Topics
- The seven basic emergency drugs that all dentists should have in their office
  - Epinephrine - in depth
  - Flumazenil
  - Airway!

Emergency Drugs
- Non-injectable:
  - Oxygen
  - Albuterol (inhaler)
  - A form of glucose
  - Nitroglycerin
  - Nitrostat (sublingual tablet)
  - Nitrolingual spray (translingual)
  - Aspirin
Emergency Drugs

- Injectable:
  - Epinephrine
  - Epi-Pen, TwinJect
  - Diphenhydramine

Diphenhydramine

- IM administration
- 50/25/12.5 mg
- Continue PO four times daily for three days

Oxygen

- Must be available in an E-Cylinder
- Nasal Cannula - 1-3 lpm
- Nasal Hood - 4-8 lpm
- Full Face Mask - 10 lpm
- Positive Pressure Ventilation - 15 lpm

Albuterol

- Beta-2 specific agent
- Onset of action within 1 to 5 minutes and produces bronchodilation that lasts for about 2 to 6 hours
GLUCOSE

- Orange Juice
- Pepsi®, etc. (Not Diet)
- Cake Icing
- NEVER PUT ANYTHING INTO THE MOUTH OF AN UNCONSCIOUS VICTIM!

NITROGLYCERIN

- Nitrostat or Nitrolingual Spray
- 9.99 vs 236.29
- Vasodilator
- Blood Pressure
- If no relief AFTER ONE DOSE* consider it to be an acute myocardial infarction.


ASPIRIN

- Prevents further clotting
- 325 mg
- 20 minute onset
- Allergy

The arachidonic acid cascade and its lipoxygenase branch, determinants of aspirin side effects

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Epinephrine

- Alpha-1, Alpha-2, Beta-1, Beta-2 agonist
- Increases systolic blood pressure more than diastolic
- Heart rate, cardiac output, stroke volume, and left ventricular work per beat are increased

Epinephrine

- For IM, SC, SL use, 1:1,000
- 0.3 mg (0.3 ml) every five minutes
- 0.15 mg (0.15 or 0.3 ml) every five minutes
- IV - cardiac arrest [1:10,000]

The diagnosis and management of anaphylaxis: An updated practice parameter. Lieberman et al 2005

No established dosage or regimen for intravenous epinephrine in anaphylaxis is recognized.

Note: Because of the risk for potentially lethal arrhythmias, epinephrine should be administered intravenously only during cardiac arrest or to profoundly hypotensive patients who have failed to respond to intravenous volume replacement and several injected doses of epinephrine.

Epinephrine Dosing

- Intramuscular injection in lateral thigh produces most rapid rise in blood level
  - 0.01mg/kg in children, 0.3-0.5mg in adults
- Data suggest that as many as 30-35% of patients require more than a single epinephrine injection

**Epinephrine Injection: Route and Site Do Matter**

<table>
<thead>
<tr>
<th>Injection route</th>
<th>Injection site</th>
<th>C-max: mean ± SD (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EpiPen IM</td>
<td>Thigh</td>
<td>12.22 ± 3.839</td>
</tr>
<tr>
<td>EpiPen IM</td>
<td>Thigh</td>
<td>9.72 ± 4.801</td>
</tr>
<tr>
<td>EpiPen IM</td>
<td>Arm</td>
<td>1.82 ± 4.26</td>
</tr>
<tr>
<td>EpiPen SQ</td>
<td>Arm</td>
<td>2.87 ± 6.67</td>
</tr>
<tr>
<td>Saline IM</td>
<td>Arm</td>
<td>1.46 ± 4.64</td>
</tr>
<tr>
<td>Saline SQ</td>
<td>Arm</td>
<td>1.16 ± 5.24</td>
</tr>
</tbody>
</table>

*P < .01 from all arms values. | Intranasal epinephrine

Epinephrine absorption in adults. Intramuscular versus subcutaneous injection.


**Epinephrine Injection: IM vs. SQ**

T-max (time to C-Max) was 8 ± 2 minutes after injection of epinephrine 0.5 mg from an EpiPen IM in the vastus lateralis vs. 34 ± 14 minutes (range, 5 to 120) after injection of epinephrine 0.01 mg/kg SQ in the deltoid region.

**Overview of Available Auto-Injectors**

<table>
<thead>
<tr>
<th></th>
<th>Twinject™</th>
<th>EpiPen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Packaging</td>
<td>Permanently attached wrap label patient instructions</td>
<td>Updated instructions attached to auto-injector New plastic sleeve with 5 clip</td>
</tr>
<tr>
<td>Needle Size</td>
<td>25 gauge</td>
<td>22 gauge</td>
</tr>
<tr>
<td></td>
<td>1/4 inch exposed needle length</td>
<td>1/4 inch exposed needle length</td>
</tr>
<tr>
<td>Noise Level</td>
<td>Quiet operation reduces risk of removal from injection site</td>
<td>Slightly louder firing mechanism</td>
</tr>
<tr>
<td>Cost / Formulary Position</td>
<td>$68.04</td>
<td>$34.58</td>
</tr>
<tr>
<td></td>
<td>AWP Single</td>
<td>AWP 2 Pack</td>
</tr>
<tr>
<td></td>
<td>$314.16</td>
<td>$815.25</td>
</tr>
</tbody>
</table>

**Epinephrine content vs. Time past expiration**

![Image showing epinephrine content vs. Time past expiration](chart)

$r = 0.63$
Reversal Agent:
- Romazicon (flumazenil)
- MUST be given IV only
- Concentration => 0.1 mg/ml
- Duration ~ 45 minutes
- Dose => 0.2 - 3.0 mg
- Cost: $ 2.50 per ml

Reversal:
- After IV administration, plasma concentrations of flumazenil follow a two-compartment, open pharmacokinetic model with an initial distribution half-life of 7 to 15 minutes.
- Approximately half of patients respond to doses of 0.4 mg to 0.6 mg, while the other half responded to doses of 0.8 mg to 1 mg.

Reversal:
- Eighty-one percent of patients sedated with midazolam responded to flumazenil by becoming completely alert or just slightly drowsy.
- Of those patients, 36% responded to doses of 0.4 mg to 0.6 mg, while 64% responded to doses of 0.8 mg to 1 mg.
- Resedation in patients who responded to ROMAZICON occurred in 10% to 15% of patients studied.

Reversal:
- Management of Suspected Benzodiazepine Overdose in Adults:
  - Of the patients who responded to flumazenil, 75% responded to a total dose of 1 mg to 3 mg.
  - Six seizures were observed in 446 patients treated with flumazenil in these studies.
WARNING:

- The use of Romazicon has been associated with the occurrence of seizures.
- Practitioners should individualize the dosage of Romazicon and be prepared to manage seizures.

Reversal:

- The availability of flumazenil does not diminish the need for prompt detection of hypoventilation and the ability to effectively intervene by establishing an airway and assisting ventilation.
- Necessary measures should be instituted to secure airway, ventilation and intravenous access prior to administering flumazenil.

ROMAZICON has not been established in patients as an effective treatment for hypoventilation due to benzodiazepine administration.

Although reversal of midazolam-induced respiratory depression was successful with all injection methods, the mean reversal time was significantly shorter with intravenous administration (120 +/- 24.5) versus sublingual administration (262 +/- 94.5) versus intramuscular administration (310 +/- 133.7) seconds.
Flumazenil Reversal of Sublingual Triazolam: A Randomized Controlled Clinical Trial. Pickrell, Masahiro Heima and Peter Milgrom Kazuo Hosaka, Douglass Jackson, Jacqueline E. J Am Dent Assoc 2009;140:559-566

- Incremental sublingual (SL) dosing of triazolam has emerged as a popular sedation technique.
- Nevertheless, few studies have evaluated the technique’s safety or efficacy. Given its popularity, an easily administered rescue strategy is needed.

Results/conclusions

- The OAA/S and BIS scores increased after the flumazenil injection at the 30-minute observation point, but they were not sustained.
- Six hours after the initial dose of triazolam had been administered (four hours after the flumazenil or placebo challenge), all patients could be discharged from the dental clinic.

Conclusions

- Deep sedation from incremental SL dosing of triazolam is incompletely reversed by a single intraoral injection of flumazenil.
- The reversal did not persist.
- The authors discharged the patients from the dental clinic at 360 minutes.

Clinical Implications

- A single intraoral injection of flumazenil (0.2 mg) cannot immediately reverse oversedation with triazolam.
- A higher dose might be effective.
- Reversal for the purpose of discharging the patient early is neither appropriate nor safe.