Methyl-B_{12}: Myth, Masterpiece, Or Miracle?

(Dr. Neubrander's protocol can be found at the end of this document)

Miracles: None Have Been Seen To Date.

After giving 50,000 to 60,000 methyl-B_{12} shots and after evaluating thousands of Parent Designed Report Forms, I can tell you that *there are no Miracles* from methyl-B_{12} therapy. However, when done correctly, when incorporating all the important factors at one time, when taking no shortcuts, when adding the adjunctive therapies that provide synergy after the initial 5-week evaluation period, when pushing through "tolerable" side effects to maximize the dose, and when continuing therapy long-term, *Masterpieces are common.* To some parents, their Masterpieces are nothing short of a Miracle. These parents had been told that their children would never speak and that they would most likely have to be institutionalized. These parents were also told that they would have to lower their expectations for their child and for themselves. Despair, despondency, and discouragement were the norm. Then, after starting methyl-B_{12} shots their children start to be aware of everything around them, start speaking, starting acting like other children, and climb from the bottom to the top of their special ed classrooms, and some advance so far that they lose their diagnosis, attend mainstream schools, and cannot be detected as ever having been affected by anyone other than those most trained in dealing with children on the spectrum. Therefore, these parents believe they have witnessed a miracle! Who am I to argue; though I know that all that has happened is that *methyl-B_{12} has done its biochemical job and that it has done it well for these children*?

Myth: Methyl-B_{12} Only Works For 30-40% Of Children:

From my research, methyl-B_{12} is seen to be active in 94% of children. The significant underreporting by clinicians or parents is directly due to the fact that whatever evaluation tool being used is not sensitive or specific enough to indicate all the improvements methyl-B_{12} is responsible for in addition to "the biggies" – executive function, speech and language, socialization and emotion. Spontaneous letters or reports from parents to clinicians will typically report only the most obvious, exciting, or hoped-for findings. Unless clinicians and parents are aware of "all the other things" methyl-B_{12} is responsible for, in addition to the major things that parents and clinicians want to see early in therapy, many responders will never be reported as being responders and therefore will never be treated. *That is why the Parent Designed Report Form is singly the most critical factor in differentiating responders from non-responders. Because the Parent Designed Report Form is the most sensitive and specific evaluation tool available*, I fondly call it The Little Green Hairs -- Red Freckles Form. The reason I call it this is because parents would not care if one of the things methyl-B_{12} did was cause little green hairs to grow out of their child's ears, nor would they care if one of the things methyl-B_{12} did was turn their child's brown freckles red! In fact, most parents who were even savvy enough to observe these things happening to their child would never attribute them being a result of methyl-B_{12} therapy and therefore they would never alert their clinician about these findings. This silly analogy clearly illustrates that unless parents and clinicians know everything methyl-B_{12} is repeatedly reported to be responsible to do, they will misdiagnose many children that are actually responding to methyl-B_{12} therapy, but responding in ways that are not immediately obvious or even desired. The consequence is that these children will not be treated or alternatively, if treated, they will not be treated long enough for the long-term effects of methyl-B_{12} therapy to be realized. It has been my experience that children such as these were originally misdiagnosed as non-responders. Once these children were restarted on the shots using the complete protocol recommended, and were reevaluated by the Parent Designed Report Form at the end of the 5 week clinical trial period, they were now diagnosed as "missed responders" or what I call "hidden responders". They did well when the shots were continued for 18 to 24 months. [See the related

discussion below regarding the importance of correctly diagnosing responders and treating long-term in the section entitled, "Myth: The Intensity Of Responses And Not The Number Of Responses On The Parent Designed Report Form Indicates Whether Or Not A Child Is A Responder And Predicts A Child's Long-Term Prognosis."

Myth: Methyl-B_{12} works better for younger children than it does for children older than six to seven years of age:

Nothing could be farther from the truth! To date, there has been no age between 9 months to 18 years that has not responded equally as well. As long as the complete protocol was followed *exactly as described* below and the results evaluated by completing in detail the Parent Designed Report Form and Parent Specifics Documentation Letter, the results are the same.

Myth: Routes Of Administration Other Than Subcutaneous Injections Will Work Just As Well:

Based on my research evaluating children from all over the country who were receiving methyl-B_{12} either orally, sublingually, transdermally, intranasally, or intramuscularly, when no other changes were made to the child's program except switching to subcutaneous methyl-B_{12}, before and after Parent Designed Report Forms showed undeniable increased benefits. Sublingual is only theoretical in the autistic population and in the rare case that it may be achieved it is pulsatile in nature. Methyl-B_{12} is easy to do orally but is pulsatile in nature. Its absorption requires a healthy terminal ileum, the region in the intestine documented by the work of Dr. Krigsman, Dr. Wakefield, and others, to be inflamed in a high percentage of children on the spectrum. Therefore the total amount of methyl-B_{12} absorbed cannot accurately be determined, nor can it consistently deliver the same dose due to exacerbations or remissions of ileitis. Intra-nasal administration is pulsatile, the dose delivered is unable to be accurately determined, and inserting an intra-nasal cannula once or twice daily is more traumatic than subcutaneous injections to the vast majority of children unless they are very high functioning. Transdermal administration is delivered into the subcutaneous tissue rendering it non-pulsatile in nature and therefore theoretically it should work like a subcutaneous injection. However, due to several variable factors, the amount delivered is unable to be accurately determined, especially when no data is available documenting its ability to achieve higher than normal tissue concentrations that are easily accomplished with injections. More important, however, is that clinically the degree of response, as evaluated by before and after Parent Designed Report Forms, and from communication with parents seeking advice who were using large amounts of transdermal methyl-B_{12}, was eclipsed by the benefits from methyl-B_{12} injected into the fat of the buttocks once they made the switch. Children frequently were brought to my office that were already receiving intramuscular injections of methyl-B_{12}. At times, the doses these children were receiving were 200 to 500% higher than my standard dose of 64.5 mcg/kg/once every three days. Sometimes these extremely higher than standard doses were being given daily. Red or pink urine was common. The majority of parents who were giving their children these intramuscular methyl-B_{12} injections were reporting benefits, oftentimes to moderate or greater degrees. However, once switched to the lower dose once-every-3-day protocol given shallowly to the subcutaneous fat in the buttocks from 25 mg/ml stock, before and after Parent Designed Report Forms documented an even better clinical response. If shots were being given daily, it allowed a less frequent shot schedule to realize the same or even better clinical response. In 100% of the cases the red/pink urine resolved immediately. [See the related discussion below regarding the importance of steady state delivery in the section entitled, "Myth: Methyl-B_{12} And The Benefits Seen For Children On The Spectrum Are Due To A Deficiency."]

Myth: The Concentration Of The Methyl-B_{12} Solution Does Not Matter As Long As The Total Dose Remains The Same And That The Volume To Deliver The Equivalent Dose Is Adjusted.

Another type of child that frequently comes to my office is one that has been receiving methyl-B_{12} injections made from a 12.5 mg/ml stock solution and has been using twice the volume to achieve the standard dose I typically recommend. Typically these children have been seeing at least mild to moderate benefits. However, when all other factors remain the same and when the shots are switched to those made from a 25 mg/ml methyl-B_{12} stock solution, with rare exception the before and after Parent Designed Report Forms demonstrate an obvious and undeniable improvement. Three factors are involved in the reason that this is true: 1) Experts familiar with the kinetics of adipose tissue agree that different types of fat show differing degrees of accumulation, storage, and release of various substances; 2) Principles of pharmacology indicate that the more dense a substance is within its delivery system, the slower and more uniform the rate of dispersion that will follow. This is the reason pellets are used over depot substances over time-release oral substances over non-time-release oral substances when a steady-state continuous dose of a medication is needed; 3) The surface area of a drop of methyl-B_{12} made from a 12.5 mg/ml concentration is much greater than the surface area of a drop of methyl-B_{12} made from a 25 mg/ml concentration when one is attempting to achieve equivalent doses. Therefore, when the concentration of methyl-B_{12} that is delivered subcutaneously into adipose tissue is from a lesser concentration, due to its significantly increased surface area, the methyl-B_{12} will be released into the bloodstream and lymphatic system much more rapidly. Therefore, to get equivalent clinical benefits from a 12.5 mg/ml subcutaneous injection as from a 25 mg/ml subcutaneous injection, the frequency of injections needs to be increased. Because regression or lack of progression is not typically seen within a day, and because lower concentrations do produce many benefits, without using the Parent Designed Report Form comparing the before and after effects of 12.5 vs. 25 mg/ml injection strengths, the fact that the higher concentration produces significantly better results is easily missed. [See the related discussion below regarding the importance of steady state delivery in the section entitled, "Myth: Methyl-B_{12} And The Benefits Seen For Children On The Spectrum Are Due To A Deficiency."]

Myth: The Fat In The Arm, Abdomen, Or Thigh Produce The Same Results As From The Buttocks.

As previously discussed, experts familiar with the kinetics of adipose tissue agree that different types of fat show differing degrees of accumulation, storage, and release of various substances. One study that I conducted took very high dose large volume of methyl-B_{12} and injected it into the subcutaneous tissue of the deltoids, abdomen, and buttocks of an adult and observed for color changes in the urine. Both the deltoid and abdomen injections produced bright reddish-pink urine with the next voiding whereas the buttock injections produced urine that was only slightly pinkish in color. Therefore, by using the buttocks as the injection site allows for a lesser-shot frequency schedule due to its slower rate of release of the medication from the adipose tissue. [Refer to the document entitled "Injection Instructions for Methyl-B12 Shots" found on my website.]

Myth: The Total Dose Is Not Standard For Most Children.

One of the studies I conducted was the result of my initial belief that I was dealing with a B_{12} deficiency and that a standard *relatively* high dose (but not excessively high dose) of methyl-B_{12} would quickly resolve any deficiency that was present regardless of whether the child was small, medium, or large in size. Therefore the dose I gave all my patients was 1500 mcg twice weekly. Clinically I noticed the children who seemed to be having the best response with some side effects were children that weighed around 45 pounds. The children that showed little to no benefit and who had almost no side effects were children that weighed over 55 pounds. The children who showed benefits but also had the most side effects were children that weighed

around 35 pounds or less. This intrigued me so I reviewed all the children's charts to study this weight to benefit vs. side effect discrepancy more closely. What I learned was that those children who had the best benefits with the fewest significant side effects (though side effects of the type now defined as tolerable were sometimes present) fell within the range of 72 to 78 mcg/kg twice weekly. Therefore the average effective treatment dose I chose for my first official protocol was 75 mcg/kg administered subcutaneously at 45 to 60 degree angles twice weekly. Over the years I estimate that about 15% of my patients do better with higher doses though most do not require it. Interestingly, those children who seem to need higher doses do not seem to have more side effects from the increased dose.

Myth: Varying Shot Frequencies Can Still Give The Same Results.

From my original protocol of 75 mcg/kg/twice weekly, it soon became apparent that the positive benefits many children were getting were wearing off before they would get their next shot. This became even more obvious because the majority of parents who were giving their children twice-weekly shots were giving them on Sunday and Wednesday evenings. This was a 4-day/3-day split. In general, the shot benefit was still seen by Wednesday, the 3rd day. However, many parents said their child really needed another shot before Sunday, the 4th day. It was from this observation coupled together with the observation that most children did not need more than 75 mcg/kg/twice weekly that I modified my previous protocol to the one I now recommend. I kept the total weekly dose the same (150 mcg/kg/week). However, I increased the shot frequency from twice weekly to once every 3 days and used the equivalent dose of 64.5 mcg/kg/once every three days. In general this works well for those parents following the injection technique very closely. The kinetics of methyl-B_{12} dispersion from the subcutaneous tissue of the buttocks for most children seems to be about 3 days before another injection is needed. If a parent reports that the effects are wearing off too quickly, and/or the benefits are showing up within hours after an injection, almost 100% of the time they are injecting too deeply and are either in the muscle or close to the SQ:IM junction. Once technique is perfected, the majority of parents report that the shots now hold the 3 days and increasing the frequency to once every other day or even to a daily routine is not necessary. Exceptions, however, do occur. With those children whose movement during a shot cannot be controlled enough to guarantee adequate subcutaneous delivery, shot frequency will need to be increased. Also, in children who are extremely thin that no matter how shallow one injects the muscle or the SQ:IM junction cannot be avoided, the frequency of injections will need to be increased. When I increase shot frequency, I decrease the total dose and shot volume proportionately in order to still be close to the total weekly dose of 150 mcg/kg/week.

[Current dosing and delivery schedule: 64.5 mcg/kg once every 3 days to the adipose tissue of the buttocks at an angle severe and horizontal enough to guarantee a "shallow" subcutaneous delivery from a BD 3/10 cc insulin syringe with an 8 mm, 31-gauge needle, item #328438 only, and made from a 25 mg/ml methyl-B_{12} stock solution.]

Myth: A 30-Degree Angle Is The Ideal Angle Of Injection.

In the past, I initially taught that a 45-60 degree angle should be used. I soon learned that this angle of injection was not shallow enough for many children in order to guarantee a shallow subcutaneous injection. This was especially true for smaller children and for very thin children of any size. What I observed was that I was not seeing as many benefits in these children, that the benefits would come on too quickly after a shot, and that the benefits would often fade by the 3rd day. This pattern of "benefits produced to benefits fading" was the same pattern I saw when the shots were given either IM or too close to the SQ:IM junction. Therefore my next protocol stated that the injections should be 30-degrees or less. Unfortunately parents heard the "30-degree" part of my message and not the "or less". Therefore, because the goal is to deliver a subcutaneous

injection away from muscle, I now teach my parents that "the shallower the injection the better" is the safest general rule to follow.

Myth: Children Will Get The Same Benefits By Lowering The Dose Enough To Take Away Side Effects.

Initially, I was influenced to lower the dose of methyl-B_{12} I was using when side effects appeared. I did this for about a year but observed that my methyl-B_{12} dropout rate varied markedly between two groups. The group with the highest dropout rate was from methyl-B_{12} responders with side effects and whose dose was lowered to reduce or eliminate the side effects. The group with the lowest dropout rate was from methyl-B_{12} responders with side effects and whose dose was maintained as we worked through the side effects until they lessened, diminished, or resolved within 2 to 6 months. What I learned was that the reason parents stopped the methyl-B_{12} shots was exactly the opposite of what I expected it to be. Logically parents would be more likely to stop the shots if their child had side effects and they would be more likely to continue the shots longer if their child had none. *This was not the case at all!* The parents whose children had the most side effects also represented the group that "hung in there" the longest because they were "getting their children back" as they would frequently say. The other group of parents whose children were shown to be responders, but did not want to deal with the side effects requested the treatment doses be lowered to diminish or take the side effects away. This group of parents would usually not return after one or two 6-week follow-up cycles because they were not seeing enough benefits to justify continuing the shots. Therefore, it was due to these *profound observations* that I redefined "side effects" as they pertain to methyl-B_{12} injections. It was at that time I learned how vitally important is was to teach parents to accept and work through tolerable side effects as part of the process just as much they would accept pain as part of the process of a successful operation. Fortunately, the good news is that within 2 to 6 months the majority of side effects diminish in intensity or disappear completely while at the same time the child continues to make moderate to significant advancements in executive function, speech and language, socialization and emotion, and is reported by the parents to "just being doing better overall in almost all phases of life!"

Side Effects: The most common side effects are hyperactivity with or without increased stimming, changes in sleep patterns, and increased mouthing of objects. I classify side effects as nuisance (tolerable) vs. intolerable. For side effects that are intolerable and so disruptive that a child can no longer function or learn, I stop the shots. Should an older or larger child become uncontrollable and potentially dangerous to others, this is always considered an *intolerable* side effect and the shots *must be stopped*. Reintroduction of the shots, if possible at all, is part of my advanced protocols and beyond the scope of this discussion.

When considering side effects, I believe it is important to redefine them in a way that allows parents to better understand what is a nuisance or tolerable side effect vs. an intolerable side effect. The primary concept for this redefinition when the problem is increased activity is to observe what is happening to the child in a controlled environment as compared to what is happening to the child in a non-controlled environment. In a home environment, 90% of the parent's time is dedicated to loving their child, letting the child feel worthwhile and valuable to the infrastructure of the family, and in creating a safe haven in which the child can "just be". Only 10% of the time is spent educating and disciplining their child. At school, in a controlled environment, exactly the opposite is true. Here 90% of the teacher's time is spent educating and disciplining the child while only 10% is dedicated to making the child feel loved, valued, and important in the world. (This statement is not meant to diminish the fact that the overall atmosphere and tone that a good teacher portrays is one designed to be loving and meant to always make the child feel worthy.) *Therefore, as long as a child can learn, attend to tasks, stay*

focused in the controlled classroom and do well in school, the side effect is tolerable no matter how much increased activity there may be at home in the child's safe haven environment when he can just let loose. In general the increased activity levels diminish or resolve within 4 to 6 months. When considering whether the side effect of a sleep disturbance is tolerable or intolerable, I consider these things. First, I am giving a substance that is known to "give energy and wake up the tired", e.g. Grandma, Grandpa, and people with chronic fatigue. Many of the children being treated with methyl-B_{12} already have excess energy and do not need more. Many of these children already have disordered sleep patterns that do not need to be disrupted further. However, just because "convention says" a child needs a certain number of hours of sleep a night does not mean that is true when a child is being treated with methyl-B_{12}. In my practice, *unless the child is falling asleep during the day and is needing more naps, I define the need for less sleep or the new disrupted sleep patterns as tolerable and not as intolerable as long as I am seeing improvement in the other areas that methyl-B_{12} is famous for: executive function, speech and language, socialization and emotion.* In general the disrupted sleep patterns take 2 to 4 months to readjust and normalize. True PICA is not a problem with methyl-B_{12} whereas *mouthing objects, and playing with the mouth, lips, and tongue is common.* This is always a side effect indicating that the peripheral nerves are being activated and this side effect *represents a "positive negative".* It is a sign that methyl-B_{12} therapy is working. It always resolves within 4 to 6 months though it can occasionally be severe in the meantime.

Myth: Methyl-B_{12} And The Benefits Seen For Children On The Spectrum Are Due To A Deficiency.

One of the common mistakes clinicians make in treating with methyl-B_{12} is to approach it from the conventional viewpoint we all learned in medical school. We were taught that B_{12} is a vitamin and when we see a positive response by using it therapeutically that the response was due to correcting a B_{12} deficiency. With methyl-B_{12} therapy, a major roadblock to reproducing the 94% response rate and obtaining the high percentage rate of long-term improvement is partly due to semantics and how one defines a deficiency. In medical school we were all taught that a B_{12} deficiency could be easily resolved. We learned that the liver and the B_{12} transcobalamin transport systems could be repleted with just a few injections and that because of these few injections there would be enough B_{12} now stored in the body to meet B_{12} deficiency needs for a year or two. However, this classic definition and original work was done on adults with pernicious anemia, not on children with autism. What is true with one disorder is not necessarily true with the other. What is observed in children with autism being treated with methyl-B_{12} injections is that they frequently regress or that they do not progress at the same rate they were progressing if they stop their methyl-B_{12} injections. It is interesting to note that most children found to be methyl-B_{12} responders have high-normal to high baseline serum B_{12} levels prior to starting the shots.

Therefore a true "nutritional deficiency" interpreted by conventional laboratory data and explained by conventional wisdom cannot account for the clinical observation why children respond so well to methyl-B_{12} in the first place. Even more so does conventional interpretation of conventional definitions of deficiency fall far short of explaining why these children regress or not progress as rapidly as they were progressing when they stop the shots. This is because conventional wisdom believes that the B_{12} stores will have undoubtedly been repleted! What we need is a new definition of deficiency as it applies to methyl-B_{12} and to children with autism and to other neuropsychological delays or disorders. This new definition for methyl-B_{12} needs to combine the old definition – "not enough of something" – with a new one that is time sensitive – "during this specific period of time" – and includes the metabolic rationale – "because of these metabolic abnormal pathophysiological mechanisms of action". Because the continuous supply of methyl-B_{12} that results from the slow leaching effect of subcutaneous injections produces far

greater clinical response, the biochemistry and pathophysiology implies that there is a transport disorder and/or a metabolic processing disorder that may be overcome if the system is fed in a steady-state and non-pulsatile fashion. *Therefore a definition more appropriate for what is seen clinically is "a nutritional methyl-B_{12} time sensitive dependency with or without a true B_{12} deficiency that is modulated by atypical or alternative biochemical processes".*

In addition to the long overdue need to redefine methyl-B_{12} deficiency as a nutritional dependency with or without a true B_{12} deficiency, we also need to rethink how we view the methyl-B_{12} molecule itself, independent of the methionine synthase enzyme. Though convention has only investigated B_{12} and methyl-B_{12}'s role from the perspective of "the deficiency model", new research must address whether methyl-B_{12} produces other effects in and of itself when all the transport systems and storage systems for B_{12} have been saturated.

Myth: Parents Can Add Several Variables At The Same Time Methyl-B_{12} Is First Introduced And Still Be Able To Differentiate What Are Methyl-B_{12} Benefits And/Or Side Effects From Those That Are The Result Of Other Things.

This is one of the most serious errors that is consistently being made by parents and allowed by clinicians. After 50,000 to 60,000 shots and thousands of Parent Designed Report Form evaluations, and after "initiating" methyl-B_{12} shots 100% of the time for the first 5 weeks of therapy with no concurrent changes, I can say with certainty that if I cannot tell one benefit vs. side effect from another benefit vs. side effect, it is anyone else's guess. Positives and negatives can both occur and to varying degrees. Being able to differentiate what effects may be additive or synergistic manifestations between items is a problem. Alternately, being able to differentiate what effects may offset other affects is equally problematic. And the unknown effect of the positive results as they interact with the negative results is even more problematic. Therefore, unless one evaluates the effects of methyl-B_{12} alone, the 94% initial response rate will be missed. The degree of the initial responses will never be known. Many children that would do well on long-term methyl-B_{12} therapy will never be started. The 6% of children that should not be taking it may continue using it when it should not be used, not only for its ineffectiveness, but also due to the needless cost involved.

Myth: The Parent Designed Report Form Is Not Necessary To Determine Whether Or Not A Child Is A Methyl-B_{12} Responder.

The Parent Designed Report Form is the most sensitive and specific tool to evaluate methyl-B_{12} responses. It is not specific to autism but goes beyond spectrum disorders to include many neuropsychological disorders. Its sensitivity and specificity are only valid if used to evaluate the 5-week initiation period of methyl-B_{12}. Afterwards it can be used to monitor overall progress but not to validate methyl-B_{12}'s effectiveness as a single agent unless, for whatever reason, an additional 5 to 6 weeks of methyl-B_{12} is prescribed and the child is still not allowed to make any other changes to his or her program. Though this situation occurs rarely, it does exist but its circumstances are beyond the scope of this discussion.

Myth: The Intensity Of Responses And Not The Number Of Responses On The Parent Designed Report Form Indicates Whether Or Not A Child Is A Responder And Predicts A Child's Long-Term Prognosis.

This is a common misunderstanding of parents and clinicians. Without a doubt it is the number of responses on the initial evaluation form that represent the greatest predictive value for whether a child will be a mild, moderate, or significant responder over the next 2 year period of time. The majority of parents score the intensity of initial responses as one's and two's. The average number of responses, both positive and negative, is 28. Each parent and clinician needs to rethink what methyl-B_{12} is doing and how fast one can expect it to mature. Using methyl-B_{12} is

analogous to growing a tree. First we plant the seed. It sprouts quickly and within 5 weeks we see a little tree where no tree has ever grown before. However, it takes years for the tree to reach its full height and strength. So it is with methyl-B_{12}. The more symptom improvements seen on the initial evaluation, the more likely the child is to have a forest a few years later. Fortunately methyl-B_{12} tree seeds sprout quickly within the initial 5-week period of time. The parents are told to watch the "X" on the ground where they planted their methyl-B_{12} tree and they get excited when they see it pop through the X and grow. Initially they were focusing at the X on the ground while their peripheral vision encompassed an additional 3-foot circle. However, after a few months the tree will be too big for them to gaze down upon and in order to view the tree to see if its still growing they will have to step back quite a distance to take it all in. Unfortunately, now when the parents view the tree it sits against the horizon and its backdrop is no longer a 3-foot circle of ground but instead the sky and the entire universe. Its growth now becomes imperceptible and can only be evaluated over a span of many months to years and is no longer discernible if measured in only weeks. So it is with methyl-B_{12} and evaluating whether it is continuing to work and whether or not it is still needed. Truly, the only job a parent and clinician has to do at the end of the first 5 weeks of methyl-B_{12} therapy is to determine if the child is a methyl-B_{12} responder – did the methyl-B_{12} tree seed sprout? If so, as long as one does not kill the tree seed and as long as one waters the tree, within a couple of years the tree will become tall and strong! When children on the spectrum who are receiving methyl-B_{12} injections per protocol are followed over a two-year period of time, a high percentage of them are found to have elevated themselves above their baseline "relative position" in the classroom at school and in the classroom of life. It is not uncommon for a child that was at the bottom of his class to be found at the top or in another higher-functioning classroom altogether in 1 ½ to 2 years.

Myth: Parents Will Not Take The Time Or Be Bothered To Complete The Parent Designed Report Form Because It Is So Long.

Parents with children on the autistic spectrum are some of the most motivated people in the world. When they understand "the why" behind what is required of them, with rare exception they are more than happy to comply, grateful for the opportunity, and thrilled that a professional is really interested about their child and will read what they have written! Whenever I initiate methyl-B_{12} therapy, I teach the parents why doing this is probably one of the most important things they will ever do and that all the time and the effort they invest to fill out the Parent Designed Report Form and Parent Specifics Documentation Letter as accurately and as completely as possible will help me to help their child sooner than I may have been able to do otherwise. To date I have 100% compliance! I also teach the parents that one of the most common comments I get at the end of the 2nd or 3rd Parent Designed Report Form evaluation is, "Thank you for making us be so thorough in the beginning. We would have never believed how much progress there has been if we hadn't been able to go back and read our previous letters. It is amazing!"

Myth: Other Standardized Evaluation Tools Are Equally As Sensitive And Specific To Be Used Instead Of The Parent Designed Report Form To Determine Which Children Are And Which Children Are Not Responders.

Repeatedly in my practice parents have completed other forms. These include the forms common to DAN! and common to the major universities that deal with autism. To date none of the forms were able to capture all of the children that the Parent Designed Report Form was able to capture. Some were not even close! Sadly, many of the children that are doing extremely well with long-term methyl-B_{12} therapy were missed and would have never received the methyl-B_{12} treatment that is proving so valuable in their lives.

Myth: Long-Term Methyl-B_{12} Is Not Needed In Children Shown To Be Responders Who Have Been On The Treatment For Several Months And/Or Their Dosing Frequencies Or Total Dosage Can Be Adjusted Downward.

Many of my patients who have been on methyl-B_{12} for 6 months to 2 years and then stopped the shots, lowered the frequency, or lowered the total dose per shot have shown regression that began anywhere from days to weeks to months later. At this time the percentage of children who will regress or who will not progress as far as they would have otherwise progressed is unknown. However, I have accumulated enough evidence among my large patient population that those who have been on methyl-B_{12} for 2 to 3 years represent many of my children who have come the farthest. Several of them have lost their diagnosis – a diagnosis that previously included statements from their neurologists saying they would never talk, never be able to attend school with other children, and that they would probably need to be institutionalized. Therefore, because of what I am seeing in my practice as my children stay on the shots long-term and what happens when they quit or get sloppy, I am presently encouraging parents to make a long-term commitment of no less than two years for the use of methyl-B_{12} therapy.

Myth: TMG (Betaine) Helps Methyl-B_{12} Work Better.

After studying numerous children's before and after responses with the aid of the Parent Designed Report Form, and from studying the biochemistry involved, my research indicates that the addition of TMG is rarely needed if methyl-B_{12} dosing is adequate and if it is delivered by a slow steady continuous rate in order to establish a state of constant methyl transfer equilibrium. Children presenting to me on high dose TMG from intramuscular injections, or children presenting to me who were receiving subcutaneous injections made from 12.5 mg/ml concentrations of methyl-B_{12} substrate frequently related that the addition of TMG improved some symptoms. By switching the patients to the concentrated 25 mg/ml form of methyl-B_{12} and insuring shallow subcutaneous injections, most of the children were able to discontinue TMG. Some parents noticed undeniable symptom improvements with decreased side effects once methyl-B_{12} was increased to its optimum dose while the TMG was simultaneously discontinued.

When considering the biochemistry involved, homocysteine either accepts a methyl group from methyl-B_{12}/methionine synthase or from TMG/betaine homocysteine methyltransferase (BHMT). Methionine synthase is found throughout the body whereas BHMT is only found in the liver and kidney. Each homocysteine molecule that is available to accept a methyl group from either methyl-B_{12} or TMG can only accept one methyl group at a time. *Therefore the limiting factors to this reaction are the amount of methyl-B_{12} present, the amount of TMG present, the activity of the enzymes themselves, the location of the pool of homocysteine being used at any moment in time, e.g. the total body pool or the pool within the liver and kidney, and the availability of key nutrient cofactors.*

It has been my experience that if the methionine synthase enzyme is intact, methyl-B_{12} can be used alone to produce the desired benefits but only if the dose is adequate and only if the delivery system is continuous. Because the methionine synthase enzyme is present throughout the body and because the betaine homocysteine methyltransferase enzyme is only present in the liver and kidney, it appears that methyl-B_{12} can provide all the methyl groups necessary for homocysteine to use but only if it is dosed high enough and delivered continuously. It has been my experience that when patients who are already taking methyl-B_{12} injections notice an increase in symptom improvement after the addition of TMG, the total number of methyl groups able to be donated from methyl-B_{12} was too few because the dose of methyl-B_{12} was too low. The incremental addition of more methyl-B_{12} then allowed TMG to be discontinued while symptom improvements remained at the same level or improved even more. In the 6% of patients where methyl-B_{12} fails, a trial of TMG is warranted to see if the entry pathway necessary to reach homocysteine by using

betaine homocysteine methyltransferase is needed, possibly due to a theoretical methionine synthase enzyme damage, deficiency, mutation, or block. It should also be noted that the addition of extra methyl-B_{12} to the shots from the pharmacies I use does not add to the cost of the shot whereas the addition of oral TMG does add to the parent's monthly expenses. Without a doubt the majority of my parents would rather give shots than any oral supplement or medication and the addition of oral TMG just represents "one more fight to fight" – a fight that I believe is unwarranted if the incremental increased subcutaneous dosing injection schedule is worked with long enough to establish the optimum dose of methyl-B_{12}.

Another time to add TMG *after the maximum saturation state of the methyl-B_{12} system has been achieved and clinical benefits are not being realized or are being realized at a very mild level* is when the question of adequate enzyme activity arises. Because the methionine synthase and betaine homocysteine methyltransferase enzyme systems are also limiting factors to the homocysteine reaction, should methionine synthase be inadequate or "damaged", the addition of TMG may be able to add additional methyl groups to the methyl pool homocysteine still requires. However, the clinical challenge is to first systematically saturate the methyl-B_{12} system without causing significantly increased side effects and while objectively noting that increased clinical benefits are no longer forthcoming. Only after that set of clinical trials has been satisfactorily answered is it advised to try a 5-week TMG clinical trial. As with methyl-B_{12}, the TMG clinical trial should allow no other concurrent changes to be made and the improvements or side effects should be evaluated by using the Parent Designed Report Form in the same manner it was used for methyl-B_{12}.

Myth: Folinic Acid And/Or 5-Methyltetrahydrofolic Acid (Folapro) Helps Methyl-B_{12} Work Better.

In my practice the addition of folinic acid always follows the first 5-week initiation period of methyl-B_{12} therapy. To date I have noticed very little significant clinical improvement with this substance alone, but as stated, I add it after I have initiated methyl-B_{12} therapy for 5 weeks. Early in my research I was not adding folinic acid for several months, not by design but rather because I was new to the entire field of folate/B_{12} biochemistry and was just focusing on methyl-B_{12}. Therefore, many of my current conclusions are based on those early years when folinic acid was added later in my treatment regimen without significant symptom improvement having been realized by the parents. Biochemically this makes sense because the need for B_{12} to receive its methyl group from 5-methyltetrahydrofolic acid is being bypassed by the direct addition of methyl-B_{12}. Therefore, though folinic acid and 5-MTHF are still vital for many other bodily functions, the methyl-B_{12} – methionine synthase - homocysteine – methylation -- transsulfuration methyl group transfer pathways are satisfied and therefore no significantly greater symptom improvement would be expected. This is not to say other symptoms not directly related to this biochemical pathway may not be affected positively and therefore symptom improvement due to other pathways may be simultaneously realized.

Myth: Methionine And/Or SAMe Help Methyl-B_{12} Work Better.

Children on the spectrum have been shown by GL Arnold's study to frequently have low plasma amino acids. Methionine is one of the essential amino acids and it is the nutritional starting point for the methylation/transsulfuration pathways. Both methyl-B_{12} with methionine synthase and TMG with betaine homocysteine methyltransferase allow homocysteine to be recycled into methionine that goes to SAMe, then to S-adenosylhomocysteine (SAH), and back to homocysteine in preparation to spin the cycle again. Additionally, some homocysteine goes down the metabolic pathway and ultimately becomes glutathione. Due to the side effect response rate of 70% in my practice when children received SAMe who had already been stabilized on methyl-B_{12} according to protocol, it quickly became apparent that it was more important to

activate the recycling of homocysteine to methionine than to load the system with more substrate, e.g. methionine and/or SAMe. By increasing the total load of either methionine or SAMe without providing adequate methyl-B_{12} to recycle the "*relative*" accumulating homocysteine or SAH, the body must once again try to figure out how to process these metabolites to move them to the next metabolic step. Though the need for these substrates is undoubtedly documented by plasma amino acid testing, the clinical catastrophes I experienced must thoughtfully be reviewed as to why. Because some of my colleagues did not report the significant and severe side effects I was noticing, e.g. head banging, hitting, and aggression when they added SAMe in high doses, the explanation must lie within the differences, not similarities of the protocols we were using. Therefore, for the protocol I am recommending, the use of SAMe and methionine must be added extremely cautiously, when added be added individually, and observed very closely for clinical response, both positive and negative.

Myth: High-Normal To High Levels Of Serum B_{12} Indicate That B_{12} And Methyl-B_{12} Are Not Needed.

B_{12} levels are high-normal to high in almost all children documented to be methyl-B_{12} responders. When B_{12} approaches the methionine synthase enzyme and cannot be reduced and recycled, the oxidized form of B_{12} just sits outside the cell and builds up in the plasma. The easiest clinical analogy to understand this phenomenon is diabetes where the blood sugar that cannot enter the cell builds up in the plasma.

Myth: Other Forms Of B_{12} Will Work Equally As Well Or Better Than Methyl-B_{12}.

There are five known forms of cobalamin, "B_{12}": a) cyanocobalamin; b) hydroxycobalamin; c) adenosylcobalamin; d) glutathionylcobalamin; and e) methylcobalamin. Cyanocobalamin and hydroxycobalamin interact with glutathionylcobalamin to form methylcobalamin. Adenosylcobalamin is made in the mitochondria. There are only two "coenzyme forms" of B_{12}: methylcobalamin coenzyme and adenosylcobalamin coenzyme. The rest of the B_{12}'s have one purpose in mind, that being to become one or the other of these active B_{12} molecules. Therefore the popularity of hydroxcobalamin that is presently occurring seems to be missing two important facts. One is that the entry of B_{12} into the homocysteine pathway is from methyl-B_{12} coenzyme, not from any other form of B_{12}. The second is that clinically I had been using hydroxycobalamin injections in children with autism for years with some benefit but no marked or incredible symptom improvements. My evolution into the methylcobalamin phenomenon had its roots in cyano-B_{12} and hydroxy-B_{12}. Eventually I was only using hydroxyl-B_{12} because it seemed to work a little better than cyano-B_{12}. Though I had been using low dose methyl-B_{12} in IV's for chronically ill adults for 2 years, I had never used it in children on the spectrum. One day in 2002 in my office I said to myself, "I wonder if this Japanese form of B_{12} will be any different than cyanocobalamin or hydroxycobalamin?" The rest is history. Within seven days of giving my first injection, Dylan, who previously spoke only in four word cryptic sentences with essentially no spontaneous speech, began talking to everyone he met in seven and eight word sentences!

Myth: The MTHFR Enzyme Mutation Test And The Genomics Test Indicate Which Child Needs Methyl-B_{12} And Which Child Does Not Need Methyl-B_{12}.

Unfortunately there is no test at this time that will predict which child will and which child will not benefit from methyl-B_{12}. When methyl-B_{12} is introduced alone for 5 weeks, when each criterion for success is in place, when no other variables are introduced or deleted, when the Parent Designed Report Form is completed at the end of the 5 week "pure" clinical trial period, and when the reason for every entry in the columns of the Parent Designed Report Form is described in detail in the Parent Specifics Documentation Letter, then the response rate to methyl-B_{12} will be over 90%. All tests to date that indicate there are problems in certain genomes or biochemical pathways miss a huge portion of this 90% of children that are shown to be clinical

responders and who should be treated. Therefore, until pure science and funded research studies catch up with the current clinical science, the only ethical thing to do is treat all the children for at least the initial 5 weeks in the manner described throughout this document. Because each child is his or her own best laboratory, we should never discount the findings observed in these children's "personal" clinical labs as being the premier lab test!

Myth: Overmethylators Do Not Need Methyl-B_{12}.
The same argument can be made here that was made above. Laboratory tests used to document "overmethylators from undermethylators" may be applicable in certain biochemical pathways and the percentages given for each may apply to certain clinical conditions, e.g. schizophrenia but not necessarily autism. However, the greater than 90% response rate I observe with children on the autistic spectrum that are given methyl-B_{12} injections does not jive with the percentage rates theoretically stating methyl-B_{12} is not indicated for "overmethylators". Once again, the child's body is the primary clinical laboratory in contrast to some in vitro test and evaluating the child's response objectively with the Parent Designed Report Form will differentiate which overmethylator can and which overmethylator cannot receive methyl-B_{12}.

Myth: If A Child Is A Responder, Even If A Significant Responder, Other DAN! Principles Are Not Necessary To Also Be Incorporated Into The Child's Total Program.
As the Parent Designed Report Form shows so eloquently, methyl-B_{12} does methyl-B_{12} things and nothing else. It is ridiculous to think that the rest of the DAN! biomedical principles should not be instituted. In all my patients I incorporate as many of the other modalities as possible. In general, the synergy that exists by using many treatments is a powerful healer. More specifically, methyl-B_{12} needs many other cofactors to be optimally active.

Myth: Methyl-B_{12} Is The Same No Matter What Compounding Pharmacy Produces It And Therefore Any Local Compounding Pharmacy Can Be Used.
This is a serious error and one that I discovered only through hundreds of failed and/or painful injections. By the end of my first year of methyl-B_{12} clinical research, and especially after my initial presentation May 2002 in Philadelphia, parents from all over the country were requesting their favorite compounding pharmacies make methyl-B_{12} at the 25 mg/ml strength. Suddenly my office was getting inundated with calls from frustrated parents and clinicians reporting that the shots were not working as I stated they should, and/or that they were hurting the children. At this point in time, at my own expense, I began to run potency tests on batches of methyl-B_{12} from various compounding pharmacies that were indicating on their labeling that the potency was 25 mg/ml. Wrong! The results of my studies indicated that the range of methyl-B_{12} could be anywhere from a low of 16 mg/ml to a high 28 mg/ml – all sold to parents as "methyl-B_{12} 25 mg/ml". To me as a clinician, this seemed odd so I asked several of my trusted compounding pharmacists. Each of them told me that it requires special effort in order to get methyl-B_{12} in solution and to have it stay in solution. Therefore, those pharmacies that I have found to give accurate potencies and that I can trust to make methyl-B_{12} to my standards are: (Listed in alphabetical order)

1. Coastal Compounding Pharmacy: phone (912) 354-5188; fax (912) 355-3685.
2. College Pharmacy: phone (800) 888-9358; fax 800-556-5893.
3. Hopewell Pharmacy: phone (800) 792-6670; fax (800) 417-3864.
4. Lee-Silsby Compounding Pharmacy: phone (800) 918-8831; fax (216) 321-4303.
5. Wellness Health and Pharmacy: phone (800) 227-2627; fax (800) 369-0302.

Have Your Pharmacy Provide For You Certificate Of Analysis Potency Reports.

Each pharmacy that wants to work with you and your patients should be willing to provide for you its history of certificate of analysis reports. Because methyl-B_{12} is so difficult to get into solution, and because the density effect is so important for the effectiveness of the medication clinically (as described above), it is very important to know "within reason" what dose and density a child is getting. The five pharmacies mentioned, Coastal, College, Hopewell, and Lee-Silsby, and Wellness have all been willing to do their homework, put in the effort to learn the intricacies of the process, and spend the money necessary for frequent certificate of analysis reports to guarantee that the final concentrations of methyl-B_{12} are typically within plus/minus 5%. Pharmacies "new to the process" cannot assume that their reconstituted product will produce a final concentration similar to the consistency seen with the five pharmacies mentioned above. Therefore, if they want to play the game and throw their hat into the ring, they must be able to show you certificates of analysis to assure you that what you are receiving can compare to the leaders in the methyl-B_{12} industry for children with autism.

*** Please note that any pharmacy willing to provide to me the same information that is required from the five pharmacies listed above will be able to request that they also be listed in this document and on the methyl-B_{12} program [available to clinicians and pharmacists] ***

Myth: The Shots Are Painful.
With the correct pH balance, any good compounding pharmacy should be able to make shots that are painless. Even the best pharmacies make a bad batch from time-to-time that can causes pain. This occurs for no obvious reason that the pharmacies have been able to explain other than "it just happens". With 50,000 plus shots to my credit, I have experienced only two bad batches that I know of where my patients noted discomfort or even pain. As far as I know, should this ever happen the pharmacy will replace your syringes with a new batch tested to be painless. My latest injection instructions teach how to avoid this ever happening in the first place.

Myth: Pink Urine Can Be Seen Even With Subcutaneous Injections And/Or It Indicates That The Body Has All The Methyl-B_{12} It Needs And That It Is Building Up To Levels That Are Too High For The Body And Is Becoming Toxic.
Pink urine from methyl-B_{12} stock solutions of 25 mg/ml, when given shallowly into subcutaneous adipose tissue of the buttocks at the standard doses recommended never produces pink or red urine. 100% of the time when I have been challenged on this point, once I helped the parents "tweak their technique" and no longer be near the SQ:IM junction, the pink urine they were seeing disappeared. The only exception to this has been in children that have essentially no subcutaneous adipose tissue so that muscle or the SQ:IM junction cannot be avoided.

Pink urine is a function of these factors: *Primary factor #1* -- total volume [not dose] of the "red substance" administered whether from a stock solution of 1 mg/ml or 25 mg/ml; *Primary factor #2* -- the relative speed of entry of the total volume of red substance into the bloodstream which is much faster when given IM or near the SQ:IM junction; *Secondary factor #1* -- the rate of filtration by the bloodstream to clear the red coloration; *Secondary factor #2* – the time of injection. Shots given at night that are IM, shots near the SQ:IM junction, shots at higher doses than the standard doses recommended, shots with higher volumes to produce the same total dose or to produce greater than standard doses, and shots made from less concentrated solutions with greater surface areas will all appear in the bloodstream relatively quickly and pass into the urine. Once present, nighttime urine will be concentrated and therefore whatever color the filtered substance is, whether yellow or red, etc., it will appear darker in a morning urine specimen.

It is important to note that pink/red urine is not a function of some buildup of methyl-B_{12} finally getting "high enough" and spilling over. It is not a function of some gradual toxicity level

appearing because the dose of B_{12} [for the standard recommended dosage ranges] is below doses that have been safely used for years, e.g. in patients with pernicious anemia. It is not a function of the cobalt atom because the cobalt atom is inactive when "contained" within the corrin ring structure and therefore does not cumulatively bind to tissues and color the urine pink/red.

Myth: The Needle Can Injure The Sciatic Nerve When Shots Are Given In The Buttocks. Simply stated, this is ridiculous when one follows the protocol I suggest! By applying simple trigonometry, one of the professionals whose child is a patient of mine gave me this "rule of thumb" when the BD #328438 needle is used as per my protocol: a) shots injected at a 30 degree angle give an *effective needle length* of approximately 4 mm; b) shots injected at a 20 degree angle give an *effective needle length* of approximately 2.7 mm; c) shots injected at a 10 degree angle give an *effective needle length* of approximately 1.4 mm. Not even the smallest premie has a sciatic nerve this shallow and because we are treating children much larger than premies, there is no possibility of ever injuring the sciatic nerve from a BD #328438 3/10 cc insulin syringe with an 8 mm, 31-gauge needle!

Myth: Pinching The Fat Will Assure That The Injection Is Administered Subcutaneously. Professionals often teach parents to "pinch the fat" to give a subcutaneous injection. Unfortunately with small children, the "tenting effect" that occurs not only brings with it subcutaneous fatty tissue but also "a ribbon of muscle" that is just as likely, if not more likely to receive the methyl-B_{12} that is thought to be being administered into the subcutaneous tissue. Therefore, *never pinch the fat* in order to insure a subcutaneous injection. Instead, go as shallow as necessary, often just under the skin in a nearly horizontal plane in order to deliver the methyl-B_{12} into the subcutaneous tissue.

Painting Your Masterpiece – The Necessary Ingredients For A Pretty Picture
(Dr. Neubrander's Protocol)

1. Total dose [for approximately 85% of children 64.5 mcg/kg/every 3 days works well].
2. Methyl-B_{12} concentration [25 mg/ml provides the least surface area resulting in a slower and more uniform rate of release].
3. Injection into the adipose tissue of the buttocks [less vascular; slower rate of release].
4. Injections that are "shallow/closer to the horizontal than vertical plane" in the subcutaneous tissue far away from the SQ:IM junction or the muscle itself and without "pinching the fat" [see Injection Instructions for Methyl-B_{12} Shots from my website].
5. The first 5-weeks of methyl-B_{12} use must allow absolutely no additions and allow absolutely no deletions to the child's current program. This 5-week period can be started early in the child's program or later on depending on the clinician's preference. However, whenever methyl-B_{12} is initiated, it is then that the 5-week "no change time clock" begins ticking. Of course if the child becomes ill and needs standard medical treatment, this must be done.
6. The Parent Designed Report Form, the most sensitive and specific tool available to evaluate the effects of methyl-B12 must be used to evaluate the clinical responsiveness. There can be no exceptions to this for at least for the first 5-week clinical trial. After that, completing the Parent Designed Report Form should still be required for at least the next two reviewing cycles because from the letter portion of the exercise, parents will be able to observe the subtle changes that will continue to occur that they would have otherwise missed.

7. Parents must understand and continually be reminded that it is not the intensity of the responses they see in their child that is the most important prognostic indicator but rather it is the number of responses they see that predicts whether or not a child will be a mild, moderate, or significant responder over the next 1.5 to 2.5 year period of time.
8. Parents need to thoroughly understand how to differentiate tolerable vs. intolerable side effects. If their child's side effects are tolerable, even though severe at times, parents should continue the shots without altering doses and understand that these side effects will usually diminish or disappear within 2 to 6 months. Parents must be thoroughly trained in differentiating tolerable vs. intolerable side effects so that methyl-B_{12} therapy can be discontinued when a true intolerable side effect is present. Otherwise therapy should be continued unchanged.
9. If a child is found to be a responder, the parents need to be taught and frequently reminded that the process is a slow steady one that needs to be continued long-term. Parents need to be taught not judge whether or not their child no longer needs methyl-B_{12} therapy because they no longer see obvious changes as those noted during the first 5-15 weeks. Currently I am recommending no less than 18 to 24 months of treatment.
10. Parents should be advised that my research indicates many, if not most children will have some form of regression and/or will lack the same degree or rate of progression they would have had if the shots had not been stopped.
11. Folinic acid should be added after the first 5-week clinical trial but not at the same time as methyl-B_{12}. It should be added alone and its dose should start low and then be incrementally increased to see how it is tolerated. From my research, approximately 20% of children become hyper and/or cannot sleep when folinic acid is added.
12. Liposomal glutathione may be tried in an effort to enhance the glutathione portion of methyl-B_{12}'s effects. As with all members that participate in the homocysteine recycling biochemical pathway, each addition should be made singly and observed over a period of time when no other changes are being made to the child's treatment program.
13. TMG should not be part of the initial protocol and should only be added after escalating doses of methyl-B_{12} fail, if methyl-B_{12} produces "intolerable" side effects according to the definitions given above, or if methyl-B_{12} produces no significant benefits.
14. SAMe and methionine should not be added until the maximum benefit or failure of methyl-B_{12} is determined. If these amino acids are then added, they should be initiated at low doses, added incrementally, and no other concurrent changes should be allowed to the child's treatment program while the parent's closely monitor the results of this clinical trial.

The Basics: Current dosing and delivery schedule: 64.5 mcg/kg once every 3 days to the adipose tissue of the buttocks at an angle severe and horizontal enough to guarantee a "shallow" subcutaneous delivery from a BD 3/10 cc insulin syringe with an 8 mm, 31-gauge needle, item #328438 only, and made from a 25 mg/ml methyl-B_{12} stock solution. * Be sure to understand each part of the injection instructions and follow them *exactly*! *****

Advanced Programs And Protocols: Available to be discussed only with clinicians and on a limited basis. Contact our office at (732) 985-6600.

Available for you from our website at www.drneubrander.com

1. Numerous video examples of parents discussing the positives, negatives, frustrations, and failures of methyl-B_{12} shots.
2. The Parent Designed Report Form.
3. Injection Instructions for Methyl-B_{12} Shots.
4. The Methyl-B_{12} Dosing Chart, Program, And Protocol. [Clinicians and Pharmacists may call to request the password. Leave both your phone and fax numbers as well as your office address and email address.]
5. List of references regarding methylcobalamin and related articles.