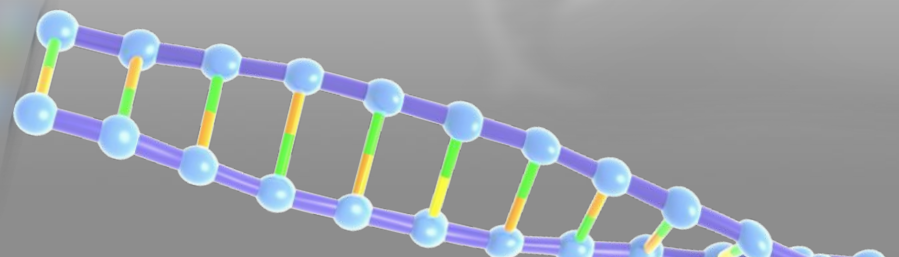

OR

PHARMACOGENOMICS

I can't even say it… How can I understand it???

OBJECTIVES

1. UNDERSTAND THE CONCEPT OF PHARMACOGENETIC TESTING
2. UNDERSTAND WHY THE TESTING IS IMPORTANT
3. Learn how it can it can be used to better support specific populations.
4. HAVE FUN AND LEARN SOMETHING



PLEASE KEEP IN MIND

At the end, you may still have questions. That's OK. We aren't afraid of questions… mostly.

The overall concept and basics of Genetic Testing will be presented as a tool that can be used to assist in choosing a medication regimen that is more "personalized." The goal is to eliminate polypharmacy and troublesome side effects.

The goal is to provide enough workable understanding of the testing and results to help in being the best advocate possible for the one being tested.

WORDS YOU WILL HEAR THROWN AROUND…

Pharmaco*genomics* – how the *genetic* makeup of an individual affects their response to medications. Sometimes called "precision medicine" or "personalized medicine".

Pharmaco*genetics* – inherited genetic difference in the metabolic pathways which includes receptors, enzymes.

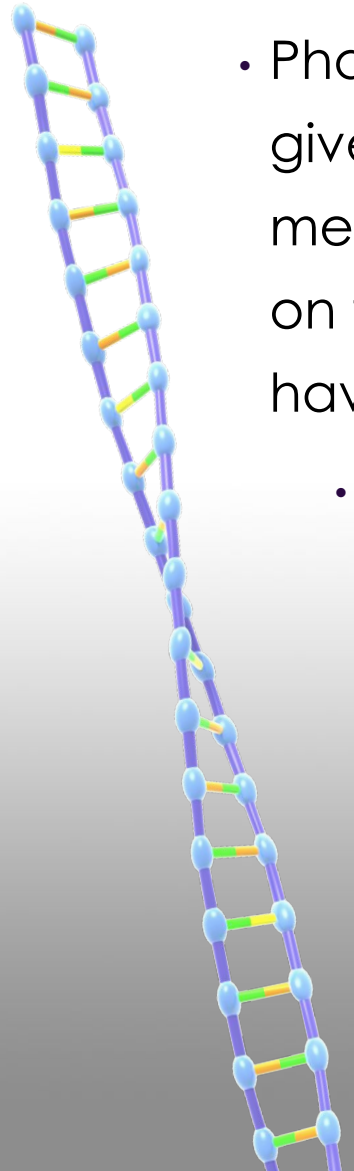
Pharmaco*dynamics* – the mechanism of the drug's action on the body.

Pharmaco*kinetics* – the absorption, distribution, metabolism and excretion (ADME) of the medication within the body.

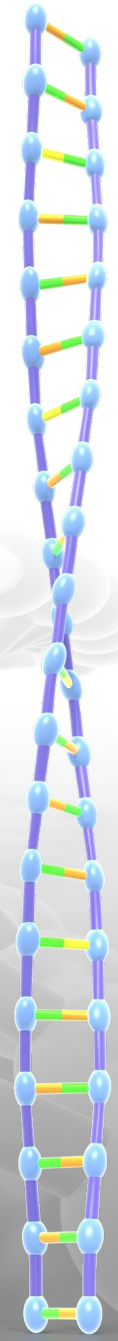
For more definitions, refer to Appendix 1

WHAT IS PHARMACOGENETIC TESTING?

(AND WHAT IT IS NOT)

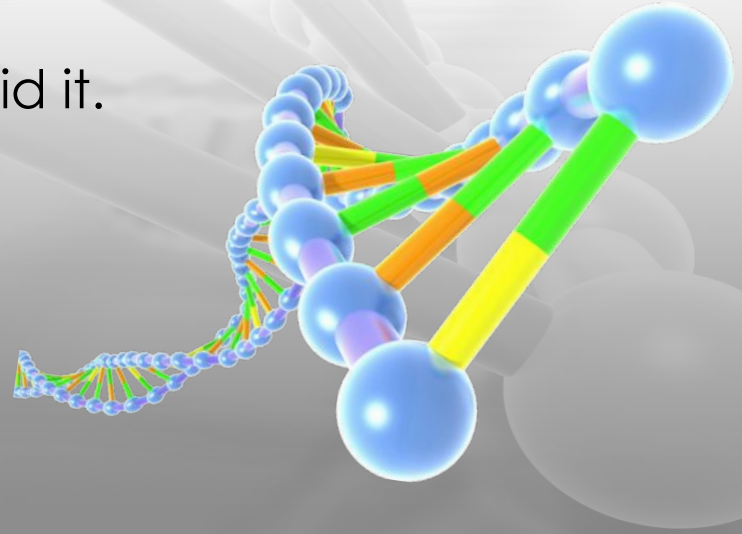


- Pharmacogenetic testing is a DNA based test that gives insight to a provider about how certain medications are **METABOLIZED** by your body based on the availability of the cytochrome pathways you have.
  - It shows which medications may be effective, ineffective, effective at a lower or higher dose or may be prone to cause increased side effects in an individual.
    - Medications include Antipsychotics, Antidepressants, Anxiolytics, Sedative/Hypnotics, ADD/ADHD and certain Mood Stabilizing/Seizure medications



WHAT PHARMACOGENETIC TESTING WILL NOT DO

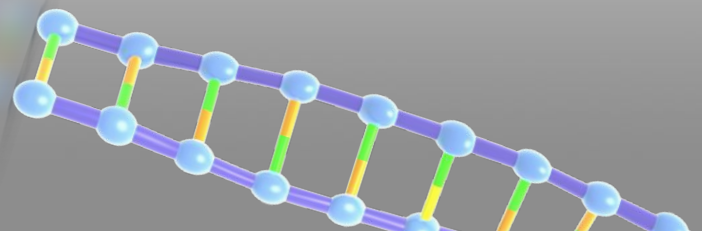
- Tell you if you are related to someone famous(or infamous).
  - Get you on an episode of Cold Case Files if you are a wanted serial killer/bank robber, kidnapper or such.
    - Tell us once and for all if O.J. really did it.



LET'S TALK DRUGS!

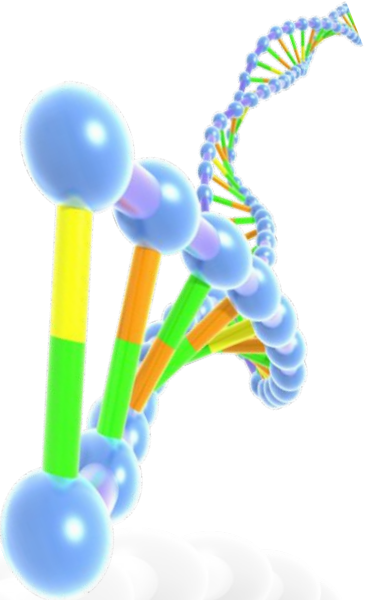
- ALL medications undergo four phases(A,D,M,E)

  - **A**bsorption- How the medication gets into the body
  - **D**istribution- Where the medication goes in the body
  - **M**etabolism- How the medication is broken down by the body
  - **E**xcretion- How the medication is expelled from the body

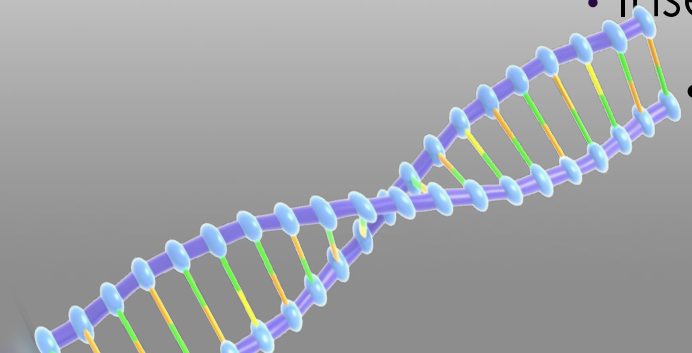


ABSORPTION

- HOW DO WE GET MEDICATIONS INTO OR ONTO THE BODY

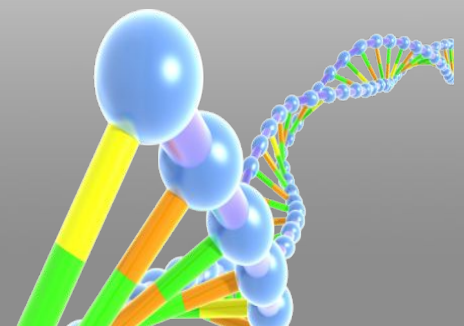


  - By mouth- oral, sublingual, buccal, oral disintegrating tablet
    - Injected- Sub cutaneous, Intravenously, Intramuscularly
      - Topical- Patches, creams, lotions, ointments, eye/ear drops,
        - Inserted- Suppositories, tablets, cream
          - Inhaled



METABOLISM

- HOW THE BODY BREAKS DOWN A MEDICATION
  - Most metabolism is carried out by the enzymes of the liver but there are other areas that can break down drugs (cilia on the kidney)
    - Cytochrome P450(CYP450) is the most common group of enzymes used in metabolism- but not the only ones
      - The process can either form an active or inactive metabolite
        - Each drug is unique in how and to what extent it is metabolized



DISTRIBUTION

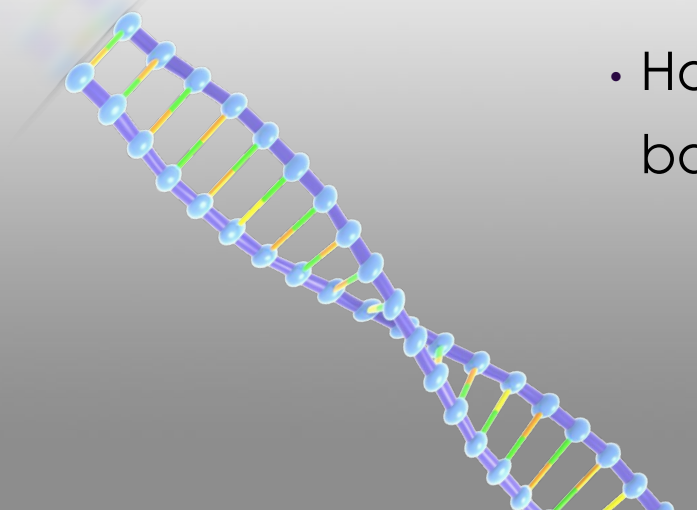
- WHERE DOES THE MEDICATION GO TO WHEN IT REACHES THE BODY

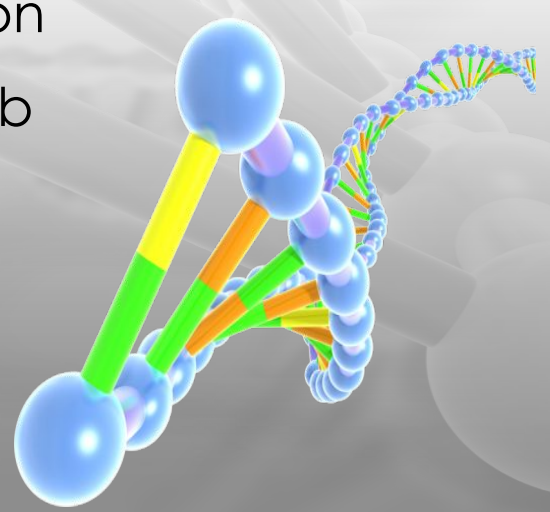
  - MANY VARIABLES(The higher the Volume of Distribution(Vd) the higher the dose level needs to be to achieve the same blood levels

    - Blood flow to a given area

      - Fat or water solubility of the medication

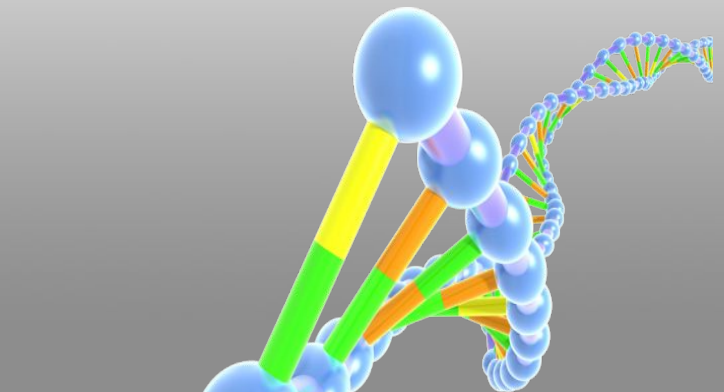
        - How much we can actually absorb based on the given route

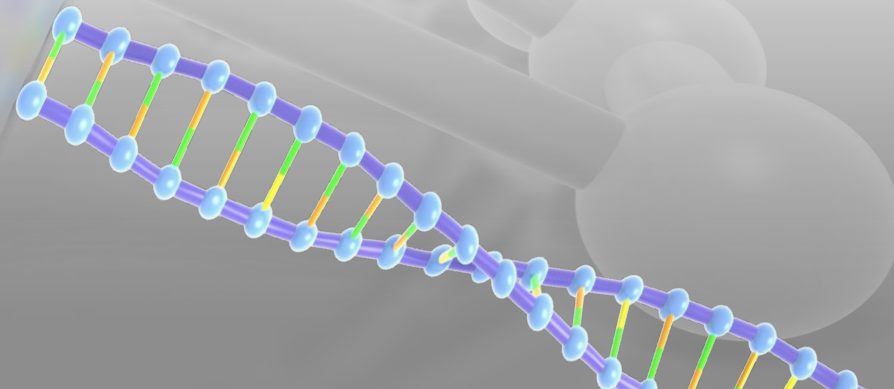




METABOLISM

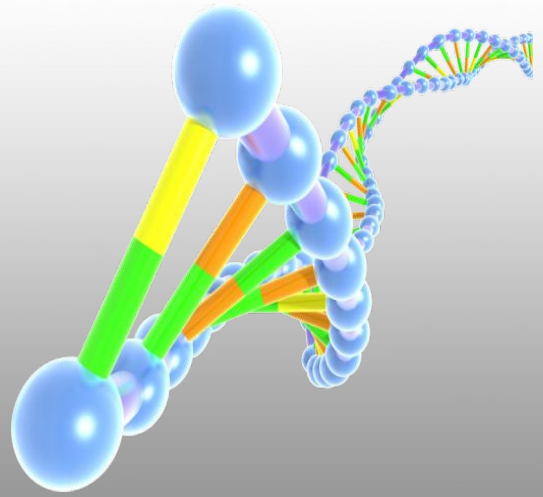
- Cytochrome P450 can be effected by several things
  - Liver damage
    - Heart disease
      - Alcohol
        - Other medications
          - Age- may decrease capability by 30% or more
            - Sex
              - Race





EXCRETION

- HOW THE BODY GETS RID OF THE MEDICATION
  - Via the urine
    - Via the gut



LET'S GO BACK A BIT.....

ALL MEDICATION IS METABOLIZED IN EITHER THE LIVER OR THE KIDNEY.

FOR OUR PURPOSES, WE WILL BE FOCUSING ON THOSE MEDICATIONS THAT ARE BROKEN DOWN IN THE LIVER.

Remember Craig told you about Cytochrome 450?

THINK OF THE CYTOCHROME 450 (CYP 450) AS A BIG UMBRELLA ENZYME

AND UNDER THE BIG UMBRELLA ARE OTHER SMALLER UMBRELLAS

In just a moment, we are going to compare these to roadways.

Based on a person's pharmaco*genetics* some of the CYP enzymes are efficient, inefficient, not working, or over achievers.

The enzymes render an individual either

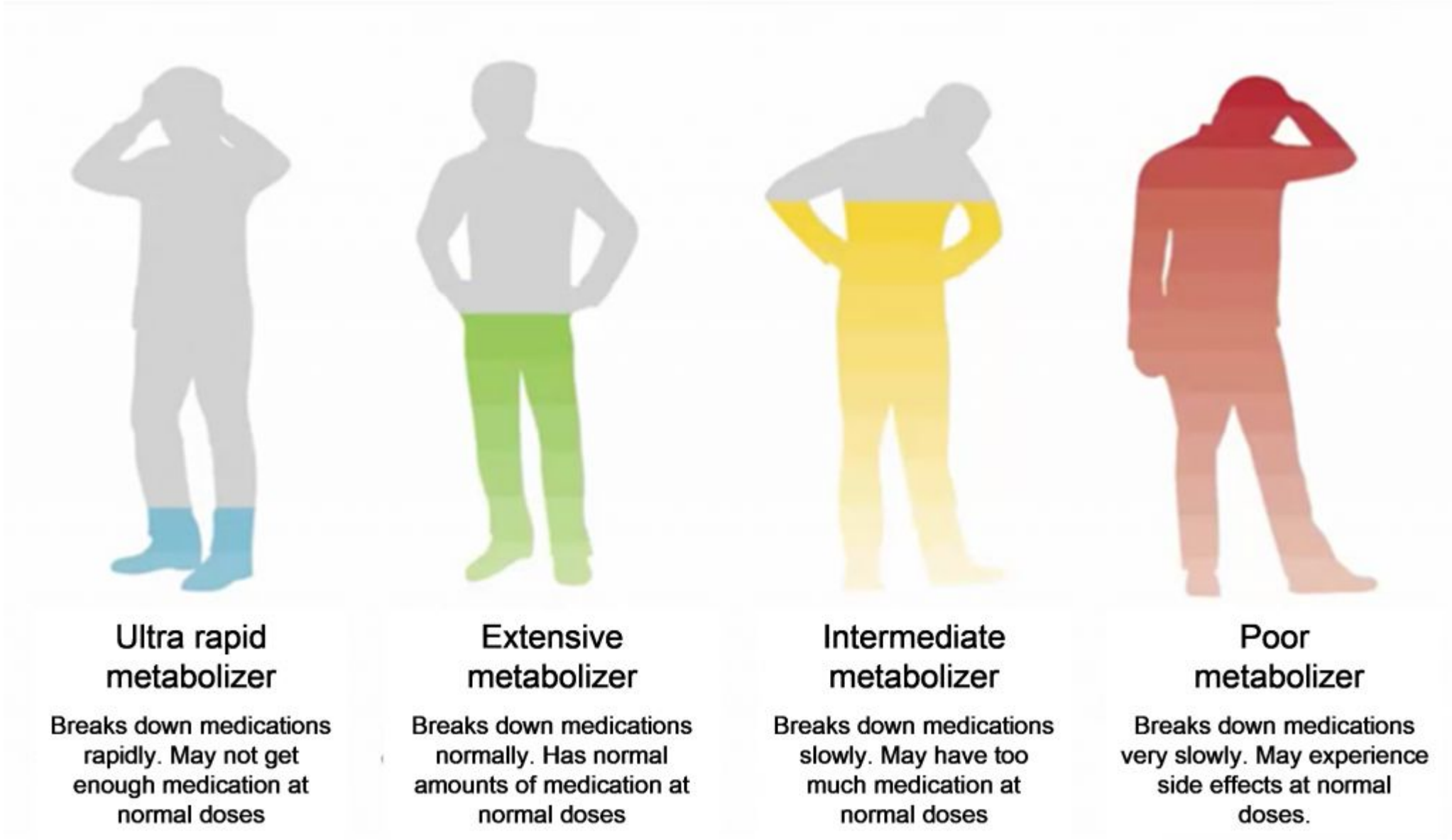
"extensive metabolizer" – meaning that their pharmacogenetics allow them to efficiently break down use the medications based on the manufacturer's dosing recommendations.

"intermediate metabolizer" – their pharmacogenetics do not allow them to break and use all of their medication dose. These individuals are at an increased risk of SEs, ADRs, and toxicity. If the medication is to be used, a lower dose would be required.

"poor metabolizer" – their pharmacogenetics make them unable to break down and use a medication. These individuals are at the higher risk of SEs, ADRs, and toxicity.

"rapid or ultra rapid metabolizer" - their pharmaco*genetics* quickly "burn up" the medication potentially requiring above recommendations of maximum dosage.

Many medication use more than one enzyme pathway in metabolizations which result in combinations of the things mentioned above.



Ultra rapid metabolizer

Breaks down medications rapidly. May not get enough medication at normal doses

Extensive metabolizer

Breaks down medications normally. Has normal amounts of medication at normal doses

Intermediate metabolizer

Breaks down medications slowly. May have too much medication at normal doses

Poor metabolizer

Breaks down medications very slowly. May experience side effects at normal doses.

https://genesight.com

IT HELPS TO THINK OF THE ENZYME PATHWAYS AS ROADWAYS.

IF THE MAIN ROAD HAS A PROBLEM…

TRAFFIC JAM!!!!!

Think of poor or intermediate metabolizers

IF THE “TRAFFIC” ON THE ROADWAY IS SPEEDING…

cars are moving too fast….

Some medications will use smaller pathways or “county roads”. If it is the only “road” open To all of the traffic, you have another TRAFFIC JAM!

NOW DOES THIS SLIDE MAKE MORE SENSE TO YOU?

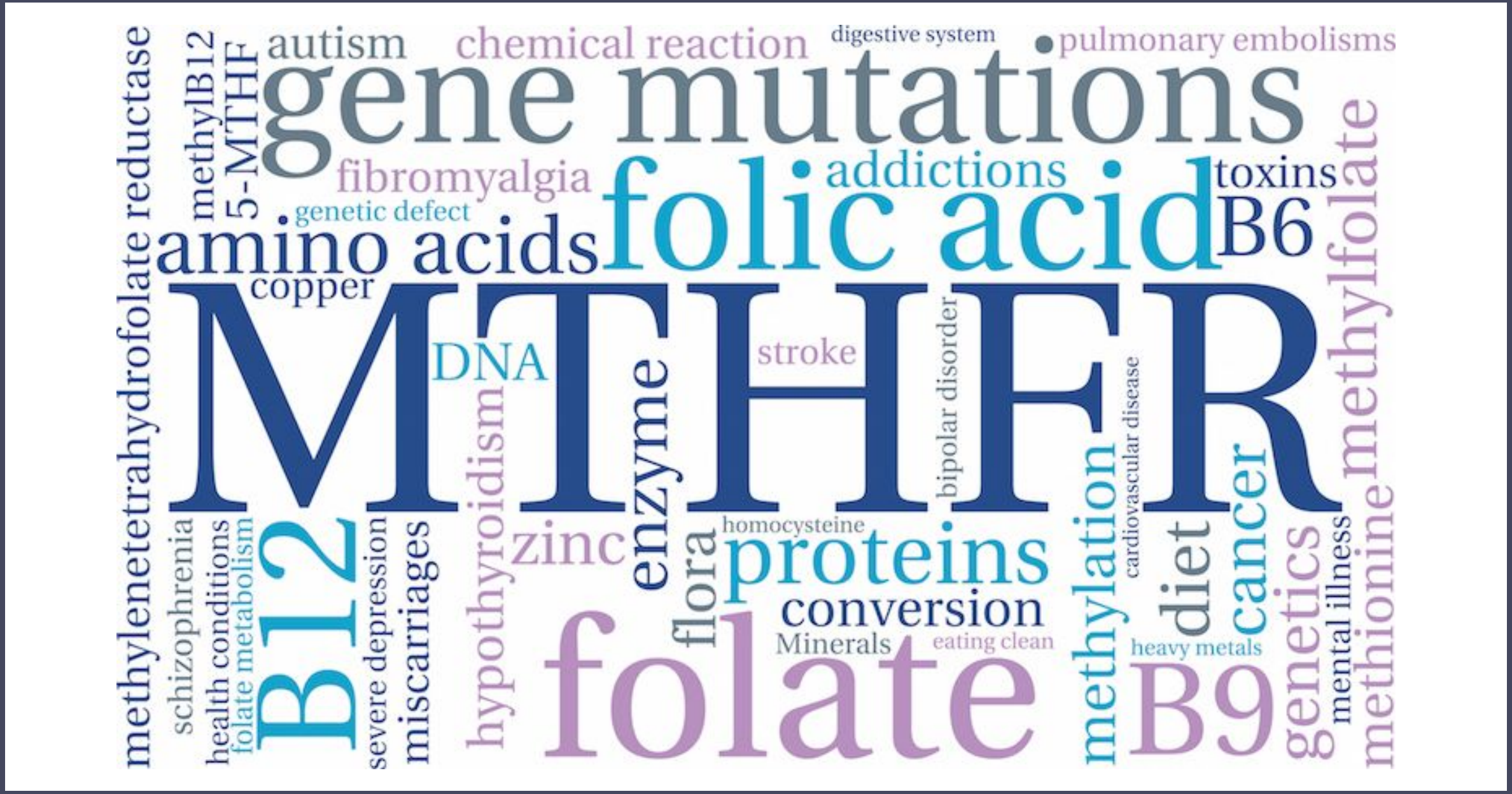
Not many cars on the roadway

Normal traffic flow

Traffic Jam

Things move slowly; One lane may be blocked

LEST IT BE TOO EASY……


methylenetetrahydrofolate reductase
schizophrenia
health conditions
folate metabolism
B12
severe depression
miscarriages
methylB12
5-MTHF
autism
chemical reaction
digestive system
pulmonary embolisms
gene mutations
fibromyalgia
addictions
toxins
genetic defect
amino acids
folic acid
B6
copper
MTHFR
DNA
stroke
hypothyroidism
zinc
enzyme
bipolar disorder
homocysteine
flora
proteins
conversion
Minerals
eating clean
folate
methylation
cardiovascular disease
diet
heavy metals
B9
cancer
genetics
mental illness
methionine
methylfolate

Here's another word…….

"MUTATION"

SIGNIFICANT TO INTERACTION AND METABOLIZING OF MEDICATIONS…..

MTHFR gene

Folic Acid Conversion

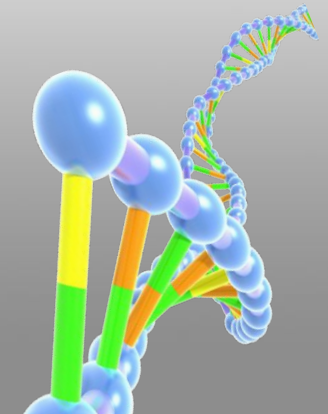
No conversion issue

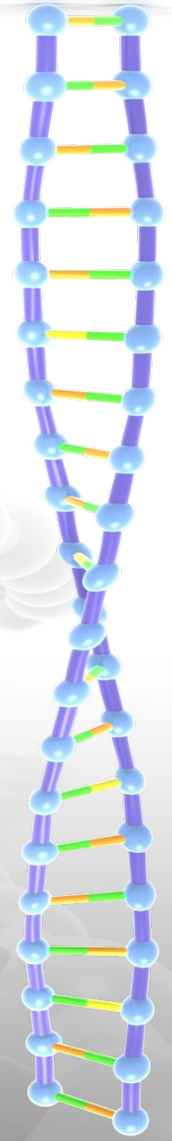
Reduced Folic Acid Conversion

Significantly Reduced Folic Acid Conversion

WHAT IS FOLIC ACID AND WHY DO I CARE

- Folic acid is a water soluble B vitamin also known as B 9
  - The body converts Folic acid to the usable form of L Methyl Folate
    - Some individuals show a diminished or inability to convert Folic acid
      - Evidence suggests low levels of L Methylfolate to be associated with Major Depressive Disorder(as can low Vitamin D levels), Schizophrenia and Alzheimer's
        - Evidence also suggests low levels can lead to treatment resistance





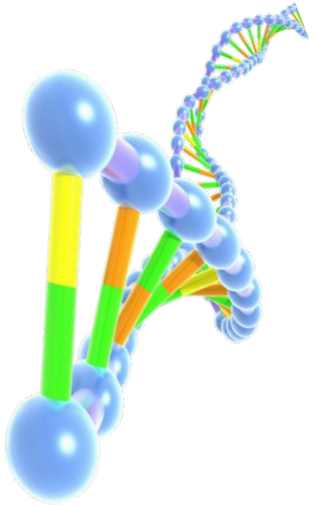
WHY IS KNOWING IF A PERSON CAN CONVERT FOLIC ACID IMPORTANT?

*"Folic acid is crucial for proper brain function and plays an important role in mental and emotional health." Folate is Vit. B-9

A folic acid conversion issue can affect how well some medications that work on the brain and emotional health actually do their job.

*https://www.mountsinai.org
Please refer to Appendix 1 where there is an excellent article sited in Medical News today

CAN TOO MUCH FOLIC ACID BE A BAD THING?



- YES! Everything can be bad if not used appropriately and monitored correctly
  - Excessive Folic Acid levels can lead to a wide range of side effects
    - Decreased appetite, Disturbed sleep, Depression, Overexcitement, Irritability, Psychological behaviors, Weakness/fatigue, Trouble concentrating, Confusion, Seizures
      - We need to be aware that supplementing with Folic acid in a "Non-Converter" can cause as much harm as good
        - If we supplement with Folic acid levels should be monitored for safety reasons- especially in patients with certain diagnosis

WHAT IS THE BENEFIT OF HAVING THIS TEST DONE?

- It can assist the physician in finding the right medication for the individual. (pharmacogenomics). It can "tailor" the medication regimen unique to genetic pre-disposition.
- It literally removes the "guesswork"; the "let's try this" syndrome in prescribing mind- altering medications.

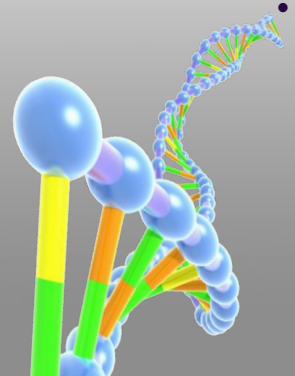
- Can improve drug safety by reducing side effects and adverse drug reactions.
- Provides a clearer picture of how effectively a medication will be metabolized and used by the individual (pharmacogenomics/pharmacokinetics)

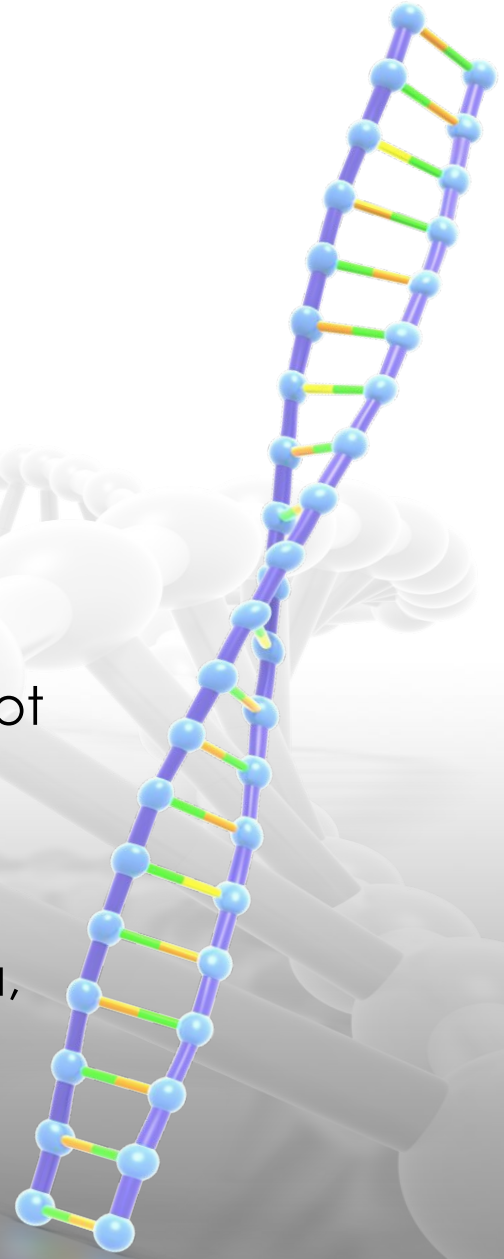
WHO CAN BENEFIT FROM TESTING AND WHY

- ANYONE currently receiving Antipsychotics, Antidepressants, Anxiolytics, Sedative/Hypnotics, ADD/ADHD medications or SELECT Mood Stabilizers/Seizure medications

- Anyone with a psychiatric or mood disorder not currently on a medication

- Anyone with a diagnosis of early dementia, dementia, stroke, TBI, Parkinson's, Down Syndrome, possibly seizure diagnosis, receiving meds for MD appts.

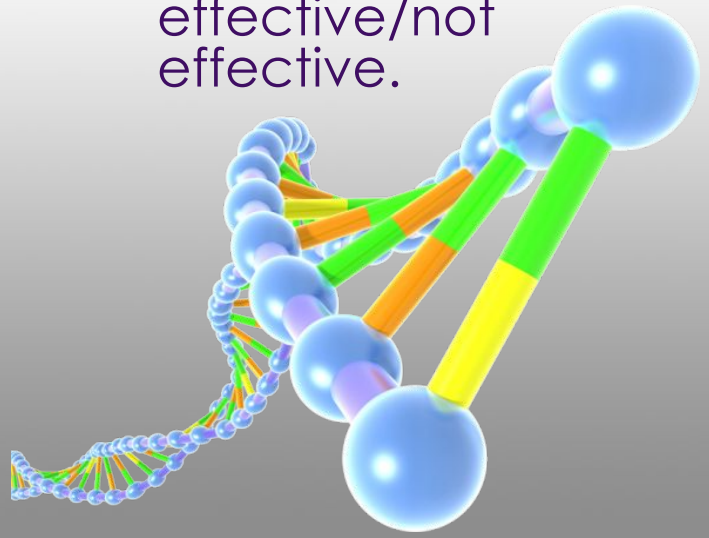




SO NOW YOU ARE ASKING…."Why again do we need this?"

Because until now we have been guessing and doing a terrible job of guessing right!

Based on the first 65 individuals we did pharmacogenetic testing on this is what we found. Based on two groups – Effective and possibly effective/not effective.

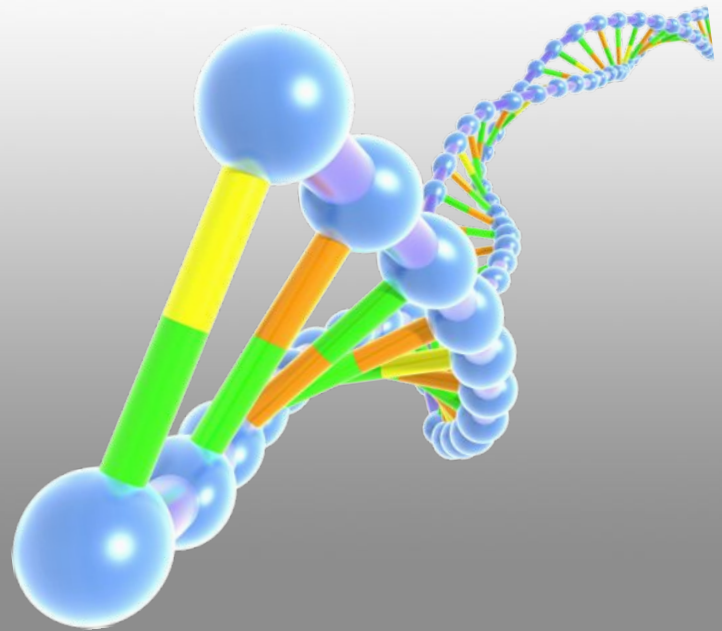


Medication	#	Effective	Possibly/Not Effective	%
Antipsychotics	74	35	39	47%
Antidepressants	53	18	35	34%
Anxiolytics	16	15	1	94%
Sedative Hypnotics	10	9	1	90%
Mood Stabilizers	34	30	4	88%
TOTALS	187	107	69	61%

RESULTS

Results are categorized as Effective, NOT effective or POSSIBLY Effective based on certain qualifiers such as smoking or possible dose changes.

This data is based on two groups. Effective/ possibly and not effective.



Medication	#	Effective/ Possibly Effective	Not Effective	%
Antipsychotics	74	61	13	82%
Antidepressants	53	41	12	77%
Anxiolytics	16	16	0	100%
Sedative Hypnotics	10	10	0	100%
Mood Stabilizers	34	31	3	91%
TOTALS	187	159	28	85%

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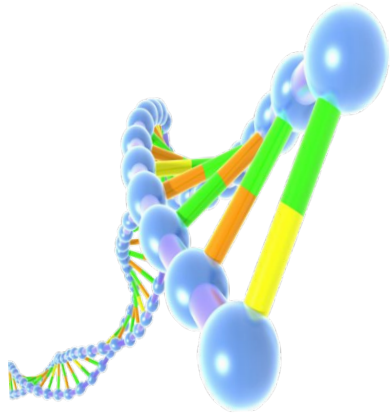
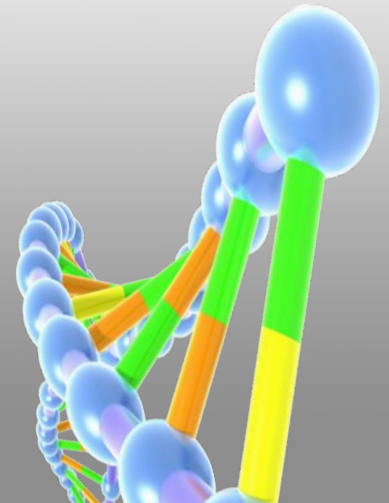


Here we see the results indicating two variations. The difference is where the POSSIBLY effective results are placed.



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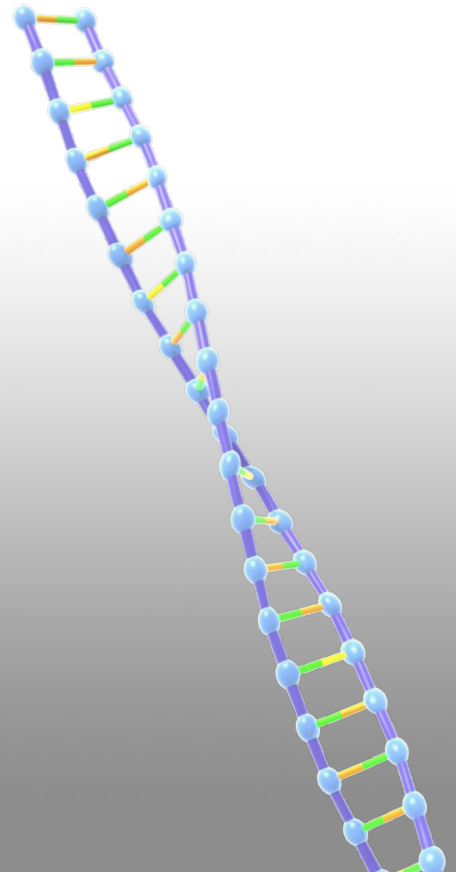
RESULTS

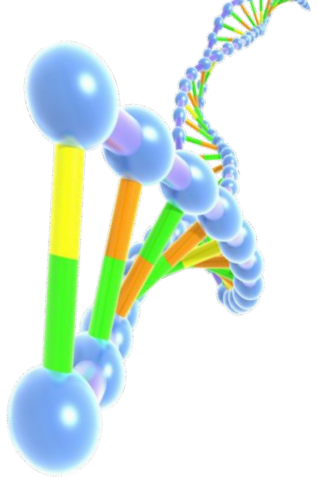
What happens if we split the data into three groups?

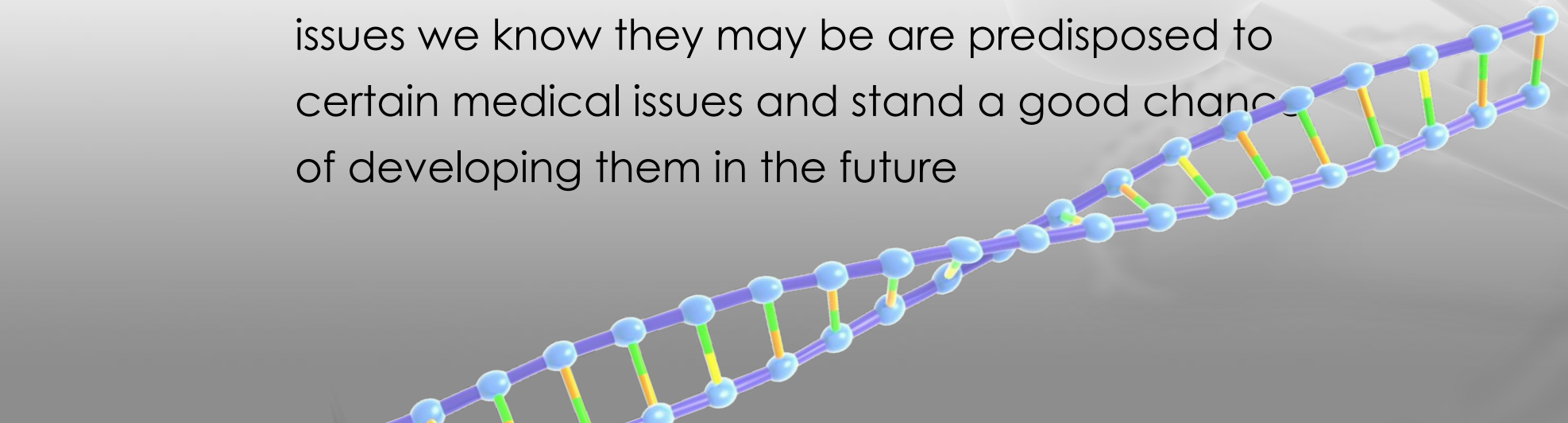


Medication	#	Effective	Possibly Effective	Not Effective
Antipsychotics	74	35	26	13
Antidepressants	53	18	23	12
Anxiolytics	16	15	1	0
Sedative Hypnotics	10	9	1	0
Mood Stabilizers	34	30	1	3

WHY THIS TESTING IS IMPORTANT

- Because our patients are often times unable to express what they are feeling because they are non verbal
  - Or because they can not accurately explain what they are experiencing in terms we comprehend
    - Our patient population is getting older and just because they do not show signs and symptoms or issues we know they may be are predisposed to certain medical issues and stand a good chance of developing them in the future





FROM A NURSING PERSPECTIVE

Again, many of the individuals we support (IDD/Dual Diagnosis/Senior) are unable to express what they are feeling due to challenges with cognition and insufficient vocabulary

Too many medications have become a “go to”. We tend to see the same medications being prescribed over and over.

Over-prescribing to manage behaviors may result in a hospitalization, detoxing and ”starting fresh”.

Over years, many meds have been added to the medication regimen. Few, if any have been taken away.

As people age, it is conceivable that they need less medication, not more. Yet we see the opposite happening.

HOW IS THE TESTING DONE?

1. Cheek swab
2. Buccal Swab (boo - cal)
3. Buccal Swab (buck-cal)
4. All of the above

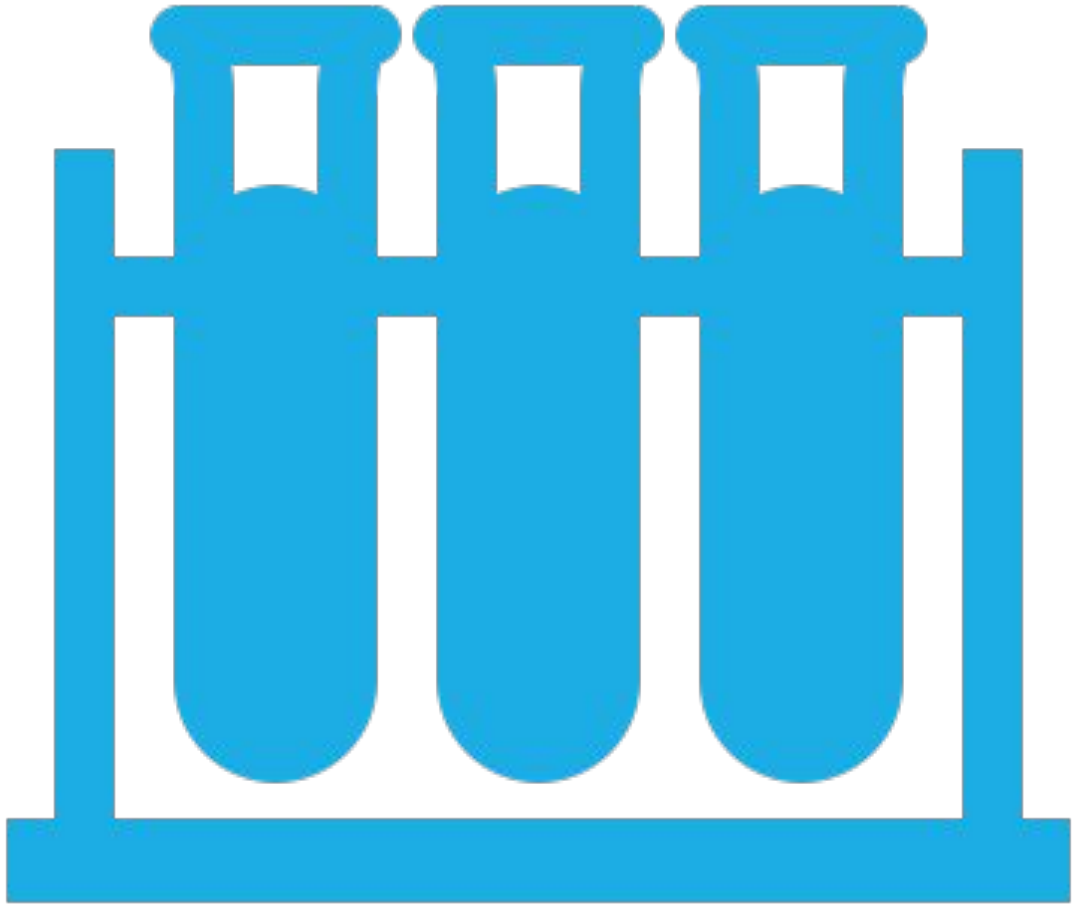
THERE ARE MANY DIFFERENT LABS THAT DO PHARMACOGEN OMIC TESTING

Please find the one that suits your needs best.

Some labs do only panels for mind or conscious altering medications.

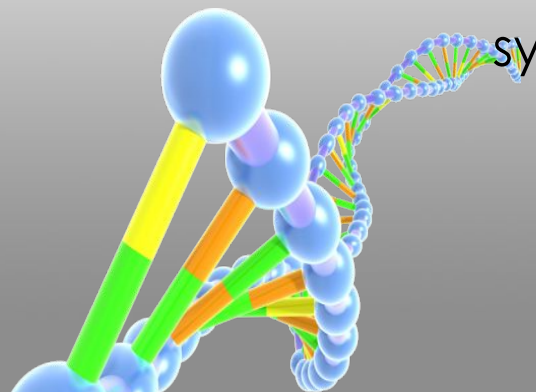
Some labs also include medications for medical issues.

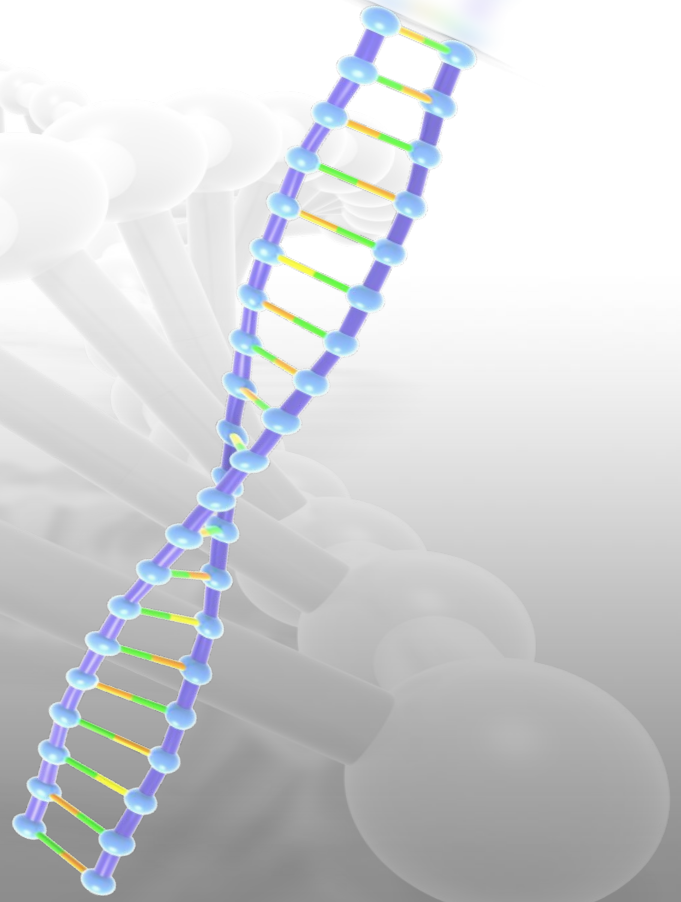
Make sure the lab provides support.



GREAT!

- **NOW WHAT DO WE DO WITH IT???**
  - If ain't broke don't fix it
    - If the individual has lost stability or is beginning to experience side effects we have a road map on where to go next
      - OR if the individual is now showing symptoms





How Do I Decide?

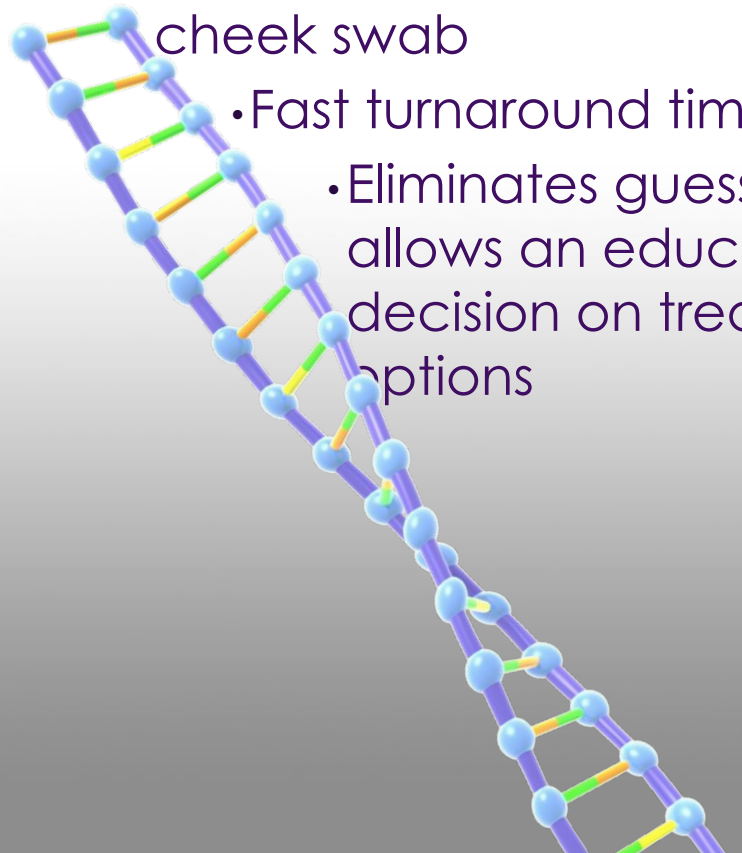
Or is it worth the effort

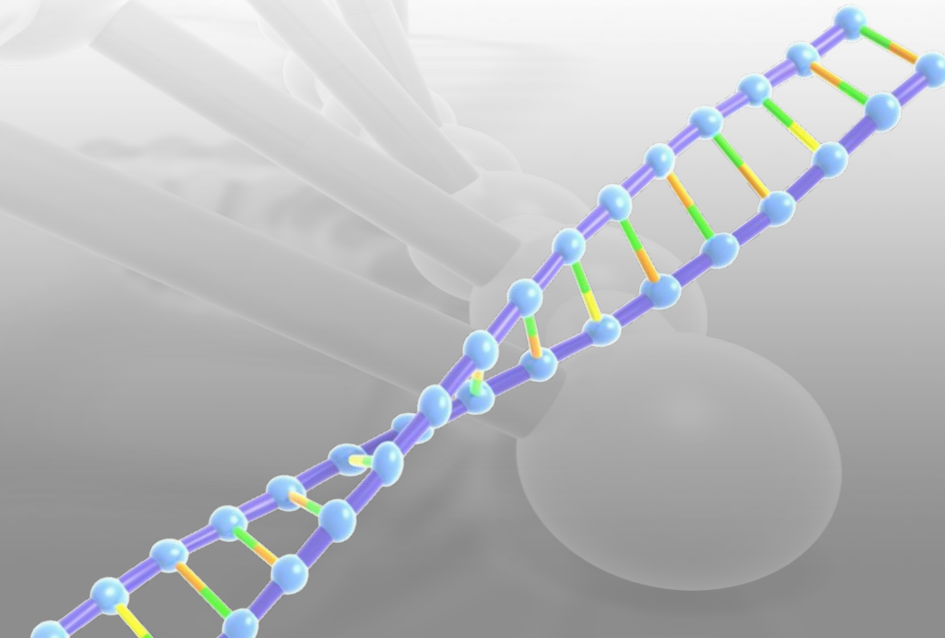
PROS

- Developed in Conjunction with the Mayo Clinic
  - Is covered by MOST pay plans
    - Low impact- requires only a cheek swab
      - Fast turnaround time
        - Eliminates guesswork and allows an educated decision on treatment options

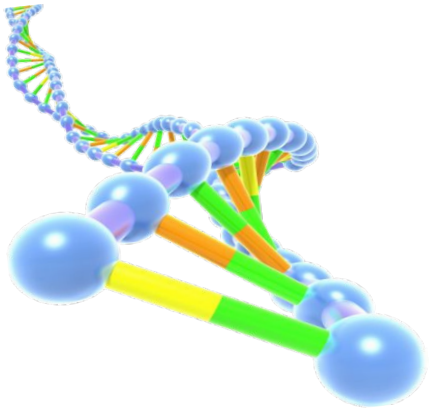
CONS

- Prescriber reluctance to accept
  - Knowing how to interpret results and plan a course of treatment
    - Explaining to family and guardians can be complicated/confusing

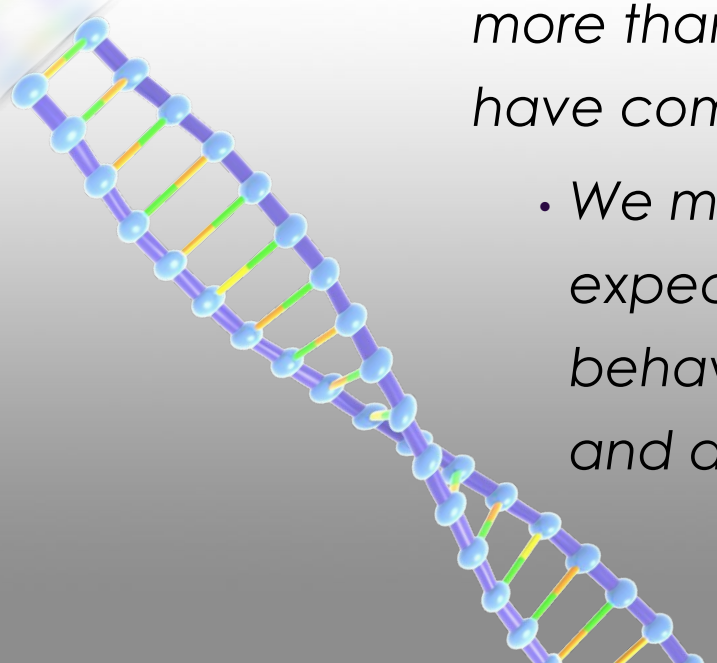




MY OPINION AND OUTLOOK ON TESTING

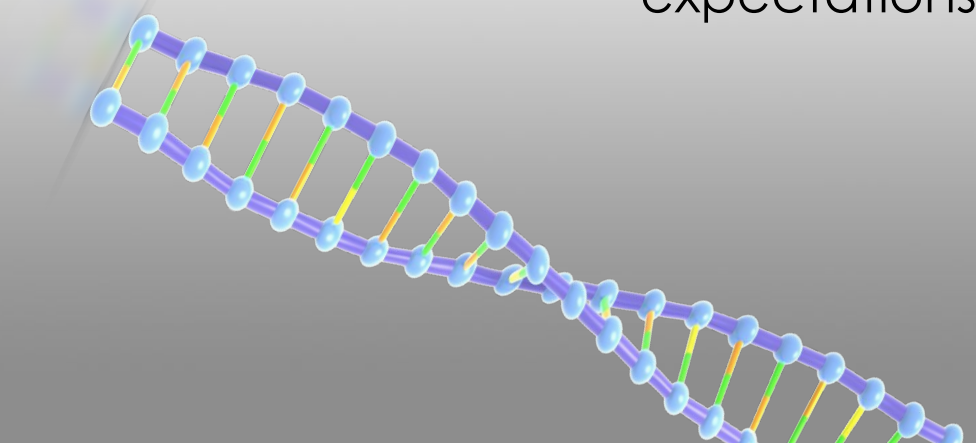


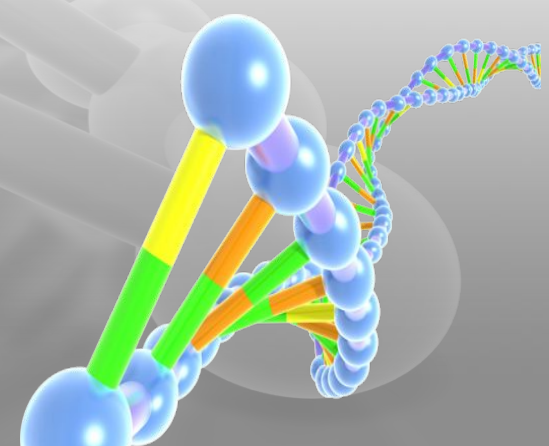
- *It provides another tool to help us provide better and quicker treatment options*
  - *What we have been doing is the best we could do with our "old" toolbox*
    - *If changing to more appropriately metabolized medications does nothing more than decrease our side effects we have come out ahead*
      - *We must have reasonable expectations, well designed behaviors plans that are adhered to and appropriate diagnosis*



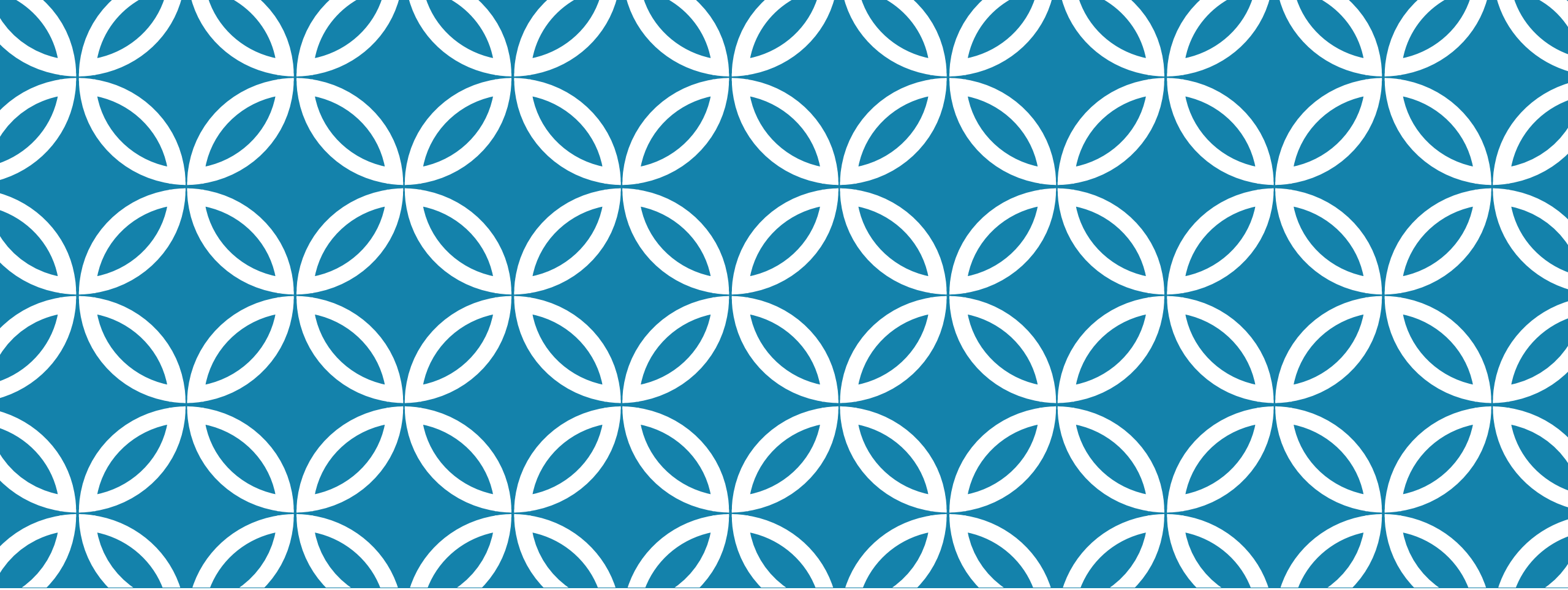
FINAL THOUGHTS

- **DO NOT Expect Miracles**
  - Supplementation with L- Methyl folate takes about 6 months to start showing effectiveness
    - 1 out of 3 folks will never respond to medications
      - Incorrect diagnosis(not recognizing autism) will only cloud our expectations





Any Questions?



WE THANK YOU FOR YOUR TIME!

THANK YOU !!
Questions? Need More Information?

Feel free to contact me.

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