Estrogen Testing and Interpretive Guide

Stacy J Cocilova – Physicians Lab

Quantitative values vs. Relative values

When deciding how to incorporate or modify estrogen therapy, 2 things must be considered; the actual amount of each analyte (quantitative) and the ratios of each analyte relative to one another (relative).

Each PhyL hormone profile includes quantitative values for;

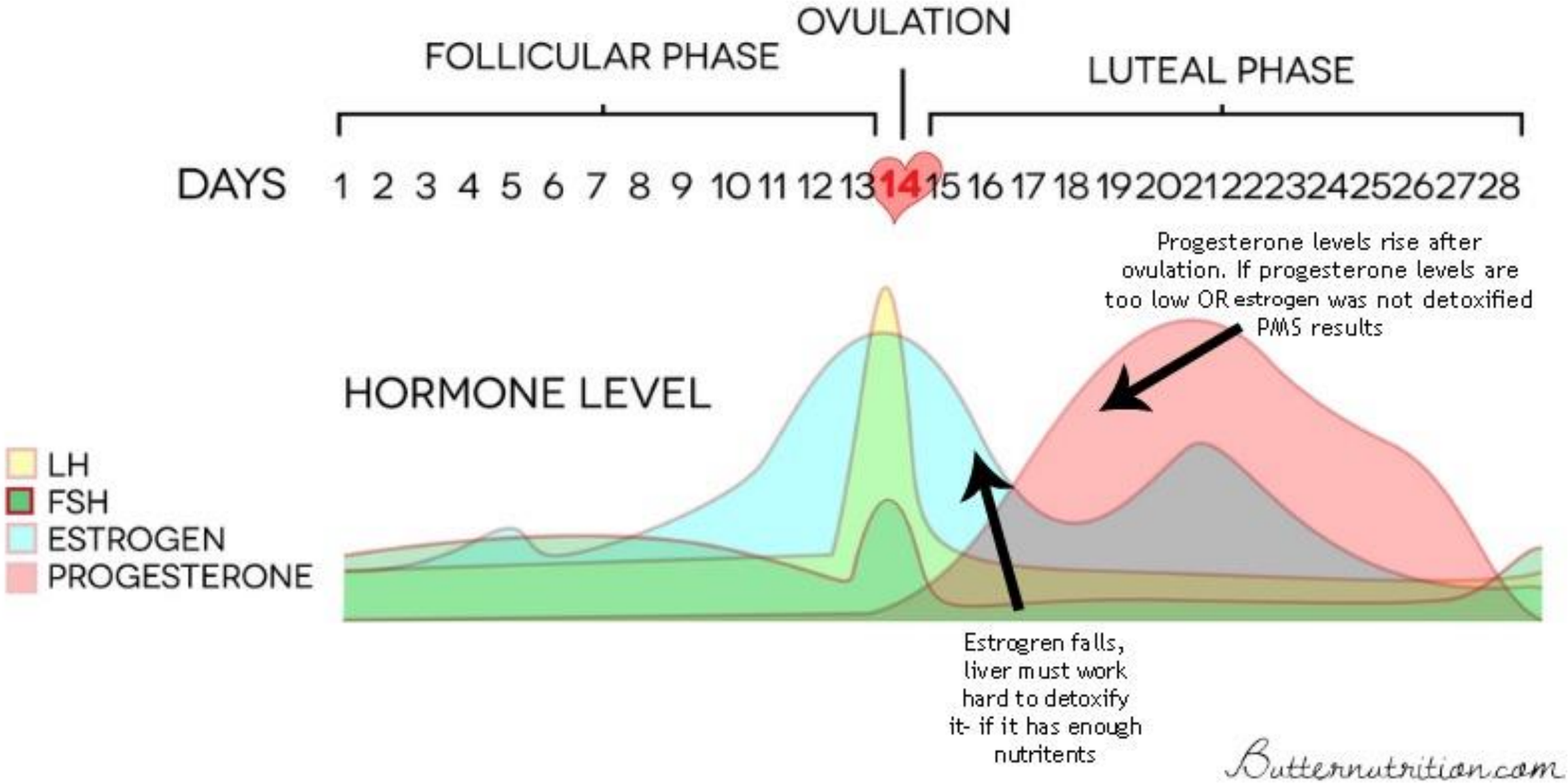
- Estrone
- Estradiol
- Estriol
- 16 – alpha-hydroxyestrone
- 2-hydroxyestrone
- 2-methoxyestrone
- 4-hydroxyestrone
- 4-methoxyestrone

Additionally, the report includes 3 estrogen ratios

- Estrogen Quotient
- 2:16 Ratio
- Methylation Ratio
- Total Estrogen Load
- Progesterone Ratio

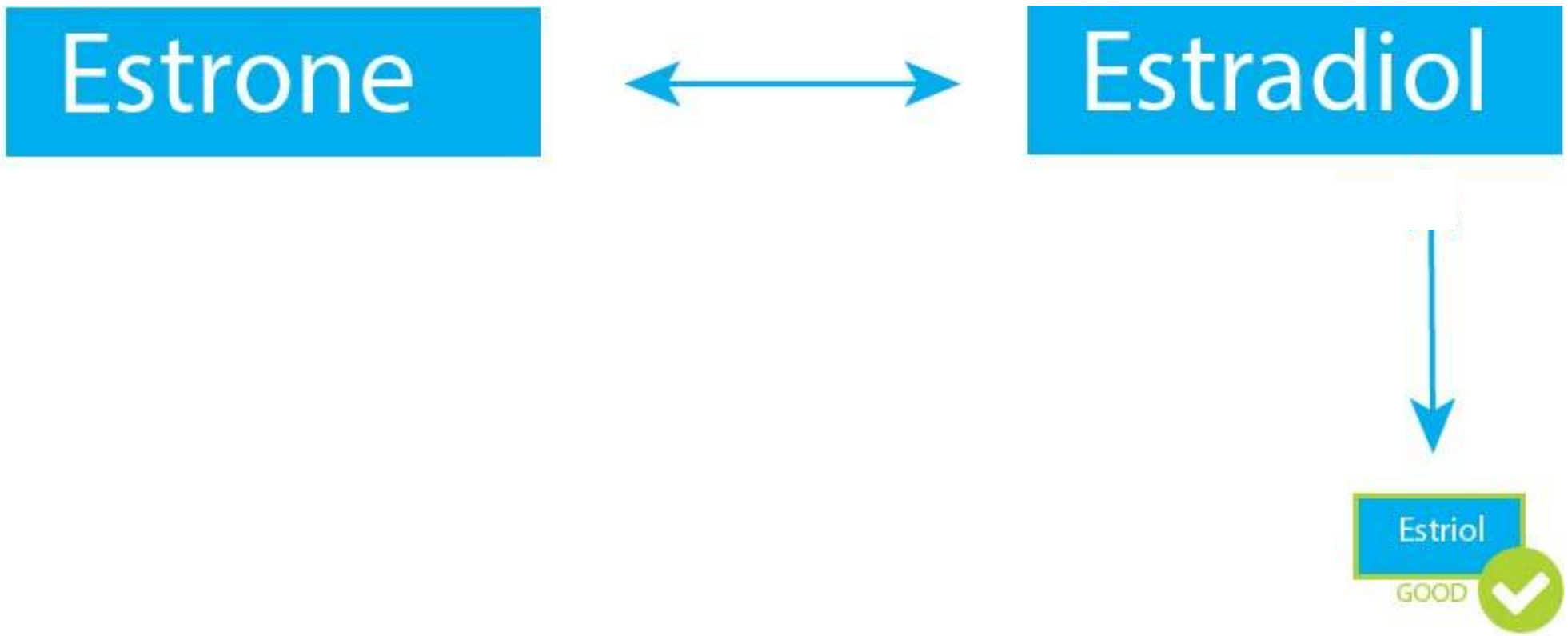
- These ratios show the balance between the quantitative values

Estrogen in Cycling Women

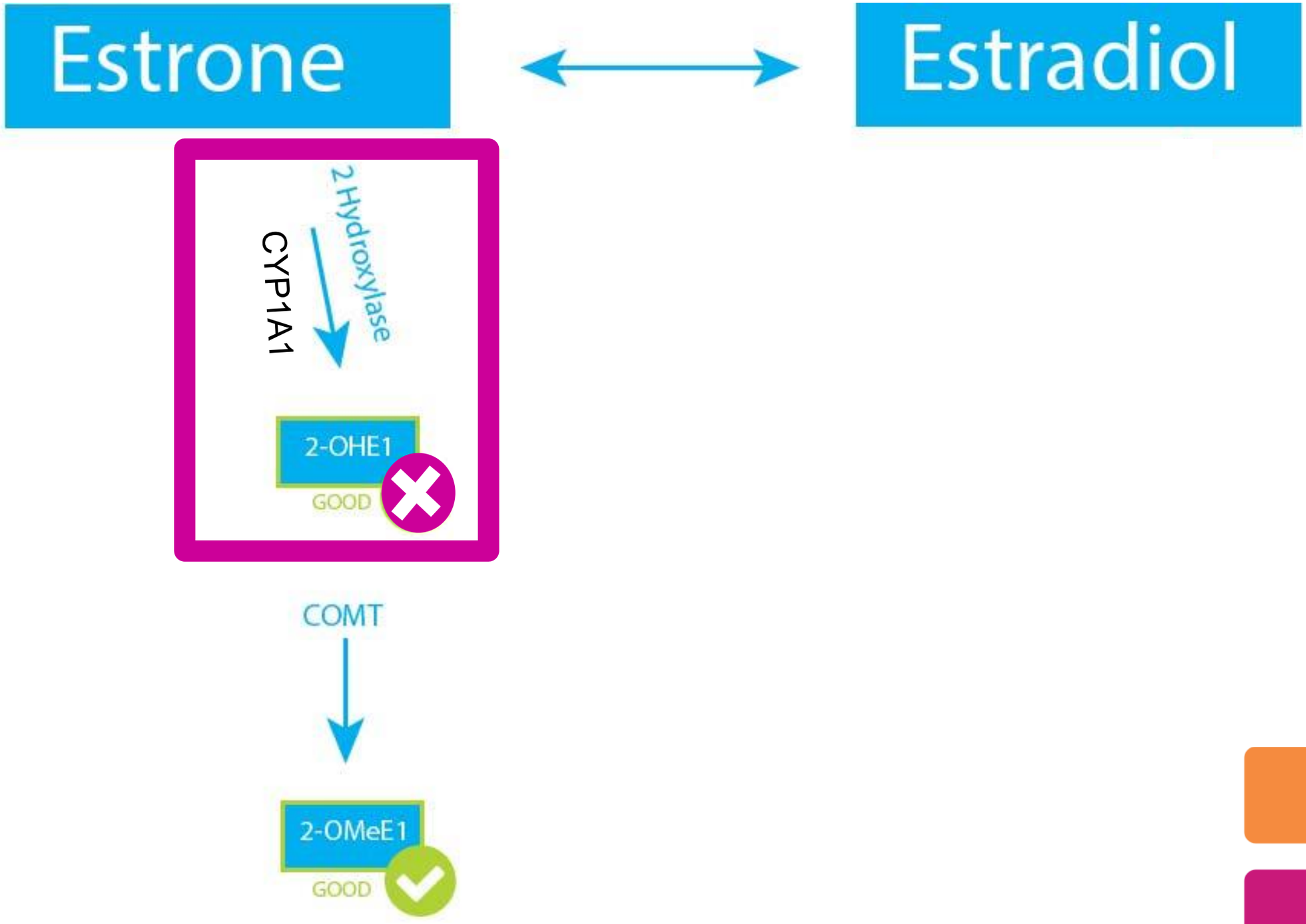


physicians LAB
State-of-the-art Science. Superior Solutions.

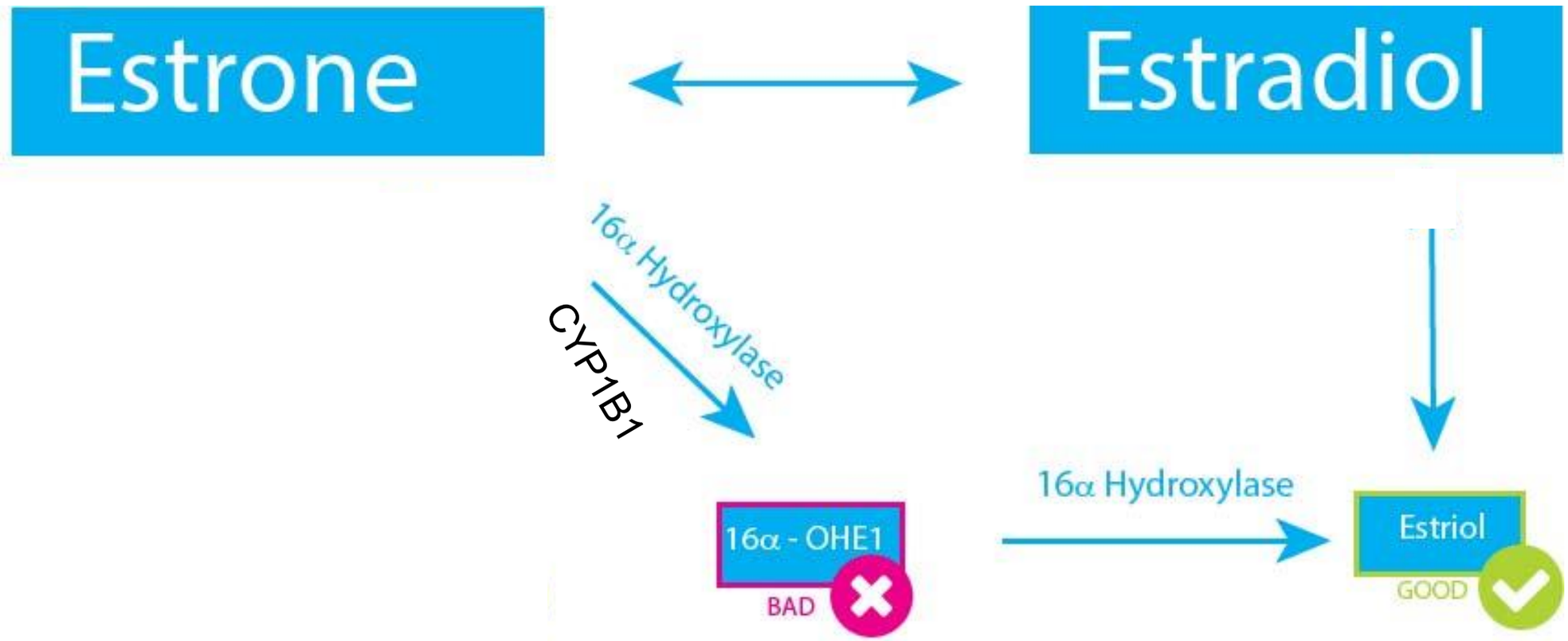
Estrogen Metabolism



Estrogen Metabolism 2-Pathway

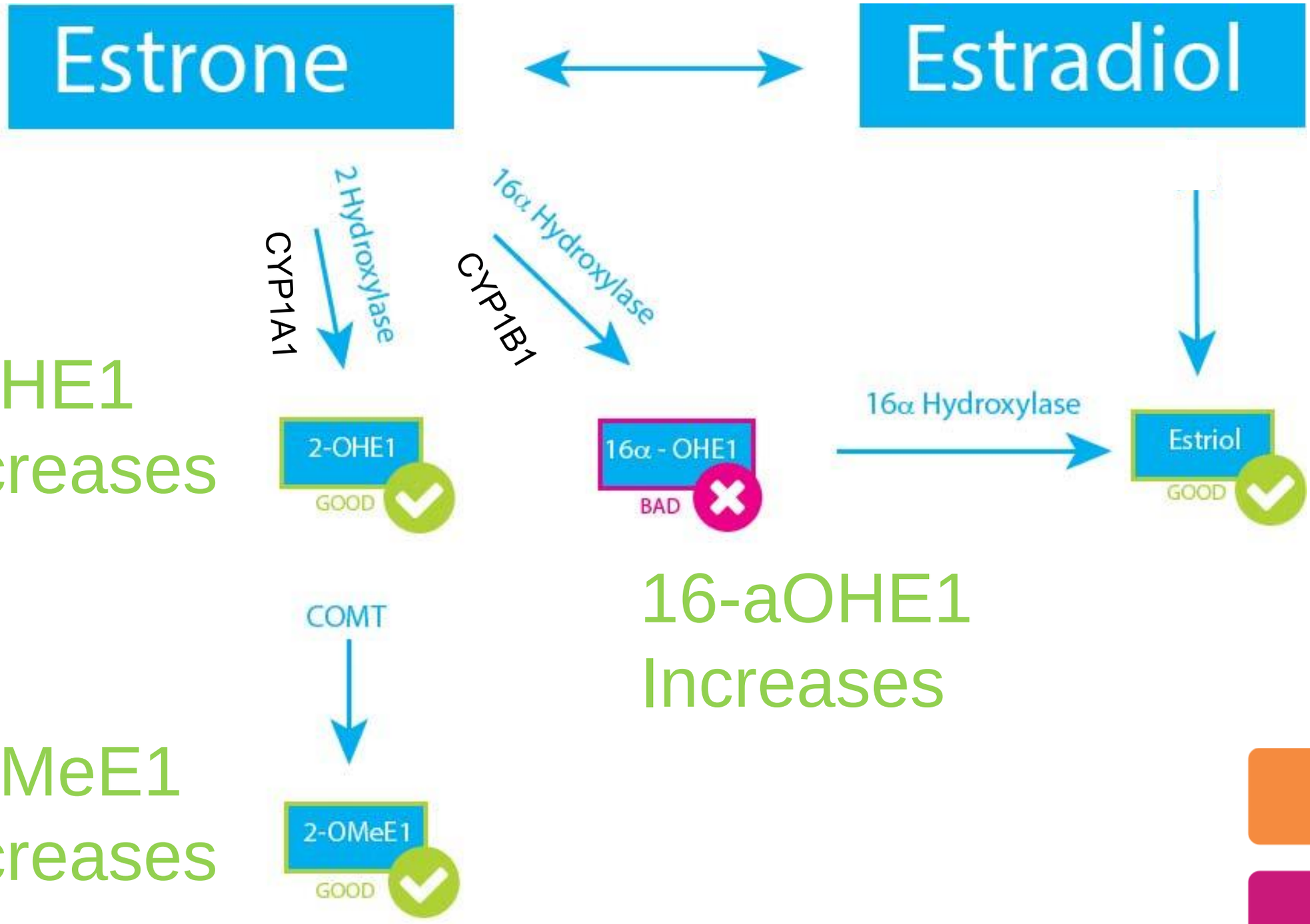


Estrogen Metabolism – 16-Pathway and E Quotient



physicians LAB
State-of-the-art Science. Superior Solutions.

Estrogen Metabolism – Inflammation

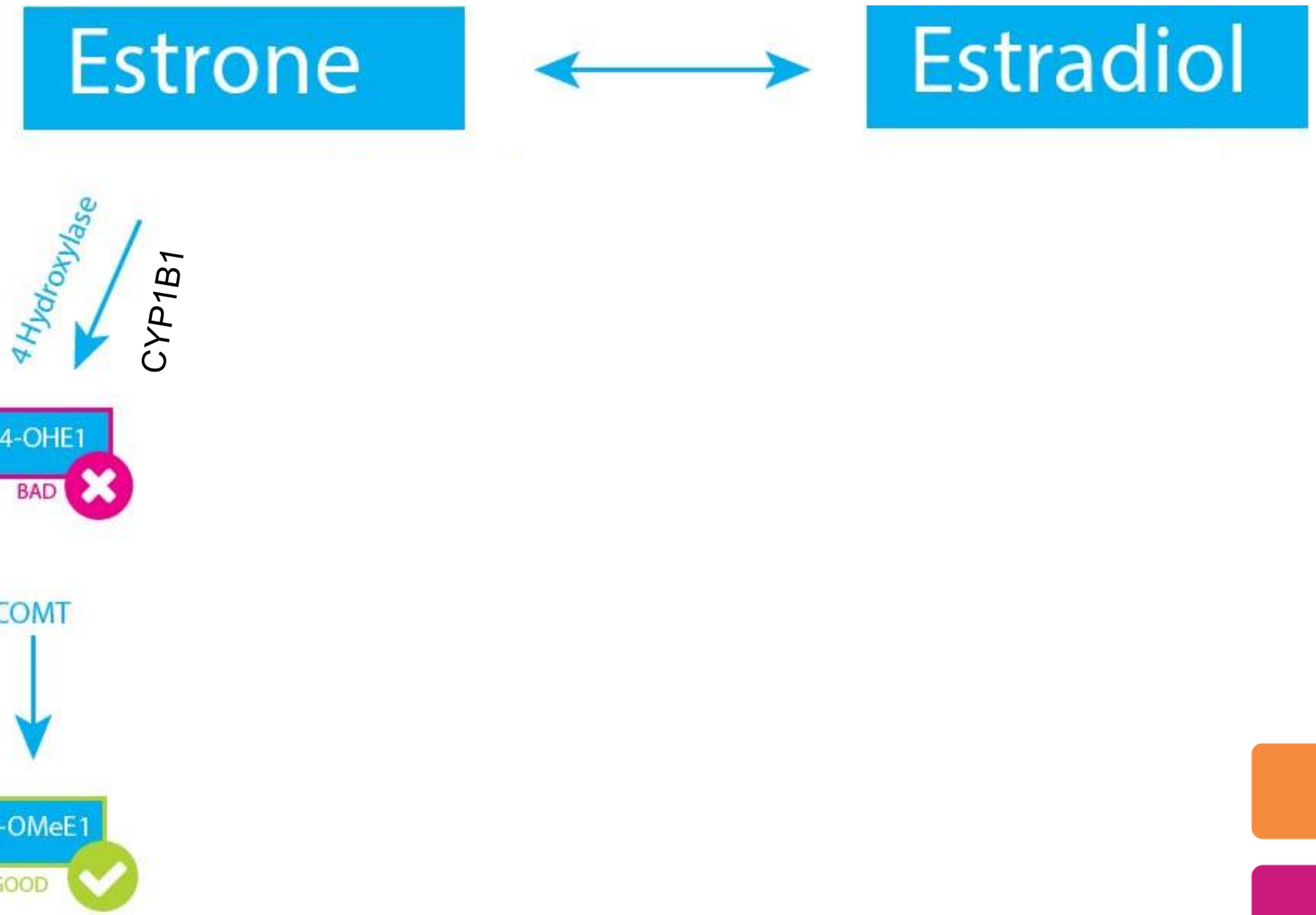


2-OHE1 Decreases

16-aOHE1 Increases

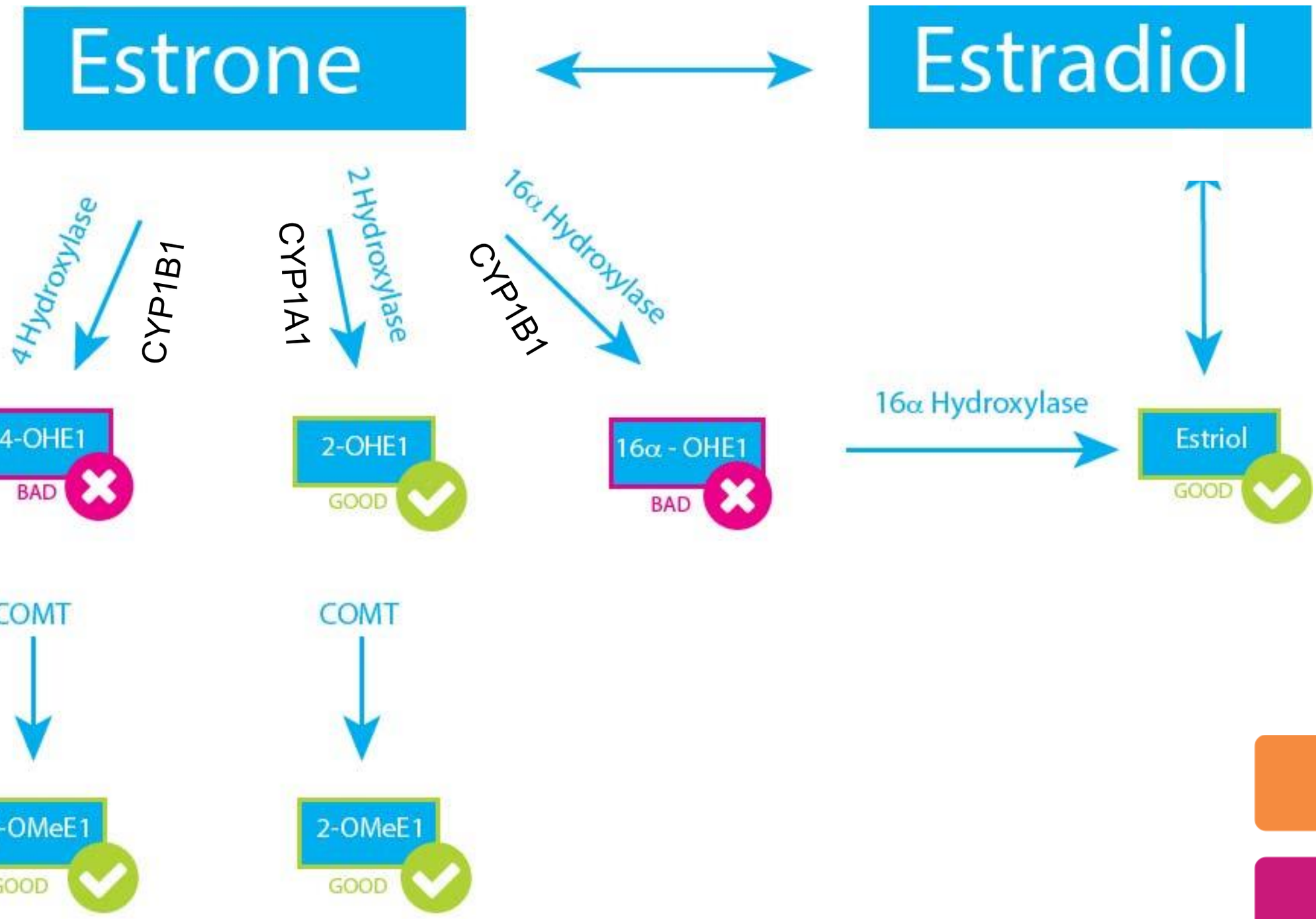
2-OMeE1 Decreases

Estrogen Metabolism 4-Pathway



physicians LAB
State-of-the-art Science. Superior Solutions.

Estrogen Metabolism



physicians LAB

State-of-the-art Science. Superior Solutions.

Monitoring Estrogen Dosing vs. Metabolism

TEST	RESULT	UNITS	TARGET RANGE
Pregnanediol - FMV (FMV - Female (supplemented - bedtime dose range 2000-8000))	4448.6	ug/mg CR	1000-6000
Total Estrogen Load (Female)	145.6	Total	40-150
Estrone - FMV (FMV)	8.9	ug/mg CR	1-12
Estradiol - FMV (FMV)	1.6	ug/mg CR	0.6-5
Estriol - FMV (FMV)	10.3	ug/mg CR	2.5-25
E Quotient (E3/(E1+E2) (Optimal = greater than 1)	Optimal 1.0		>=1
16-Alpha-hydroxyestrone	5.8	ug/mg CR	0.2-15
2-Hydroxyestrone	15.0	ug/mg CR	4.2-15.6
4-Hydroxyestrone	<0.5	ug/mg CR	<3.5
2:16 Ratio	Low 2.6	Ratio	>4
2-Methoxyestrone	1.1	ug/mg CR	0.5-6.1
Methylation Ratio	(low) 7.2	Ratio	>10

physicians LAB

State-of-the-art Science. Superior Solutions.

Monitoring Estrogen Dosing vs. Metabolism

TEST	RESULT	UNITS	TARGET RANGE
Pregnanediol (Female Cream/No supplemented range)	3324.0	ug/mg CR	400-2000
Total Estrogen Load (Female)	(High) 253.3	Total	40-150
Estrone	10.6	ug/mg CR	1-12
Estradiol	(high) 5.1	ug/mg CR	0.6-5
Estriol	(high) 47.8	ug/mg CR	2.5-25
E Quotient (E3/(E1+E2) (Optimal = greater than 1)	Optimal 3.0		>=1
16-Alpha-hydroxyestrone	3.8	ug/mg CR	0.2-15
2-Hydroxyestrone	(elevated) 28.2	ug/mg CR	4.2-15.6
4-Hydroxyestrone	Elevated 3.7	ug/mg CR	<3.5
2:16 Ratio	Favorable 7.5	Ratio	>4
2-Methoxyestrone	6.5	ug/mg CR	0.5-6.1
Methylation Ratio	Favorable 22.9	Ratio	>10

physicians LAB

State-of-the-art Science. Superior Solutions.

Monitoring Estrogen Dosing vs. Metabolism

TEST	RESULT	UNITS	TARGET RANGE
Pregnanediol (Female Supplemented range)	3025.0	ug/mg CR	1000-6000
Total Estrogen Load (Female)	(High) 589.4	Total	40-150
Estrone	3.6	ug/mg CR	1-12
Estradiol	1.8	ug/mg CR	0.6-5
Estriol	(high) 28.0	ug/mg CR	2.5-25
E Quotient (E3/(E1+E2) (Optimal = greater than 1)	Optimal 5.2		>=1
16-Alpha-hydroxyestrone	Elevated 55.2	ug/mg CR	0.2-15
2-Hydroxyestrone	(elevated) 15.8	ug/mg CR	4.2-15.6
4-Hydroxyestrone	<0.5	ug/mg CR	<3.5
2:16 Ratio	Low 0.3	Ratio	>4
2-Methoxyestrone	<0.5	ug/mg CR	0.5-6.1
Methylation Ratio	(low) 0.8	Ratio	>10

physicians LAB

State-of-the-art Science. Superior Solutions.

Monitoring Estrogen Dosing vs. Metabolism

TEST	RESULT	UNITS	TARGET RANGE
Pregnanediol (Female Supplemented range)	4137.0	ug/mg CR	1000-6000
Total Estrogen Load (Female)	(High) 192.3	Total	40-150
Estrone	3.9	ug/mg CR	1-12
Estradiol	1.2	ug/mg CR	0.6-5
Estriol	>50	ug/mg CR	2.5-25
E Quotient (E3/(E1+E2) (Optimal = greater than 1)	Optimal 11.2		>=1
16-Alpha-hydroxyestrone	8.9	ug/mg CR	0.2-15
2-Hydroxyestrone	13.5	ug/mg CR	4.2-15.6
4-Hydroxyestrone	<0.5	ug/mg CR	<3.5
2:16 Ratio	Low 1.5	Ratio	>4
2-Methoxyestrone	<0.5	ug/mg CR	0.5-6.1
Methylation Ratio	(low) 1.0	Ratio	>10

physicians LAB

State-of-the-art Science. Superior Solutions.

Monitoring Estrogen Dosing vs. Metabolism

TEST	RESULT	UNITS	TARGET RANGE
Pregananediol - FMV (FMV - Female (Cream or non-supplemented range))	3143.0	ug/mg CR	400-2000
Total Estrogen Load (Female)	(High) 162.0	Total	40-150
Estrone - FMV (FMV)	8.1	ug/mg CR	1-12
Estradiol - FMV (FMV)	3.6	ug/mg CR	0.6-5
Estriol - FMV (FMV)	(High*) 45.8	ug/mg CR	2.5-25
E Quotient (E3/(E1+E2) (Optimal = greater than 1)	Optimal 3.9		>=1
16-Alpha-hydroxyestrone	2.2	ug/mg CR	0.2-15
2-Hydroxyestrone	13.4	ug/mg CR	4.2-15.6
4-Hydroxyestrone	<0.5	ug/mg CR	<3.5
2:16 Ratio	Favorable 6.1	Ratio	>4
2-Methoxyestrone	1.8	ug/mg CR	0.5-6.1
Methylation Ratio	Favorable 13.3	Ratio	>10

2-Hydroxyestrone

When within range and with proper methylation, 2-hydroxyestrone is considered a “good” estrogen metabolite and the 2-hydroxyl pathway is considered the most favorable path for detoxification of estrogen.

LOW 2-OHE1

- Low 2-OHE1 + Low 16-aOHE1 + Low Primary Estrogens
  - consider an increase in estrogen therapy
- Low 2-OHE1 + Low 16-aOHE1 + High Primary Estrogens
  - Support Phase I metabolism
- Low 2-OHE1 + High 16-aOHE1 + Low Primary Estrogens
  - Consider bi-est to treat
  - Inflammation indicator – support gut health and Phase I + Phase II

Methylation not as critical

HIGH 2-OHE1

- High 2-OHE1 + High 16-aOHE1 levels
  - consider reducing estrogen therapy is TEL is high
  - Increase 2:16 Ratio
- High 2-OHE1 + Low 16-aOHE1
  - Make sure primary estrogens and TEL are good, otherwise consider changing to bi-est or reducing therapy
- High 2-OHE1 + Low 2-OMeE1
  - See therapies for increasing methylationMethylation ratio (Slide 14)

16-alpha-Hydroxyestrone

Considered a “bad” estrogen. Can increase the rate of existing cancer growth and is found at higher levels than 2-OHE1 in breast cancer patients.

LOW 16alpha-OHE1

- Considered favorable
- **Low levels** combined with low 2-OHE1 can indicate the need for primary estrogen therapy – patients who are already on a treatment plan may consider an increase in estrogen therapy.

HIGH 16alpha-OHE1

- **High levels** of 16-aOHE1 combined with high 2-OHE1 levels
  - consider reducing estrogen therapy
- **High levels** of 16-aOHE1 combined with low 2-OHE1 levels
  - Increase the 2:16 Ratio

4-Hydroxyestrone

Considered a “bad” estrogen, 4-hydroxyestrone is reported to have carcinogenic effects on estrogen–sensitive tissues and may even indicate when a tumor exists. During Phase I detoxification, 4-hydroxyestrone can be metabolized into quinone estrogens that can cause genetic mutations and further increase the risk of cancer.

LOW 4-OHE1

- Considered favorable

.

HIGH/ANY 4-OHE1

- High levels of 4-OHE1 combined with high 2-OHE1 levels
  - consider reducing estrogen therapy
  - Increase Phase II detoxification by up-regulating COMT (increasing Methylation)
  - Stop Oral Estrogen therapy

- High levels of 4-OHE1 combined with low 2-OHE1 levels
  - Do not supplement without addressing COMT activity by increasing Phase II detoxification

2-Methoxyestrone

Considered a “good” estrogen with anti-carcinogenic effects. 2-methoxyestrone both decreases the risk of developing cancer and slows proliferation of existing cancer cells.

LOW 2-OMeE1

- **Plus Normal/elevated 2-OHE1**
  - Increase methylation through diet, supplements, lifestyle
- Plus Low 2-OHE1
  - Not relevant

HIGH 2-OMeE1

- **High levels** of 2-OMeE1 combined with **high** 2-OHE1 levels
  - consider reducing estrogen therapy
- **High levels** of 2-OMeE1 combined with **low** 2-OHE1 levels
  - Considered Favorable
  - If symptoms are present and primary estrogen levels are low, estrogen supplementation can be considered

2:16 Ratio

Low 2:16 Ratio (ratio less than 4)

Risks Associations: Cancer, PCOS

Possible causes:

- INFLAMMATION
- Reduced CYP1A1 activity (inhibiting 2 – OHE1 production)
- Estrogen therapy dosing is too high (when combined with a high 2-OHE1)
- Oral estrogen supplementation
- Decreased Methylation activity
- Caffeine/coffee consumption
- Poor GI health

Treatments to consider:

- GI DETOX supporting Phase I and Phase II metabolism
- Increase methylation
- Supplement with I3C or DIM
- Increase fruit and vegetable intake, especially cruciferous vegetables or supplement with cruciferous veggie drinks/capsules
- Change to a non-oral estrogen therapy
- Increase omega-3 fatty acids
- Avoid caffeine/coffee in diet
- Increase detoxification and methylation with folic acid, B vitamins, as well as SAMe and sulfer supplements
- Encourage a Paleo-like diet
- Regulate sleep
- Increase exercise

2:16 Estrogen Ratio

High 2:16 Ratio (ratio more than 35)

Risks Associations: Although a 2:16 ratio above 4 is associated with reduced risk of breast cancer, when a patient presents with a HIGH 2-OHE1 AND a HIGH 2:16 ratio, this can be associated with some cancers and increases as the 2-OHE1 value increased above norms.

Methylation Ratio

Low Methylation Ratio (ratio less than 10)

Risks Associations:

If quantitative values of 2-OHE1 are low, the risk is also lower and the patient may require estrogen therapy (check the primary estrogen levels).

Possible Causes:

- Decreased Methylation due to:
  - Low COMT activity
  - Inflammatory responses (stress)
  - Diet

Treatments to consider:

- GI DETOX Supporting Phase and Phase II detoxification
- Increase methylation by the following:
- Supplement with I3C or DIM
- Increase fruit and vegetable intake, especially cruciferous vegetables or supplement with cruciferous veggie drinks/capsules
- Increase omega-3 fatty acids
- Avoid caffeine/coffee in diet
- Increase detoxification and methylation with folic acid, B vitamins, SAMe and sulfer-containing supplements
- Encourage a Paleo-like diet
- Reduce stress
- Identify possible COMT mutations

Methylation Ratio

High Methylation Ratio

Risks Associations: A High Methylation ratio is favorable and is associated with a decreased risk in developing certain cancers.

When the Methylation ratio is high AND the level of 2-OHE1 is Low, the ratio can be ignored

When the Methylation ratio is high AND the level of 2-OHE1 is also high, the patient may be at greater risk for inflammation due to estrogen dominance

Look for signs/symptoms of methyl trapping

Methyl Trapping

Risks Associations:

If someone has an MTHFR mutation, methl trapping can occur during therapy with folate, SAMe, B-Vitamins or other methyl donor supplements.

Some other causes of methyl trapping:

- Infection
- Autoimmunity
- toxic body burden
- problems with blood sugar and fat metabolism
- other inflammatory indications

Treatments to consider:

Non-methylating nutritional support should be provided for mutations in:

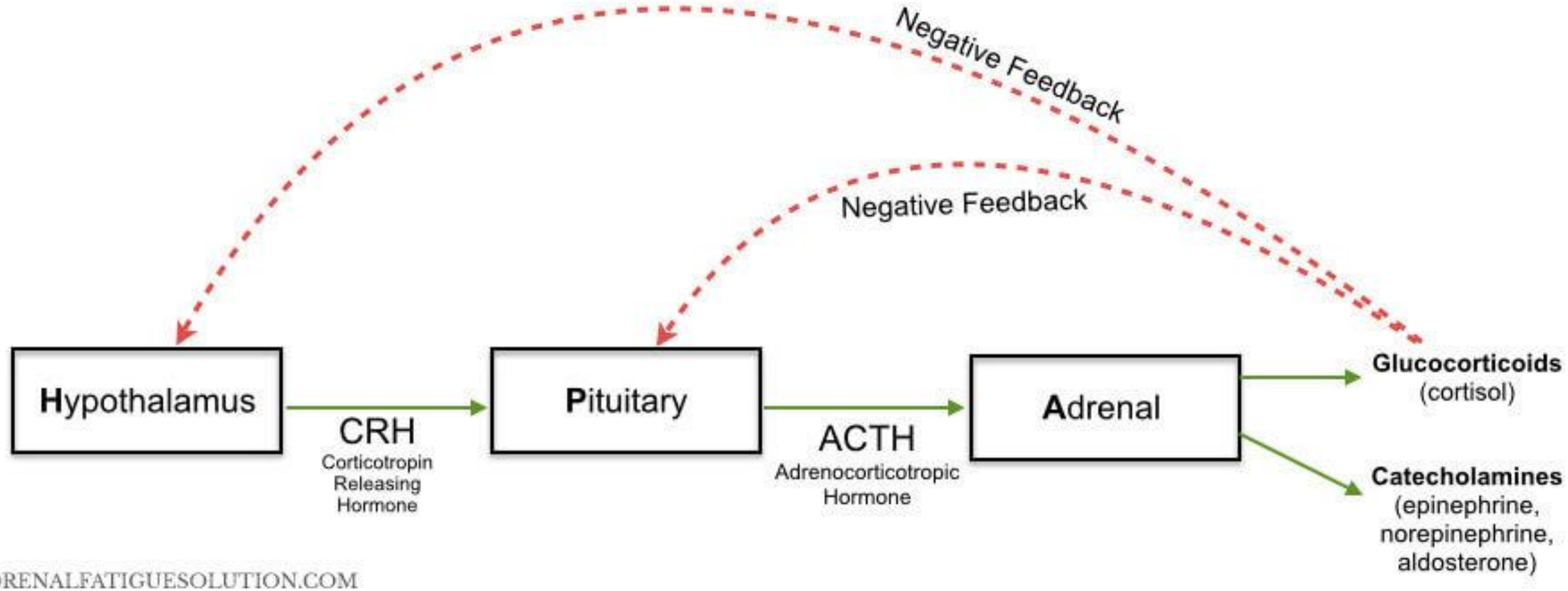
- MTR/MTRR, BHMT, SHMT2, MAT1A, CBS, QDPR, OTC, CPS, ARG2, PCBD1, MAOA or B, COMT, HNMT, DHPR, NOS1, 2, 3, SOD1, SOD2, PEMT, PON1, ABCB1, cytochrome P 450 genes and Soluble Carrier Family transporter protein SNPs

Cortisol Testing

Stacy J Cocilova – Physicians Lab

physicians LAB

State-of-the-art Science. Superior Solutions.

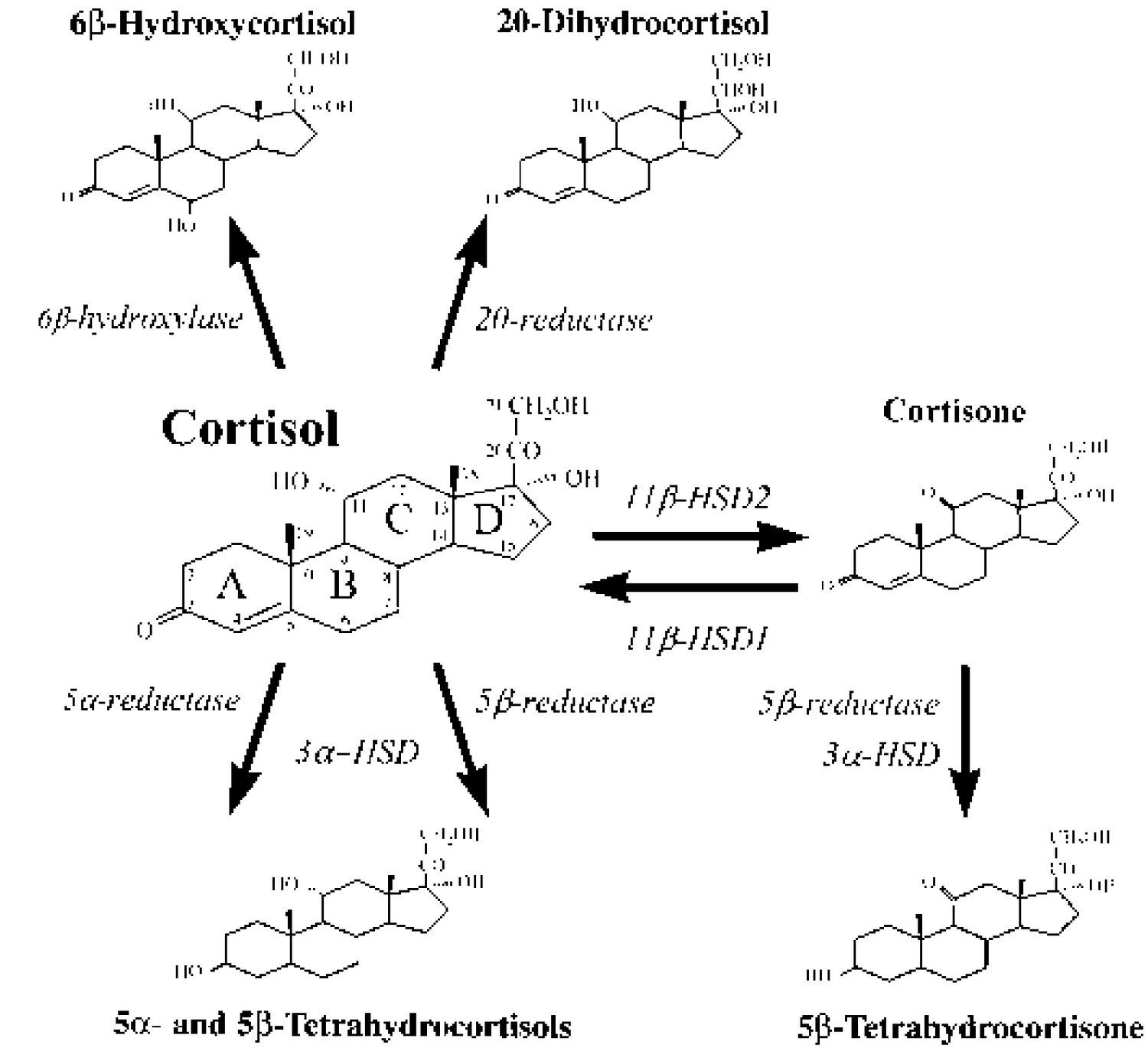


ADRENALFATIGUESOLUTION.COM

Cortisol Metabolites

- Cortisone
- Corticosterone
- DHEA-S
- Pregnanetriol
- Tetrahydroaldosterone
- αTHF (allo-tetrahydrocortisol)
- αTHB (allo-tetrahydrocorticosterone)
- THA (tetrahydro-11-dehydrocorticosterone)
- ACTIVE: THF (tetrahydrocortisol)
- INACTIVE: THE (tetrahydrocortisone)
- THB (tetrahydrocorticosterone)
- THS (tetrahydrodeoxycortisol)
- 11-Deoxycorticosterone
- 11- Deoxycortisol

Cortisol Metabolites



Cortisol, which is the active hormone, can convert into cortisone, the inactive form.

Cortisol and Cortisone convert back and forth in various places in the body.

By looking at whether cortisol metabolites (aTHF, bTHF) or coritsone metabolites (bTHE) are made more (compared to what is normal), we can report a total cortisol vs a total cortisone.

Why Cortisol vs Cortisone?

There are certain lifestyles and disease states that drive cortisol metabolism to cortisone metabolism more often and we can use this information to make some changes to the patient that continues to have low cortisol.

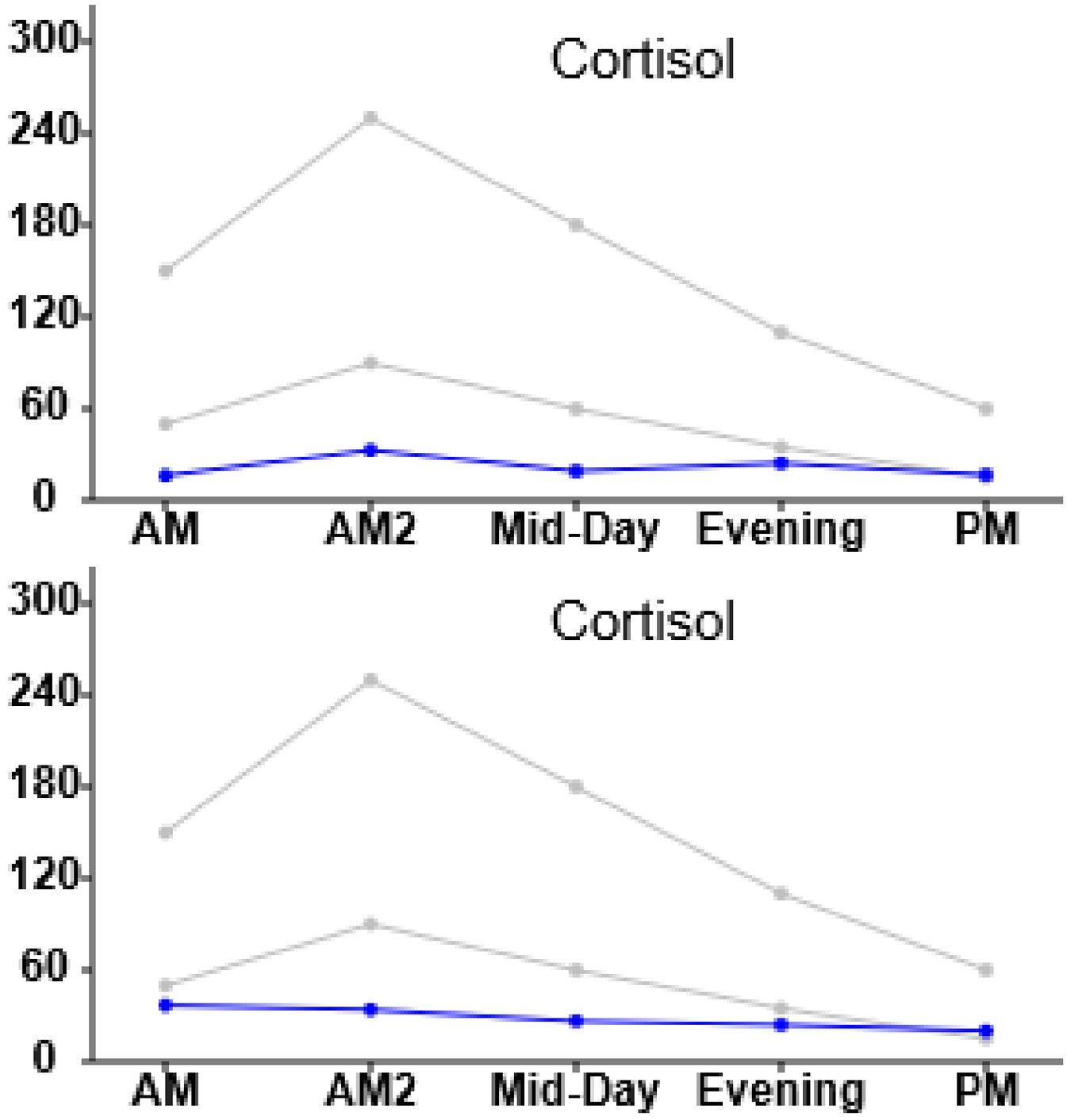
More Cortisone:
Hyperthyroidism, hGH, E2, ketoconazole, quality sleep, magnolia, scutellaria, izyphus, testosterone, citrus peel extract

VS.

More Cortisol:
Hypothyroid, licorice, grapefruit, inflammation, visceral obesity, high insulin, excess sodium

physicians LAB
State-of-the-art Science. Superior Solutions.

Why Cortisol vs Cortisone?

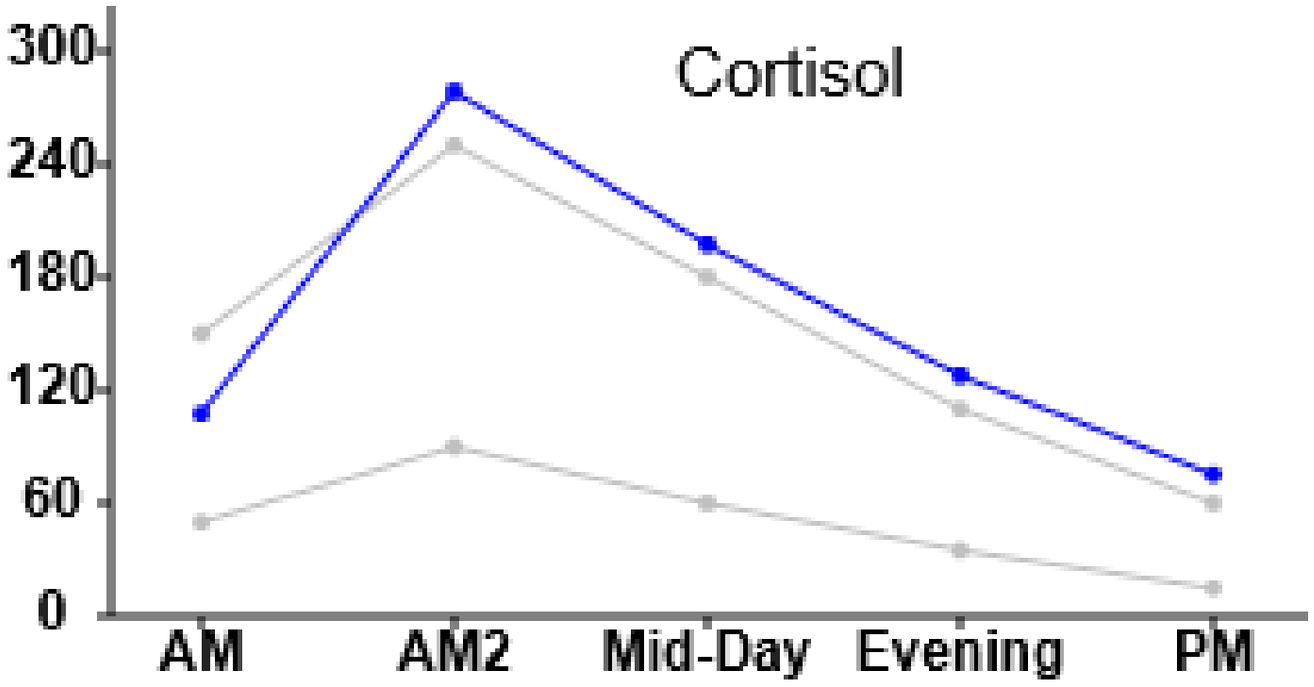


Addison Disease patient

Obesity patient

physicians LAB
State-of-the-art Science. Superior Solutions.

Why Cortisol vs Cortisone?



Hypothyroid?

Sluggish Metabolism?

Inflammatory Response/ Elevated ACTH?

physicians LAB
State-of-the-art Science. Superior Solutions.

Transdermal Progesterone
Saliva/blood spot vs Urine