These patients don’t always come in with the pill bottle taped to their hands so, start with a really good approach to undifferentiated hypotension. May I suggest:

Walk up to the bedside with an ultrasound. Look at the monitor and then do your RUSH exam (rapid ultrasound of shock and trauma) follow through the ABCDE’s, H’s and T’s (hypovolemia, hypoxia,
hypo/hyperthermia, hyper/hypo-lytes, head injury, mi, acidosis, drug OD, PTX, embolism, tamponade

1. First – start at the beginning of the BP equation above and address the heart rate. If it’s too fast or too slow then fix it (PALS/ACLS algorithms).
2. Second - move to the end of the equation and quickly rule in/out neurogenic shock, anaphylaxis, sepsis, adrenal crisis.
3. You should be finishing up your RUSH exam and be able to determine preload (IVC) and Contractility.

WITHIN 2-3 MINUTES YOU CAN NARROW YOUR DIFFERENTIAL TO THE DRUGS!!!!

Airway:

Treat the airway with respect. Most CCB ODs will not need intubation, but do not be shy from it and find yourself playing catch-up.

INTUBATE EARLY: for respiratory failure, if the case portends to a poor outcome, or if you need to do a bunch of things quickly to that child that they are not going to like (ie. Charcoal, CVL, IO).

Be appropriately afraid:

• Your induction agent will worsen hypotension just like in cases of hemorrhagic shock. You may think Etomidate is safe, for its’ cardio-protective profile, but Ketamine is probably safer.
• I suggest: Ketamine: 0.5mg/kg IV to start. Add a second 0.5mg/kg if needed and the BP is holding. (kids and adults)
• For paralytics: I like rocuronium. If there is any concern that Digoxin is still a possible culprit then I would stay away from succinylcholine (hyperkalemic affects).
• If you have time, an awake-sedated-intubation is much better! I would still use Ketamine as my sedating agent.
• Pre-treat with Atropine (and pray b/c it probably won’t help)

Breathing/Circulation:

• Get access quickly. If you have access that is sufficient for the medications you need then move on. Usually these patients will need IO/Central access for pressor support. This is not the time for multiple RN sticks; punch at least one IO. Get a second IO if necessary.
• Try the “Femoral IV” cannulation with US
• US guided CVL
• Once you have access continue PALS/ACLS
- Fluids
- Atropine
- Pacing
- Push dose epinephrine/phenylephrine

- Don’t forget the CXR/ECG

Disability/Exposure/Extemities:

- Toxicology Exam = “Strip, Flip, Touch and Smell”
  - Strip – full exposure everything off, head to toe for trauma, tract marks, rashes, etc.
  - Flip – look at their back for the exact same reasons
  - Touch – start to put them into a toxidrome.
    - Put a hand in the armpit. Are the dry there (anticholinergic) diaphoretic (cholinergic)?
    - Are they cold and not perfusing well (Clonidine, oral hypoglycemics, opium, liquor, sedatives) = COOLS.
    - Are they hot (Nicotine, anticholinergics, amphetamines, antihistamines, sympathomimetics, antidepressants) = NASA
    - Neuro exam: pinpoint pupils (clonidine?)
    - Focal deficits – CVA, Diabetes
  - Smell
    - Alcohols
    - CN – Almonds, Organophosphates – onions/garlic, etc
    - Keytones

Once you have narrowed it down to drugs, there are only 4 that can cause bradycardia and hypotension. All four have some specific bedside tests that can help you ascertain the most likely culprit.

1. Digoxin
   - Lab - Hyperkalemia
   - EKG –
     - scooped T waves (indicates on Dig, not toxicity)
     - Bidirectional tachycardia
     - AV Blocks
2. Clonidine
   - Exam- Pinpoint pupils and opiate toxidrome
   - EKG - Sinus brady
3. Beta Blockers
   • Lab – Hypoglycemia

4. CCB
   • Lab – Hyperglycemia

**TREATMENT**

There are 3 categories of treatment options. ALL SHOULD BE TRIED, but some will probably not be helpful. As long as they don’t hurt the patient and there is the possibility of benefit then I’m going to “give them up.” No one goes to the morgue without a full-court press! These are labor-intensive patients. Pull an extra RN or tech, you’re going to need them.

Treatment should have been started yesterday. It should take you 5-10 total minutes to run through the above ABC’s, undifferentiated hypotension algorithms and the RUSH protocol. During that time PALS/ACLS treatment should be started concurrently.

Things that will probably not be beneficial but worth trying:

- **Pacing** – you will most likely get capture, but if you repeat your RUSH exam you will not get a benefit in the EF. Don’t waist a lot of time with TV pacing initially, but come back to it if all else fails.
- **Charcoal** – may work with sustained release; it is not going to hurt. Make sure you trust your airway before you give it; intubate if necessary.
  - Dose – 1g/kg
- **Fluid Bolus** - don’t give to much, the heart may have a hard time with the volume load. Start with 10cc/kg in a kid and repeat the RUSH IVC exam until the IVC has <25% collapse
- **Atropine** – again you may increase the rate, but if you repeat the ECHO your not going to get a significant increase in squeeze
  - **Kids dosing:**
    - 0.02mg/kg, min 0.1mg, may repat x one
  - **Adult dose:**
    - 0.5mg, may repeat x3 up to a total of 1.5mg
• **Glucagon** – increases cAMP up-regulation. The final common pathway to myocyte contraction is the calcium channel. Beta channels stimulate cAMP which stimulate the calcium channel. The calcium channel then triggers the myocyte to contract. Poisoning the calcium channel with CCBs kills the entire cascade. Since cAMP occurs before the calcium channel it should not work well in stimulating inotropic/chronotropic affects.
  
  o Kids dosing:
    - Bolus - 0.05mg/kg, may repeat once at 5 minutes
    - Infusion – 0.07mg/kg/hr
    - PRE-TREAT WITH ZOFTRAN – THEY WILL VOMIT!
  
  o Adult dosing:
    - Bolus – 3-5mg IV (after Zofran, I like 5mg)
    - Infusion – 5-15mg/hr (I like 15mg)
    - I prefer the bigger doses, b/c it is probably not going to work. If it has any chance it will be at the larger dose.
Band-Aids (Temporizing support):

These are medications that should be started in tandem with the therapies above and have a much better chance at holding the fort until you can get an antidote.

CALCIUM

- Calcium Gluconate/Chloride – CaCl has 3 times the elemental calcium as Ca Gluconate. Calcium Chloride is available immediately while Ca Gluconate has to be broken down in the liver so the affect is slower. CaCl can cause severe sclerosis of the peripheral veins leading to the need for skin grafting. Calcium chloride should be given through central access/IO if possible; don't withhold it from a good peripheral IV in a code. Again, if the final common pathway (calcium channel) is poisoned it will probably have a small transient affect at best.
  - Kids dosing:
    - CaCl (one amp = 3x the elemental Calcium has Ca Gluconate)
      - 20mg/kg over 5min, repeat x 5 doses
    - Ca Gluconate
      - 60mg/kg over 5min, repeat x 5 doses
  - Adult dosing
    - CaCl – give at lease 2 amps before you give up
    - Ca Gluconate – give at least 6 amps before you give up, 3 at a time

Remember that a calcium level over 13 or Ca x Phos >70 will cause permanent precipitation of calcium into the intra/extravascular spaces.
PRESSORS

- Phenylephrine – I prefer this for pure CCB ODs. No need to flog the heart the heart with unneeded beta affects.
  - Kids dosing:
    - Bolus = 5-20mcg/kg - I recommend to start 5-10mcg and then double every 2-5 minutes until affect achieved
    - Infusion = 0.1-0.5mcg/kg/min, max 5mcg/kg/min
  - Adult dosing:
    - Bolus = 40-500mcg. I start 50-100mcg and recheck in 2 minutes.
    - Infusion = 100-180mcg/min

- Epinephrine – I prefer this for Beta Blocker ODs. The added beta affect may give you some pick-up in EF; a little extra squeeze.
  - Kids dosing:
    - Bolus 5-20mcg – I recommend starting with 5-10 mcg and double every 2-5 minutes until affect achieved
    - Infusion 0.1-1mcg/kg/min IV
  - Adult dosing:
    - Bolus = 20-250mcg – I start 50mcg and double every 2-5 minutes.
    - Infusion = 2-10mcg/min

Remember Epi 1:10,000 code dosing is 0.1ml/kg or 0.01mg/kg IV or IO. It is always easier to calculate this in milliliters because it is to complicated to convert mg/kg to mg/ml. Now follow the math:
Epinephrine 1:10,000 comes 1mg/10ml vials. 1mg/10ml = 0.1mg/ml = 100mcg/ml = 10mcg/0.1ml. For push dosing, you take 1ml out of a 10cc NaCl flush. That gives you a 9ml NaCl flush that you mix with 1ml (0.1mg = 100mcg) epinephrine you now have a total 100mcg of epinephrine that is diluted to 10mcg/ml. Code dosing in 0.01mg(=10mcg) /kg or 0.1ml (=10mcg) per kg. So in a 10kg child you are giving 10mcg/kg = 100mcg. I only tell you this so you are not scared to give 5-20mcg of epinephrine to a nearly coding CCB OD.

Milrinone and Dobutamine are options, but beware worsening hypotensive affects. Use bedside ED TTE to gauge contractility or
quality of squeeze in order to make a determination of potential benefit vs harm with these vasodilating inotropes.

**Preventing phenylephrine as a push-dose pressor**
- Phenylephrine is supplied in a 1 ml vial at concentration of 10mg/ml
- Take 1ml vial & inject into a 100ml bag of NS
- You now have a bag of phenylephrine at a concentration of 100mcg/ml
- Draw up 3-5ml in a syringe
- Push 0.5-2ml (50-200 mcg) at a time, q2-5 minutes for gentle BP control
- Response within 1 minute, lasts ~5 minutes

**Preventing epinephrine as a push-dose pressor**
- Code box vial: 10 ml vial at concentration of 1mg/10ml (1:10,000)
- Take 10ml of NS (i.e. saline flush) & dump 1ml = 9ml NS syringe
- Draw up 1ml of epinephrine vial in the same syringe
- You now have an epinephrine syringe at 10mcg/ml
- Push 0.5-2ml (5-20 mcg) at a time, q5 minutes

Antidotes:

High Dose Insulin: In shock: the heart changes from preferentially running on free fatty acids to using carbohydrates (glucose) for energy. CCBs block insulin release from the pancreatic islets cells. In a CCB OD the heart is in a state of shock from the drug’s direct negative inotropic/chronotropic affect at the calcium channel and b/c it prevents the myocyte from processing the glucose that it needs by robbing it of the insulin needed to drive glucose into the cell. Now there is plenty of glucose in the blood, but the myocyte never sees it b/c there is no insulin to drive it into the cell. *It takes high doses of insulin to overcome this conundrum!*

- Kids and adult dosing:
  - Bolus - 1U/kg – I recommend that you give a test dose of 10% (0.1U/kg) dose, wait 3-5 minutes and then if the glucose remains the same or goes up. Give the full dose and have D50 at the ready.
  - Insulin Infusion – 0.5–1U/kg/hr

- **Monitor the glucose every 15min!!**
- Have a dextrose drip ready to go, but you will probably not need it for a while. D10-D50 suggested. This is not the time to give D5; at least start with D10.

- Toxicologists believe that when the glucose starts to go down, the toxidrome is improving. When it goes up, the patient is getting worse!

- I start the glucose infusion when the glucose <250
  - Beware the K
    - Check the K every 30 minutes. Again you will probably not see it move for a while. Most of what you see is just shifts of K, not depletion.
    - Start K replacement at 2.5

**Intralipids:**

Based on a bunch of case reports out of anesthesia literature: Useful in local anesthetic, TCA, Beta and CCB ODs, but probably useful in any medication that is lipophilic. Probably acts as a sink/resin for excess CCBs to bind to and/or bathes the heart in FFA to provide it its’ preferential energy source and/or potentially re-activates blocked calcium channels.

  - Kid and Adult Dosing:
    - 1.5ml/kg/min bolus over one minute
    - 0.5ml/kg/min up to 8ml/kg
    - Total infusion time is 13 minutes

Consider Intralipids early. There has been no real report of adverse effects and it is inexpensive. It will likely become an “intravenous charcoal” equivalent in the unknown unstable toxic ingestion.

**The Kitchen Sink!**

When all else fails..... ECMO and Balloon Pumps may save your skin! Once I have fired my last “medical bullet” and I have no therapies left to offer the patient, I start making phone calls to my CV Surgeon (ECMO) and my Interventional Cardiologist (Balloon Pump). These are band-aides, but they may keep the patient alive until the CCB has gone through several half-lives. Don’t wait until you are out of bullets.... call early (when you are starting intralipids).
Summary:

Once I confirm that this is most likely a CCB OD: I start all the treatments “that probably won’t work” at the same time; usually while I’m finishing the ABCDEs and getting access/intubating. I get the D10/25/50, insulin, pressors, and intralipd ordered and to the bedside at the same time I put the orders in for all the other therapies “that probably won’t work.” Next, give the insulin test dose followed by the full dose. If that does not change things within 5-10 minutes I start pressors. I would advocate giving a push dose of pressor in between trials of calcium and during the period when you are waiting for the insulin to have its’ affect. I continue to give calcium and measure the Ca(Phos) multiplier. If there is no affect from all of those therapies then I give the intralipid and call CV Surgery (ECMO) and cardiology (Balloon Pump) and a priest.

Briefly on Beta Blockers:

The therapies for BB and CCBs are so similar that they have to be mentioned.

*Beta-blockers cause hypoglycemia* and this is the **MAIN WAY** to rapidly distinguish the two OD’s.

*Calcium and Glucagon should work better* on BBs than CCBs because the final common receptor (calcium channel) has not been poisoned. Glucagon increases CAMP-dependent phosphorylation, which in turn stimulates the calcium channel. Calcium obviously binds directly to the calcium channel for direct stimulation.

Whole Bowel Irrigation is indicated in Beta Blocker toxicity, but not in CCBs. I recommend you put the NG tube in and put the GoLytely on a infusion pump rather then have the patient drink to clear bowel effluent, but make sure you have confidence in your airway.

Dialysis works for BBs not CCBs, but only shown a morbidity benefit in Atenolol.
Be cautious with high dose insulin. Kids get commonly get hypoglycemic seizures with BB toxicity. Stay on top of your glucose. Check q 15min!

Links

- UT Houston EM Critical Care Conference – email me and I’ll send you a copy of the newsletter.