



Mrkq#1#E dln | #M1/#P G

P relh/#Daledp d

584#67509776

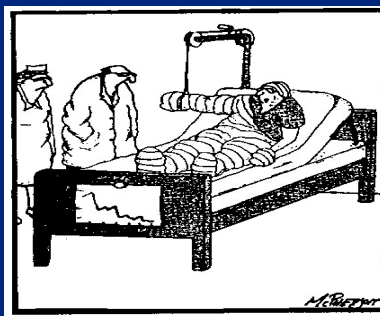
DGKG #dgg#Jhælhg#F rggLwrv#q#F k.lgjhq# #Dgxow

zzz FDOr:P relhfrp

dgggrfC ehærxw.kjhw



# WHY I LEFT FAMILY PRACTICE FOR PSYCHIATRY



*“ Your insurance company is refusing to pay your medical bills. They say you were already an idiot before you decided to roller-blade down the interstate. ”*



# DISCLOSURE

- Paid participant:
  - Real-world Adderall® Studies, 1990's
    - Adderall® IR
- Paid participant:
  - LADD-CAT Study, 2001
    - Adderall XR®
- Paid speaker:
  - Tris Pharma, 2016 ->

Otherwise, since 2001, I have had no financial involvement with any entity involved with ADHD some travel expenses for ADHD conferences at which I spoke *gratis*.



# PSYCHIATRIC TREATMENT



# - ADHD MEDS 101 -

For Home, School, &  
Work



## TREATMENT SUCCESS

-- Bailey's 1<sup>st</sup> Law of Medication --

*“SUCCESS IN LIFE WITH ADHD  
IS PROPORTIONAL TO  
THE PERCENTAGE  
OF LIFE TREATED WELL”*



# TREATMENT SUCCESS

-- Bailey's 2nd Law of Medication --

*"LIFE'S HARDER  
IF THE MEDICINE ISN'T RIGHT"*



# TREATMENT SUCCESS

-- Bailey's 2nd Law of Medication --

*"LIFE'S HARDER  
IF THE MEDICINE ISN'T RIGHT"*

- Drug*
- Delivery System*
- Dose*
- Frequency*
- Timing*



## SLIM OUTLINE

- Available medications
- Non-stimulants & stimulants
- What's officially OK & what's not
- What works - what doesn't
- Forms & delivery systems
- Dosages
- Durations of action
- Engineering continuous action



## CAVEATS *and all that stuff*

- What I say isn't all you need to know nor gospel.
- Information presented is for general medical education.
- It is not intended to establish a standard of care or to bear upon any specific patient.
- I am not endorsing or condemning any product.
- I may use brand names at times because of audience familiarity, not recommendation.
- Any drug may be the best drug for any 1 patient.



# CAVEATS *and all that stuff*

- Ages, dosages, frequencies, durations, indications, etc. discussed will not all conform to FDA's or manufacturer's product information.
- Not every statement or treatment possibility mentioned has received ideal scientific study. Some have received none.
- Some is fact, some is observation, some is opinion.
- Don't rely on or do anything treatment-related in this presentation unless your doctor agrees with it.
- Follow label directions, cautions, & all drug laws.
- Your mileage may vary.



# PSYCHIATRIC APOTHECARY

<u>DIAGNOSIS</u>	<u>AVAILABLE MEDS</u>	
Depression	25 +	00000000000000000000000000000000
Anxiety	18 +	000000000000000000000000
Sleep	17 +	000000000000000000000000
Cyclic Moods	11 +	000000000000
<u>ADHD</u>	6	000000



## ADHD APOTHECARY

<u>NON - STIMULANTS</u>	Adrenalin Inhibitors	clonidine
		guanfacine
	N-T Magnifier	atomoxetine
	<i>Miscellaneous</i>	<i>(none are "indicated")</i>
<u>STIMULANTS</u>	N-T Releaser & Magnifier	amphetamine
		methamphetamine
	N-T Magnifier	methylphenidate



## “ADHD MEDS“

### NOT INDICATED FOR ADHD

*Off-Label Usage with Minimal Evaluation*

- Antinarcotics
  - Provigil®, Nuvigil®
- Appetite Suppressants
  - Adipex-P® (phentermine), Tenuate®, Bontril®, Didrex®
- Antiparkinsonians
  - Symmetrel® (amantadine), Requip® (ropinirole)
- MAOI's
  - Parnate®, Nardil®, Marplan®, Emsam® (selegiline patch)
- Antidepressants
  - Wellbutrin®, Effexor®, Cymbalta®, tricyclics



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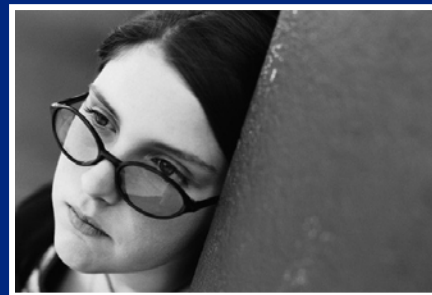
## WHY ANTIDEPRESSANTS ?

### DEPRESSION

Mimics

ADHD

Memory  
Concentration  
Focus  
Motivation  
Interest



*TWICE AS HARD --  
-- HALF AS FAR*

--ADDA Conference Theme, 1996





HERBALS  
NUTRACEUTICALS  
NOOTROPICS  
HOMEOPATHIC MEDS  
DIETARY SUPPLEMENTS

No rigid, placebo-controlled, scientific study  
has ever shown a useful  
and statistically valid benefit  
from any such agent.\*



**WHAT IS A DRUG?**



## DRUG

A substance which,  
when administered to a rat,  
produces a doctoral dissertation.



## ADHD MEDICATION FIELD



## ADHD MEDICATION FIELD

Left Field  
amantadine  
phentermine  
modafinil

Center Field  
amphetamine  
methylphenidate

Right Field  
guanfacine  
clonidine

Stay on the Bus  
methamphetamine  
MAOI's  
tricyclic anti-d's

Dugout  
atomoxetine  
bupropion  
venlafaxine

Center for  
Attention  
& Learning

## 'APPROVED' ADHD FIELD

Left Field  
amantadine  
phentermine  
modafinil

Center Field  
**AMPHETAMINE**  
**METHYLPHENIDATE**

Right Field  
**GUANFACINE**  
**CLONIDINE**

Stay on the Bus  
**METHAMPHETAMINE**  
MAOI's  
tricyclic anti-d's

Dugout  
**ATOMOXETINE**  
bupropion  
venlafaxine

Center for  
Attention  
& Learning

# ADHD STIMULANT FIELD

Left Field  
amantadine  
phentermine  
modafinil

Center Field  
**AMPHETAMINE**  
**METHYLPHENIDATE**

Right Field  
**GUANFACINE**  
**CLONIDINE**

Stay on the Bus  
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Dugout  
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bupropion  
venlafaxine

Center for  
Attention  
& Learning

## STRATTERA®

### Atomoxetine

- Failed Antidepressant
- Non-Stimulant
  - Better P.R.
  - In drug-misuse patients?
- Non-Controlled
  - Can be called in
  - Can be refilled
- OK: 6 YO - Adults
- Doses 'missable'
  - Effect rolls over
- Main engine vs helper-engine
  - Booster?



## STRATTERA®

### Atomoxetine

- Frequent Side Effects . . .
  - GI upset common - 20% - nausea, vomiting, pain
  - Poor appetite common
  - Sleepiness frequent
  - Headache
  - Urinary flow problems
- Other Issues . . .
  - 'Black-box' warning - suicide discussion required
  - Blows up bipolar & cyclothymia - especially teens?
  - Liver damage occasional



## STRATTERA® Atomoxetine

- Nuisances
  - Rarer success than stimulants - 75% vs 95%
  - Slow onset - 1 month -- *after* target dose
- Concerns
  - Unpredictable metabolism
    - Dosage & frequency vary
  - Drug interactions
  - CV cautions suggested
    - -- as with stimulants
- 2 Achilles' Heels !!
  - Vague, indistinct effect
    - Harm from missed doses not noticed
  - Initial reassurance . . .
    - ---> *stealthy fadeaway*
  - *Frequently works for 4-6 months - only !!*

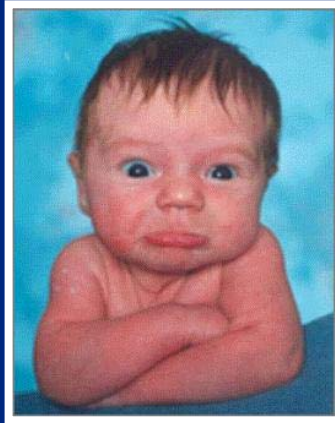


## ALPHA-2 AGONISTS 'INHIBITORS' Clonidine - Guanfacine

- Inhibit norepinephrine signaling in brain
  - Reduces overactivation
- Best ---- ADHD w/ *Oppositionality, Agitation, Anger, & Aggression*
- Good ---- *Impulsivity & Distractibility*
- Fair ---- *Physical Hyperactivity*
- Poor ---- *Inattention & Focus*
- Helpful with tics
  - Virgin or stimulant-augmented (disputed)
- “De-fuser”



## ALPHA-2 AGONISTS



DE-FUSING CANDIDATE



## CLONIDINE

- **OLD ADULT ANTIHYPERTENSIVE - *Catapres*®**
  - Short-acting tabs not indicated for ADHD
  - Not practical
    - 4 doses/day - ADHD rebound 3 X a day if dose late
  - Daytime sleepiness
  - Kapvay® - time-release
    - No adult or long-term studies
    - Tic treatment consideration
- **BEST FOR HYPERACTIVITY - IMPULSIVITY**
  - Good inhibitor
  - Poor attention magnifier
- **BEST USES:**
  - Tabs as sleep agent (*not indicated*)
  - Add to stimulants



## GUANFACINE

- Old adult antihypertensive drug - *Tenex*®
  - Better for ADHD than for HBP
  - Most US use is ADHD
- Inherent 8-12 hour duration
- Economical - generic long and short work well
- Useful addition to stimulants
- First-line / safest agent for tics (*disputed*)
- Suppresses night ADHD awakenings
- Intuniv® - 12-24 hour duration
  - More 'magical' than generic guanfacine
  - Most prefer to generic
- Best for **Irritability, Anger, S.T.O.** (*Status Ticked Off*)
  - “*He’s nicer!*”



## GUANFACINE DEFICIENCY





# STIMULANTS



## STIMULANT DRUG

One which causes a temporary arousal of central nervous system activity, resulting in increases in:

- Alertness
- Wakefulness
- Consciousness
- Awareness
- Stimulus recognition
- Sense of well-being
- Mood
- Energy
- Interest
- Motivation



## STIMULANT DURATIONS -- VIP!

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Rit.® Tabs			?												
Focalin® Tabs															
Dex Tabs															
'Adderall®' Tabs				?											
Dextroamphetamine ER															
F-XR® R-LA® M-CD®															
Aptensio XR®															
Adderall XR®							?								
Concerta®							?								
Vyvanse®															
Dyanavel XR®															
Mydayis®											?			?	



DISPENSING or CONCENTRATION

CURVES

VS

EFFECTIVENESS

CURVES

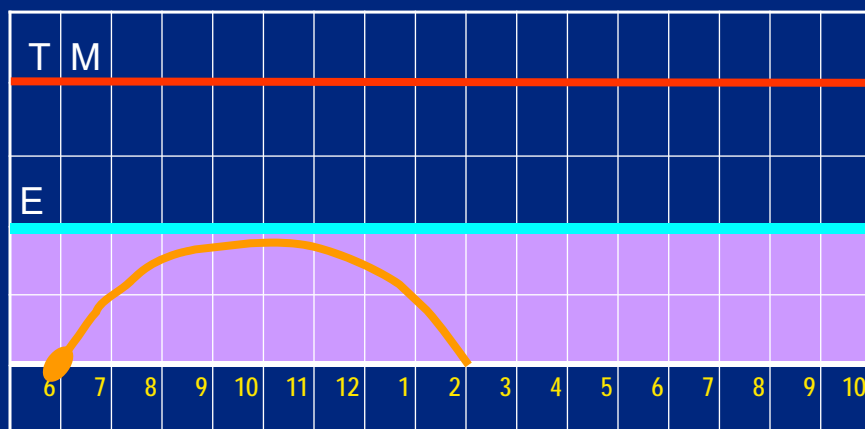


# CONCENTRATION $\neq$ EFFECTIVENESS



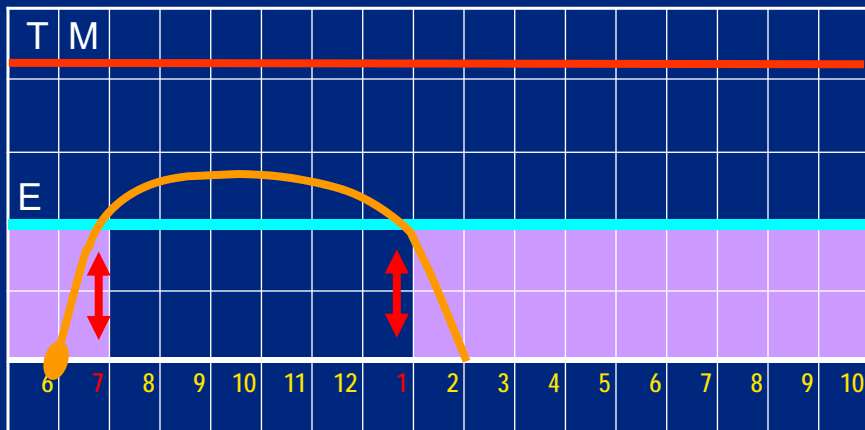
Center for  
Attention  
& Learning

# GENERAL EFFECTIVENESS CURVE



Center for  
Attention  
& Learning

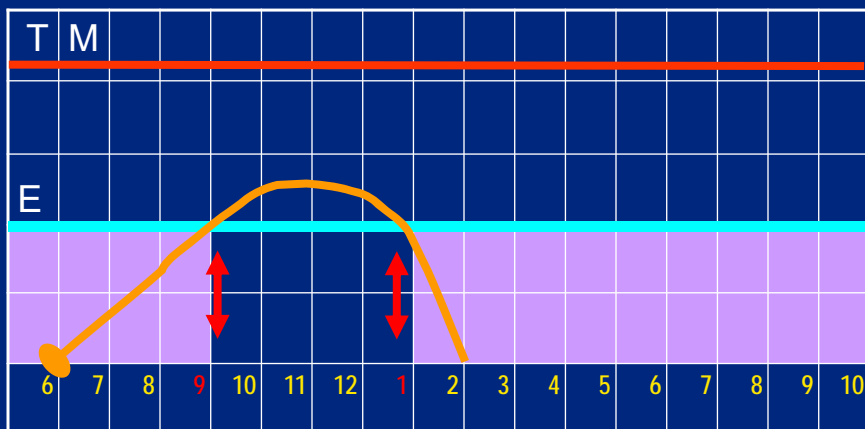
# GENERAL EFFECTIVENESS CURVE



Rapid Onset



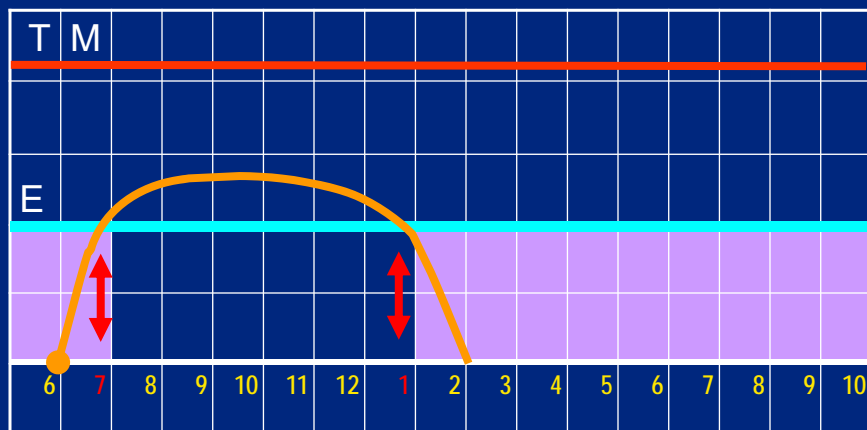
# GENERAL EFFECTIVENESS CURVE



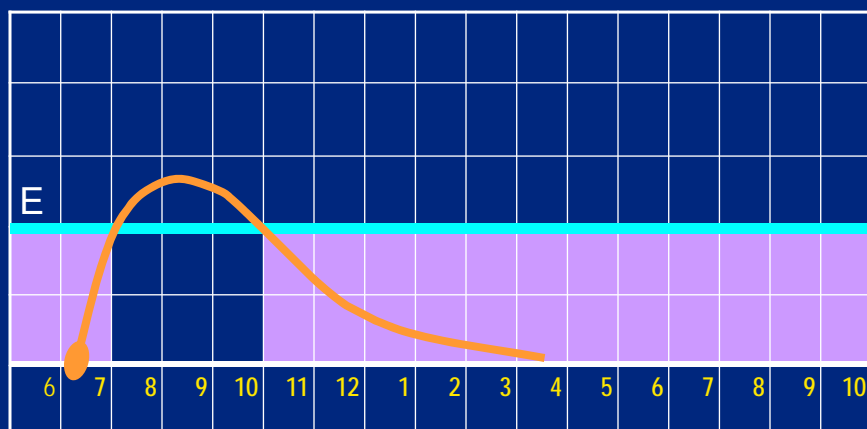
Slow Onset



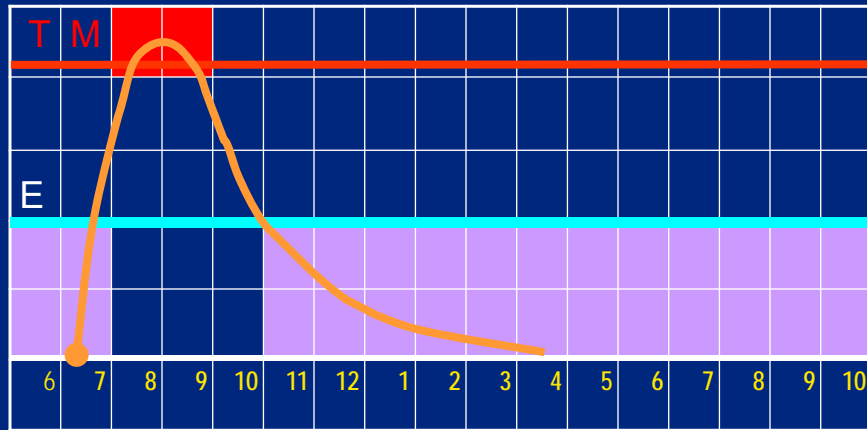
# "SOAPBOX MODE"



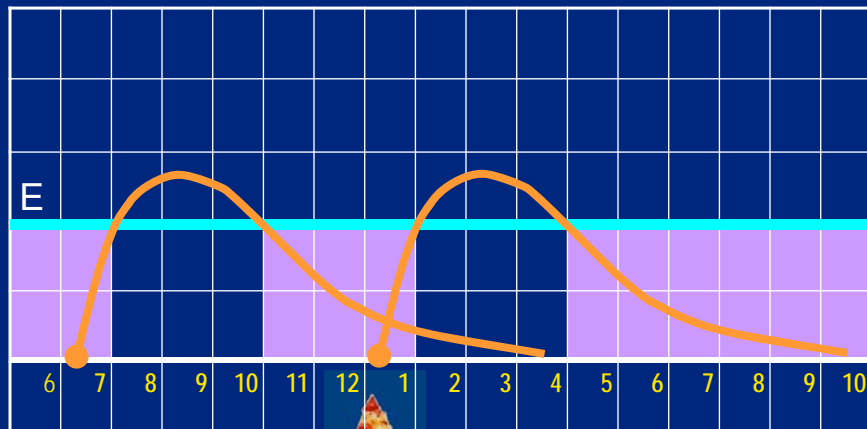
# NOT LONG ENOUGH



# SO GIVE MORE ?



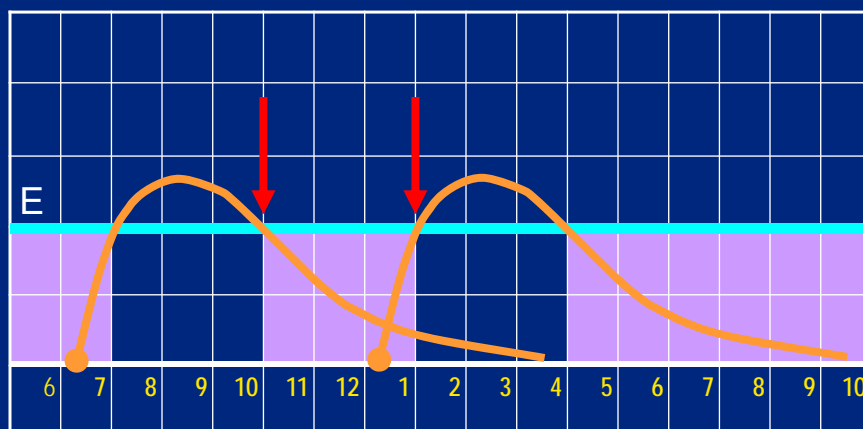
# PLAN B - ALL TOO COMMON



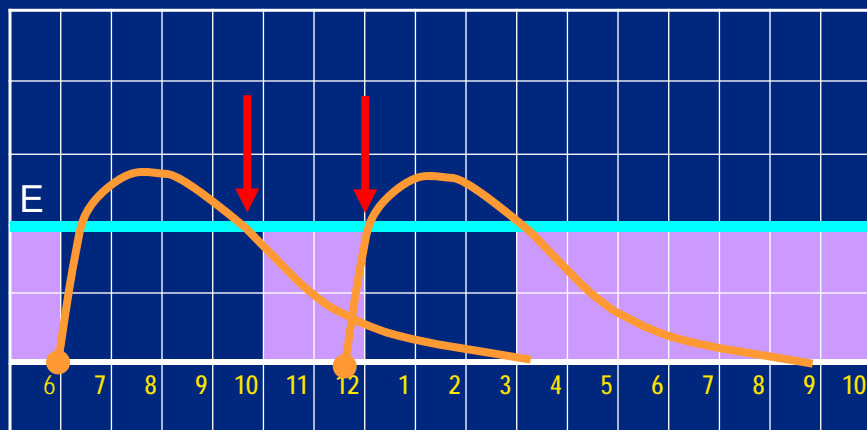
# ALL TOO COMMON



# PLAN B - MIDDAY GAP

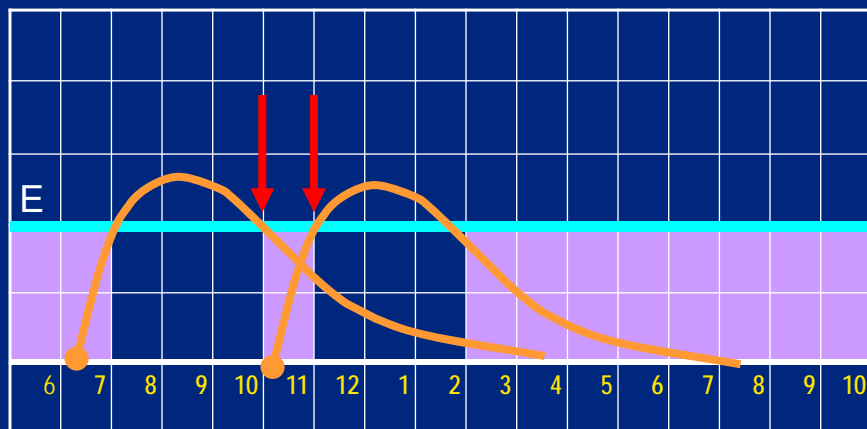


# GAP CURE? - FAIL !



Center for Attention & Learning

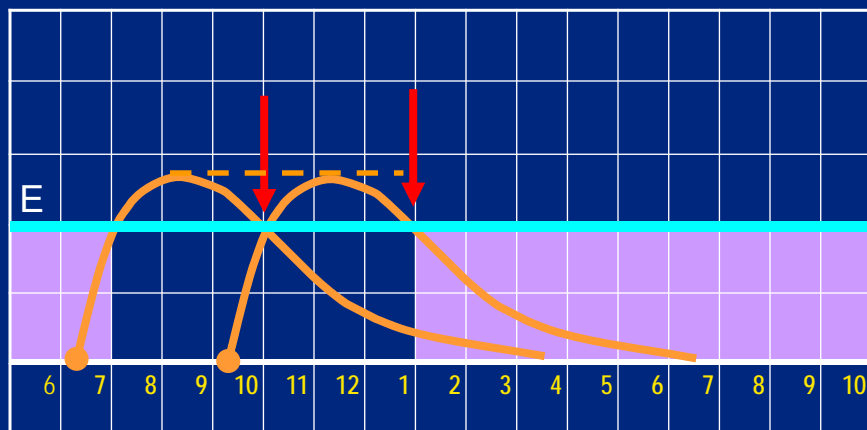
# GAP CURE? - FAIL !



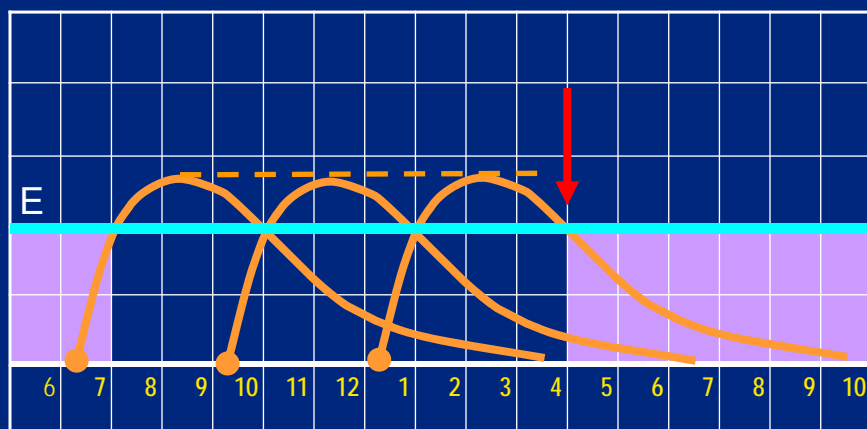
Center for Attention & Learning



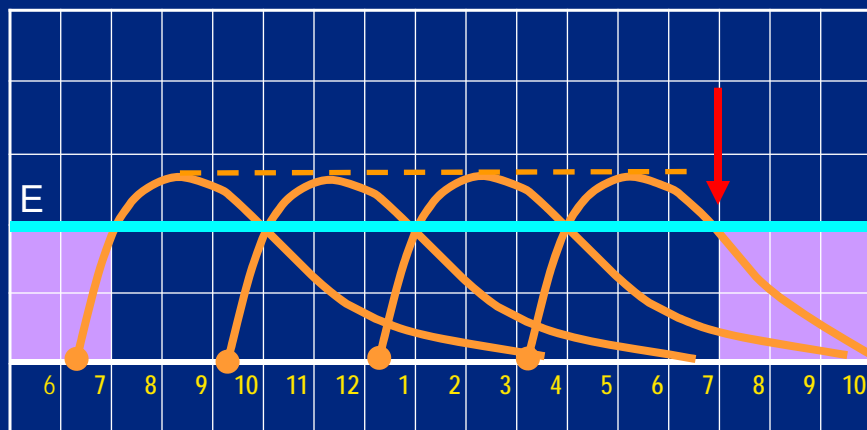
# GAP CURE ... but ...



# GAP CURE ... better, but ...

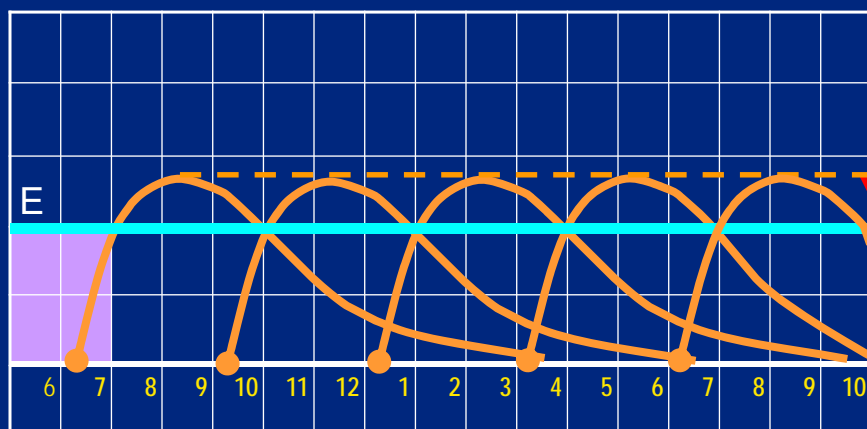


## GAP CURE . . . *betterer, but . . .*



Center for  
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& Learning

## NEW PROBLEM . . .



Center for  
Attention  
& Learning

# METHYLPHENIDATE



## METHYLPHENIDATE - *The Early Years*

- 1955 – Ritalin®
- 1982 – Ritalin SR® discontinued
- 1999 – Metadate ER®
- 2000 – Concerta®
- 2001 – Metadate CD®
- 2001 – Focalin®
- 2002 – Ritalin LA®
- 2002 – Methylin® IR liquid & chewable tabs
- 2005 – Focalin XR®
- 2006 – Daytrana® patch

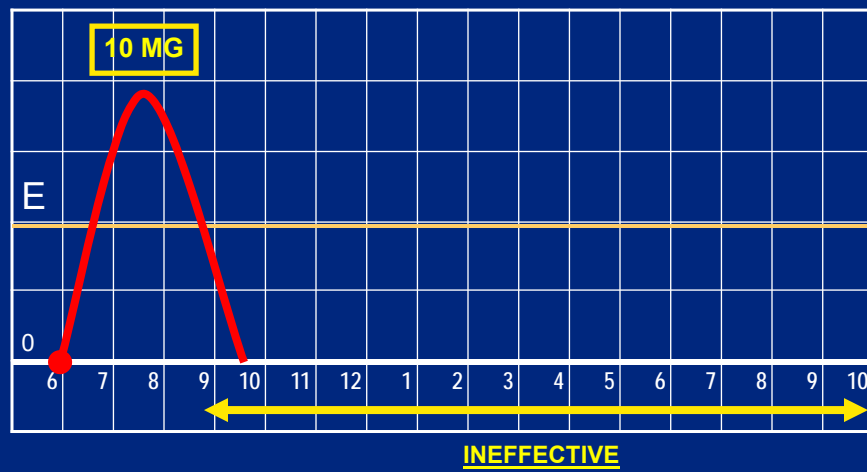


## METHYLPHENIDATE - *The Recent Years*

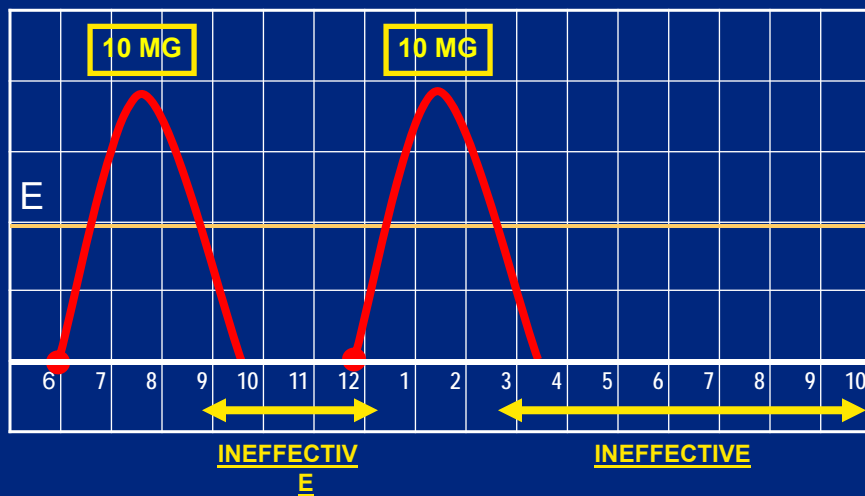
- 2012 – Quillivant XR® liq
- 2015 – Aptensio XR® cap
- 2015 – QuilliChew ER® tab
- 2017 – Cotempla XR-ODT orally dissolving



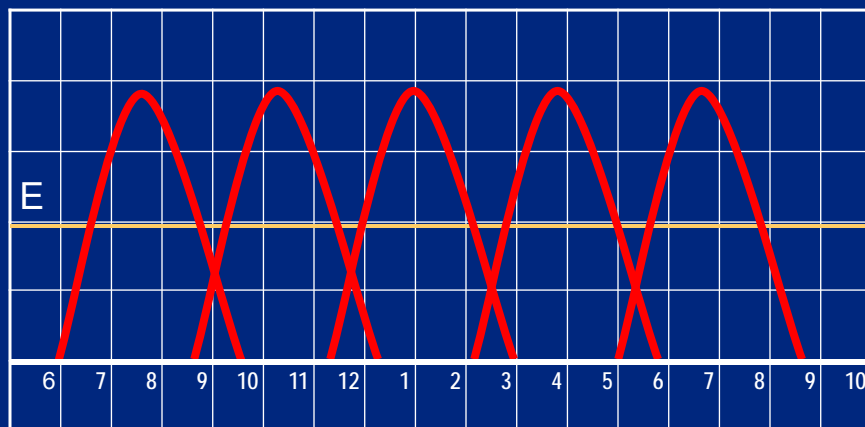
## METHYLPHENIDATE IR – 10 mg



# METHYLPHENIDATE IR – 10 mg



# METHYLPHENIDATE IR – 10 mg

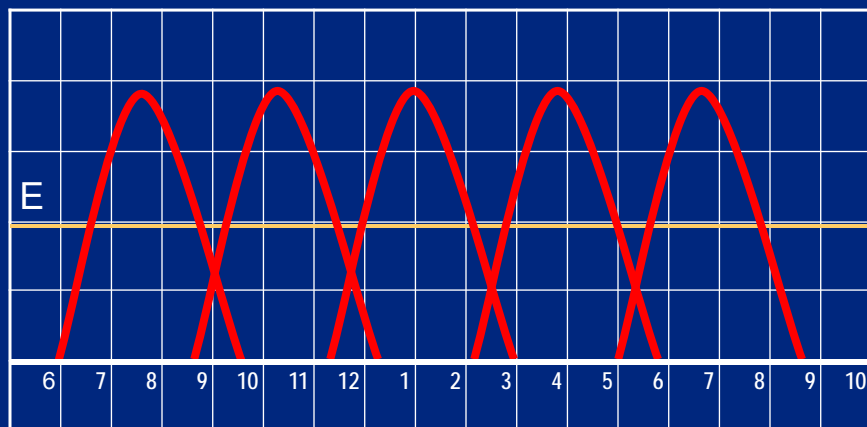




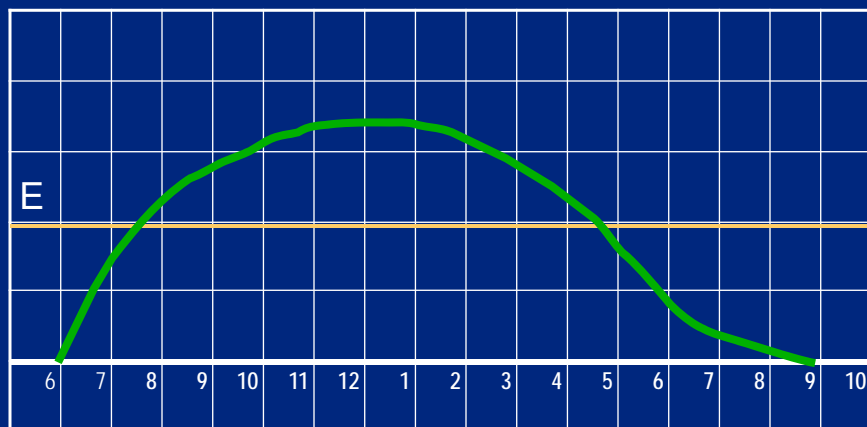
TEXAS LIMOUSINE



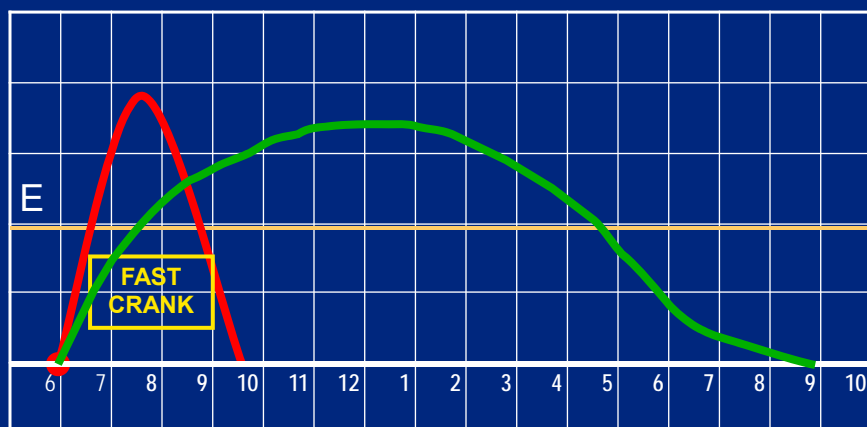
## METHYLPHENIDATE IR – 10 mg



## GENERAL LONG-ACTING CURVE

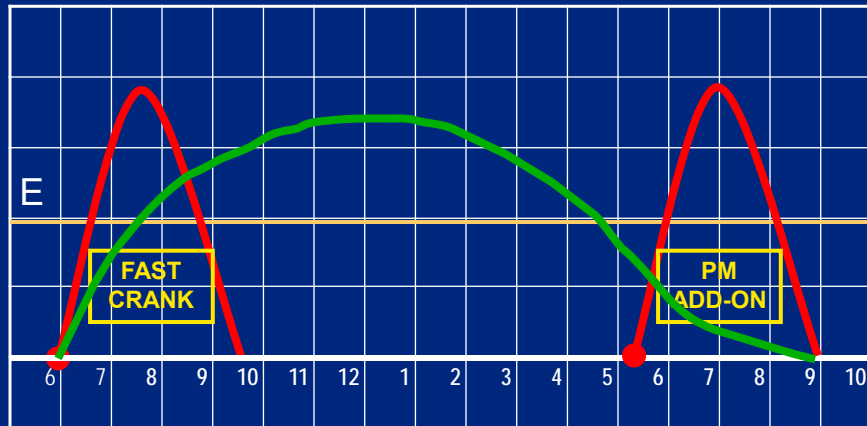


## METHYLPHENIDATE IR Useful for Short Treatment Periods



# METHYLPHENIDATE IR

Useful for Short Treatment Periods



# DELIVERY SYSTEMS





## IMMEDIATE - RELEASE DELIVERY SYSTEM

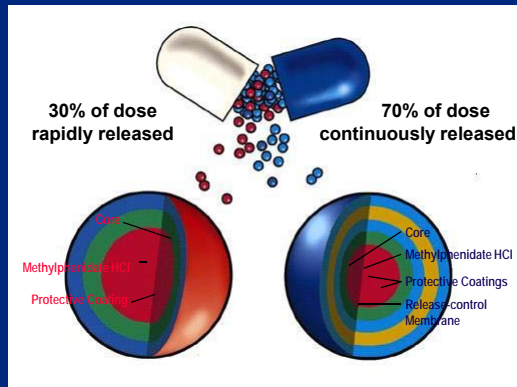


## EXTENDED - RELEASE DELIVERY SYSTEM



# Metadate<sup>®</sup> CD Delivery System

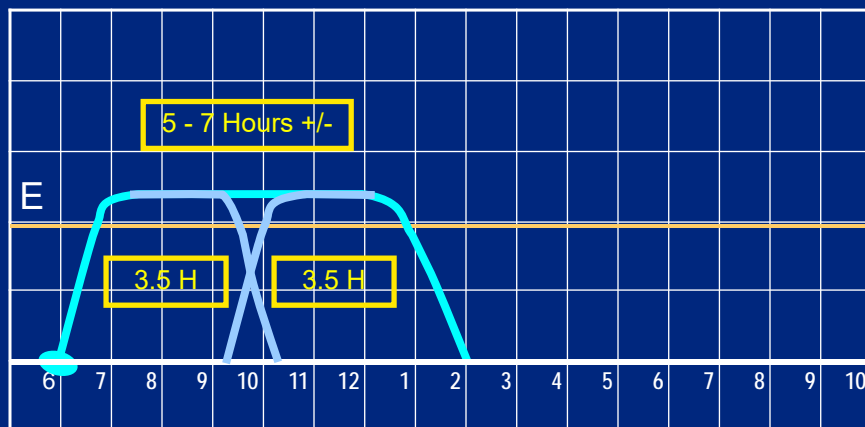
30% - Rapid Release (IR)  
70% - Continuous Release (ER)



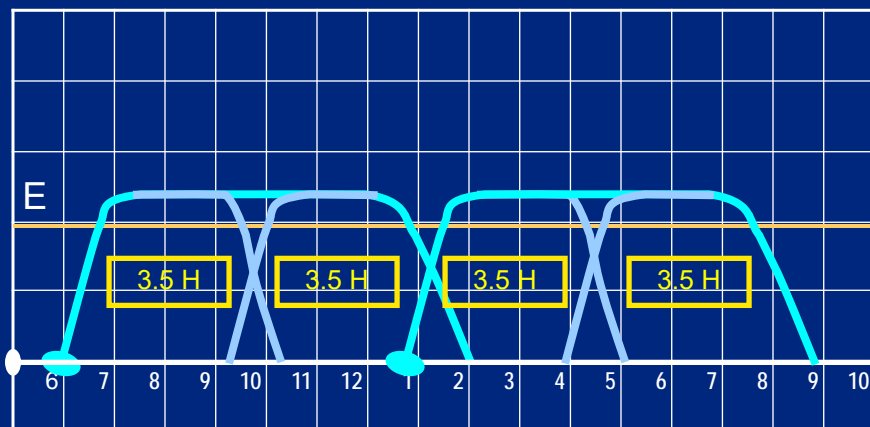
Beads shown are not actual sizes  
Metadate is a registered trademark of Celtech Pharma, Ltd.



## 2-PHASE SYSTEM - 1X

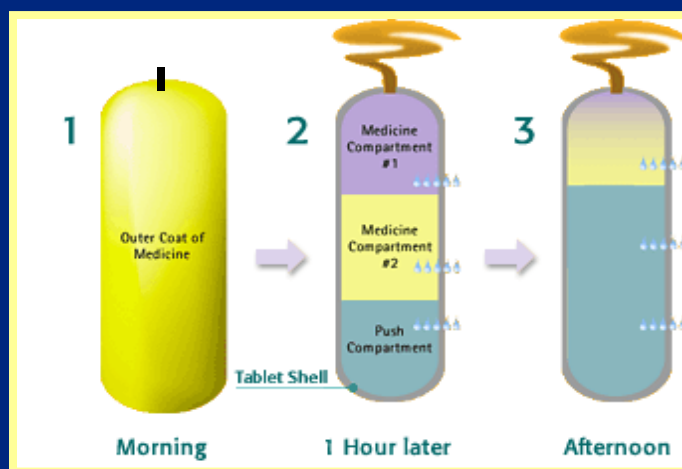


## 2-PHASE SYSTEM - 2X



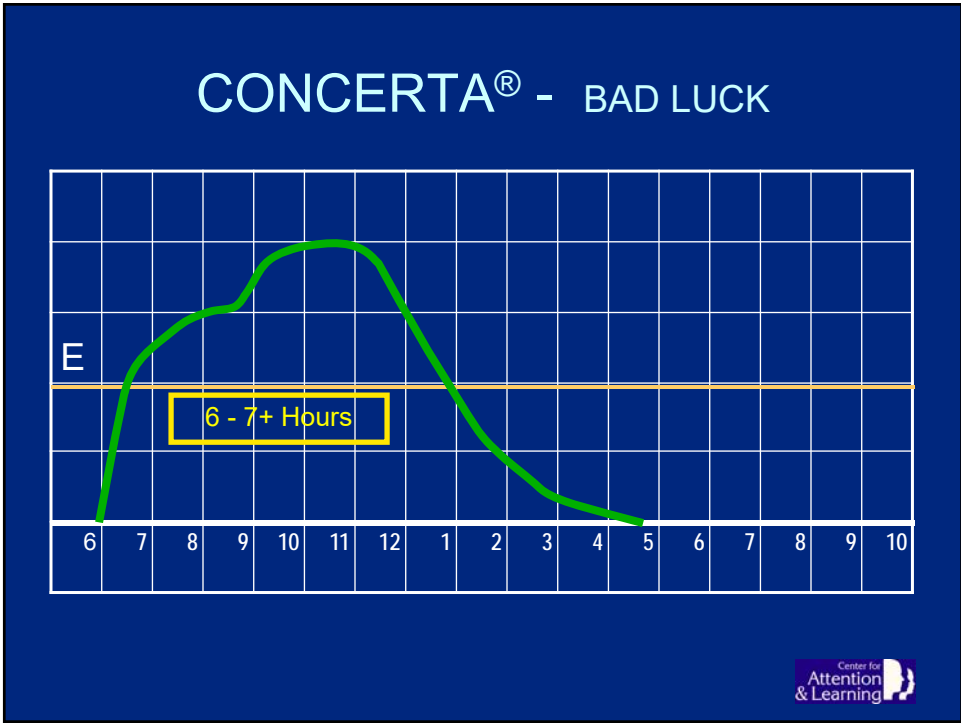
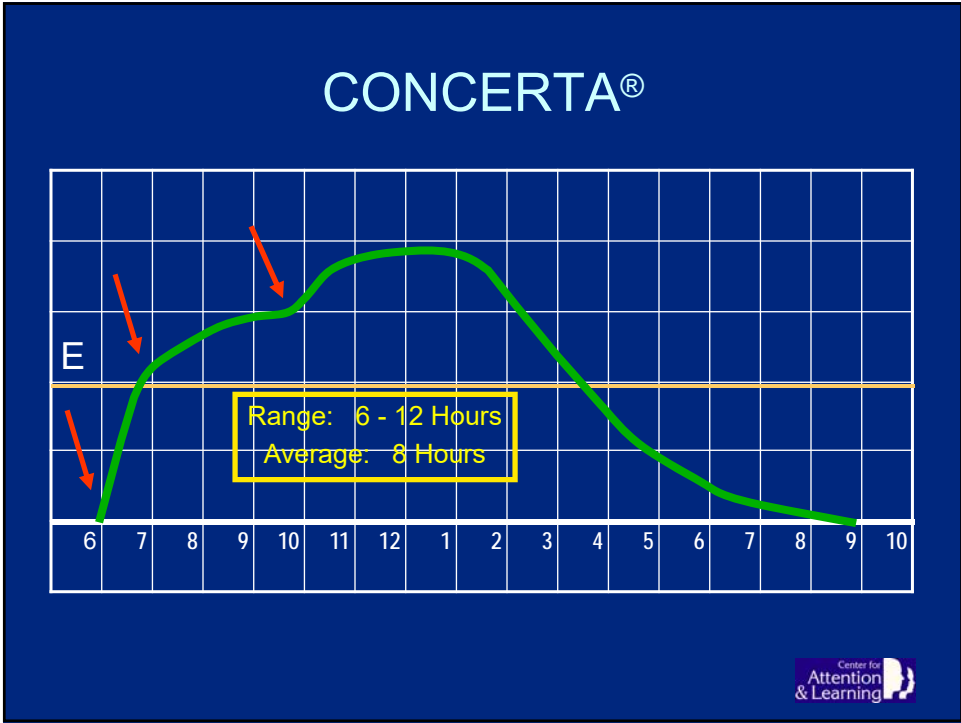
Center for Attention & Learning

## CONCERTA<sup>®</sup> - Delivery System

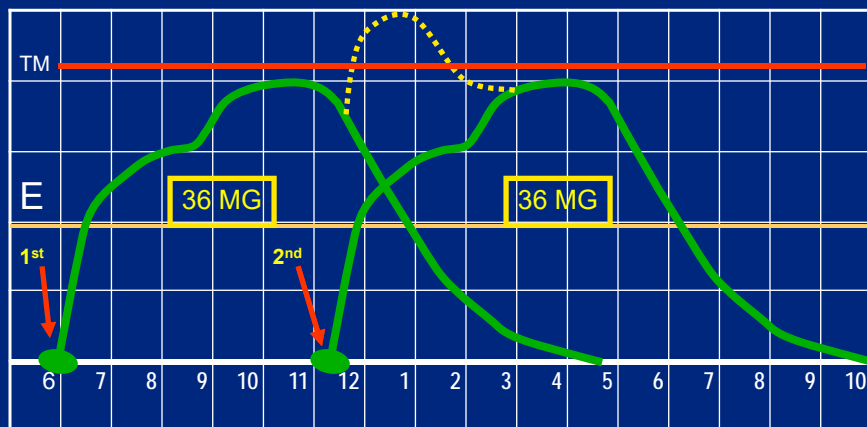


©Janssen Pharmaceuticals, Inc.

Center for Attention & Learning



# CONCERTA® 2X



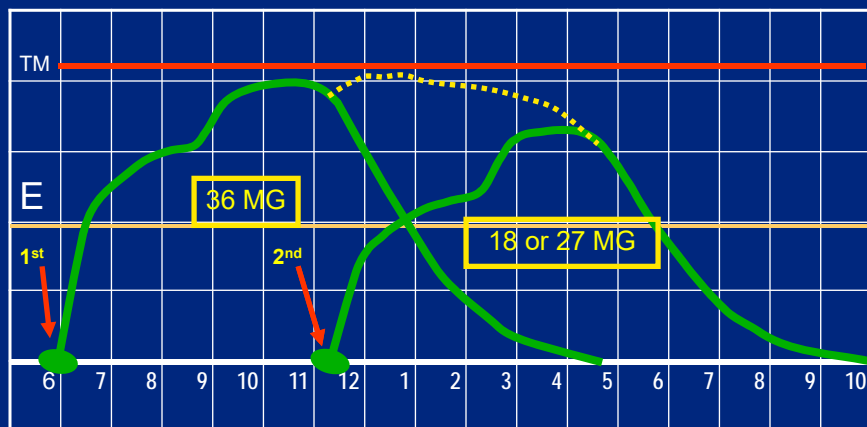
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# BUMPY DAY

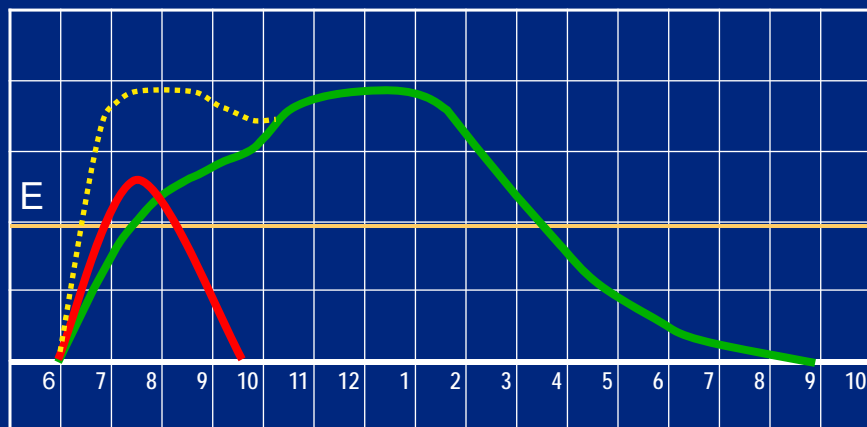


Center for Attention & Learning

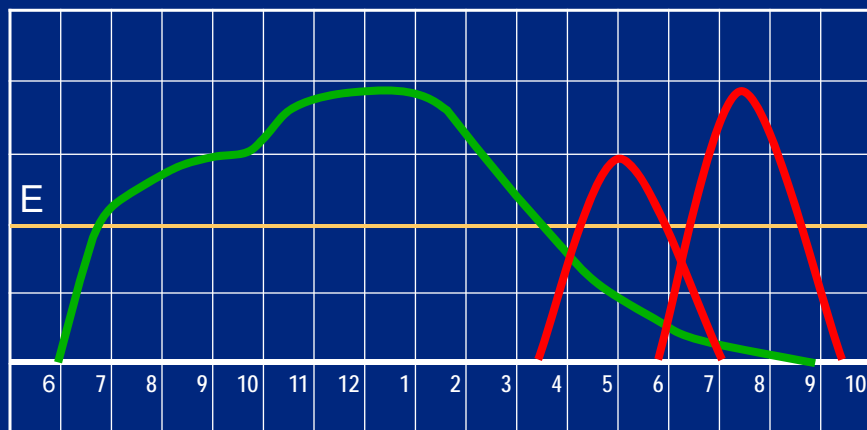
# CONCERTA® 2X



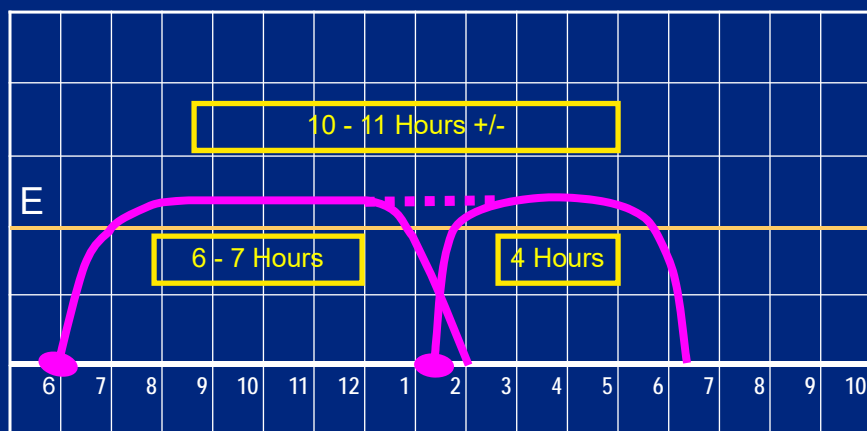
# CONCERTA® + MPD-IR BOOST



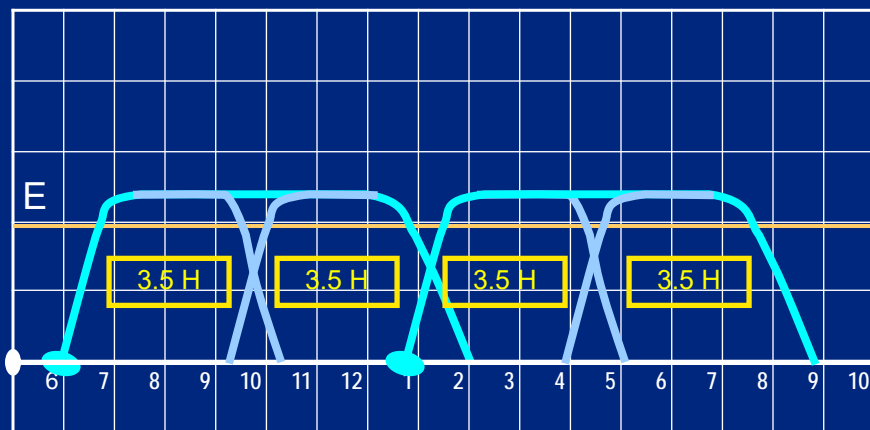
# CONCERTA<sup>®</sup> + MPD-IR - PM 2X



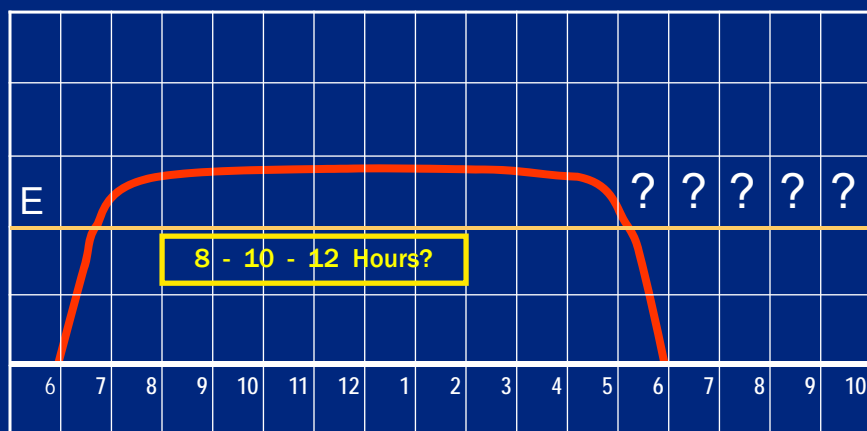
# MID-RANGE + SHORT



## 2-PHASE SYSTEM - 2X



## LONG-ACTING PRODUCT





## DAYTRANA® PATCH

*“Ritalin Patch”*

- 4 patch sizes - \$13/patch/day
- Not adult indicated
- Hold to hip x 30 seconds
- Slow to crank - 2 hours
- Only ADHD Rx must remember to start and stop!
- Must remember to remove at 9 hrs
  - Then remains 3 hours - problem for sleep-sensitive patients
- Beware:
  - Waistbands, water, contact sports, application difficulties, impatience, heat, forgetfulness, skin irritation
- Irritated skin absorbs more\*
- Contact sensitization is rare, but: be aware that if it happens, it may preclude oral MPD treatment -- for life.



## AMPHETAMINES



## AMPHETAMINES - *The Early Years*

- 1887 - Amphetamine **synthesized in Germany**
- 1893 - Methamphetamine synthesized
- 1932 - Benzedrex® **OTC amphetamine inhaler** – till 1959
- 1935 - Methamphetamine study #1
- 1937 - Benzedrine for headaches - Chas. Bradley, MD\*
- 1937 - Dexedrine® **marketed by SKF** – fatigue, etc
- 1940 - Dextroamphetamine **in WWII** – ‘go pills’
- 1942 - Benzedrine® **ADHD study #1 published** – Bradley
- 1950 – Marketing explosion – not for ADHD



## AMPHETAMINES – *The Later Years*

- 1960 - Obetrol® - dex + meth
- 1976 - Dexedrine Spansules® - **1<sup>st</sup> E-R ADHD Rx**
- 1994 - Obetrol® - meth removed, reformulated as MSA
- 1996 - Adderall - Obetrol renamed. **approved for ADHD**
- 2001 - Adderall XR® - **1<sup>st</sup> good ER system**
- 2007 - Vyvanse® - **very long acting**, approved for ADHD



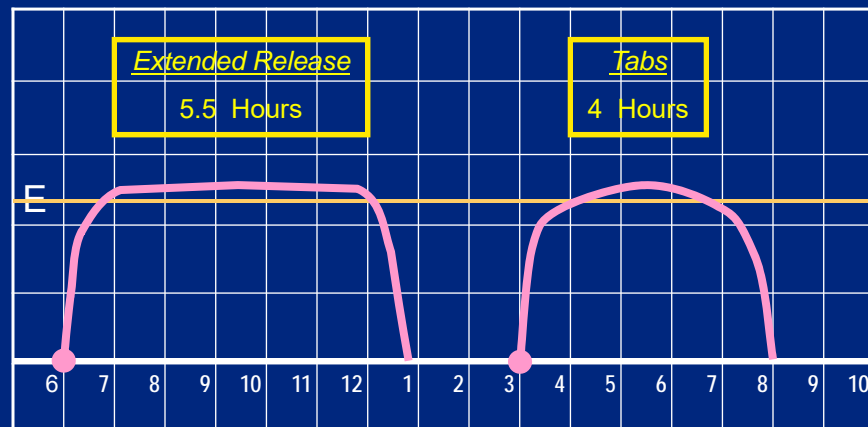
## AMPHETAMINES – *The Recent Years*

- 2013 - ProCentra® - dex IR liquid
- 2015 - Vyvanse® - new approval for Binge Eating Disorder
- 2015 - Evekeo® - the return of Benzedrine®
- 2015 - Zenzedi® - dex tabs
- 2015 - Dyanavel XR® - dex time-release liquid
- 2016 - Adzenys XR-ODT® - orally dissolving tablet
- 2017 - Mydayis® - 3-phase capsule

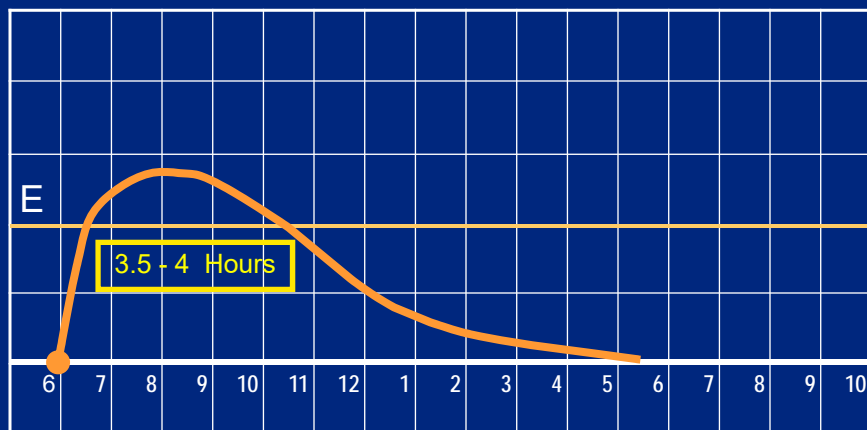


## DEXTROAMPHETAMINE

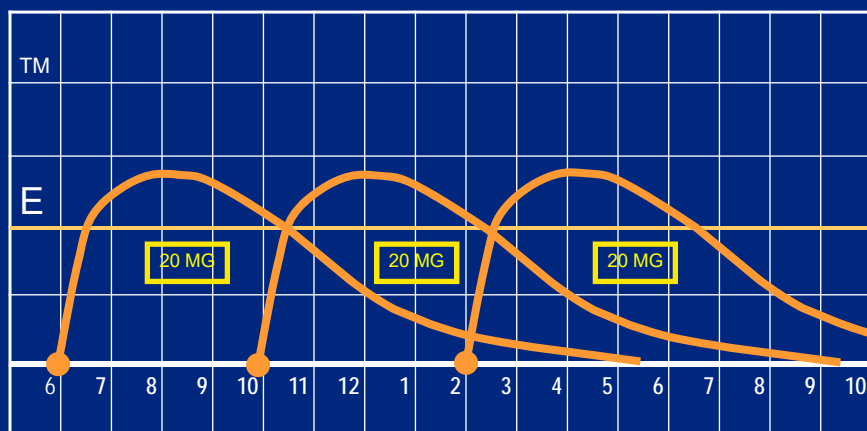
Dextroamphetamine Tabs - 2.5-30 mg  
Dextroamphetamine ER - 5, 10, 15 mg



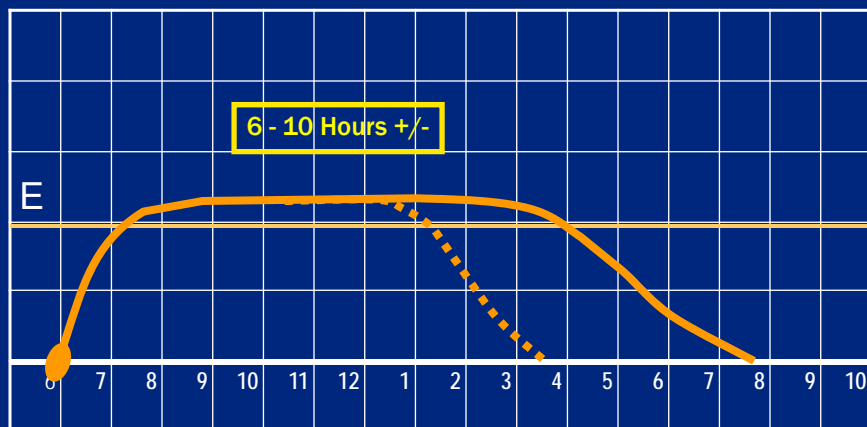
# ADD-ER-ALL<sup>®</sup> TABS 1X



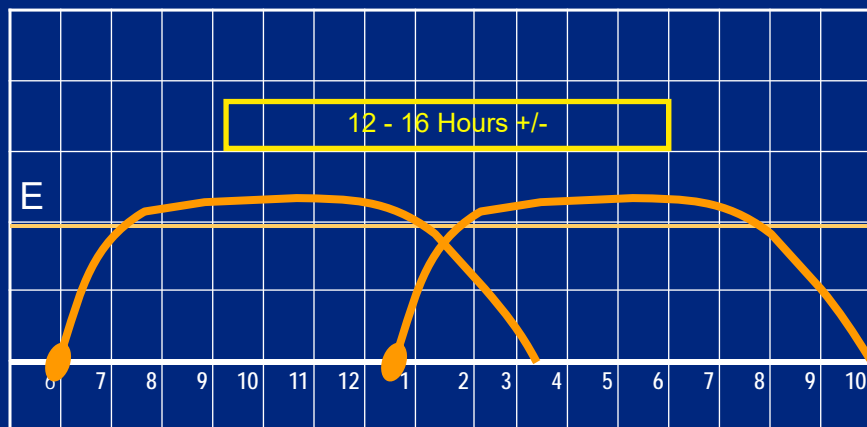
# ADDERALL<sup>®</sup> TABS 3X



# ADDERALL XR® 1X



# ADDERALL XR® 2X

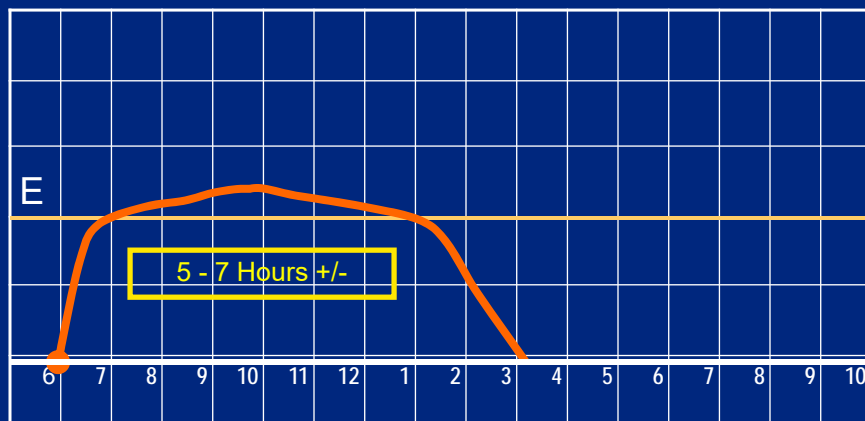


# COMMON STIMULANT DOSING & DURATION

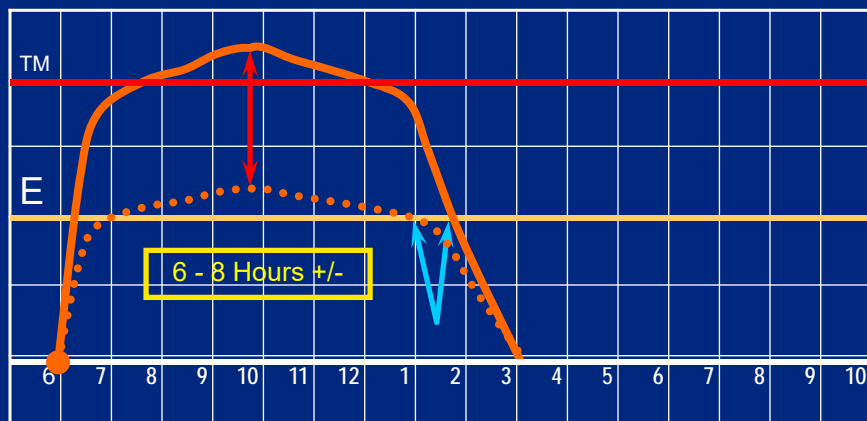
INCREASING THE DOSE  
OF MOST STIMULANTS  
INCREASES THE CONCENTRATION --  
*NOT THE DURATION*



## MPD ER – 20 mg 1X

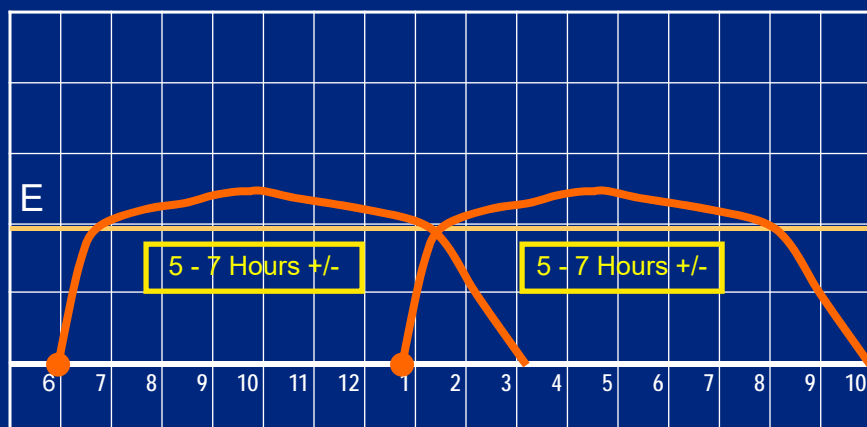


### MPD ER – 40 mg 1X



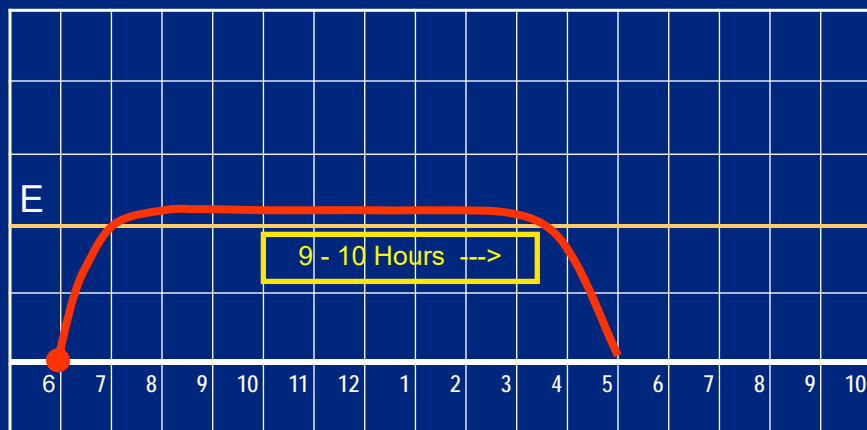
Center for  
Attention  
& Learning

### MPD ER – 20 mg 2X



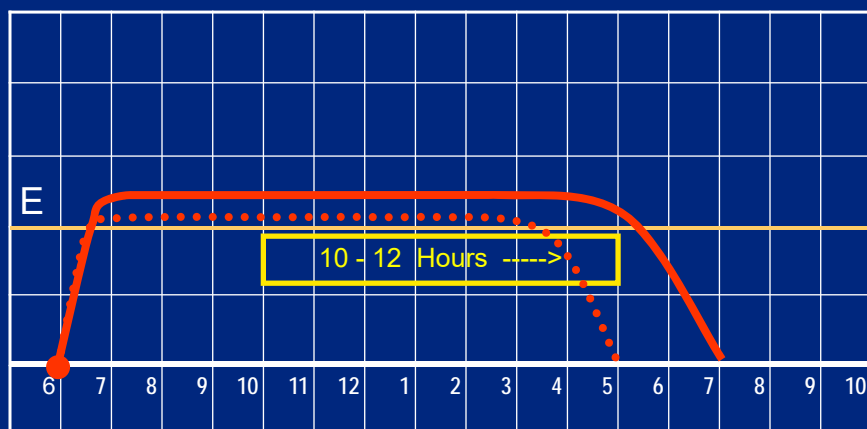
Center for  
Attention  
& Learning

## VYVANSE® 30 mg



Center for  
Attention  
& Learning

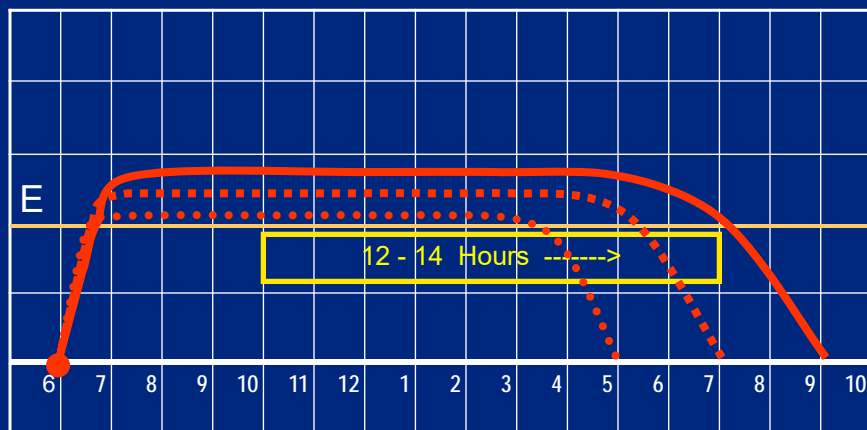
## VYVANSE® 40 mg



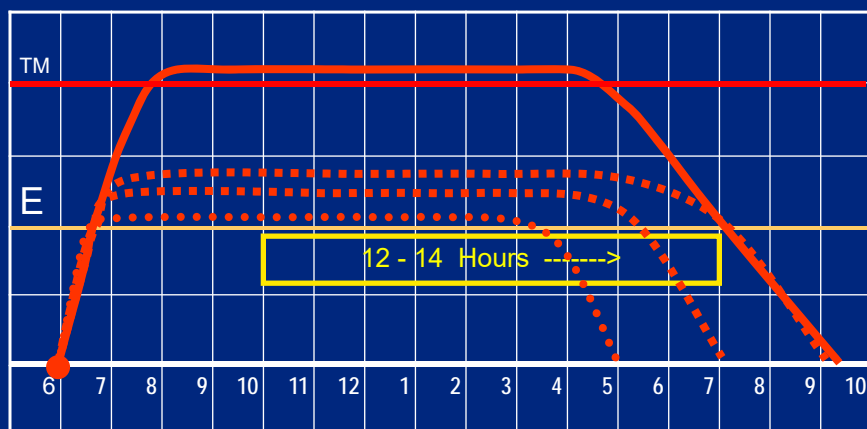
Center for  
Attention  
& Learning



# VYVANSE® 50 mg



# VYVANSE® 60 mg



## STIMULANT DOSING

### PRACTICAL BUT NONSTANDARD PROCESS FOR STIMULANT DOSING

*This must be done with thoughtful discussion  
and physician direction.*

*The patient doesn't know what 'normal' is!*

- Go up carefully until it doesn't feel right
- Drop down one notch
- That's frequently the best dose
- If then it's not good enough, change the drug!
- Even if it *seems* fine, it's OK to try a change!



## STIMULANT DOSING

Insufficient dosages  
and durations of dosing  
mislead everyone involved  
- *teachers, spouses, bosses, doctors* -  
and the patient -  
to think maximum potential  
has been reached!



## ADHD MEDS

*“I take my pill,  
but my life doesn’t seem  
to be getting any better.”*



## TREATMENT SUCCESS

*Bailey’s 1<sup>st</sup> Law:*

*SUCCESS IS PROPORTIONAL TO  
THE PERCENTAGE OF LIFE TREATED WELL*

•



## TREATMENT SUCCESS

*Bailey's 1<sup>st</sup> Law:*

*SUCCESS IS PROPORTIONAL TO  
THE PERCENTAGE OF LIFE TREATED WELL*

- Treat 7 days a week
- Treat from arising
- Treat as close to bedtime as practical
- Treat weekends, holidays, breaks, & summers
  - *Drug holidays hurt you, not help you*
- Keep level constant through the day
- Use long-acting meds whenever possible
- Combine products and even different drugs if needed



## - ADHD MEDS 101 -

*For Home, School, &  
Work*



**- ADHD MEDS -**  
*Use Your Brain All Day*



**- YOU MAY REJOICE -**





Mrkq#1#Edh | #M1#P G

P relh/#Daledp d

584#6750776

DGKG #dgg#Jhøwng#F rggLwqv#q#F k.guhq# #Dgxow

zzz FDOr:P relhfrp

dgggrfC ehøvrxw.kjhw

