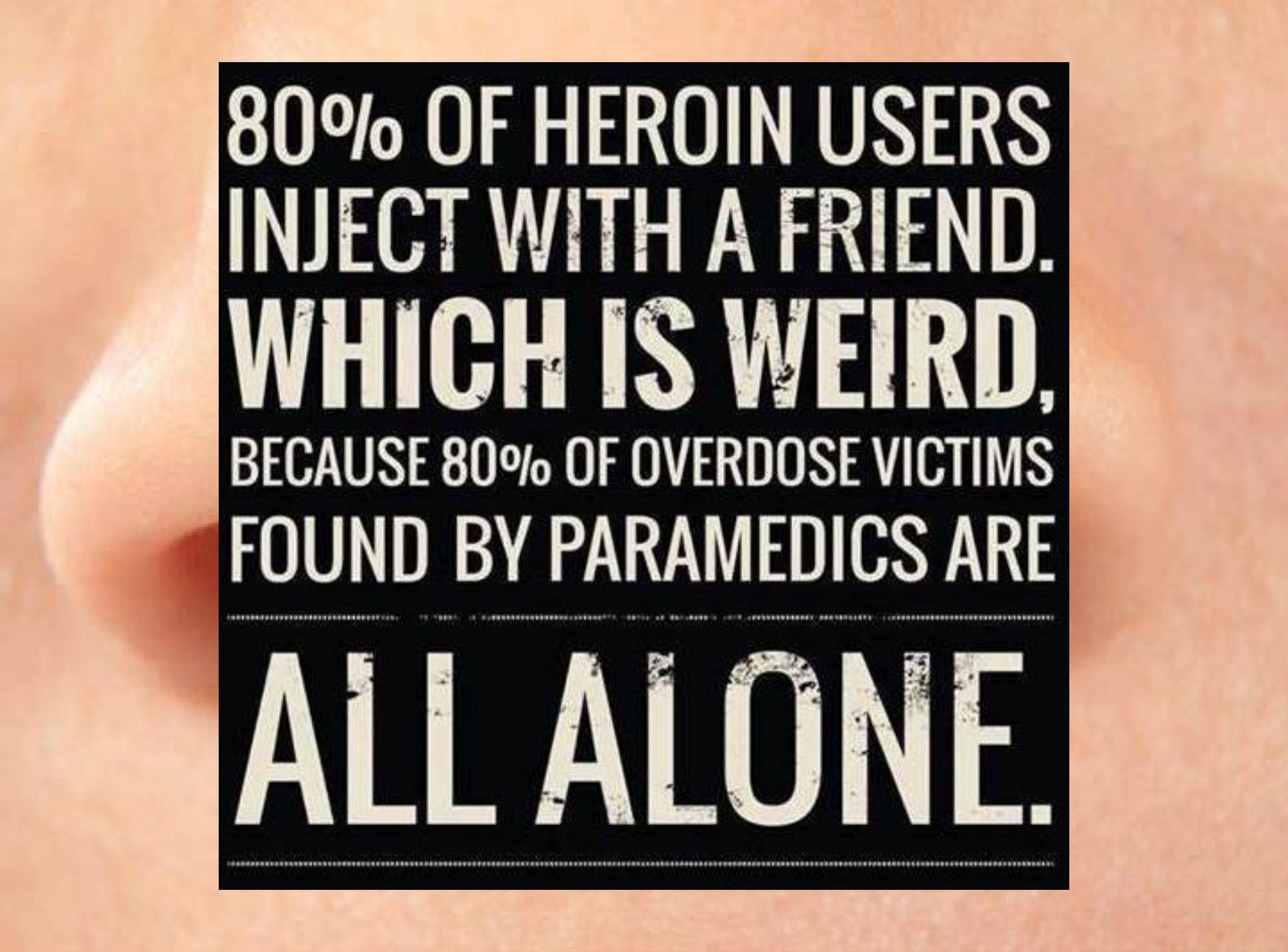
*Although the efficacy of Therapeutic Hypothermia is currently under debate, our regional protocols still reflect this option if needed using either Versed or Fentanyl.

Versed Pediatric Dose for Seizure Control

PEDIATRIC DOSAGE:

Seizure:

Midazolam (Versed) 0.1mg/kg IN to a maximum single dose of 2 mg followed by up to 1 mg every 2 min until seizure activity stops up to a total dose of 5 mg



**80% OF HEROIN USERS
INJECT WITH A FRIEND.
WHICH IS WEIRD,
BECAUSE 80% OF OVERDOSE VICTIMS
FOUND BY PARAMEDICS ARE**

ALL ALONE.

Pharmacology-NARCAN



- Used for drug overdose or suspected overdose of narcotics
- ***This medication has been de-regulated in many states just like an Epi Pen and quick kits with an intranasal device are provided to family members of some known narcotic drug overdose patients for urgent use.***

Pharmacology-Glucagon



- Pre-filled syringes may not be capable of converting over to IN use, check the packaging. Vials may be easier to administer via IN route.

Pharmacology-Glucagon

PROTOCOL

EMR	Follow <i>Universal Patient Care Protocol</i>	EMR
EMT	Obtain blood glucose level	EMT
<u>Suspected Narcotic Overdose</u>		
A	Administer <i>Naloxone (Narcan) 2 mg IV/IO, IN or IM</i> titrated to effect, Repeat dose in 5 minutes if no response	A
<u>Hypoglycemia</u>		
EMT	If consciousness is altered, if blood sugar level less than 60 mg/dL and patient can protect airway, administer <i>oral glucose</i> or	EMT
A	Administer <i>Dextrose 50% 25g (D₅₀) IV</i>	A
A	If unable to gain IV access, administer <i>Glucagon 1 mg IN or IM</i>	A
EMT	Repeat blood glucose level, administer <i>oral glucose</i> if necessary	EMT
A	Administer second dose <i>Dextrose 50% 25g (D₅₀)</i> if necessary	A
<u>Hyperglycemia</u>		
A	If blood glucose level is greater than 250 mg/dL Administer fluid bolus <i>20 ml/kg 0.9% Normal Saline up to 1000 ml</i>	A

Pharmacology-Glucagon

ADULT DOSAGE:

Altered Level of Consciousness:

If unable to gain IV access, administer *Glucagon 1 mg IN or IM*

Overdose and Poisons:

Antidote for some overdoses

PEDIATRIC DOSAGE:

Altered Level of Consciousness:

Consider *Glucagon 0.1 mg/kg IN or IM up to a maximum dose of 1mg if no IV/IO access OR if unable to administer oral glucose*

Overdose and Poisons:

Antidote for some overdoses

IN Fentanyl Use

PAIN MANAGEMENT/ORIGINAL RESEARCH

Safety of Intranasal Fentanyl in the Out-of-Hospital Setting: A Prospective Observational Study

Anders P. H. Karlsen, BM; Danny M. B. Pedersen, EMT; Sven Trautner, MD; Jørgen B. Dahl, MD, PhD;
Morten S. Hansen, MD

Study objective: Initial out-of-hospital analgesia is sometimes hampered by difficulties in achieving intravenous access or lack of skills in administering intravenous opioids. We study the safety profile and apparent analgesic effect of intranasal fentanyl in the out-of-hospital setting.

Methods: In this prospective observational study, we administered intranasal fentanyl in the out-of-hospital setting to adults and children older than 8 years with severe pain resulting from orthopedic conditions, abdominal pain, or acute coronary syndrome refractory to nitroglycerin spray. Patients received 1 to 3 doses of either 50 or 100 μg , and the ambulance crew recorded adverse effects and numeric rating scale (0 to 10) pain scores before and after treatment.

Results: Our 903 evaluable patients received a mean cumulative fentanyl dose of 114 μg (range 50 to 300 μg). There were no serious adverse effects and no use of naloxone. Thirty-six patients (4%) experienced mild adverse effects: mild hypotension, nausea, vomiting, vertigo, abdominal pain, rash, or decrease of Glasgow Coma Scale score to 14. The median reduction in pain score was 3 (interquartile range 2 to 5) after fentanyl administration.

Conclusion: The out-of-hospital administration of intranasal fentanyl in doses of 50 to 100 μg is safe and appears effective. [Ann Emerg Med. 2013;■:1-5.]

Please see page XX for the Editor's Capsule Summary of this article.

IN Midazolam/Versed Use

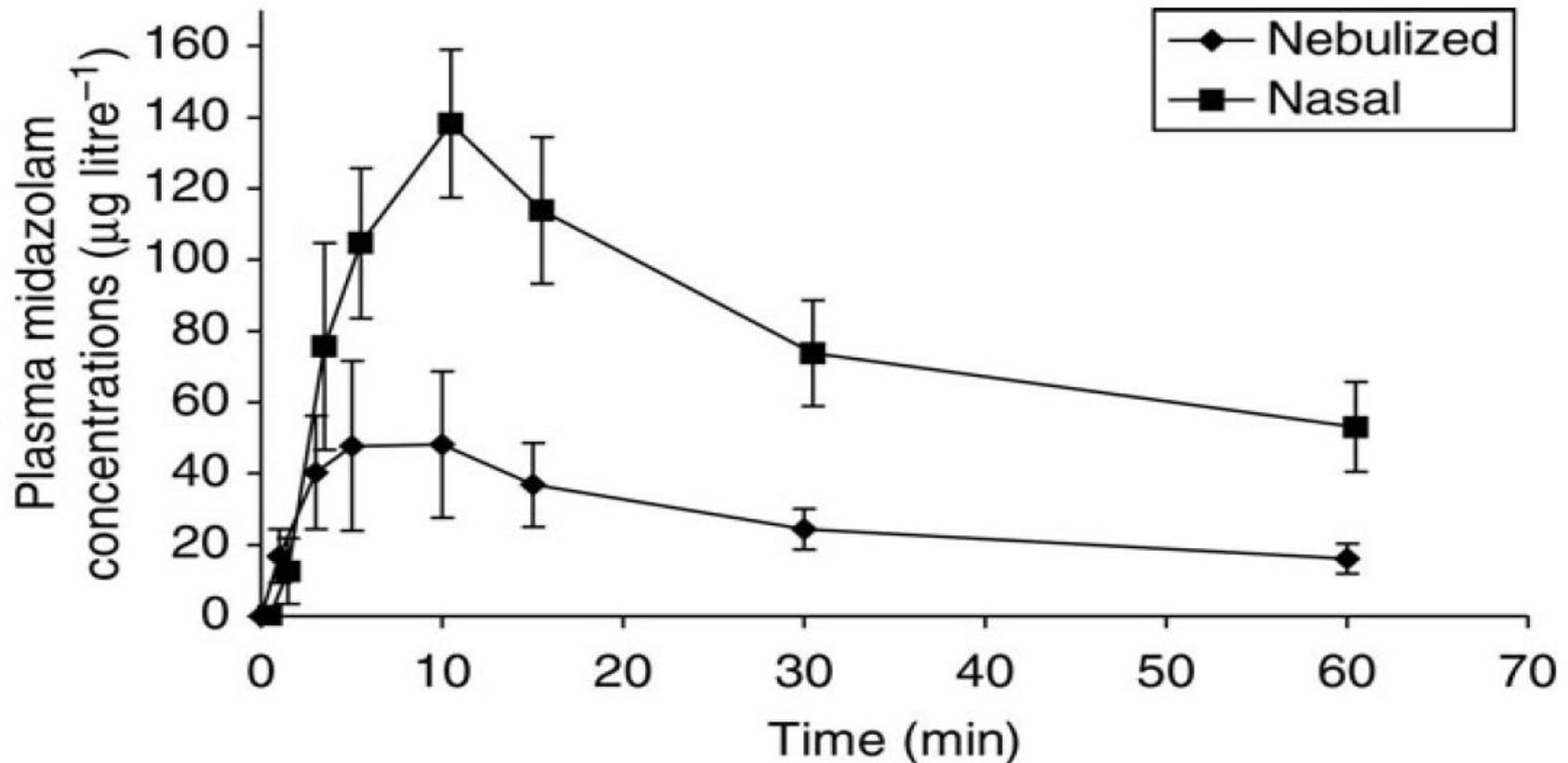


Fig 8 Plasma midazolam concentrations ($\mu\text{g litre}^{-1}$) [mean (2SEM)]. Mean (SD) AUC: nebulized=1670 (778.0), nasal=4785 (1329.6); $P<0.001$.

Seizure Meds in IN Use

Neurotherapeutics: The Journal of the American Society for Experimental NeuroTherapeutics

Intranasal Delivery of Antiepileptic Medications for Treatment of Seizures

Daniel P. Wermeling

Department of Pharmacy Practice and Science, University of Kentucky College of Pharmacy, Lexington, Kentucky 40536-0082

Summary: Acute isolated seizure, repetitive or recurrent seizures, and status epilepticus are all deemed medical emergencies. Mortality and worse neurologic outcome are directly associated with the duration of seizure activity. A number of recent reviews have described consensus statements regarding the pharmacologic treatment protocols for seizures when patients are in pre-hospital, institutional, and home-bound settings. Benzodiazepines, such as lorazepam, diazepam, midazolam, and clonazepam are considered to be medications of first choice. The rapidity by which a medication can be delivered to the systemic circulation and then to the brain plays a significant role in reducing the time needed to treat seizures and reduce opportunity for damage to the CNS. Speed of delivery, particularly outside of the hospital, is enhanced when transmucosal routes of delivery are used in place of an intravenous injection.

Intranasal transmucosal delivery of benzodiazepines is useful in reducing time to drug administration and cessation of seizures in the pre-hospital setting, when actively seizing pa-

tients arrive in the emergency room, and at home where caregivers treat their dependents. This review summarizes factors to consider when choosing a benzodiazepine for intranasal administration, including formulation and device considerations, pharmacology and pharmacokinetic/pharmacodynamic profiles. A review of the most relevant clinical studies in epilepsy patients will provide context for the relative success of this technique with a number of benzodiazepines and relatively less sophisticated nasal preparations. Neuropeptides delivered intranasally, crossing the blood-brain barrier via the olfactory system, may increase the availability of medications for treatment of epilepsy. Consequently, there remains a significant unmet medical need to serve the pharmacotherapeutic requirements of epilepsy patients through commercial development and marketing of intranasal antiepileptic products. **Key Words:** Intranasal, drug delivery, antiepileptic medications, treatment of seizures, emergency pharmacotherapy, benzodiazepines, blood-brain barrier.

How to Give Intranasal Medications

PROCEDURE



Identify the need for IN medication delivery

Prepare the delivery device and medication according to the manufacturer's recommendation

Explain the procedure to the patient

Use a method that fragments the medication into fine particles so the maximal nasal mucosal surface is covered and minimal volume runs out the nose or into the throat

Utilize both nostrils to double the surface area for absorption and halve the volume delivered per nostril

Deliver medication in the nostril, **DO NOT** exceed more than 1mL per nostril in any 10-15 minute period, **verify you are not exceeding maximum doses**

Document time of medication delivery, which nostril(s) used to deliver medication and response

Drugs which can be given by intranasal route (IN): Glucagon, Midazolam (Versed), Naloxone (Narcan), Sublimaze (Fentanyl)

Contraindications to IN Delivery

PRECAUTIONS:

- **DO NOT** Administer more than 1mL of medication/substance per nostril within a 10-15 minute period
- **DO NOT** exceed maximum doses of medication when utilizing IN initially, then moving to another delivery method such as IV/IO

CONTRAINDICATIONS:

- **DO NOT** administer Intranasal (IN) medications with any nasal/nose trauma or bleeding from the nose

LMA | MAD Nasal™

When IV delivery is less than ideal, LMA MAD Nasal™ can come to the rescue delivering safe, painless, and rapidly-effective treatment with minimal resource utilization.



Equipment for IN Delivery



Equipment for IN Use



Tim Wolfe, MD-Inventor



Tim Wolfe, MD-Inventor

“It was pretty clear to me when I conceptualized it that it had significant applications in EMS (I was an EMS director at the time). My first thought for EMS was to reduce needle stick in heroin overdose situations. Little did I know that as I experimented more and got others to do the same - that it would be so great for pain control, seizure therapy and even sedation in agitated delirium.”

Tim Wolfe, MD-Inventor

- “My biggest “insight” if you will for EMS is based on a lot of questions that I get and comments that I see that show a slight misunderstanding of the pharmacology of nasal drug delivery. Nasal drugs are NOT the same as IV drugs even though they work nearly as well (better in many settings). So – the doses are different and the time of onset from drug delivery is different.”

Tim Wolfe, MD-Inventor

- “Timing: Again it takes a little while for nasal drugs to take effect. 3-5 or so minutes to therapeutic levels depending on the drug. About 15 minutes to peak levels. For naloxone, fentanyl and midazolam or lorazepam in seizures the effect onset is 3-4 minutes but it keeps absorbing for 15. So relax, manage the airway if needed, they will wake up and breath in a few minutes which is all you really want (opiate OD) or stop seizing in a few minutes. This usually is in the time frame it takes to establish an IV anyhow – so just give the nasal drug, support their airway and don’t stress out. As long as you can oxygenate them – don’t get in a hurry with a needle. ”

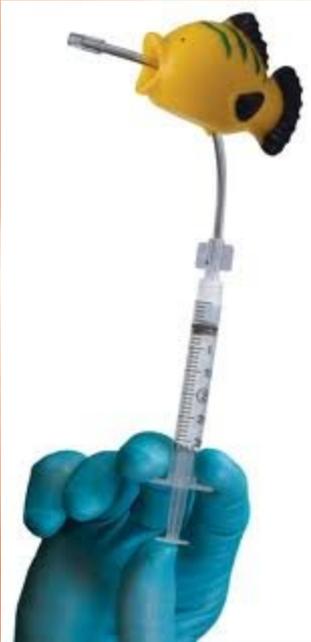
Interesting Use of Narcan



Narcan Home Use



Other Equipment Related



Maddie the Blowfish for
Pediatric IN Delivery

Intranasal Medications in Hospice

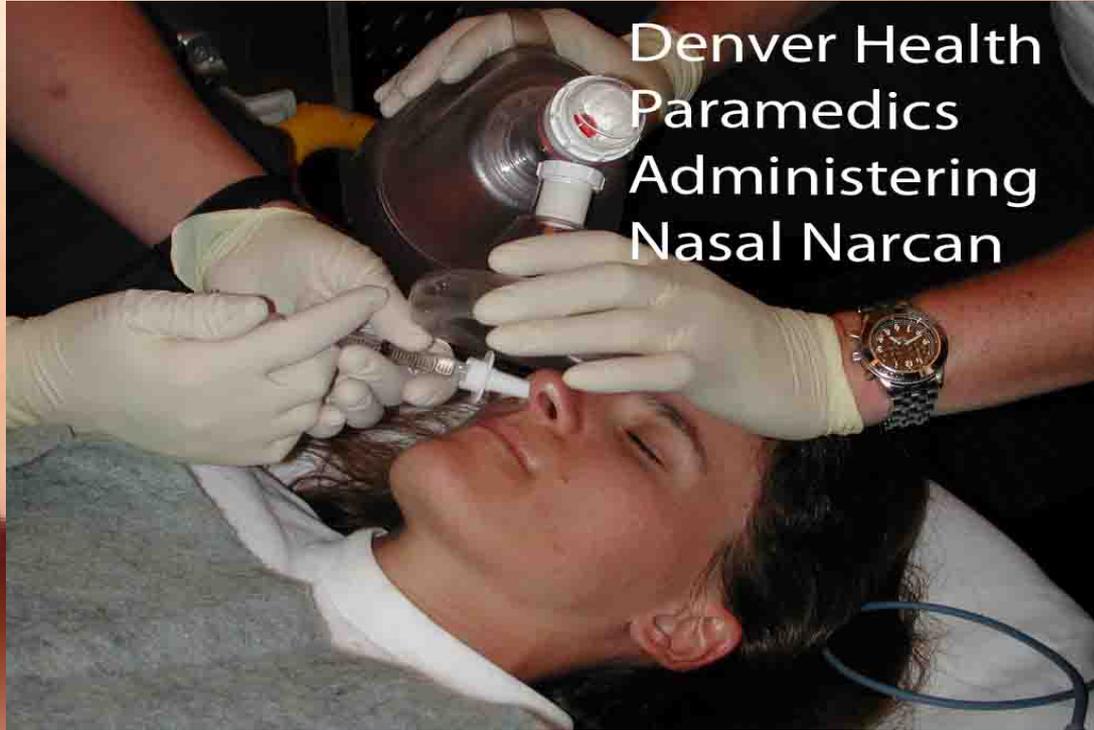
A Novel method of pain,
dyspnea, seizure and anxiety
control.





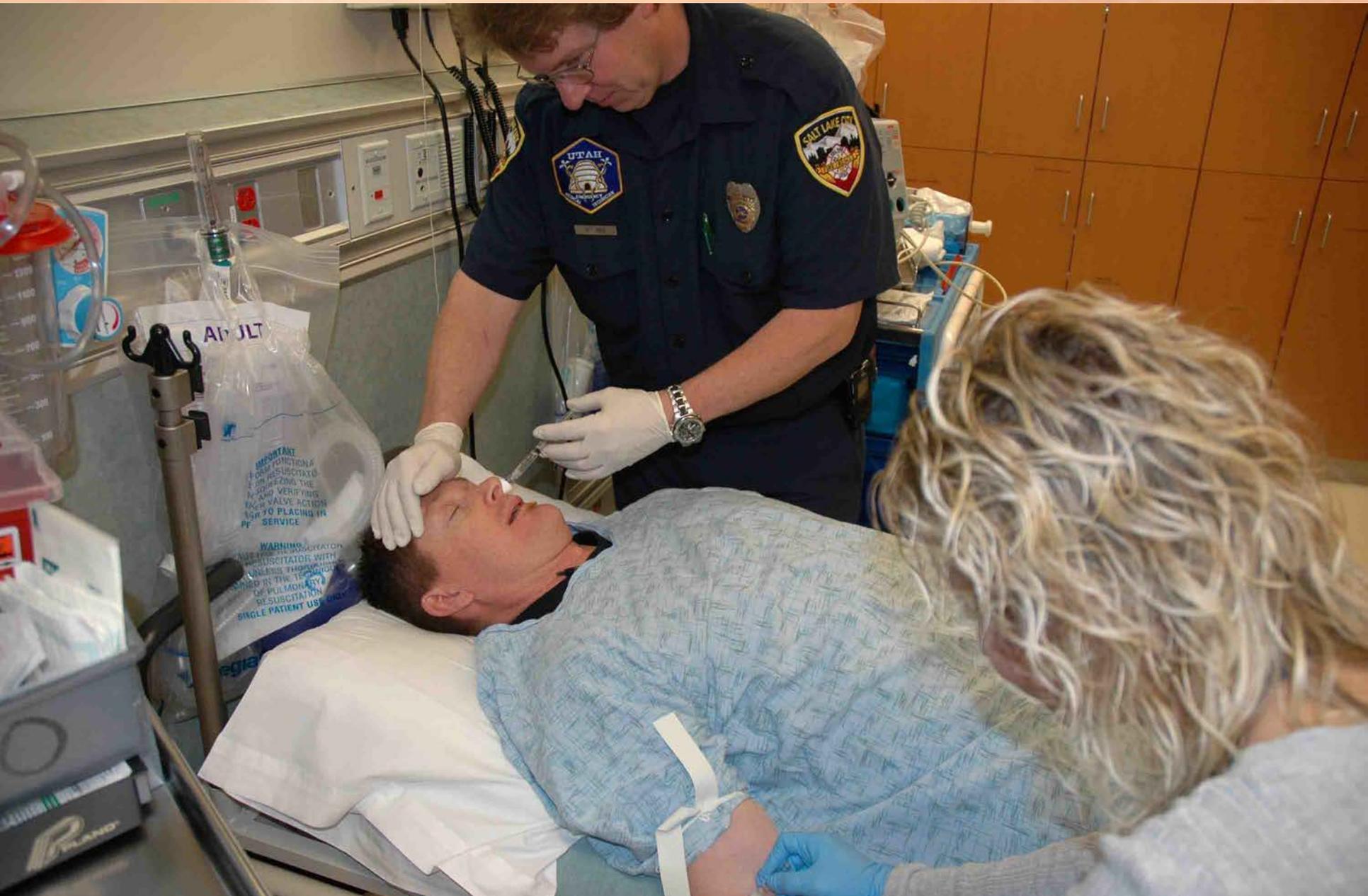


Denver Health
Paramedics
Administering
Nasal Narcan



Intranasal Medications in Anesthesia





Equipment for the Procedure

- 1cc Syringe (3cc is ok)
- MAD Nasal Device (1 is all you need)
- Blunt fill needle
- Medication to be given
- Gloves
- If patient is conscious, a tissue or 2"x2" gauze pad (comfort only)



Different Packaging of the MAD Devices



Other devices on the Market





NEEDLE-FREE TREATMENT OPTION: NASAL DRUG DELIVERY

with
MAD[®] Nasal
MUCOSAL ATOMIZATION DEVICE



So Many Advantages...

COST-EFFECTIVE

VERSATILE

QUICK TO ADMINISTER



FAST ACTING & EFFECTIVE

LESS STRESS

NO SPECIAL TRAINING

SAFER!

PAINLESS

GREATER CONTROL



WOLFE TORY
MEDICAL, INC.

Elegant solutions for complex issues.



Websites to Visit

- www.intranasal.net
- <http://www.lmana.com/pwpcontrol.php?pwplD=6359>
- <http://prehospitalresearch.eu/?p=3179>
- Blog style EMS forum that has the largest collection of medical study links for the meds given IN including many not being used by EMS IN (Atropine, Ketamine, Dilaudid, etc)

Free Product Sample Info

- <http://www.lmana.com/pwpcontrol.php?pwplD=7461>
- Fill out the fill-able online form on this page for your FREE NASAL MAD KIT

Don't miss this particular offer.



LMA MAD Nasal™
INTRANASAL MUCOSAL ATOMIZATION DEVICE

Introducing the LMA MAD Nasal™, the safe and painless way to deliver medication directly into your patient's blood stream without an intravenous line.

When it delivery is less than ideal, LMA MAD Nasal™ can come to the rescue. Delivering safe, painless, and rapidly effective treatment with minimal resource utilization.

With no danger of needle sticks, no need to stabilize, and no sedation and free monitoring it offers the intranasal mucosal atomization device with deliver a vital of essential medication that is absorbed directly into your patient's blood stream. So you spend more time caring for your patient, and less time starting a painful intravenous line.

Safe and Painless
• No needles, no sticks
• No sedation
• No monitoring

Rapidly Effective
• Rapidly effective treatment
• Minimal resource utilization
• Free monitoring

Controlled Administration
• Precise dosing
• No sedation
• No monitoring

Minimal Resource Utilization
• No needles, no sticks
• No sedation
• No monitoring

Evidence Based
• Evidence based research
• Evidence based research
• Evidence based research

LMA MAD Nasal™
delivers a treatment solution that's right on the nose.

- Needle Free, Intranasal Drug Delivery
- Safe and Painless
- Rapidly Effective
- Controlled Administration
- Minimal Resource Utilization
- Evidence Based

LMA MAD Nasal™
INTRANASAL MUCOSAL ATOMIZATION DEVICE

Learn More >>

Spend more time caring for your patients and less time starting painful intravenous lines.

Questions?

- Please feel free to bring me your flash drive & I will upload this program for you to take home if you wish.
- Contact us at melissdoak@yahoo.com & my phone is 757-256-8154 & Blake- hur5st@gmail.com and my phone is 804-313-7562
- THANKS FOR HAVING US SPEAK & for SELECTING THIS CLASS!!!