PHARMACOGENOMIC TESTING

Hard to say, but easier to understand.

OBJECTIVES of the Presentation

1. Understand what the testing is.
2. Understand why the testing is important.
3. Learn how it can it can be used as a tool to better support specific populations.

PLEASE KEEP IN MIND

At the end of the presentation, you may still have questions. That's OK. I'm not 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* – Sometimes called "precision medicine" or "personalized medicine". It is how the *genetic* makeup of an individual affects their response to medications.

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

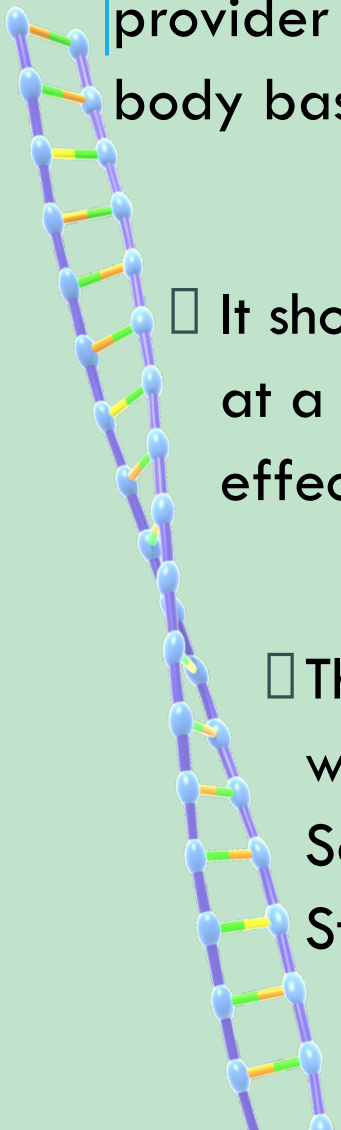
Pharmaco*dynamics* – the mechanism of the drug's action on the body. Or, how the drugs ACT in the body.

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

For more definitions, refer to Appendix 1

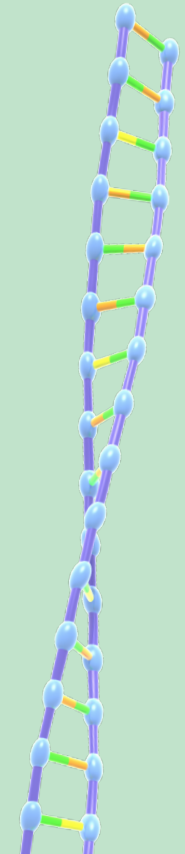
WHAT IS PHARMACOGENETIC TESTING?

- 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.

- The medications most important for the vulnerable populations we support are: Antipsychotics, Antidepressants, Anxiolytics, Sedative/Hypnotics, ADD/ADHD and certain Mood Stabilizing/Seizure medications



THIS IS HOW IT GOES…..

- Medication is absorbed into the bloodstream; stomach, intestines, topical, sublingual, inhalation, mucus membranes.
- The medication then goes either to the liver or the kidney or both to be broken down into a form that the targeted cells can use
- The cells that the medication is targeted to breaks the medication down, uses (metabolizes) it and a waste product is produced
- The waste product is then eliminated from the body.

DEFINITION OF A D M E

- 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

ALL MEDICATIONS ARE BROKEN DOWN IN THE LIVER **OR** THE KIDNEY,

Or both

To explain pharmacogenomic testing we are focusing focusing on psycho-active medications that are broken down in the Liver.

Sidebar: if a medication is broken down in all or in part in the kidney, the metabolization is based on the functioning of the kidney and is entirely different than medications who use the liver in their metaboliztion.

BROKEN DOWN IN THE LIVER (IN WHOLE OR IN PART),GOES THROUGH A MAJOR ENTRY ”PORT.”

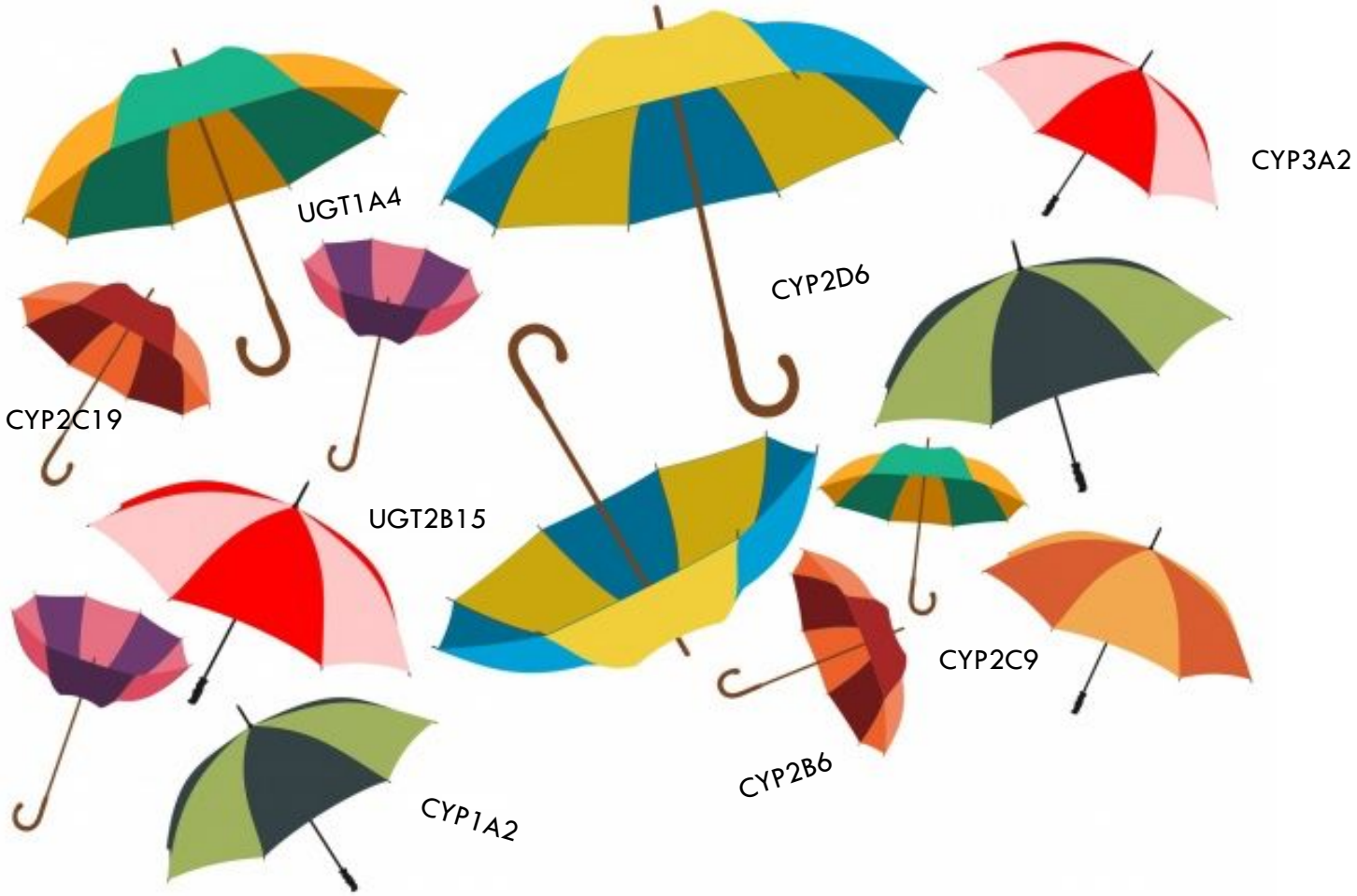
THINK..

GATEWAY.

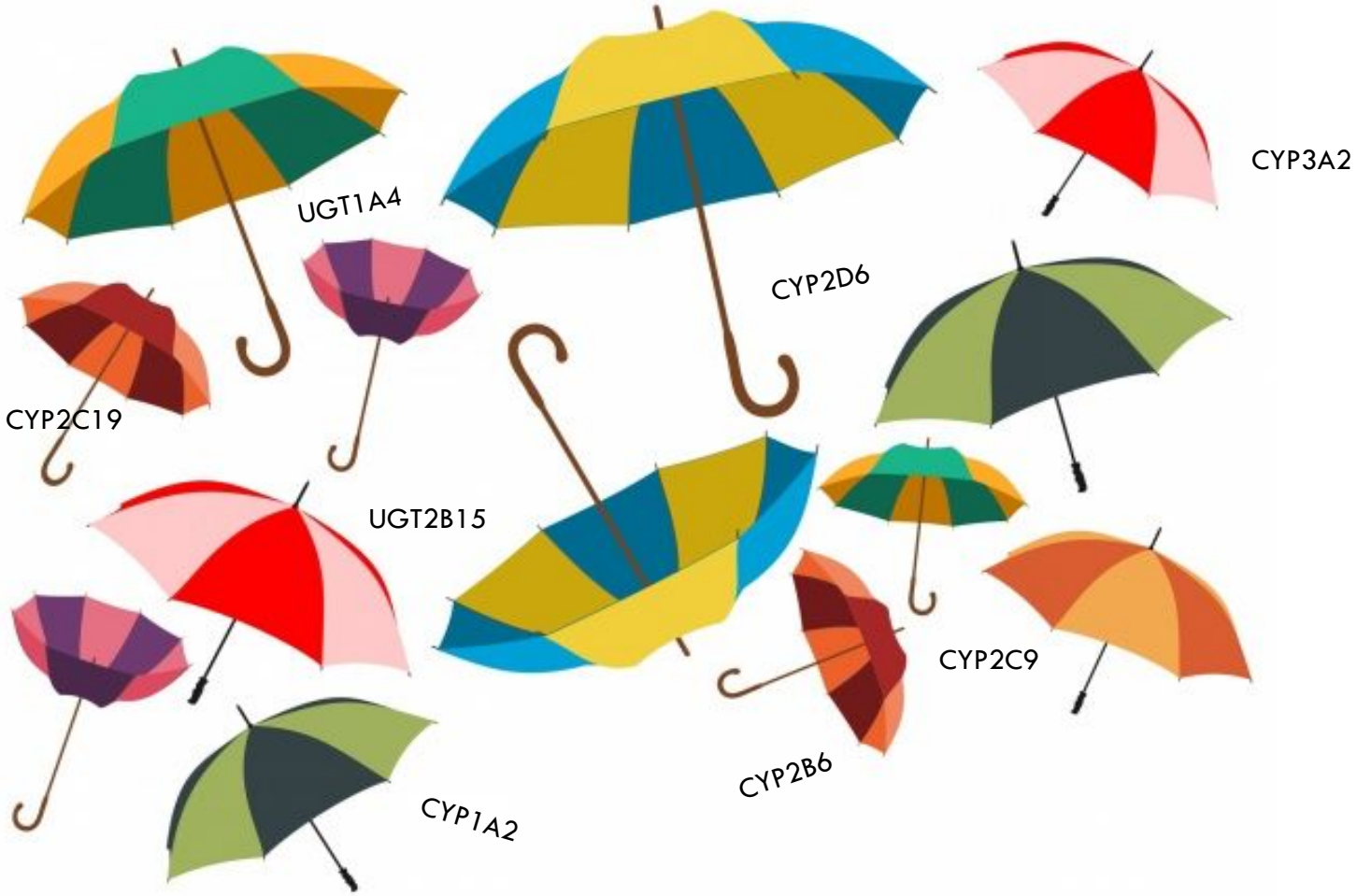
BUT REALLY?

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

AND UNDER THE BIG UMBRELLA ARE OTHER SMALLER UMBRELLAS



AND EACH UMBRELLA HAS ENZYMES LIVING UNDER THEM.



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

The enzymes render individuals either

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

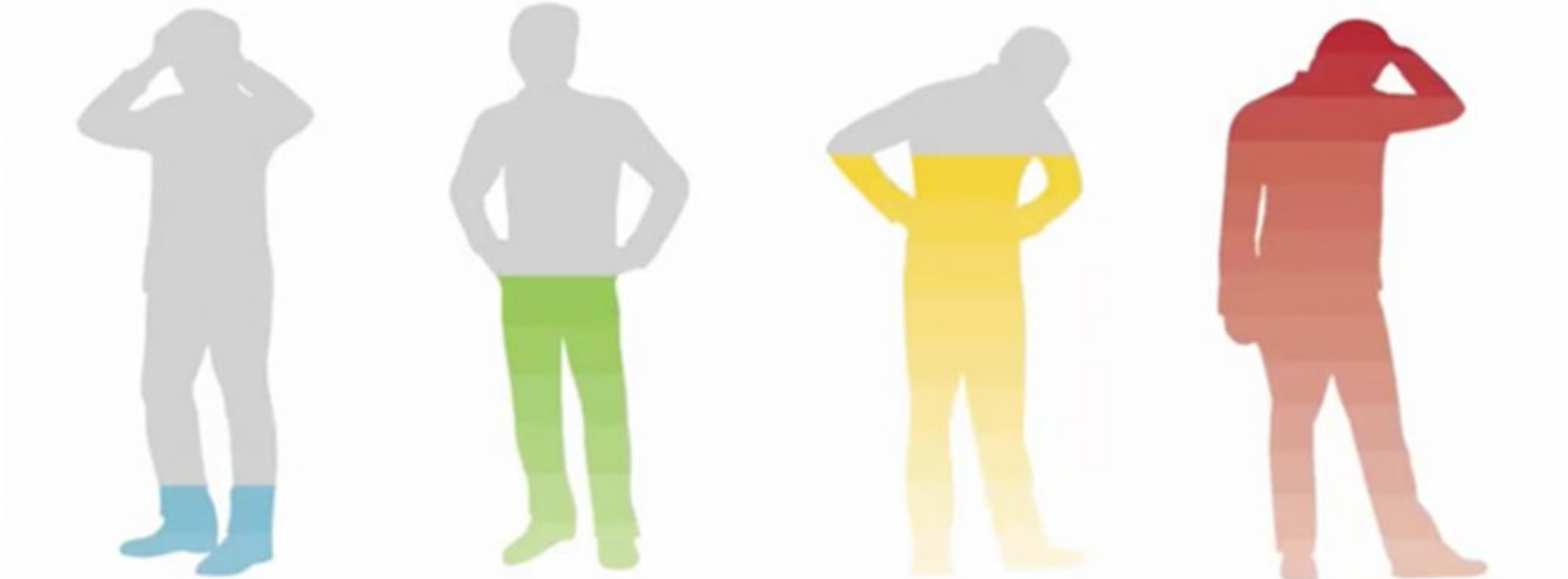
"intermediate metabolizer" – their pharmacogenetics do not allow them to break and use all of their medication dose. These individuals are at an increased risk of SEs, ADRs, and toxicity. If the medication is to be used, a lower dose would be required.

"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 (or "umbrella") in breaking down the medication, which result in combinations of the things mentioned above.

Let’s unravel this



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!

THIS IS THE SIMPLEST EXPLANATION…

And each of the major metabolic pathways, have two pathways within then.

Yeah. It's a lot.

NOW DOES THIS SLIDE MAKE MORE SENSE TO YOU?

Not many cars on the roadway

Ultra rapid metabolizer

Normal traffic flow

Extensive metabolizer

Traffic Jam

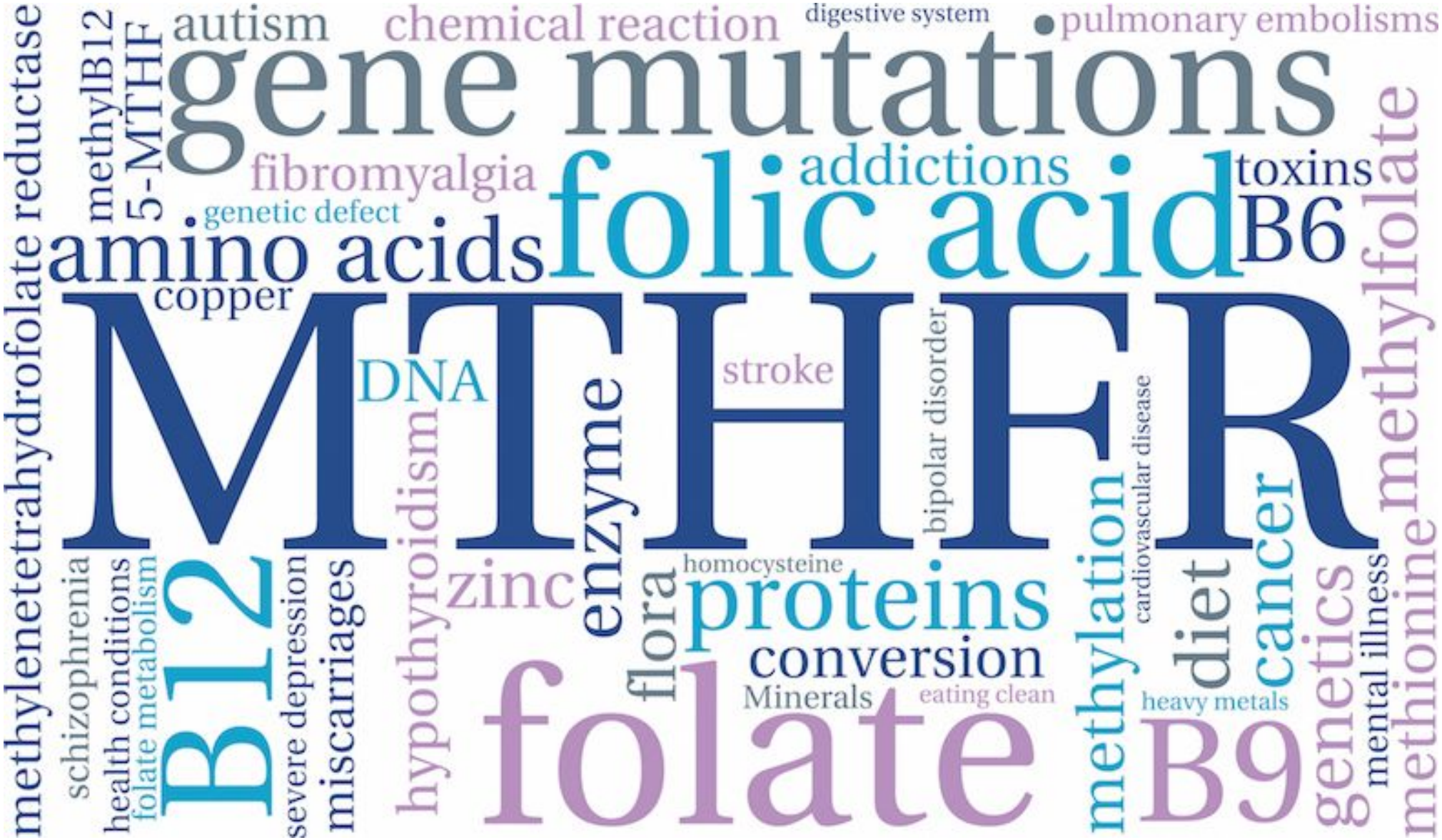
Poor metabolizer

Things move slowly; One lane may be blocked

Intermediate metabolizer

NOW THAT WE ARE HERE…

Let me further complicate things….


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
bipolar disorder
hypothyroidism
zinc
enzyme
homocysteine
proteins
flora
conversion
Minerals
eating clean
folate
methylation
cardiovascular disease
diet
heavy metals
B9
cancer
genetics
mental illness
methionine
methylfolate

Here's another word…….

"MUTATION"

Refer to article Appendix 2

SIGNIFICANT TO INTERACTION AND METABOLIZING OF MEDICATIONS…..

MTHFR gene

Converts Folic Acid into Folate

No conversion issue

Reduced Folic Acid Conversion

Significantly Reduced Folic Acid Conversion

WHAT IS FOLIC ACID?

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 into the metabolite of folate.
- 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."

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

IF THERE IS A FOLIC ACID CONVERSION ISSUE..

Generic - L-Methylfolate
Brand Name – Deplin

May take up to 6 months to be effective

WHY IS THIS TESTING IMPORTANT?

Many of the individuals we support are unable to express what they are feeling.

Cognition
Insufficient Vocabulary

Too many medications have become a “go to”. It may not be the “right” medication for the individual.

Over-prescribing, mis-prescribing may result in a hospitalization, detoxing and ”starting fresh”.

Too often we hear, “Let’s Try”. This tool eliminates that statement.

Over years, many meds have been added. Few, if any have been taken away. This testing reduces and potentially eliminates the poly-pharmacy that plagues our field.

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)

HOW IS THE TESTING DONE?

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

HOW MUCH DOES THIS COST?

Who pays for it?

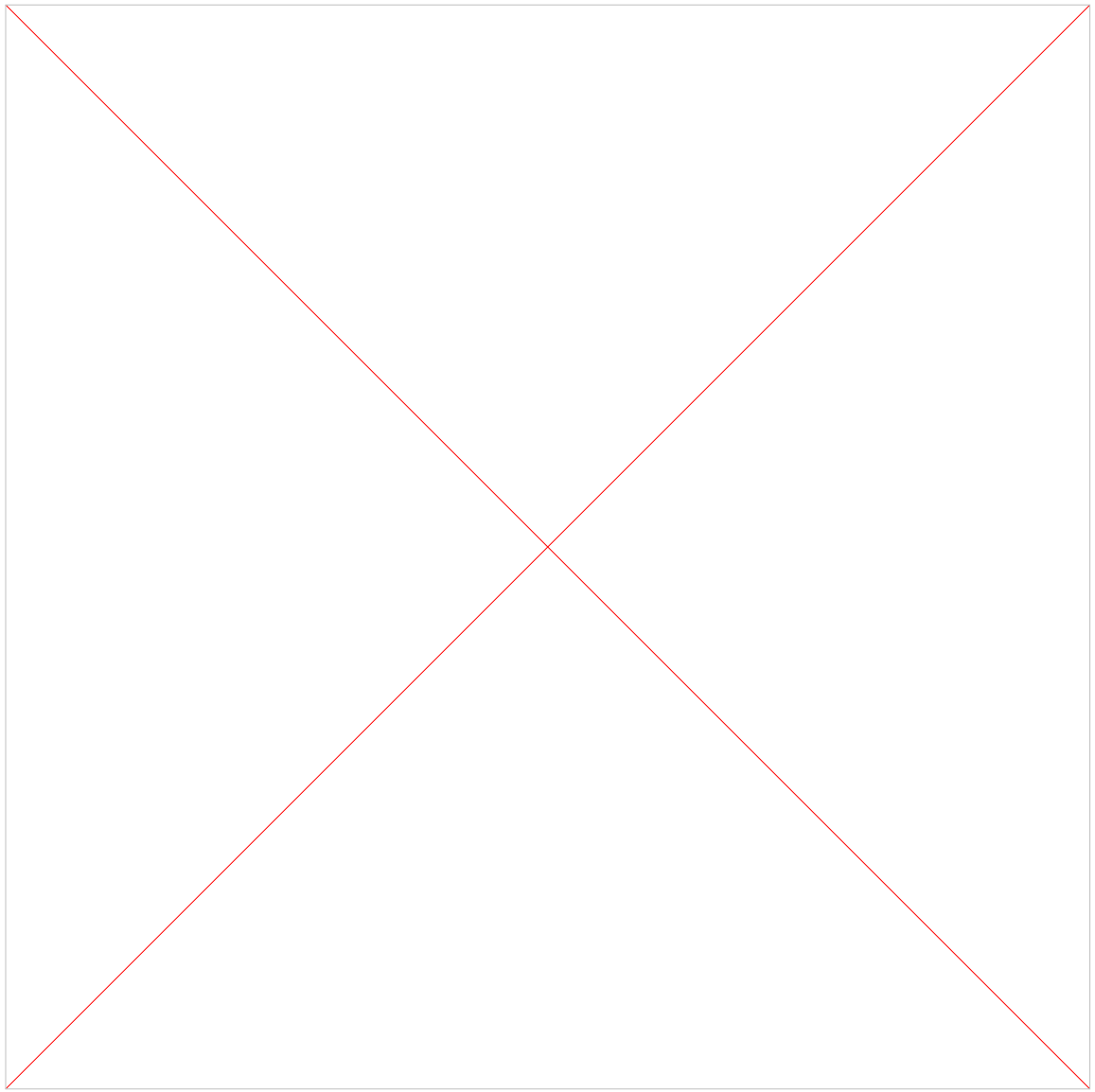
THERE ARE MANY DIFFERENT LABS THAT DO PHARMACOGENOMIC TESTING!

Please find the one that suits your needs best.

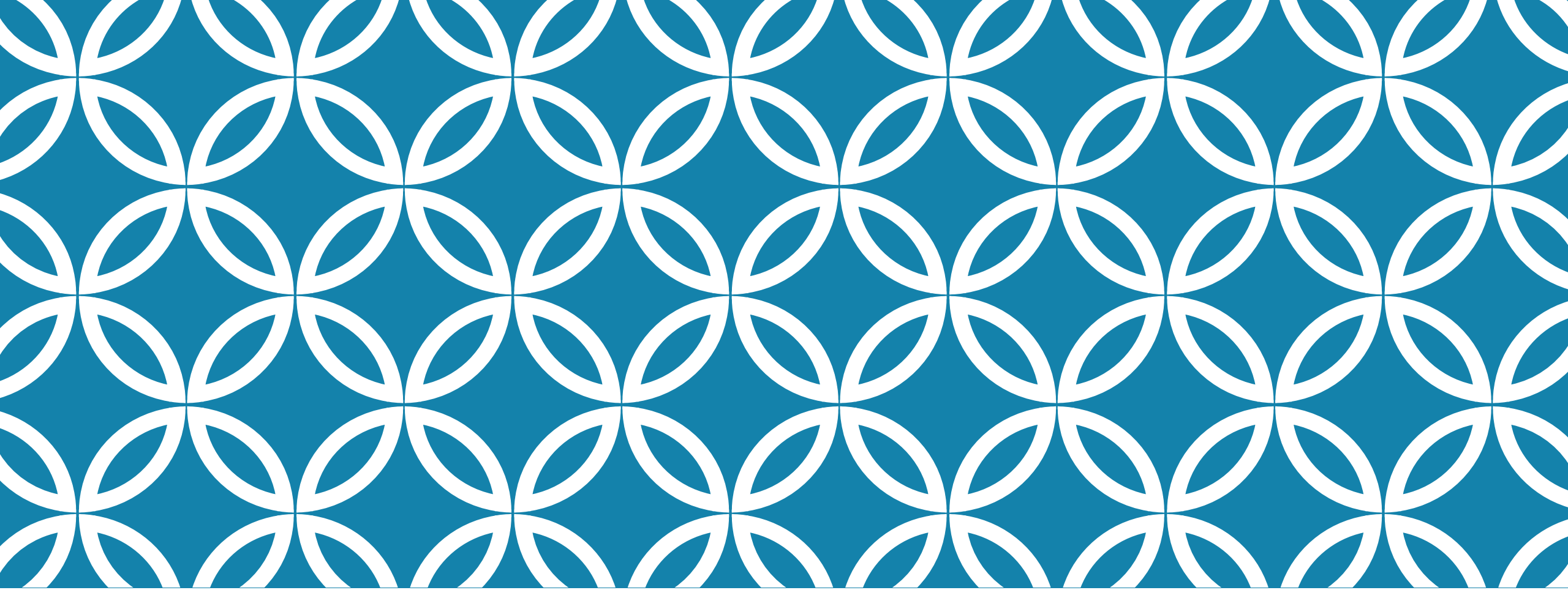
Some labs only do panels for psychoactive medications.

Some labs also include medications for medical issues.

Make sure whatever lab you use, they provide support.



ANY QUESTIONS?



THANK YOU FOR YOUR TIME!