

ADHD- Past & Present

RAY CORDRY, D.O.



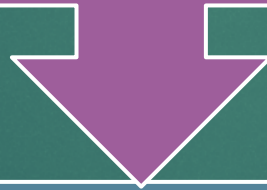
Points to Convey

- ▶ History
- ▶ Functional Symptoms
- ▶ Pathophysiology
- ▶ Clinical Evaluation
- ▶ Treatment
 - ▶ Medications
 - ▶ Other treatment modalities
 - ▶ Prognosis



Confessions

I have no affiliation with any pharmaceutical company or research grants



If I suggest any off - label use of a medication it will be presented in that manner

Past (Quite the History) !

Prior names for ADHD

1902 - defect of moral control

1908 – high – grade feeble – minded

1937 – racemic amphetamine (Benzedrine) originally for kids with severe headaches rather their behavior and school performance improved

1957 – hyperkinetic impulse control which was an improvement from 1956 and Thorazine (chlorpromazine) was tried on what Freed & Pfeifer were calling hyperkinetic emotionally disturbed children

1963 & 1966 (methylphenidate) Ritalin was introduced leading to a popular term minimal brain dysfunction syndrome

1970 – 1971 – The Comprehensive Drug Abuse Prevention and Control Act made stimulants Schedule III then 1971 changed to schedule II

History

movement greatly expands as several books helped reinforce the belief that ADHD is not a diagnosis, was created by pharmaceutical companies to make money. It was also promoted that diet, food allergies and food additives were

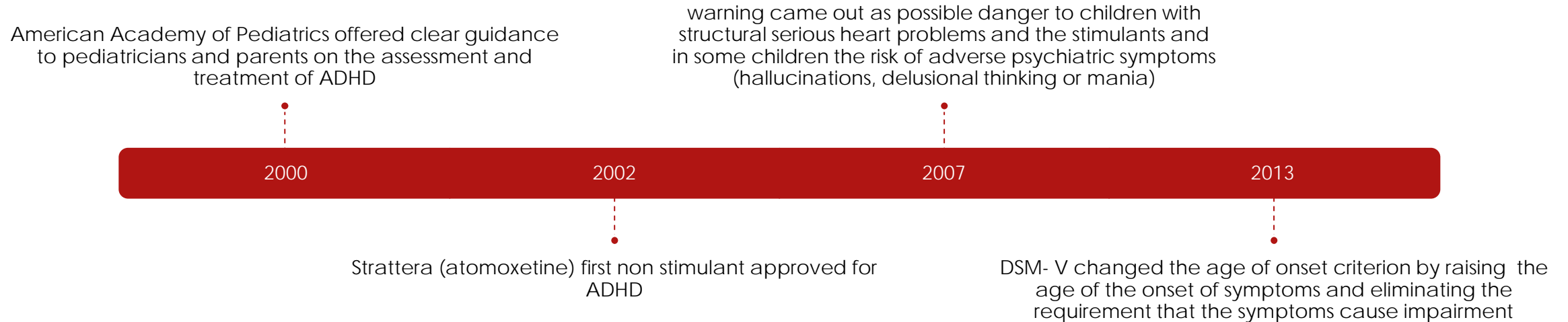


1987 – American Academy of Pediatrics changed the name to ADHD and recommendations that drug therapy in the treatment of ADHD is useful



1993 – A newsletter was begun “ The ADHD Report” followed in 1994 with DSM-IV – TR the types of ADHD were introduced – ADHD combined type, ADHD predominantly inattentive type, ADHD predominantly hyperactive type

History



History One More Time

Medication TimeLine

1937 – Benzedrine (racemic amphetamine)

1943 – Desoxyn (methamphetamine hydrochloride)

1955 - Ritalin (methylphenidate)

1955 – 1983 – Biphedemine (mixed amphetamine /
dextroamphetamine)

1960 – Adderall (mixed amphetamine/ dextroamphetamine)

1975 – 2003 – Cylert (pemoline) 2002 – atomoxetine (Strattera)

1982 – current – many long acting and delivery systems have
been introduced to the market

DSM –V ADHD

- ▶ Persistent pattern of inattention and / or hyperactivity – impulse control that interferes with functioning or development as characterized (1) and / or (2)
- ▶ 1. Inattention: Six or more of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic / occupational activities
- ▶ Note: The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or failure to understand tasks or instructions. For older adolescents and adults (17 & up) , at least 5 symptoms are required



1. Criteria - Inattention

- ▶ a. Often fails to give close attention to details or makes careless mistakes in schoolwork , at work, or during other activities (e.g.,, overlooks or misses details, work is inaccurate)
- ▶ b. Often has difficulty sustaining attention in tasks or play activities (e.g., has trouble remaining focused during lectures , conversations , or lengthy reading)
- ▶ c. Often does not seem to listen to when spoken to directly (e.g., mind seems elsewhere, even in the absence of any obvious distraction)
- ▶ d. Often does not follow through on instructions and fails to finish schoolwork , chores or duties in the workplace (e.g., starts tasks but quickly loses focus and is easily sidetracked)
- ▶ e. Often has difficulties organizing tasks and activities (e.g., difficulty managing a sequential task , difficulty keeping materials and belongings in order , messy , disorganized work , poor time management and fails to meet deadlines)

Criteria - Inattention

- ▶ f. Often avoids , dislikes ,or is reluctant in tasks that required sustained mental effort(e.g. , schoolwork , homework , for older adolescents and adults preparing reports , completing forms , reviewing lengthy papers)
- ▶ g. Often loses things necessary for tasks or activities (e.g. , school materials, pencils , books , wallets , keys , paperwork , cell phones , eyeglasses)
- ▶ h. Is often distracted by extraneous stimuli (for older adolescents and adults , may include unrelated thoughts)
- ▶ i. Is often forgetful in daily activities (e.g., doing chores , running errands , for older adolescents and adults , returning phone calls , paying bills , keeping appointments)

Criteria – Hyperactivity & Impulsivity

- ▶ Six or more of the following symptoms have existed at least 6 months and they are negative impacting social , occupational / academic activities
- ▶ The same exclusion criteria regarding other diagnosis are repeated
- ▶ a. Often fidgets, or taps hands or feet or squirms in seat
- ▶ b. Often leaves seat in situations when maintaining it is expected to remain in your seat (adults moves around the office or workplace when remaining seated is expected)
- ▶ c. Often runs about or climbs in situations when it is inappropriate (adults or adolescents may just feel restless)
- ▶ d. Often unable to play or engage in leisure activities quietly
- ▶ e. Is often on the go as if “driven by a motor” (adults or below not comfortable with being still or seated in a meeting or activities , restless hard to keep up with in places)
- ▶ f. Often talks excessively
- ▶ g. Often blurts out an answer before a question has been completed (e.g., completes people’s sentences , cannot wait their turn in a conversation)
- ▶ h. Difficulty waiting their turn
- ▶ I Often interrupts and intrudes on others

Completing the Disorder

- ▶ B. Several inattentive or hyperactive – impulse symptoms present prior to 12 Y/O
- ▶ C. Several inattentive or hyperactive – impulse symptoms present in two or more settings
- ▶ D. There is clear evidence that the symptoms interfere with or reduce the quality of , social , academic ,or occupational functioning
- ▶ E. The symptoms do not occur exclusively during the course of schizophrenia or another psychiatric disorder and are not better explained by another mental disorder(e.g. , mood disorder , anxiety disorder , dissociative disorder, personality disorder , substance intoxication or withdrawal)

Specify

1

Combined presentation – inattentive and hyperactive

2

Predominately in attentive (often missed in girls)

3

Predominantly hyperactive / impulsive presentation

Epidemiology / Comorbidity

- ▶ 45,736 parents were called by the National Survey of Children's Health about children 2 – 17 current ADHD prevalence was 8.4%. In this group 62% were on meds , 46.7% behavioral treatment and 23 % of the children received no treatment



Adult ADHD

- ▶ It is called adult ADHD but symptoms began in childhood.
- ▶ Adult ADHD can lead to unstable relationships, poor work or school performance, low self esteem difficulty paying attention, impulsive, restlessness, problems focusing leading to missed deadlines, meetings, and social plans
- ▶ Many symptoms in adults become fewer with age
- ▶ What's typical and what's ADHD & Symptoms severe enough to cause problems , problems that just began or only occasionally occur are not ADHD. Symptoms must be persistent , disruptive and noted from childhood onset originally.

ADHD in Women

- ▶ ADHD is a neurological disorder characterized by a persistent pattern of inattention – with or without hyperactivity and impulsivity that interferes with daily activities
- ▶ While prevalence rates are similar by gender the diagnosis among American men is nearly 70% higher than it is in women(5.4 % of men and 3.2% of women have an ADHD diagnosis)
- ▶ Understanding - ADHD now not totally diagnosed by hyperactivity – inattentiveness is included and can last a lifetime
- ▶ ADHD in women is weighted toward inattentiveness

ADHD Women

- ▶ ADHD Signs and Symptoms / women are prone to these symptom clusters
- ▶ Failing to give close attention to details or making careless mistakes in activities
- ▶ Trouble holding attention on tasks
- ▶ Not following through on instructions and failing to finish duties (e.g., losing focus, getting sidetracked)
- ▶ Trouble organizing tasks and activities
- ▶ Easily distracted
- ▶ Forgetfulness in daily activities

ADHD Women

- ▶ Common Comorbidities
- ▶ Anxiety (25 – 40 % of people with ADHD have an anxiety disorder)
- ▶ Mood disorders
- ▶ Dysregulated eating (bulimia most common type)
- ▶ Externalizing disorders , like oppositional defiant, conduct disorder, (mostly found in women with higher impulsivity)
- ▶ Personality disorders like Borderline personality
- ▶ Gender bias is rarely intentional, but is insidious and pervasive
- ▶ ADHD “tests” are geared more toward hyperactivity

Pathophysiology

- ▶ Research suggested that multiple cognitive deficits in children with ADHD are prominent. When measured in a laboratory setting these symptoms did not distinguish ADHD from control subjects regarding cognitive deficits
- ▶ Working memory – term for what is being considered at any moment this has been associated with prefrontal cortex and connections to parietal area
- ▶ Working memory is modulated by catecholamines dopamine and norepinephrine so interventions that increase (DA) & (NE) in the prefrontal cortex enhance working memory which improves attention
- ▶ Norepinephrine stored in locus coeruleus when stimulated by vagus nerve enhances memory




Pathophysiology

Dysfunction in the prefrontal cortex and striatum (contains locus coeruleus) are most common abnormal brain findings reported for ADHD



Judith Rapoport examined 300 subjects ½ with ADHD and ½ without in the ADHD subjects the gray matter thickness was thinner by 5% in ADHD and some as they matured and / or some with medication the thickness corrected. Study is more of an observation as many variables are being explored.



Scandinavian study located 25,000 patients with ADHD matched medication therapy with national crime registry and found an inverse relation to using medication and crime involvement this was true for stimulant and nonstimulant medications



Pathophysiology

- ▶ In this group it was felt stimulants reduced impulsiveness and complications
- ▶ To reemphasize of over 46,000 patients identified 62% were treated on medication, 46.7% were in behavior therapy but high concern that 23 % had no treatment manipulate the 46000 number and so around 11,000 were not treated

Resulting in a leaning toward getting into trouble and being less

likely to succeed to the top of their potential and even slide into

much darker ways of trying to survive

Diagnosis Co – Morbidity with ADHD

- ▶ Many facts to consider to arrive at ADHD – everything that wheezes is not asthma and everything that jumps around may not be ADHD
- ▶ Usually observe symptoms at least by 7 years old
- ▶ Co-Morbidities important to consider in assessment
- ▶ Specific learning disabilities in ADHD (10 – 40 %)
- ▶ Oppositional defiant disorder (30 – 60 %)
- ▶ PTSD
- ▶ Bipolar disorder
- ▶ Substance abuse
- ▶ Tourette's disorder and psychosocial morbidities

Mimics of ADHD

- ▶ Language disorders
- ▶ Learning disability
- ▶ Anxiety disorder/ obsessive compulsive disorder
- ▶ PTSD
- ▶ Depressive and bipolar disorders
- ▶ Oppositional defiant disorder
- ▶ Iron deficiency anemia / malnutrition
- ▶ Side effects of medication / or substance abuse
- ▶ Sleep disorder
- ▶ Child abuse/ neglect/ and or stressful home environment
- ▶ Parent problems i.e., psychological issues or inadequate educational experience



Medical Conditions Associated with ADHD

Seizure
disorder

Thyroid
disorder

Traumatic
brain injury

Fetal
alcohol
syndrome

Lead
poisoning

Tests to Consider Ideal group

- ▶ Vision / hearing
- ▶ CBC with differential to rule out anemia
- ▶ Thyroid studies to include TSH
- ▶ Lead screen
- ▶ Genetic screen
- ▶ Toxicology screen
- ▶ If available functional MRI to rule out issues with prefrontal cortex, striatum, and cerebellum
- ▶ EKG to rule out conditions before starting a stimulant

Rating Scales

- ▶ Vanderbilt useful in diagnosis and rating results of treatment
- ▶ The Swan useful for strengths, weakness and symptoms
- ▶ American Academy of Pediatrics toolkit available at
- ▶ www.nichq.org/resources/toolkit
- ▶ Important in gathering information as important as tests- child, primary care givers, teachers, parents and other caretakers
- ▶ If not improvement in 3 months refer to mental health provider

Additional Management Tips

- ▶ First people associated with the child must realize this is a psychiatric disorder with biological underpinnings not the child's fault and struggling with schoolwork, paying attention, sitting still and other behaviors are not just the child being lazy or oppositional
- ▶ Putting that energy to productive use can be helpful such as exercise
- ▶ They have more trouble staying organized than other children their age and organizational aids are helpful
- ▶ Catching the child doing something right and praise is helpful among all the redirection they get during the day

Management Tips Continued

- ▶ Individual, family therapy and medication can help – some parenting instruction to help with management of ADHD and setting boundaries within the child’s abilities. Some parents get frustrated and feel we just want them to do nothing and no boundaries this is usually because they are frustrated and at a lost point
- ▶ Appraise them of the school can work with them on an IEP or 504 plan to individualize the educational experience
- ▶ It is important to encourage the parents to also take care of them it is a stressful assignment caring for ADHD and the also need a time out

Course & Prognosis

ADHD is associated with significant morbidity. Some children have remission of symptoms as they age

Other children begin to develop serious adult sequelae to include antisocial behavior, academic underachievement, teenage pregnancy, substance abuse and poor employment records

ADHD is associated with several comorbid disorders to include anxiety 33%, depression 11%, oppositional defiant and conduct disorders 50%, learning disorders 20%, & mood dysregulation

Comorbid disorders make ADHD much more difficult to treat

ADHD like any other disorder should be treated early to get ahead of the comorbid if possible (wouldn't wait until a diabetic had HbA1c of 15 before treating along with the comorbid developments)

Prognosis

These are recent studies not gospel as yet

ADHD versus matched controls on MRI studies, displayed a global maturation delay in the development of the cortical surface area and cortical thickness in ADHD matched with controls and the delay was about 2 years

Longitudinal studies have suggested that long term stimulant use appears to be associated with some degree of normalization in cortical development in that the treated ones had reduced thinning of the cortex over development relative to those that did not stay in the treatment

Prognosis

A practical standpoint if a child obtains treatment. able to concentrate better, stand still, less intrusive, less prone to outbursts, working memory is improved among other symptoms in relation to the child with no treatment

Which child is most likely to develop an attitude, anger, do poorly in school, try drugs etc.?

Is It Really ADHD ?

- ▶ Not confusing enough?
- ▶ Between 2011 and spring 2012 , record numbers of Americans went to the pharmacy to fill Adderall only to find the medications sold out!
- ▶ DEA researched the situation and raised the quota for production of stimulants. ADHD diagnosis has ballooned over the past decade
- ▶ In 2003 , 7.8 % of 4 to 17 year olds diagnosed with ADHD according to the National Survey of Children's Health, sponsored by the CDC
- ▶ By 2007 , that number jumped to 9.5 % an increase of 22%
- ▶ In 2011 , 11 % of school age including one in five high school boys received ADHD diagnosis

Really ?

- ▶ 2/3 of the children diagnosed with ADHD take medications
- ▶ Is there a true increase in the disorder – or are we simply expanding our definition of it , or are more aware if it ? Why is the diagnosis twice as high in the Southern states compared to the Western states?
- ▶ The difficult part is that ADHD is just like depression, like autism, schizophrenia, they are all symptom based.
- ▶ It is a real diagnosis but its on a spectrum like autism, blood pressure, depression and schizophrenia
- ▶ It arbitrary as to who is above and who is below the cut because we don't know exactly where the cut is in the disorder spectrum

What is the Standard for Diagnosis?

- ▶ There has to get observations from the school , or at least ratings from the teacher, ratings from the parents and a very good developmental history of the child – its not a 10 minute office visit
- ▶ Quick can lead to overdiagnosis can miss other reasons for the symptoms
- ▶ On the same token don't fall into the trap of underdiagnosis by saying " He wasn't tearing up the office waiting room" or "She sat very still in the waiting room so she can't have ADHD"

Goals and Objectives medications

- ▶ Understand basic classes of stimulants and equivalents
- ▶ Be exposed to role of nonstimulant alternatives
- ▶ Discuss the role of therapy in the treatment of ADHD



Treatment "finally"

Stimulants the mainstay of treatment (comparisons)

AMPHETAMINES (Adderall plain half life 9-14 hours)

They are all longer acting than methylphenidate (Ritalin)

Intermediate

Adderall 15mg twice a day

Ritalin 20 mg 3 times a day

Evekeo 15 mg twice a day

Zenzedi 15 mg twice a day

Procentra 15 mg twice a day

Long acting

Adderall XR 30 mg

Adzenys XR ODT oral dissolve

Vyvanse 70 mg (more similar to
Ritalin or Adderall XR 30 mg daily)

AMPHETAMINE

- ▶ Comes many ways

Amphetamine (D, L)

Adderall

Amphetamine(D)

Dexedrine

Dextrostat

Lisdexamfetamine (prodrug)

Vyvanse

Dexedrine

- ▶ Amphetamine (D) is one half of the Amphetamine (D, L) (dextro and levo) Adderall
- ▶ (D) is a cleaner version of amphetamine (theory)
- ▶ Short acting (3-6 hours,) and long acting spansules (8 hours)
- ▶
- ▶ Spansules may be opened and sprinkled on food

Adderall

- ▶ FDA approved for ages 3 and up (IR - instant release form)
- ▶
- ▶ Try to use the XR form whenever possible
 - ▶ Comes in 5, 10 , 15 , 20 , 30 mg tablets
 - ▶ Should last about 8 – 10 hours (ideally)
 - ▶
 - ▶ Often requires afternoon boost with a dose of IR (5, 10, 15, 20 mg)
 - ▶ To get through homework and evening hours

Lisdexamfetamine (Vyvanse)

- ▶ Prodrug of dextroamphetamine, activated in the GI tract
- ▶ (Prodrug medications that turn into an active form once they enter the body)
- ▶ Longest acting of the amphetamines (10 – 12 hours)
- ▶ Comes in 10, 20, 30, 40, 50, 60, 70 mg caps
 - ▶ May be opened and sprinkled or dissolved in water
 - ▶ Usually start 20 – 30 mg and increase by 10 mg increments

Stimulant Dosing Overall View

- ▶ Stat low , go up
- ▶ Collect data from teachers and parents to assess progress
- ▶ Can tell very rapidly if a medication is going to work or not
- ▶ Side effects (esp. GI) often get better if patients can persevere

Do not exceed 2 mg / Kg / day as a rule to work

Methylphenidate Basic

- ▶ Short half life : 2-4 hours
 - ▶ First developed in 1944, Ritalin has been used in ADHD since the 1960's
 - ▶ Due to the short half life , and industry has arisen trying to get the medication to last longer and be delivered more evenly

Methylphenidate

- ▶ Short acting
 - ▶ Ritalin 20 mg 3 times a day
 - ▶ Focalin 10 mg twice a day
 - ▶ Metadate CD 30 mg daily
 - ▶ LONG ACTING
 - ▶ Focalin XR 30 mg daily
 - ▶ Quillivant 60 mg (liquid 25 mg / 5 ml) & Quillichew 60 mg daily
 - ▶ Aptensio XR 60 mg (equivalent to Ritalin 25 .9 mg twice a day)
- Concerta 54 mg (similar to Ritalin 20 mg 3 times a day in terms of total dose but may need a chaser)

Methylphenidate

- ▶ Comes in many names
- ▶ Most medications have both (D,L) sections of methylphenidate
 - ▶ Brand names Concerta, Metadate, Ritalin, Daytrana, Quillivan (liquid), Methylin, Aptensio, Quillichew
 - ▶ All are the same medication, just different packaging and delivery systems

Methylphenidate (D)

purified version of methylphenidate

Focalin

Ritalin

- ▶ The first ADHD medication used since the 1950's
 - ▶ Comes in 3 preparations
 - ▶ Immediate release (IR) (lasting 2-4 hours)
 - ▶ Sustained release (SR) (4—6 hours , seldom used)
 - ▶ Long acting (LA) (~8 hours)

Advantage of Ritalin LA versus Concerta is this may be opened and sprinkled on food

Many times the IR form will be used as a bridge for kids to get them through evenings and homework

Metadate



- ▶ Very similar to Ritalin
 - ▶ Controlled Dosing (CD) usually last ~8 hours and is comparable to Ritalin LA
 - ▶ Can be opened and sprinkled
 - ▶ Often insurance companies with approve one of the other
- ▶ Extended Release (ER) is comparable to Ritalin SR
 - ▶ Lasts 4-6 hours
 - ▶ Seldom used

Methylphenidate other Forms

Quillivant XR extended release liquid (25 mg / 5 ml)

Quillichew ER chewable 20, 30, 40 mg size tabs

Aptensio extended release tablet dissolve in your hand

Comes in 10, 15, 20, 30, 40, 50, 60 mg

Daytrana

- ▶ Transdermal patch delivery
- ▶ Lasts about 9 hours / day
- ▶ Comes 10, 15, 20, 30 mg doses
- ▶ Takes about 1-2 hours to take effect
- ▶ Rashes can be a problem
- ▶ Very expensive and can be hard to find
- ▶ Price estimate all sizes for # 30 - \$438.00

Concerta

- ▶ Pill form (not breakable)
- ▶ Long acting stimulant : 8 – 13 hours
- ▶ OROS (Osmotic Release Oral Delivery System)
- ▶ It slowly releases as the osmotic pressure causes more of the capsule to release
- ▶ Dosing : 18, 27, 36, 54 mg capsules
- ▶ Maximum: 72 mg usual dose per day maximum
- ▶ Average price from a reference for 30 caps is 380.00 to 445.00 dollars

Non-Stimulants

- ▶ Alpha – 2 agonists
- ▶
- ▶ Atomoxetine (Strattera)
- ▶
- ▶ Bupropion (Wellbutrin)
- ▶
- ▶ Viloxazine (Qelbree)

Alpha – 2 Agonists

- ▶ These are purported to work in Prefrontal Cortex for ADHD
- ▶ Also work in the Brain Stem to decrease sympathetic activity, decreasing blood pressure
- ▶ Side effects are largely from decreasing sympathetic signaling (dry mouth , sedation)
- ▶ Hypotension
- ▶ Not often used as ADHD monotherapy , very often used as an adjunct
- ▶ Takes weeks to see full effect

Guanfacine (Tenex)

- ▶ Useful for tics
- ▶ Dosing : 1, 2 mg tabs
- ▶ can often start at 0.5 mg
- ▶ can use twice a day dosing , sometimes less sedative than clonidine
- ▶ Extended release form – Intuniv
- ▶ Once a day

Clonidine (Catapres)

- ▶ Can be sedating , dry mouth , hypotension
- ▶
- ▶ Dosing : 0.1, 0.2, 0.3 mg tabs
- ▶ Can use twice a day
- ▶ Extended Release form – Kapvay
- ▶ Once a day – insurance many times hard to cover

Atomoxetine (Strattera)

- ▶ Norepinephrine Reuptake inhibitor (NRI) with secondary effects on Dopamine
- ▶ Takes time for full effect / must be taken everyday
- ▶ Side effects
 - ▶ Decreased appetite
 - ▶ Sedation and fatigue
 - ▶ Priapism
- ▶ Generally second line medication used if contraindications to stimulants or potential abuse

Atomoxetine

- ▶ Requires titration
- ▶ Lots of dosages (10, 18, 25, 40, 60, 80, 100 mg)
- ▶ Can become tricky as it often requires time to titrate
- ▶ Usually start at 0.5 mg /Kg / day , increase after a week up to 1.2 mg / Kg/ Day
- ▶ Once daily dose



QELBREE (Viloxazine)

- ▶ Selectively inhibits norepinephrine reuptake
- ▶ Dosing in the literature starts at 6 y/o
- ▶
- ▶ Adult 200 – 600 mg per day start with 200 mg titrate, 600 mg max /day
- ▶ Children 6-11 100 – 400 mg per day , 12 and older 200 – 400 mg per day 400 mg max

Bupropion Wellbutrin

- ▶ Norepinephrine / dopamine reuptake inhibitor
- ▶ Only fairly effective for ADHD
- ▶
- ▶ Does well with depression exhibiting poor motivation / energy or adjunct to SSRI to create your own dual action antidepressant