A REVIEW OF STIMULANTS FOR ADHD FOR THE PRIMARY CARE PROVIDER

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OVERVIEW

- Review Stimulant Treatment for ADHD

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STIMULANTS

- They are an approved indication for the treatment of ADHD in children
- Well documented 300+ controlled trials
- 70% or better improvement in individuals with true ADHD

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STIMULANTS

- Have been shown to decrease interrupting and fidgetiness in the classroom and increase on-task behavior in the classroom

- Improve parent-child relationships in the home as well as compliance and on-task behavior.

    - Also improves other social interactions

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STIMULANTS

- Block the reuptake of DA and NE into the presynaptic neuron
- Increase the release of these into the extra-neuronal space, but...
- Methylphenidate(s) and amphetamines have different mechanisms on release of DA

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HOW I THINK ABOUT TYPE OF STIMULANTS FOR TREATING ADHD…

- TWO groups:
  - ‘The Amphetamines’
    - Dexedrine, Adderall, Vyvanse etc.
  - ‘The Methylphenidates’
    - Ritalin, Metadate, Concerta etc.
- The short half-life of stimulants has always been the problem.
- The science is in how the newer preparations deliver the old drug.

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SOME NUTS AND BOLTS ABOUT STIMULANTS

- Some need higher doses
- Official limit is a guide, if there is a good response without side effects you could increase
- On the other hand, avoid heroic dosing
- There is evidence to support that if one stimulant fails try a different one before going to non-stimulants

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MORE NUTS AND BOLTS ABOUT STIMULANTS

- Be careful what parents mean by non-response – this can vary!
- How are you measuring response?
- Use rating scales (a lot of good ones for free)
  - Child Behavior Checklist, Conners, Vanderbilt
  - No Gold Standard
  - Different measures of drug response do not correlate with each other
- Treat mood and anxiety disorders first, then ADHD

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EVEN MORE NUTS AND BOLTS…

- How I remember it –
  - Methelyphenidate:
    - Heavy dose is 1.5 mg/kg/day
    - Medium dose is 1.0 mg/kg/day
    - Light dose is 0.5 mg/kg/day
    - Range is 0.3 to 2.0 mg/kg/day

  - Dexedrine and Focalin are twice as potent so use half as much

- **NOT AN ABSOLUTE STANDARD**

- Use recommended starting doses from reliable Rx guide and go up or down as clinically indicated
  - I use Epocrates

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AND A COUPLE MORE...

- Diagnosis demands that “several inattentive or hyperactive-impulsive symptoms were present prior to12 years of age
  - What my thoughts are
- They do get misused/abused. People without ADHD can have improvement with rote-learning tasks but do not increase IQ. They can cause euphoria but with dangerous consequences

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THE AMPHETAMINES

- Amphetamine has one chiral center, producing both *dextro* and *levo* isomers
- D isomer was felt to have more potent effects, but later found that L isomer was what some people would only respond to
- Started combining the isomers i.e. Adderall

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SOME AMPHETAMINE PREPARATIONS

- **Dexedrine**
  - Dextroamphetamine sulfate
- **Dexedrine Spansule**
  - Dextroamphetamine in waxy capsule
- **Adderall, Adderall XR**
  - Mixed salts of amphetamine and dextroamphetamine
- **Vyvanse**
  - Lisdexamphetamine
- **Adzenys XR**
  - Amphetamine extended release orally disintegrating tablets
- **Dyanavel XR**
  - Amphetamine extended release oral suspension

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ADDERALL XR – HOW'D THEY DO THAT?

- Capsule contains two types of beads, which together provide a "double pulsed" delivery of amphetamines
- This is similar to BID dosing of regular Adderall

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VYVANSE
LISDEXAMFETAMINE DIMESYLATE

- The first stimulant to be offered as a Prodrug
- “Therapeutically inactive molecule” converted to active form after being absorbed by GI tract
- It is d-amphetamine and l-lysine
- Smoother onset and offset
- Supposedly “less likeable” to substance abusers

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THE METHYLPHENIDATES

- Methylphenidate has two chiral centers, resulting in 4 isomers:
    - d-threo, d-erythro, l-threo, and l-erythro

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SOME METHYLPHENIDATES

- **Ritalin**
  - Methylphenidate
- **Focalin**
  - Dexmethylphenidate
- **Daytrana**
  - Methyl-P transdermal
- **Concerta**
  - Methyl-P extended release capsule
- **Metadate CD**
  - Methyl-P extended release capsules
- **Quillivant XR**
  - Methyl-P extended release oral suspension
- **Quillichew ER**
  - Methyl-P extended release chewable tabs
- **Ritalin LA**

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CONCERTA – HOW'D THEY DO THAT?

- Capsule is not digestible
- Methylphenidate is pumped out throughout the day
- 18mg = 5mg tid, 27mg = 7.5 tid 36mg = 10mg tid, 54 mg =15mg tid
- "Backwards engineered"

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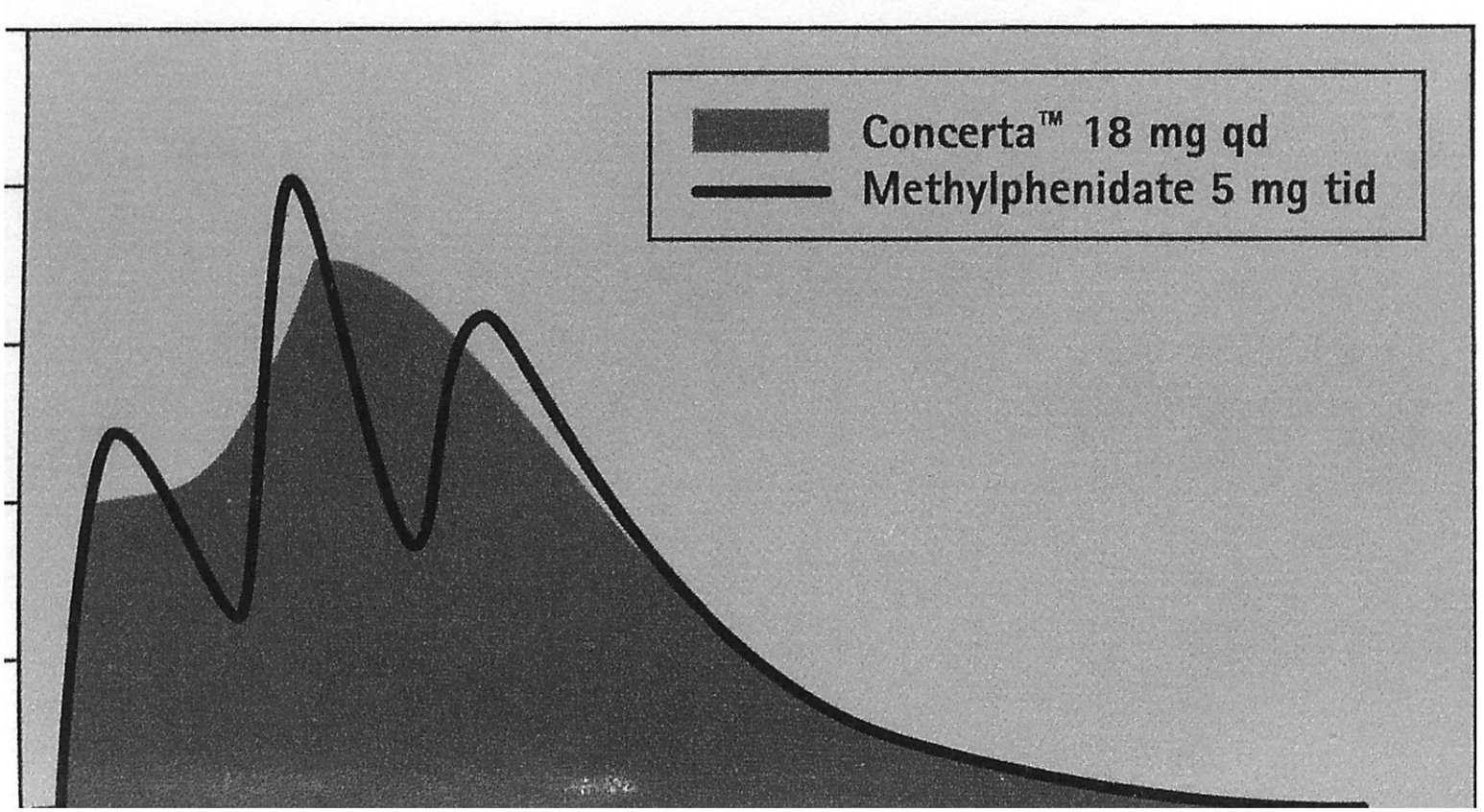
CONCERTA…



This is a cartoon, but it gets the point across.

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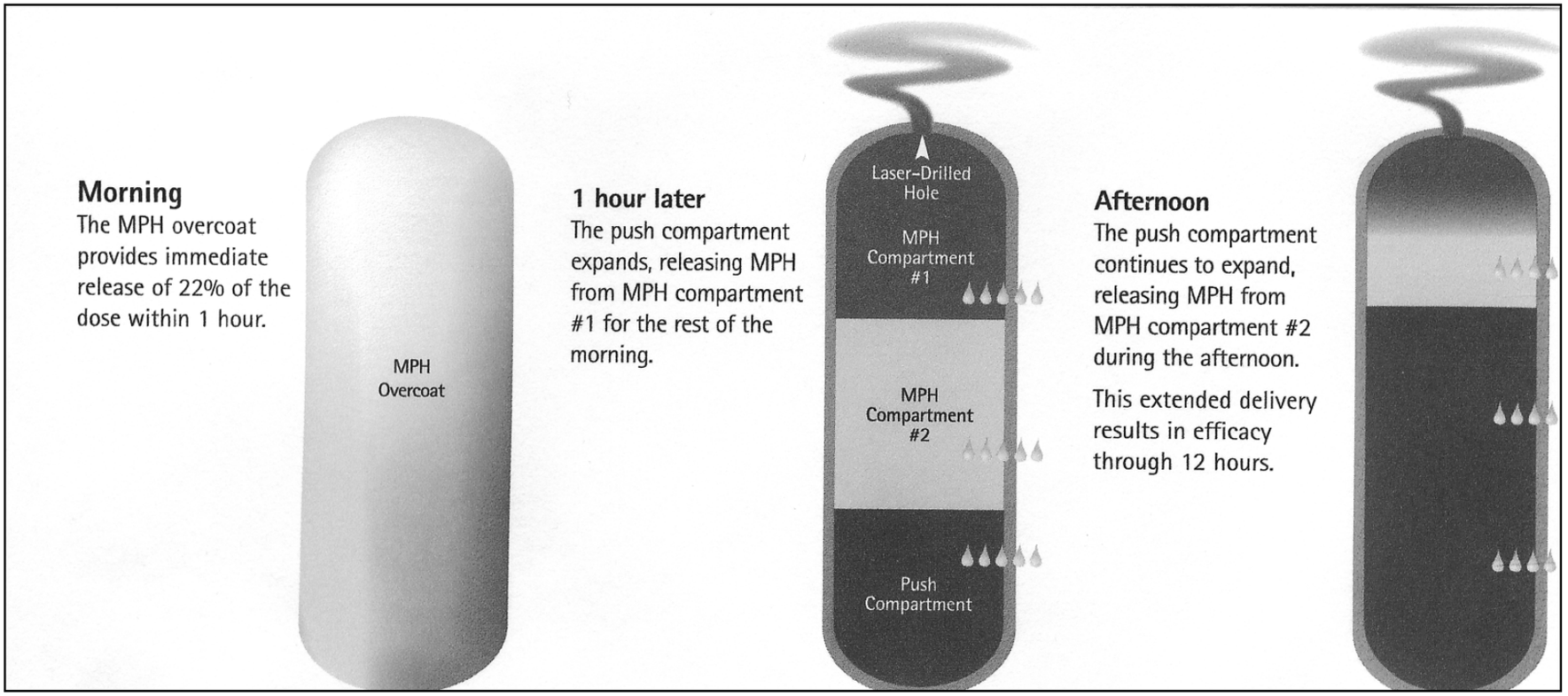
CONCERTA…



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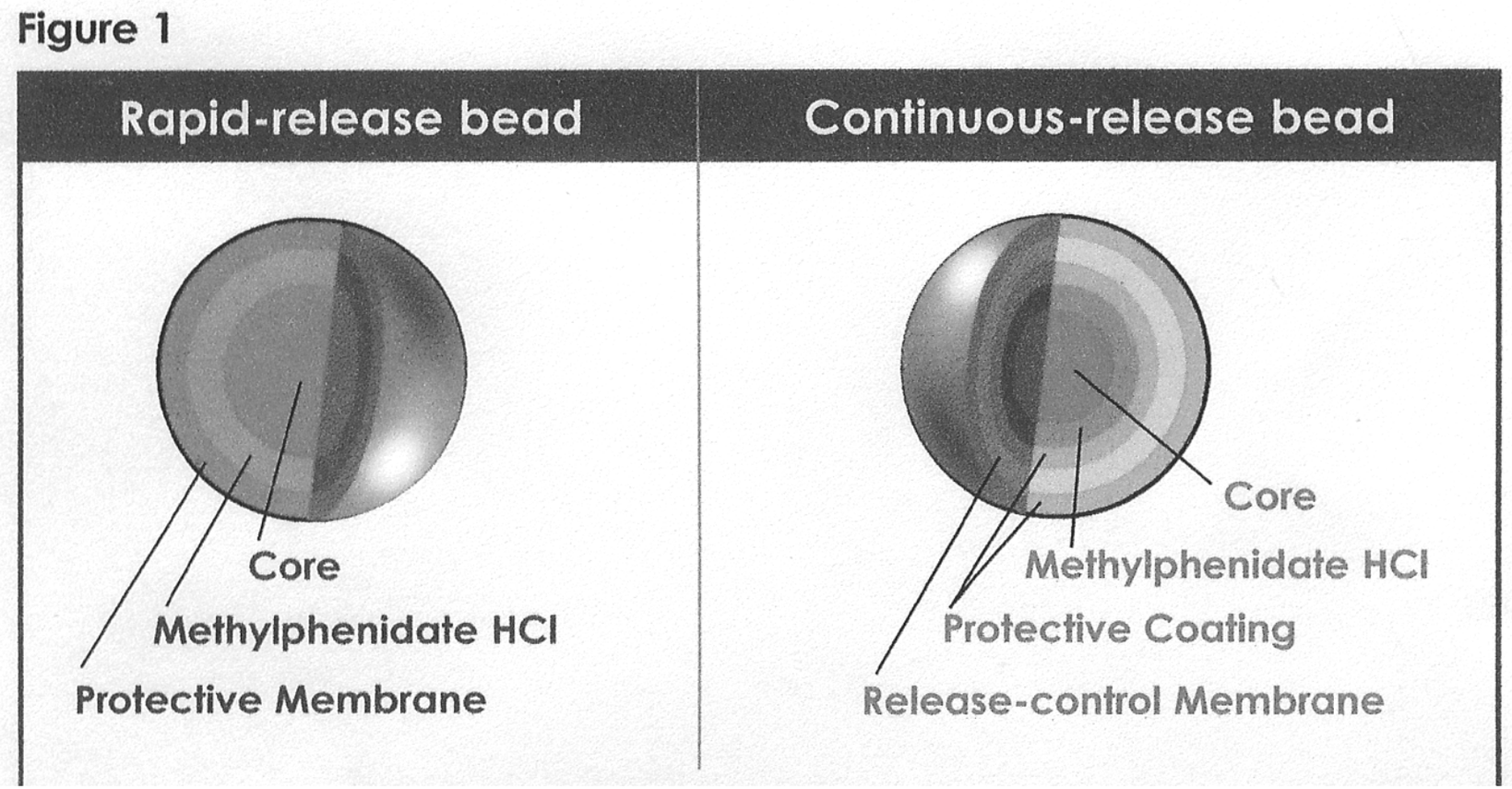
METADATE-CD: EXAMPLE OF BEAD SYSTEM

Figure 1



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METADATE CD

- Long-acting sustained release
- Mixture of long acting and short acting beads
  - 30% 6mg IR(immediate release), 70% 14mg SR(sustained release)
- Duration of action 8-12 hours

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FOCALIN

- Purified d isomer methylphenidate
- 2x as potent so use half as much
- Peak effect is 1-4 hours
- Duration of action 2-5 hours
- Use BID
- Focalin XR same daily dose as Focalin but just once a day

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TICS AND STIMULANTS

- Not an absolute contraindication
- Try different stimulants
- Weigh the cost of the tics with the cost of not successfully treating ADHD
- Some studies are suggesting stimulants decrease tics over time in kids with Tourette's and ADHD
    - Strattera

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QUESTIONS?

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