A Physician's Perspective

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Part one

- Introduction
- Who should take medications, and why?
- What improvement should be seen?
- Who should prescribe medications?
- Medical trials
- What is the correct medication?
- What is the correct dosage?
- What about "natural" therapies?
- Summary

Part two: Overview of Medications

- Non-stimulant medications
  - Atomoxetine, 24 hours (strattera)
  - Clonidine, tablets: 4-5 hours, patch: 5-6 days (catapres)
- Stimulant medications: overview, safety profile, side effects
  - Methylphenidate tablets, 2-4 hours (ritalin)
  - Dextro-methylphenidate, 4-6 hours (focalin)
  - Methylphenidate sustained release, 6 hours (ritalin sr20)
  - Methylphenidate long acting, 8 hours (ritalin la)
  - Methylphenidate controlled dispense, 8 hours (metadate cd)
  - Methylphenidate extended release, 12 hours (concerta)
  - Dextroamphetamine tablets, 4 hours (dexedrine, dextrostat)
  - Dextroamphetamine spansules 6 hours (dexedrine)
  - Amphetamine salts tablets, 6 hours (adderall tablets)
  - Amphetamine salts extended release, 12 hours (adderall xr)
  - Pemoline, 24 hours (cylert)

Introduction

Human beings are rarely created in perfect form, so we all arrive in this world with unique differences. Some differences are blessings, others are handicaps. Poor vision, for example, is a common handicapping condition that affects millions of people throughout the world. I consider poor vision a condition of "human-ness." People can also have other medical conditions such as diabetes, asthma, thyroid conditions, ADHD, etc.—all are well recognized differences that can impair the pursuit of a normal life style if not dealt with in some manner.
ADHD is characterized by a prolonged history of inattention, impulsiveness and sometimes variable amounts of hyperactivity. It is important to emphasize that all of these symptoms are normal human characteristics. Most of us are forgetful and inattentive at times. We all at times become nervous and fidgety, and we certainly are impulsive to some degree. It is part of our "human-ness." ADHD, therefore, is not diagnosed by the mere presence of these normal and characteristic human behaviors, but by the DEGREE to which we manifest these symptoms. ADHD individuals have an over-abundance of these normal characteristics. They have less CONTROL of these behaviors and therefore a more variable and frequently poor outcome of their day.

Who should take medications, and why?

If a person meets the clinical criteria for a diagnosis of ADHD and is not succeeding academically and/or socially up to age-appropriate expectations, medication should be a PRIMARY OPTION for therapeutic intervention. ADHD is a medical condition. Recent research out of Harvard University has documented an abnormality in the dopamine transporter system in the central nervous system of ADHD adults. (1) This transporter system is responsible for moving neurotransmitter chemicals from the synaptic space back into the nerve cell. ADHD adults have approximately 70% more dopamine transporter than non-ADHD individuals and thus appear to have an overactive transport system.

Returning to the vision analogy, there are a number of options open to an individual who has compromised eyesight. One option is to attempt to correct the problem by wearing glasses to improve the visual acuity. Perhaps glasses will totally correct the problem or perhaps they will help only partially. After glasses are in place, we are in a position to assess what further problems are interfering with success. Then we can address these issues as well.

The opportunity to eliminate the symptoms of a medical condition partially or completely should be available to all. Many children and adults with ADHD benefit enormously from the use of medication. The medications that are in use today act as transporter blockers, thus serving to normalize this aspect of the brain chemistry. Most families who understand ADHD and its clinical manifestations prefer to try medication as a PART of their treatment plan. Over 90% of individuals with ADHD will have a positive response to one of the medical treatments.

What improvement should be seen?

In the early 1930's, Dr. Charles Bradley noted some dramatic effects of stimulant medications on patients with behavior and learning disorders. He found that the use of stimulants "normalized" many of the systems that we use for successful living. People on medication IMPROVED their attention span, concentration, memory, motor coordination, mood, and on-task behavior. At the same time they DECREASED daydreaming, hyperactivity, immature behavior, defiance, and oppositional behavior. It was evident that medical treatment allowed intellectual capabilities that were already present to function more successfully. (2, 3)

When medication is used appropriately, patients notice a significant improvement in control. Objective observers should notice better control of focus, concentration, attending skills, and
task completion. Many individuals are able to cope with stress and frustration more appropriately with fewer temper outbursts, less anger and better compliance. They relate and interact better with family members and friends. Less restlessness, decreased motor activity and impulsiveness are noted. ADHD individuals often complain of forgotten appointments, incomplete homework, miscopied assignments, and frequent arguments with siblings, parents, spouses, workmates, along with excessive activity and impulsive behaviors. With medication, many of these problems dramatically improve.

It is very important to remember what medicine does and does not do. Using medication is like putting on glasses. It enables the system to function more appropriately. Glasses do not MAKE you behave, write a term paper or even get up in to morning. They allow your eyes to function more normally IF YOU CHOOSE to open them. You, the individual, are still in charge of your vision. Whether you open your eyes or not, and what you choose to look at, are controlled by you. Medication allows your nervous system to send its chemical messages more efficiently, and thus allows your skills and knowledge to function more normally. Medication does not provide skills or motivation to perform. Patients successfully treated with medications typically can go to bed at night and find that most of the day went the way they had planned.

**Who should prescribe medications?**

Licensed physicians, physician's assistants or nurse practitioners can prescribe medications only. This person may serve as a coordinator to assist with the multiple therapies often needed, such as educational advocacy, counseling, parent training and social skill assistance. Parents should look for a physician who has a special interest and knowledge in dealing with ADHD individuals. This professional should be skilled in working closely with families to try the many and varied medical treatments that are available until the correct therapeutic response is attained. Members of CH.A.D.D chapters are an excellent resource for referrals to appropriate professionals.

**Medical trials**

It is necessary to establish a team of observers to appropriately evaluate a medication trial. Gather information from sources that spend time with the patients. This might include significant others, parents, teachers, grandparents, tutors, piano teachers, coaches, etc. As gradually increasing dosages are administered, input is gathered from these observers. Various ADHD rating scales are available to assist in gathering factual data. The most important assessment, however, is dependent on whether the ADHD patient's quality of success in life has improved. For this information, I find no scale takes the place of conversations with patient and family members.

When evaluating patients during a trial of medication, it is important to maintain treatment throughout the waking day, seven days a week. Treating them only at school or in the workplace is totally inadequate. I need all involved observers, especially parents and/or significant others, assisting in the evaluation process. Furthermore, I want to know if treatment has an effect on non-academic issues. Recent studies have found that treatment is necessary for most ADHD individuals throughout the full day, thus allowing full development not only of academic or work skills, but also the all-important social skills that are utilized with friends and family. After the
trial of medication, if positive results are evident, then the family and the patient can make informed decisions as to when the medication is helpful. Most patients need the medication throughout the day and evening.

**What is the correct medication?**

At the present stage of medical knowledge, there is no method of predicting which medication will be most helpful for any individual. At best, physicians can make educated decisions based on information about success rates with individual medications. Over 80% of ADHD individuals will respond favorably to the stimulant medications, methylphenidate and amphetamines. Both of these categories of medications may need trials to assess which is best. If one stimulant does not work, the others should be tried, for experience has proven that individuals may respond quite differently to each one. Another good alternative medication is atomoxetine (Strattera), a new non-stimulant medication for ADHD that was approved by the FDA in December 2002. Each family and physician must be willing to try different medications in order to determine the best and most effective therapy. This is the only way to find the appropriate medical treatment. In some children who have multiple diagnoses such as ADHD and depression, or ADHD and anxiety, or ADHD and Tourette syndrome, combinations of medications are being successfully utilized for treatment.

**What is the correct dosage?**

If stimulant medications work, there is a best dose for each individual. Unfortunately, medical knowledge is not at a point where it can predict what the correct medication or dose will be. This is not an unusual circumstance in medicine, however. For a person with diabetes, for example, we must try different forms and amounts of insulin to achieve the best control of blood sugar levels. For people with high blood pressure, there are many medications that can be effective, and often a trial of multiple medications and dosages is necessary to determine the best treatment. For stimulant medications, there is no magic formula. The dose cannot be determined by age, body weight or severity of symptoms. In fact, it appears that the correct dose is extremely individual and is not at all predictable. Again, similar to people who need glasses, the kind of prescription and the thickness of the lenses are not dependent on any measurable parameter other than what the individuals say enables them to see well. The dose of medication is determined solely by what ADHD patients need to most effectively reduce their symptoms. One must be willing to experiment with carefully observed dosage changes to determine the correct dosage. The appropriate dosage does not seem to change very much with age or growth. Medication continues to work effectively through the teenage years and through adulthood.

For atomoxetine, the dosage at the present time is calculated according to weight. This is the only medication for ADHD for which this is true.

**What about "natural" therapies?**

At this time, there is no evidence that natural therapies are therapeutic. There are many anecdotes about various "magical" cures for ADHD, but none have been found to be valid. Remember: multiple anecdotes do not mean proof. Natural therapies such as grape seed extract, blue algae,
biofeedback, magnets, megavitamins, diet, and other "natural products" have not yet shown any lasting therapeutic benefit. At this time traditional medical therapy is the most effective treatment for ADHD. This is quite similar to other medical treatments such as insulin, THE best form of treatment for Type 1 diabetes, or thyroid pills THE best therapy for inactive thyroid gland. Furthermore, natural health food treatments are not regulated by the government and are therefore highly suspect for contamination. Please be cautious when experimenting with alternative therapies on your family members.

Summary

Individuals with ADHD with present with a variety of well-defined symptoms and behaviors. Medication may be extremely helpful in alleviating some of these symptoms and will allow the other therapeutic modalities to be much more successful. Families must be willing to work closely with their physician to identify the correct medications and establish the best dosage levels.

Part two: Overview of Medications

It is important to note that medical treatment should always be given for the entire waking day, seven days a week. There are few medical conditions that we do not elect to treat in the evenings, on weekends or holidays. No one chooses to turn down their brain chemistry during his or her wakeful hours. Therefore, all medical treatment for ADHD should last for at least 12 hours daily and 24 hours when possible. With this in mind, I have highlighted (*** the medications that should be preferred treatments for ADHD.

Non-stimulant medications

ATOMOXETINE 24 hours (Strattera)
This is a new medication for ADHD, which was released by the FDA in December 2002. It is a non-stimulant medication, which is not abusable and can be written without Schedule II restrictions. This is the first medication that lasts 24 hours and therefore gives full therapeutic effect throughout the day and night. It has great implications for homework, driving, and social relations in the evening, etc. It is my expectation that treatment of ADHD in the future will probably utilize more of the 24-hour continuous therapies as they become available. Early reports suggest atomoxetine works for 70% of individuals with ADHD.

Form: Capsules: 10mg, 18mg, 25mg, 40mg, 60mg.
Dosage: Weight based dose: first four days=0.5mg/kg; target dose (day five and after)=1.2mg/kg. This medication must be taken with food to prevent nausea.
Action: Very slow acting and will take 3-4 weeks (or more) to reach therapeutic effect. If the patient is already taking stimulant medications, suggest continuing them and adding the Strattera for the first 4-6 weeks, then tapering the stimulant slowly until discontinued.
Possible Side Effects: No long term safety information is available for this medication. Primary side effect in children is sleepiness. If this occurs, give the dose at night or lower the dose until this improves. Then raise dose if possible. Adults can experience more noted effects: transitory dry mouth and dizziness, insomnia, sleepiness. Other effects in adults include possible bladder spasm, sexual dysfunction (uncommon but often results in discontinuation of medication).
Occasionally a child or adult will get very agitated. If this occurs, discontinue the medication.

**Pros:**
- 24 hour coverage.
- Less effect on appetite than stimulants.
- Marked improvement in sleep pattern for many.
- Marked improvement in mood in many patients.
- Not a stimulant and not abusable.

**Cons:**
- Very little information is available at this time to fully evaluate long term safety profile.
- Short term safety profile appears to be excellent.

**CLONIDINE** tablets 4-5 hours, patches 5-6 days (Catapres)

**Form:** Patches applied to back or shoulder. Catapres TTS-1, TTS-2, TTS-3. Tablets. Clonidine tablets 0.1mg, 0.2mg, 0.3mg.

**Dosage:** Very individual, usually .1-.3mg.

**Action:** Works quickly. Tablets work within 1 hour, patches within 1 day.

**Effects:** Often will improve ADHD symptoms, particularly aggressive and hyperactive behaviors. Not too helpful for focus and attention. Decreases motor and vocal tics. Can have a dramatic effect on oppositional defiant behavior and anger management. Often used as one dose at night about 1½ hours before bedtime to assist with getting to asleep.

**Possible Side Effects:** Major side effect is tiredness, particularly if dose is raised too quickly. This disappears with time. Dizziness, dry mouth. Some will notice increased activity, irritability.

**Pros:** Excellent delivery system if patch is used.

**Cons:** Does not usually work as well as stimulants. Patch can cause skin irritation in many individuals and may not be tolerated. Can effect cardiac conduction (heart rate and rhythm) in high doses and must not be left around for animals or small children to accidentally ingest.

**Stimulant medications**

Some general comments can be made about stimulant medications as a class of medications. The longer acting medications have clear advantages over the short acting medications, not only in duration of therapeutic effect throughout the day, but also in smoothness of the therapeutic effect. It is very difficult for an individual with ADHD to remember to take multiple doses of medication during the day. Multiple dosing increases the risk of missing doses, which results in the return of symptoms at inopportune times. The afternoon dosing is frequently missed, causing significant difficulties. Furthermore, each additional dose serves as an unnecessary reminder that treatment for this condition is needed and "something is wrong."

The reason for medical treatment is to "normalize" the day. My general rule is to always use 12 hour medications unless they are not effective or have intolerable side effects. In such a case, the six or eight hour medications should be tried, because some individuals tolerate them better and find them more effective. However, if the six or eight hour medication is used, a second dose should be given to allow patients to have the therapeutic benefit for the full day.

**Safety profile**

The stimulant medications are one of the most studied treatments in the history of medicine. The medications have been used extensively in children and adults over the past 50 years with no evidence to date of long term concerning side effects. At this time there is no conclusive evidence that use of stimulants causes any long term lasting effects on growth, although there may be some delay in height and weight gain in some individuals.
The short acting stimulants are extremely abusable and are valued highly on the street. It is best to always use the long acting preparations which are not abusable to avoid the temptation of misuse and abuse.

Common side effects:
The following side effects are often noted with the use of stimulants. In general, the side effects with the short acting medications are more pronounced and bothersome than with the long acting medications. Thus, long acting meds are somewhat more tolerable for long term treatment and are certainly a marked improvement for long term therapeutic effect.

Appetite suppression: Most will note decreased appetite during the effective hours of the medication. This often means minimal lunch intake. I suggest a small protein lunch such as milk, peanut butter crackers, beef or turkey jerky to get through the day. A milk shake after school helps. Many find their appetite returns late in the evening (around 8-9pm) when their medication wears off, and they need to be allowed to eat at that time. If weight gain is a continued concern, I often add cyproheptadine (Periactin) 4mg, ½ tablet at breakfast and dinner. Periactin is an antihistamine similar to Benedryl which enhances appetite and often results in 1-2 lbs weight gain per month. Remember that good nutrition is helpful for all, and these individuals should emphasize protein intake in their diet.

Sleep disturbance: Many ADHD individuals will have sleep difficulties before they begin their medical treatment. At night, their brain continues its activity and starts thinking of the day. Using stimulant medications may either improve or worsen this problem. In those with no prior sleep difficulty, stimulants can create significant sleep issues. ADHD individuals do not usually have a problem with sleeping through the night (sleep disorder) but often do have problems with starting the sleep. A clear-cut bedtime routine helps (bath or shower and then read in bed) with the elimination of caffeine, computers, computer games and television at least one hour before bedtime. Interestingly, adding stimulant medication actually allows a percentage to sleep better at night, and this technique should be tried. It only takes one night to see if a dose of short acting stimulant will enable sleep initiation.

Some patients, however, require more assistance. Many patients will use a small dose of Clonidine tablets given one hour before bedtime to help with sleep initiation. Clonidine is a mild sedative, not a sleeping pill, and it is non addictive. Approximately 60-90 minutes after taking the medication, a brief sleepy phase will occur that lasts about 20 minutes. If the patient is in bed and trying to go to sleep, it is very effective. It will NOT make someone stop playing computer games and go to bed.

Mood changes: One of the biggest complaints about stimulants is that they can cause mood changes. These come in a number of different forms.

Rollercoaster effect: Short acting medications have a continuous cycling of the blood level, either rising or falling throughout the day. This can lead to significant mood changes, particularly at the end of the four hour cycle when the medication is wearing off. This problem with cycling is greatly diminished with the use of eight hour and twelve hour medications.
Rebound effect: Stimulants can often wear off very rapidly, and in some individuals this can cause a rebound, a marked change in demeanor often characterized by irritability, loss of patience, and a worsening of the ADHD core symptoms. Rebound can occur in the evening when the medication wears off and can also be evident in the morning on first arising. The morning rebound may require an early dose of immediate release methylphenidate (MPH) prior to the administration of the long acting dose at breakfast. Rebound effect is markedly reduced in frequency and severity in the long acting stimulants.

Irritability and anxiety: All of the stimulants have the possibility of causing a generalized irritability, and sometimes even anger, which is not tolerable over a long period of time. They can cause anxiety and panic disorder and may aggravate existing anxiety. Often, changing from one stimulant to another will reduce this side effect, so it is worth trying different stimulants to identify the best one for each patient.

Overdose effect: When using the stimulants it is necessary to gradually raise the dose to find the most effective therapeutic level. Sometimes in doing this, one gets an overdose effect. The stimulants are incredibly safe. They have been studied for over 50 years, and there is no evidence at this time of any long term serious complications when used appropriately for ADHD. However, if ADHD individuals take too high a dose, they will experience an overdose effect which appears as a dulling of the personality: They complain of being somewhat physically lethargic, subdued, dull, less conversational, less apt to laugh and be social. By simply lowering the dose for one day, these symptoms will disappear.

Tic Formation: All of the stimulants have the possibility of temporarily causing a tic disorder or aggravating an existing one. There is no evidence that the use of stimulant medications will cause permanent formation of tic disorder or Tourette syndrome. Children who already have tics (10% of children have mild tics at some point in childhood) and individuals with Tourette syndrome will find a number of different scenarios with the use of medication. Approximately 1/3 will actually notice that the tics improve (lessen) with the use of stimulants, 1/3 will see no change at all, and 1/3 will find the tics worsen with use of stimulants. If the stimulants are effective and tics are worse, a medication to help control the tics is usually added to the treatment.

METHYLPHENIDATE TABLETS 2-4 hours (Ritalin IR)
Form: Short acting tablets. Methylphenidate (MPH) 5mg, 10mg, 20mg.
Dosage: Very individual. Average 5-20mg tablets every 2-4 hours.
Action: Immediate release (IR) MPH starts to take effect in 15 minutes, which is extremely helpful for some individuals. Some children need an early morning dose 20 minutes BEFORE arising in the am, followed by a long acting medication at breakfast. Often used as a booster for evening coverage.
Possible Side Effects: See above
Pros: Very easy to use for short periods of coverage, such as early morning and evening.
Cons: Must be administered frequently during the day (3-5 times/day). Inconvenient to use at school and work. Often causes rebound and rollercoaster effect. Very abusable.
DEXTRO-METHYLPHENIDATE 4-6 hours (Focalin)
Focalin is an isomer product of methylphenidate. Methylphenidate is composed of two mirror image molecules, and it has been determined that the right-hand side of the molecule contains most of the therapeutic activity. Therefore the left-hand side has been eliminated, giving a cleaner formulation of methylphenidate.
Form: Tablets: 2.5mg, 5mg, and 10mg.
Dosage: The same as methylphenidate, but divide the dose by half.
Action: The same as methylphenidate, but in some individuals up to 6 hours duration.
Possible Side Effects: Same as MPH but possibly to a slightly less degree.
Pros: A cleaned up version of MPH that may last a bit longer with slightly decreased side effects.
Cons: Same as MPH. Very abusable.

METHYLPHENIDATE SUSTAINED RELEASE 6 hours (Ritalin SR20)
Replaced by Ritalin LA.

METHYLPHENIDATE LONG ACTING 8 hours (Ritalin LA)
Form: Capsules: 20mg, 30mg and 40mg.
Dosage: Very individual. Average: 20-40 mg daily or twice a day, every 8 hours.
Action: Same as methylphenidate, but eliminates the noontime dose.
Possible Side Effects: See above.
Pros: Eliminates midday dosing. Works more smoothly than IR methylphenidate and is more effective than methylphenidate SR.
Cons: Only works for eight hours and therefore subjects the patient to loss of focus and control in mid afternoon. This requires an afternoon booster to be administered.

METHYLPHENIDATE CONTROLLED DISPENSE 8 hours (Metadate CD)
Form: Capsules: 20mg (10mg and 30mg to be available in 2003)
Dosage: Very individual. Average: 2-3 capsules in the am.
Action: Same as methylphenidate.
Possible Side Effects: See above.
Pros: Works more smoothly than IR methylphenidate. Sometimes is effective when Concerta and Ritalin LA are not effective. Not abusable.
Cons: Works for only eight hours. (See Ritalin LA)

***METHYLPHENIDATE EXTENDED RELEASE 12 hours (Concerta)
Form: 12 hour long acting tablet. Uses a unique delivery system that delivers a constant therapeutic level of methylphenidate for twelve full hours. Concerta 18mg, 27mg, 36mg, 54mg.
Dosage: Dosage will vary as with all methylphenidate products.
Concerta 18mg = Ritalin 5mg three times a day
Concerta 27mg = Ritalin 7.5mg three times a day
Concerta 36mg = Ritalin 10mg three times a day
Concerta 54mg = Ritalin 15mg three times a day
Action: 12 hours of consistent therapy with no highs or lows throughout the day. A few individuals will only get 8-9 hours of effective therapy and will need either a higher dose or a second dose.
Possible Side Effects: See above.
Pros: Unique delivery system avoids multiple dosing throughout the day. No dosage at school. No rebounding with missed doses. Fewer side effects, less mood swings, better therapeutic response for many individuals. No daytime dosing. Less anxiety and worry. Not abusable.

Cons: Does not work for all individuals who use methylphenidate. If ineffective, should try Ritalin LA and/or Metadate CD. May need a short acting booster to cover the evening hours.

DEXTROAMPHETAMINE TABLETS 4 hours (Dexedrine, Dextrostat)
Form: Short acting tablets 5mg, 10mg.
Dosage: Very individual. Average 1-3 tablets each dose every 4-5 hours.
Action: Rapid onset of action, approx. 20 min. Lasts 4-5 hours.
Possible Side Effects: See above.
Pros: Excellent safety record. Rapid acting. Some patients who do well on dextroamphetamine prefer the tablets over the spansules. The rapid onset in tablet form is apparently more effective for these individuals.
Cons: Same as MPH. Very abusable.

DEXTROAMPHETAMINE SPANSULES 6 hours (Dexedrine)
Form: Long acting. Dexedrine Spansules 5mg, 10mg, 15mg.
Dosage: Very individual. Average is 5-20 mg.
Action: Very individual. May take up to one hour to be effective. Usually lasts 6-8 hours. In some individuals it may last all day. In others it may only last 4 hours. Most will take twice a day, six hour intervals
Possible Side Effects: See above
Pros: Excellent safety record. May be the best drug for some individuals. Long acting, smooth course of action. May avoid lunchtime dose at school.
Cons: Slow onset of action. May require a short acting medication at the start of the day. Very abusable.

AMPHE TAMINE SALTS TABLETS 6 hours (ADDERALL)
Form: Long acting tablets: 5mg, 7.5mg, 10mg, 12.5mg, 15mg, 20mg, 30mg.
Dosage: Very individual, usually between 5mg and 20mg, once or twice each day.
Action: Usually lasts 6 hours. May be given once or twice a day depending on length of therapeutic effect. Duration of effect varies from person to person.
Possible Side Effects: See above.
Pros: Only needs to be given once or twice a day. Often fewer side effects than the short acting medications.
Cons: Can cause irritability in a small percentage of patients. Very abusable.

***AMPHETAMINE SALTS EXTENDED RELEASE 12 hours (Adderall XR)
Form: Uses a unique delivery system that delivers a constant therapeutic level of amphetamine salts for twelve full hours. Capsules: 5mg, 10mg, 15mg, 20mg, 25mg, 30mg.
Dosage: Very individual. Average 15-30mg daily.
Action: Long acting 12 hour control of ADHD symptoms for coverage during most of the day.
Possible Side Effects: See above.
Pros: Very effective. Same as Adderall with longer duration of action. Cannot be abused.
Cons: May need a booster to cover the evening hours.
PEMOLINE 24 hours (Cylert)
Form: 18.75mg, 37.5mg, 75mg tablets. 37.5mg chewable tablets.
Dosage: Very individual.
Action: Good medication for ADHD symptom relief, similar to other stimulants.
Possible Side Effects: Cylert has a BLACK BOX warning from the FDA. This medication is associated with risk of liver failure leading to death, and its use requires blood tests every two weeks. It should be used as a last resort with very careful and continuous supervision.
Pros: Not abusable.
Cons: Significant risk.

References
