

# How to reset your stress response: function, evaluation, and considerations

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**DUTCH TEST**



# DISCLAIMER

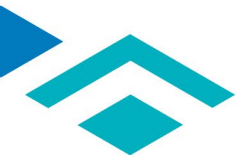
- The purpose of this discussion is for education and information purposes only and not intended for treatment or to be used in place of medical evaluation or care.





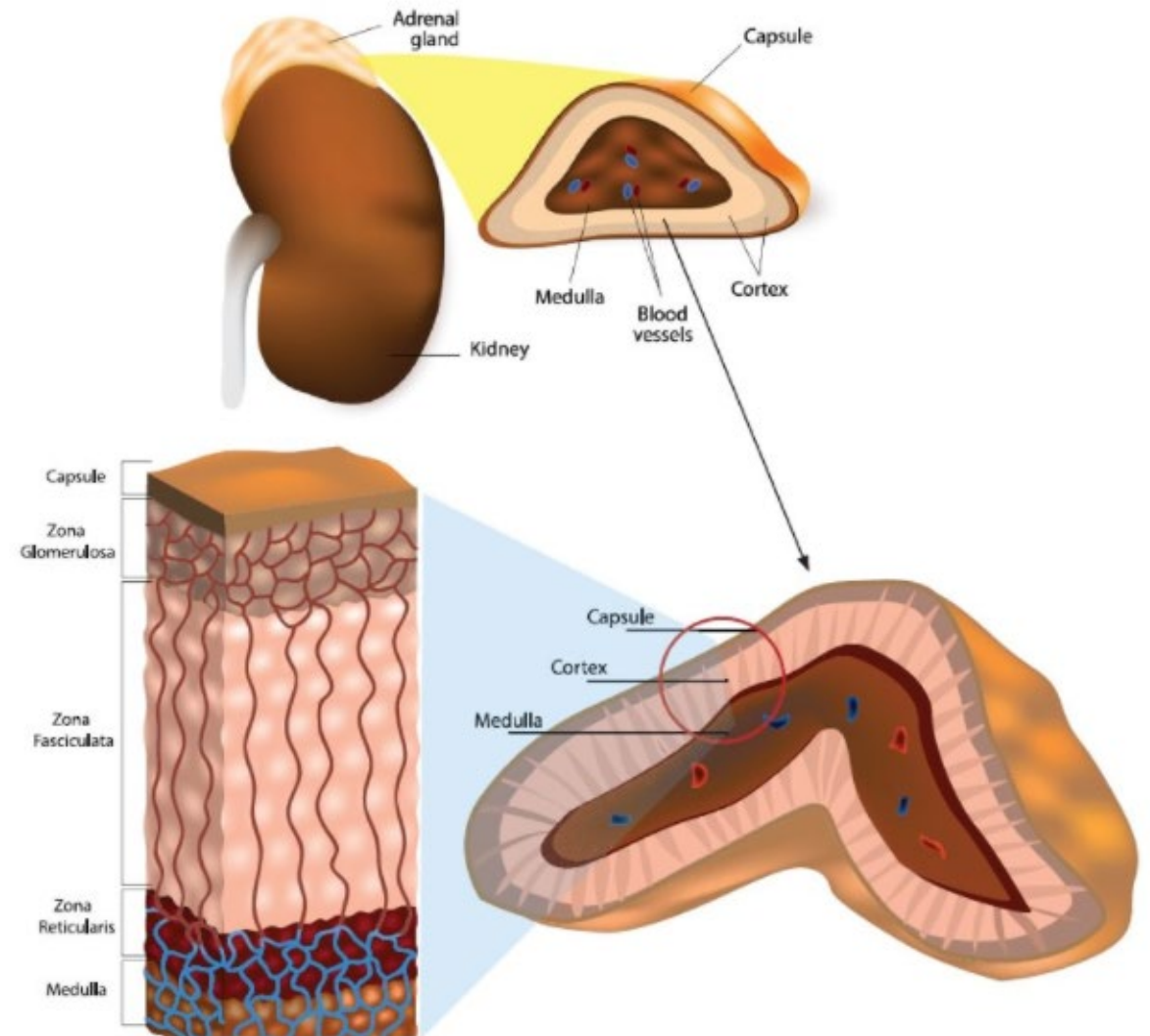
# STRESS RESPONSE

- What is Stress?
  - Stress is anything that creates an imbalance in your system
  - Homeostasis: maintain a steady state, or optimal stability (think temperature, fluid balance, mood, energy, blood sugar, etc)
- Where does stress come from?
  - REAL vs
  - PERCEIVED
    - All the same response
    - The body does not have a “good” or “bad” category of stress



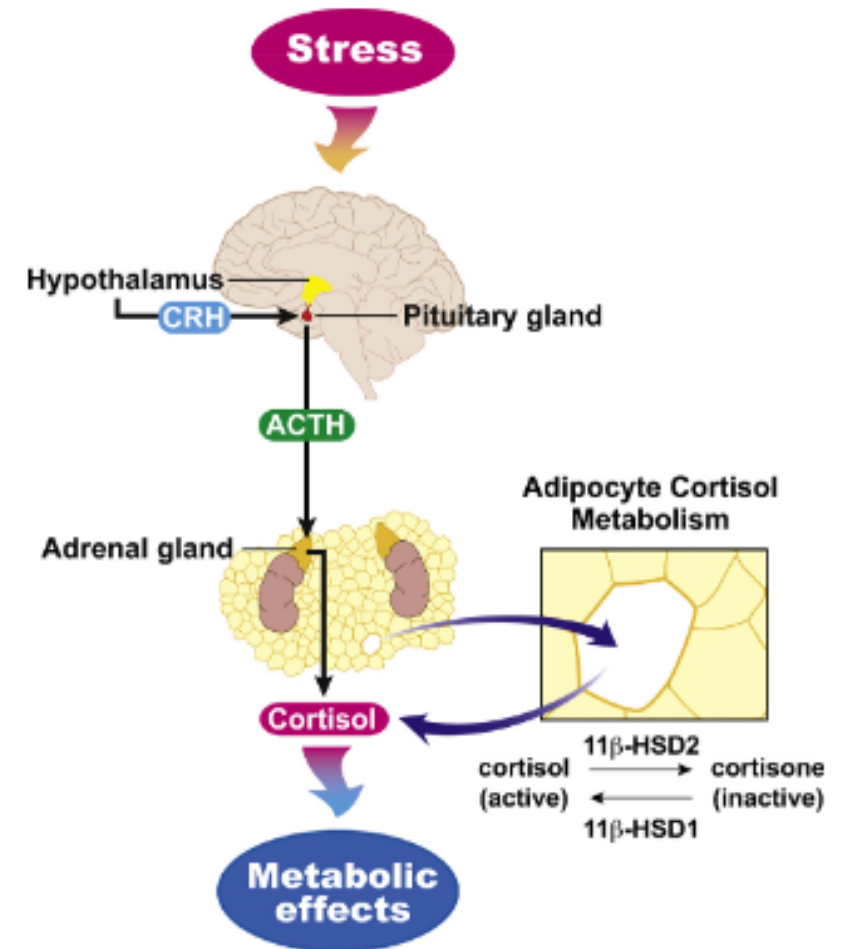
# STRESS RESPONSE – hormones involved

- Adrenal Glands Produce:
- (3 zones for hormone production in the adrenal cortex)
  - **Cortisol**
    - Adrenal Cortex: Zona Fasciculata
  - **DHEA/DHEA-s**
    - Adrenal Cortex: Zona Reticularis
  - **Aldosterone**
    - Adrenal Cortex: Zona Glomerulosa
  - **Catecholamines**
    - Adrenal Medulla: Epinephrine and
    - Norepinephrine



# STRESS RESPONSE – HPA Axis

- HPA = Hypothalamic – Pituitary – Adrenal Axis
- Hypothalamus → CRH/CRF (In the PVN)
- CRH → Pituitary Gland
- Pituitary Gland → ACTH
- ACTH → Adrenal Glands
- Adrenal Glands → Cortisol





# STRESS RESPONSE – HPA Axis

- Cortisol Response vs Catecholamine Response
- Cortisol (Adrenal Cortex) - SLOW
  - The body makes cortisol **as needed** when signaled – it is not made then stored
  - This usually occurs after a stressor signals the BRAIN
  - Lag time is usually about 10 minutes after Epi/Norepi have been released
- Catecholamines (Adrenal Medulla) - FAST
  - Immediate release of stored epinephrine and norepinephrine
  - These are amines the body makes then stores to be at the ready for a threat!
    - This is signaled through the spinal cord and not through the brain





# STRESS RESPONSE – Cortisol Response

- **Cortisol**
  - Produced in the zona fasciculata in the adrenal cortex of the adrenal glands
  - It is a glucocorticoid (steroid hormone that utilizes sugar and fats to mediate an anti-inflammatory response; can influence immune response)
  - Cortisol is released in response to stress. It is also released in the presence of low blood sugar (which is a stressor).
    - Cortisol blocks insulin to keep glucose in the blood stream
    - Cortisol induces gluconeogenesis (break down of glucose from fat cells/liver)
    - Cortisol reduces protein uptake (diverts it to gluconeogenesis to keep glucose in circulation)
    - Cortisol suppresses the immune system to deal with the stress
    - Cortisol increases blood pressure (vasoconstriction)
    - Cortisol improves focus (mental and physical), improves eyesight





# STRESS RESPONSE – Cortisol Response

- **Short Term Effect of Cortisol Release:**
  - Anti-inflammatory
  - Ability to have energy to fight, deal with stress
  - Increased focus
  - Increased blood pressure (vasoconstriction)
  - Increased HR and blood flow to muscles
  - Decreased digestive effort
  - Decreased sex hormone response
  - Decreased immune response





# STRESS RESPONSE – Cortisol Response

- **Long Term Effect of Cortisol Release:**
  - Insulin dysregulation
  - Blood sugar irregularities/dysglycemia - diabetes
  - Weight gain, specifically around the middle
  - Immune suppression, immune dysregulation
  - Chronic Fatigue
  - Gastrointestinal Issues – parasympathetic nervous system suppression
  - Cardiovascular Concerns – blood vessel constriction, over compensation of the cardiovascular system (high blood pressure)
  - Sex Hormone Imbalances, infertility, irregular periods, heavy periods, low libido/sex drive





# STRESS RESPONSE – Cortisol Highs and Lows

- **HIGH Cortisol**
  - Cushing's – a pathology of consistently high levels of cortisol, usually from a tumor that encourages improper and constant signaling to release cortisol
- **LOW cortisol**
  - Addison's – when the body does not have enough cortisol (or aldosterone). This can be a life-threatening disease and needs appropriate treatment





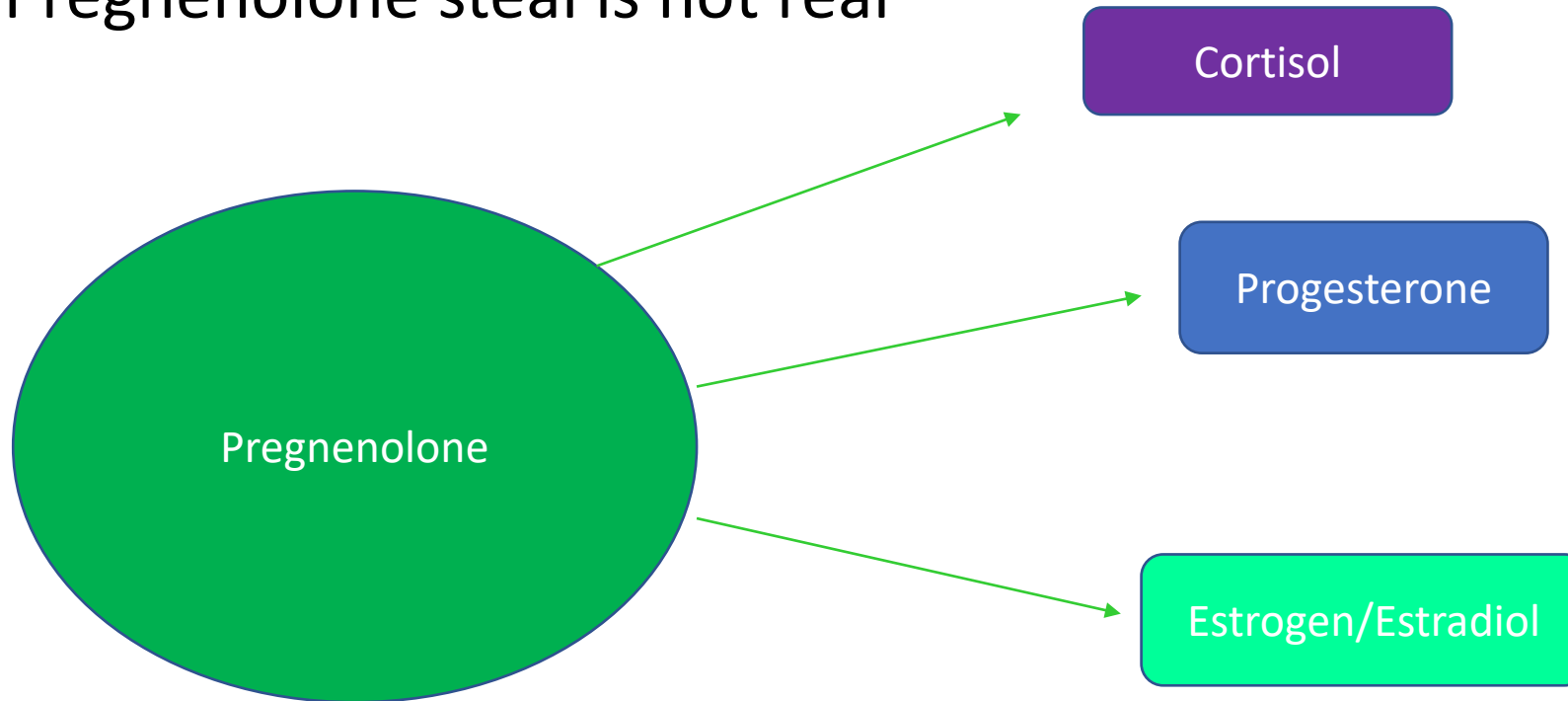
# STRESS RESPONSE – “Adrenal Fatigue”

- Old school thought process for adrenal function
  - Implies the adrenal glands are not able to respond
- More appropriately, it is categorized as HPA (axis) dysfunction or HPA (axis) imbalance
  - This points more specifically and accurately to poor functioning of the brain to adrenal communication
  - Support appropriate language to clarify the need for how to evaluate the issue and best treatment modalities (Hypothalamic and/or Pituitary vs adrenal gland support)



# STRESS RESPONSE – Accurate Physiology

- Pregnenolone steal is not real



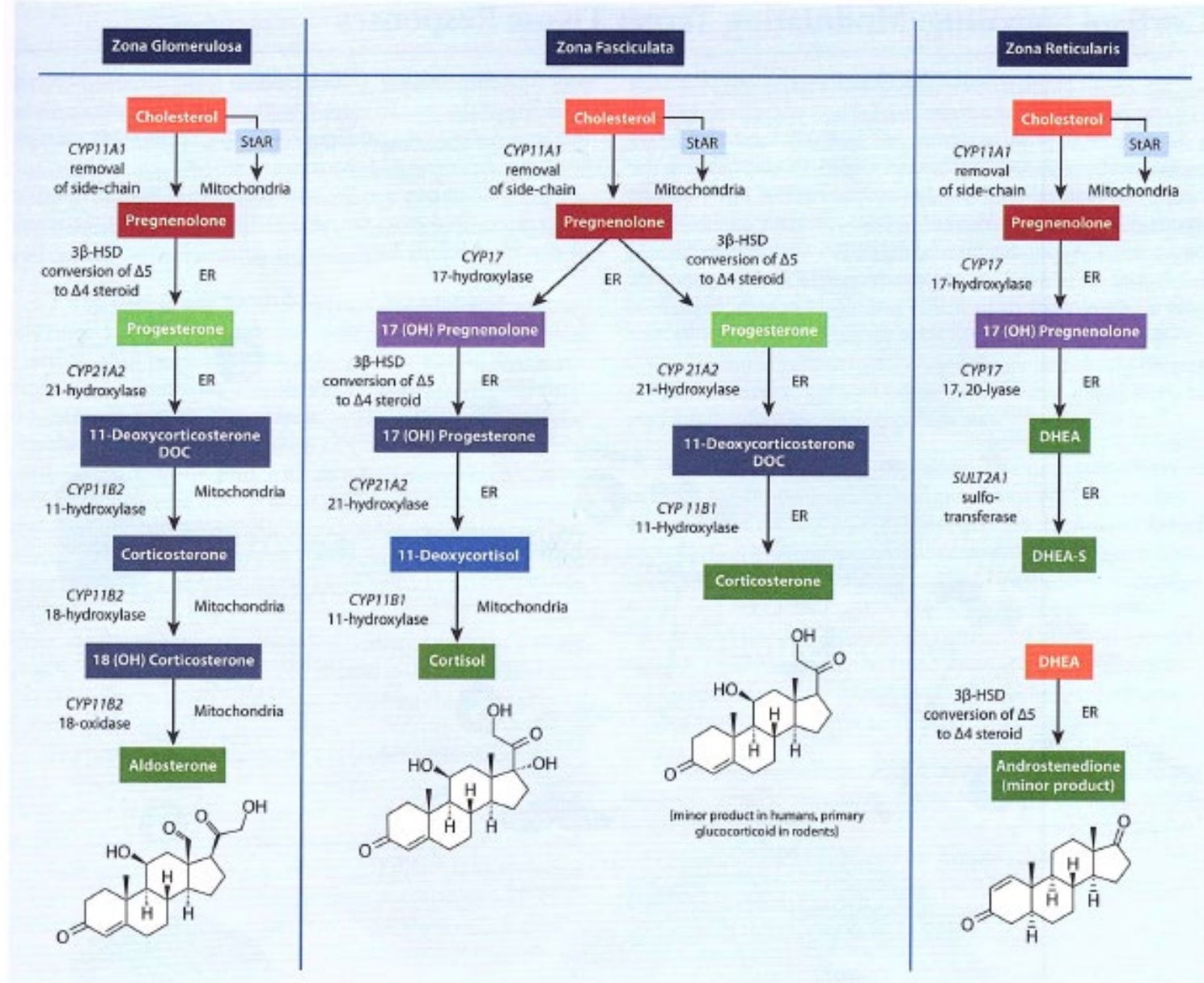


# STRESS RESPONSE – Pregnenolone and appropriate metabolism

- Cholesterol is the backbone for hormone production
- Different cells have different responsibilities with different enzymes to do their job
- Zona Fasciculata makes cortisol. It has to have specific enzymes to do this from cholesterol.
  - (ie the ovaries have a specific job to make progesterone but they use a particular cell with specific enzymes to make progesterone once that particular cell pulls cholesterol in)



# STRESS RESPONSE – cholesterol metabolism in adrenal function



- Guilliams, Tom. 2019. The Standard. Maintaining HPA Axis
- Adaptability: Vol 15; 11.

Figure 5: Adrenal Cortex Steroidogenesis.



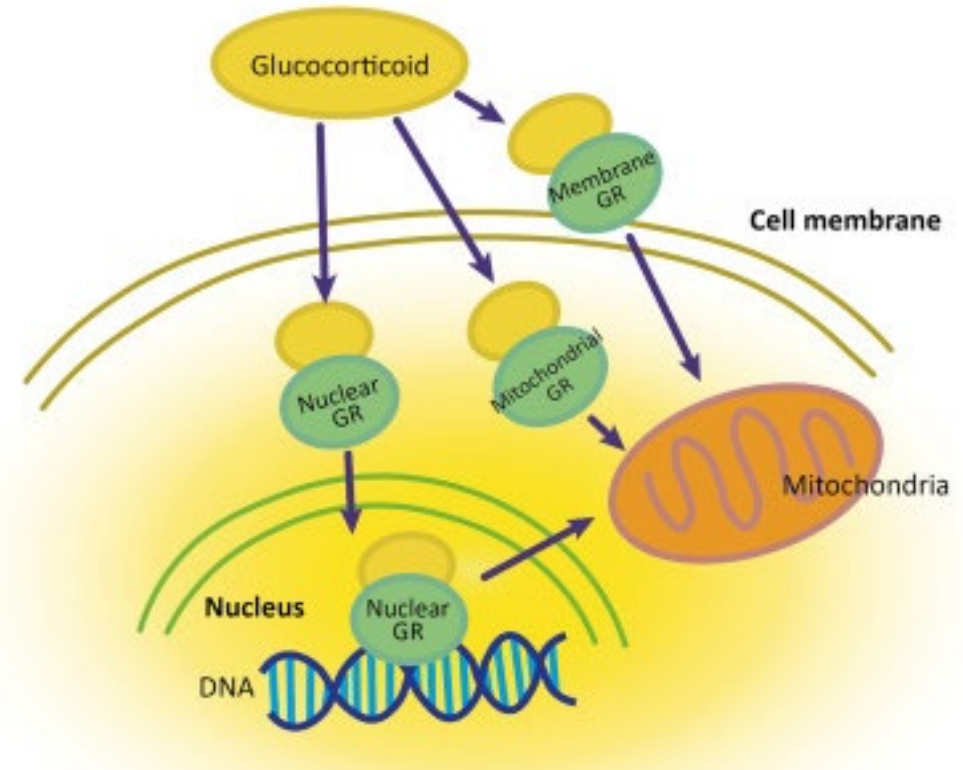
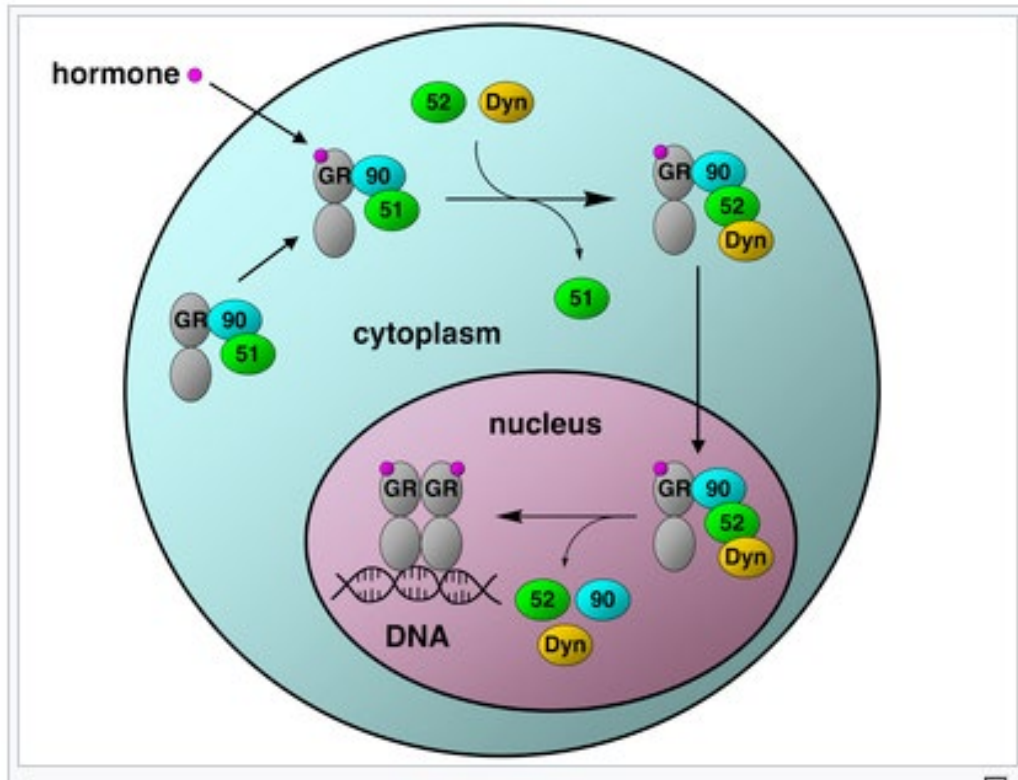


# STRESS RESPONSE – how it works

- The glucocorticoid must be transported into the cell
- Cortisol does not need a transporter to get inside the cell
- Once inside the cell it binds to a Glucocorticoid Receptor (GR)
- Once bound, the GR carries cortisol with help of a “chaperone” called HSP90
- HSP90 is the carrier to pull cortisol via the GR from the cytoplasm of the cell to the mitochondria of the cell
- Once inside the mitochondria, HSP90 allows cortisol to unbind from the GR and act on the cell for the cortisol response



# STRESS RESPONSE – how it works







# STRESS RESPONSE – how it works

- GR
  - The GR can bind to multiple steroid hormones including estradiol, androgens like Testosterone, Aldosterone, and progesterone; here the focus is on Cortisol
- HSP 90
  - Heat Shock Protein 90
  - Protects cells from “heat shock” but also from a multitude of stressors
  - Also known as “stress proteins”



# STRESS RESPONSE – how it works

- Heat Shock Protein (HSP)
  - Responsible for appropriate “presentation” and “folding” of proteins
  - Think of how a DNA helix is organized - if this is not organized in a particular manner, the DNA does not work appropriately. This is the same for other proteins
  - HSP is responsible for watching over and ensuring all proteins have appropriate structure to do their job(s)
- Heat Shock Protein 90
  - Helps with appropriate protein folding
  - Maintains an open site for GR binding
  - Assists in transport of glucocorticoids and other hormones
  - Assists in cell signaling
  - Supports angiogenesis (good and bad)
- Heat Shock Protein 70
  - Protects cells from Oxidative Stress
  - Disposes of damaged proteins
  - Inhibits apoptosis
  - Hsp90/Hsp70 can work together to transfer proteins

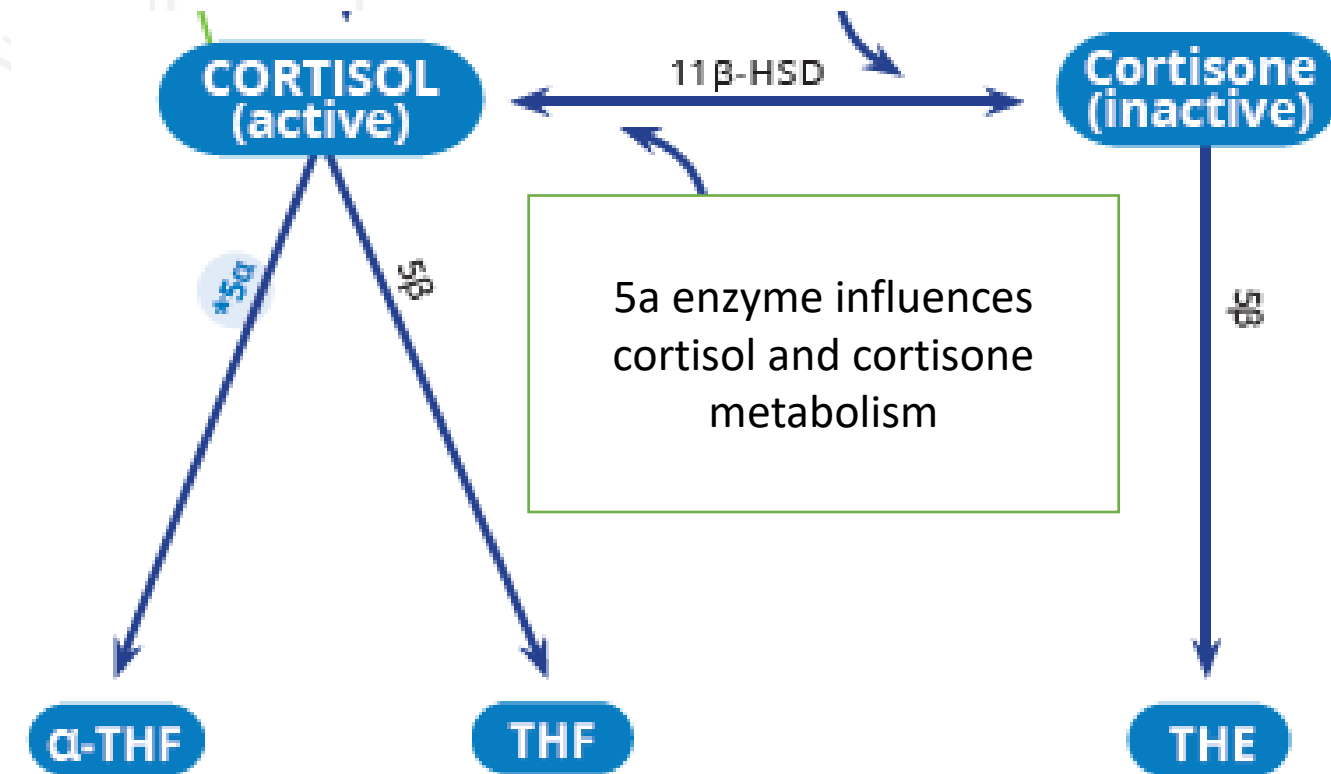


# STRESS RESPONSE – how it works

- HSP
  - Organizes
  - Transports
  - Protects
  - Realigns



# STRESS RESPONSE – how it works



- Deactivation happens in the kidney
- Reactivation can occur in fat cells and the liver

- >5% of cortisol is free
- THF = Cortisol Metabolites
- THE = Cortisone Metabolites
- 11b-HSD 1
  - Activates to cortisol
- 11b-HSD 2
  - Deactivates to cortisone

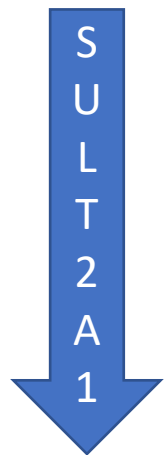


# STRESS RESPONSE - DHEA

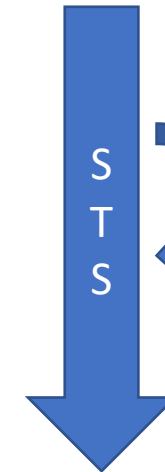
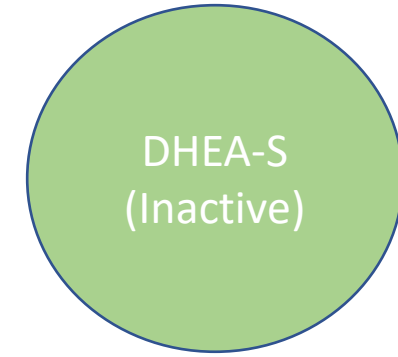
- DHEA – Dehydroepiandrosterone; produced in the adrenal glands (adrenal cortex), gonads, and the brain
- DHEA is seen as a parent hormone – it is a major precursor to most other steroid hormones
- DHEA plays in both the sex hormone and adrenal hormone worlds
  - DHEA supplies about 75% of estrogens to pre-menopausal women, and in menopause [androgens] supply 100% of estrogens
  - DHEA-sulfate does not cross the blood brain barrier
  - DHEA-sulfate does not follow a diurnal pattern through the day, it is constant and most abundant, and is therefore a better measurement of adrenal/stress reserve
  - DHEA and DHEA-S have been found to heavily influence brain and nervous system functions – specifically mood, neurotransmitter regulation and production (more specifically with dopamine), immune function, and endothelial function
  - DHEA is still not greatly understood though there is a lot of new information and research regarding its purpose and function



# STRESS RESPONSE – how it works

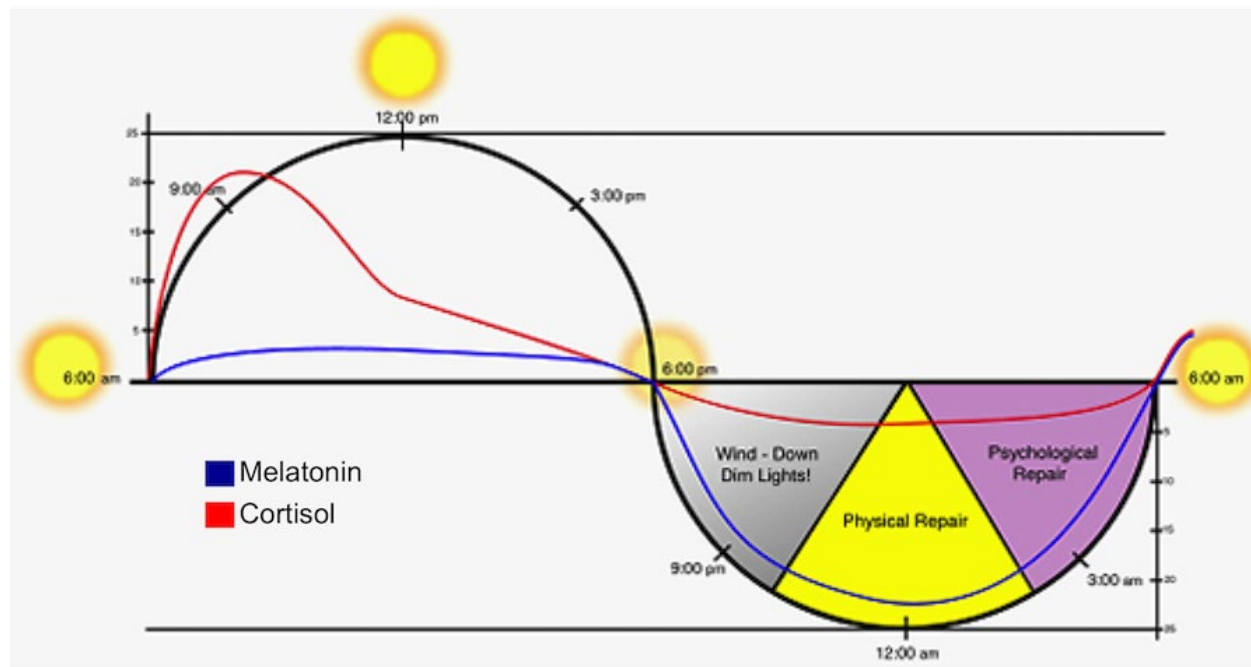



- DHEA to DHEA-s needs a sulfur donor
- DHEA-s to DHEA requires cysteine
  - DHEA has a diurnal rhythm
- DHEA-s does not have a diurnal rhythm



# STRESS RESPONSE – Diurnal Pattern

- DHEA has a diurnal pattern similar to Cortisol
- Cortisol should follow a diurnal [circadian] pattern
- Cortisol starts to rise before waking
- Cortisol peaks as the sun peaks, then wanes into the evening
- Melatonin takes over at night when cortisol levels should be low





# STRESS RESPONSE – Sympathetic vs Parasympathetic Nervous System response

- Sympathetic Nervous System
  - Run, Fight, Flight
  - Action
- Parasympathetic Nervous System
  - Rest
  - Digest
  - Calm







# STRESS RESPONSE – how to evaluate

- Understand **physiology and function**
  - The how and what (what hormones do what and how)
- Understand **the players in the game**
  - The what (enzymes, protein carriers, signalers, etc)
- Understand **the influencers**
  - These are the contributing factors to the situation
- Understand **how and what to test**
  - Which hormones are we looking at
  - What are the best methods to measure function





# STRESS RESPONSE – how to evaluate Influencers

- The Influencers:
  - Lifestyle
  - Stressors
  - Sleep pattern
  - Blood sugar regulation
  - Inflammatory triggers
  - Oxidative stress
  - Mitochondrial health





# STRESS RESPONSE – how to evaluate Influencers

- Mitochondrial Health = Cellular Health
- Manage your Mitochondrial House
- Weak Mitochondria = weak cellular function = weak metabolism of hormones and execution of overall function
- Individual components
  - HSP – less damage to cells, less shock to cells, improved cellular function





# STRESS RESPONSE – how to evaluate Influencers

- Support cellular and mitochondrial health
- Diet: anti inflammatory, individualized
- Sleep and Circadian hygiene
- Optimal immune function
- Optimal glycemic regulation (blood sugar)
- Supportive nutrients and supplements



# STRESS RESPONSE – Supportive Measures

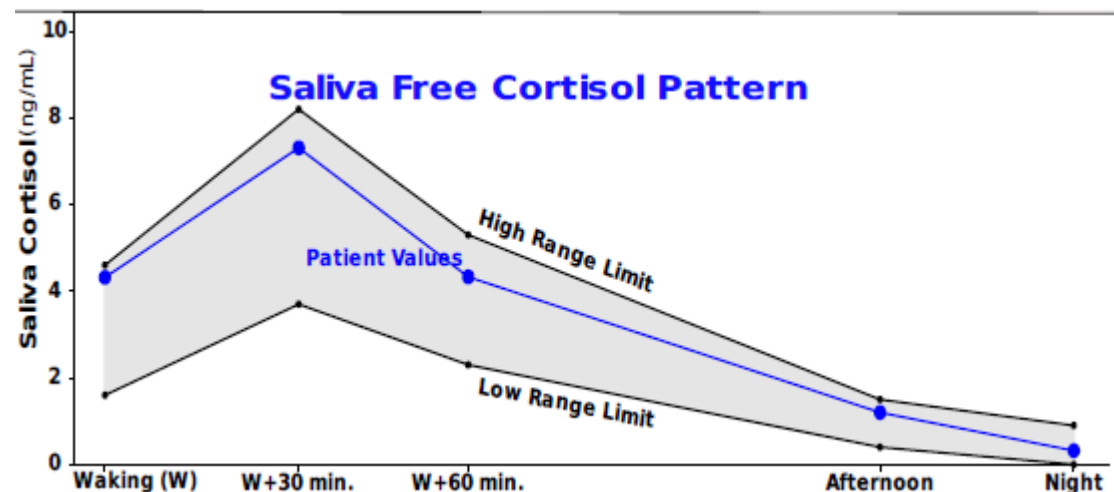
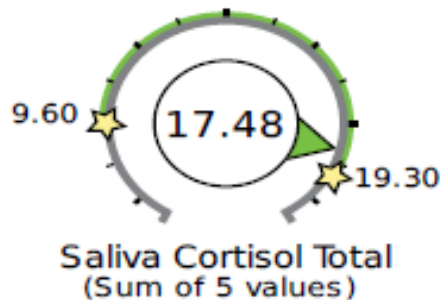
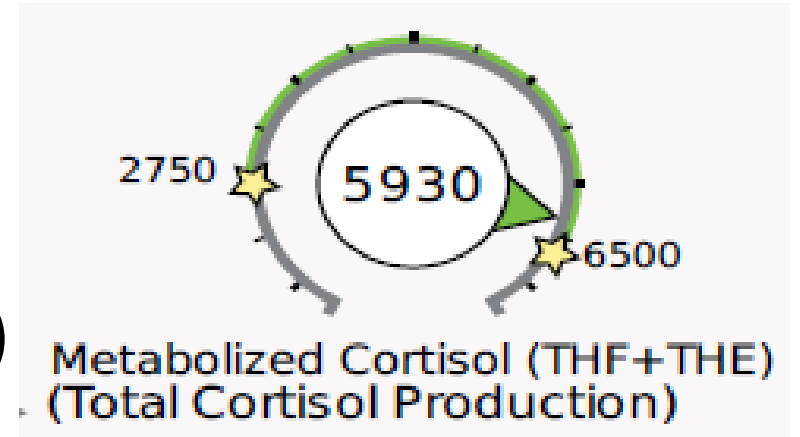
## Mitochondrial and Cellular Health

- CoQ10
- Sufiorophane
- Quercetin
- Alpha Lipoic Acid
- Glutathione
- NAC (N-Acetyl-Cysteine)
- Resveratrol
- Vit E
- B Vitamins
- PQQ
- Melatonin
- Think of cofactors for Mitochondrial function:
  - NAD
  - FAD
  - Carnitine
  - Magnesium
  - Iron
  - Oxygen
  - Strength Training/movement
  - Anti-Inflammatory Foods
  - Routine sleep
  - Detox Support:
    - Sauna
    - Infrared
    - Hot/Cold



# STRESS RESPONSE - testing

- We want to see:
- Cortisol Production capacity (Met Cort)
- Amount of Free Cortisol
- How the cortisol is used throughout the day (pattern)



# STRESS RESPONSE - testing



Flagship test: **DUTCH COMPLETE**

Dried Urine only

4 **urine** samples done throughout the day and dried

1. Dinner time
2. Before bed
3. First thing upon waking
4. 2 hours after waking
  - Optional 5<sup>th</sup> (3<sup>rd</sup>) strip if wake and urinate in the middle of the night



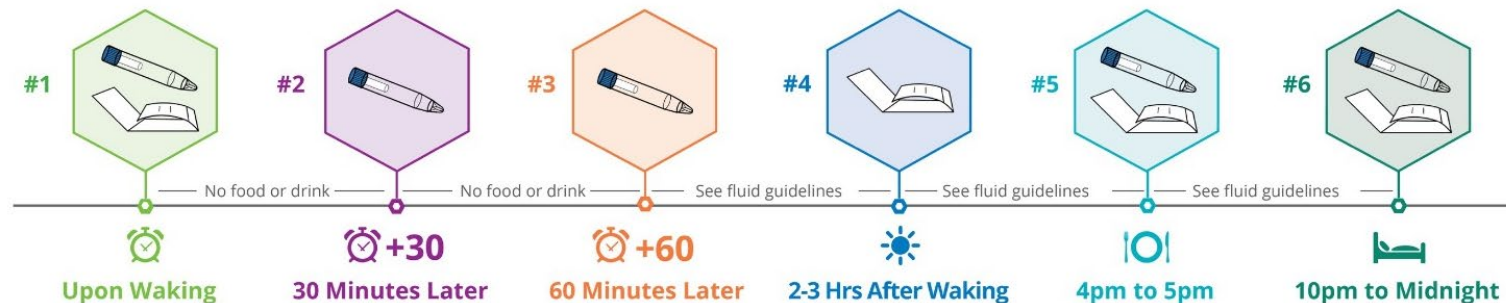
# STRESS RESPONSE - testing

DUTCH PLUS – Urine PLUS Saliva for the CAR

## 5 Saliva collections

- Waking, +30 min, +60 min, 5pm, Bedtime
- Easier collections using cotton swabs

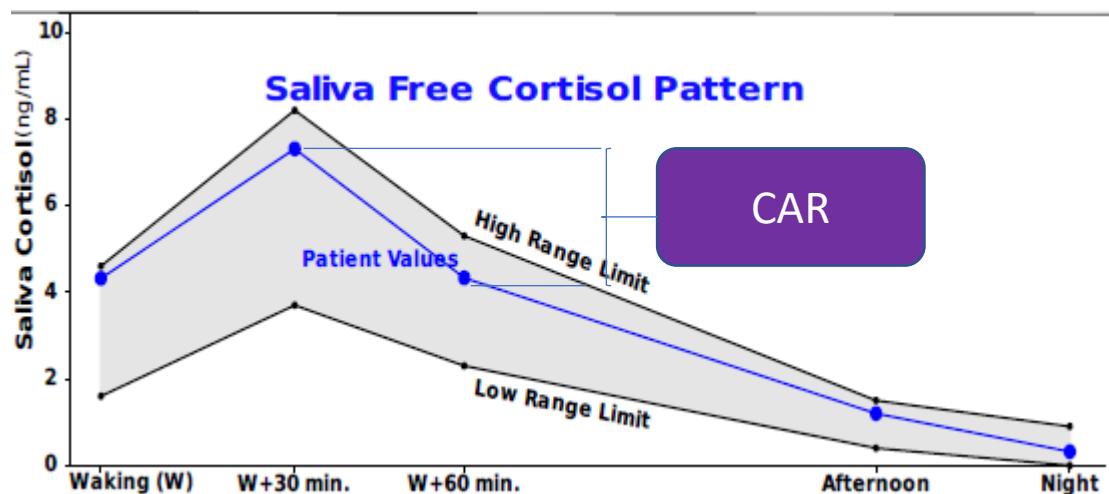
## 4 Dried urine collections (for metabolites)





# STRESS RESPONSE - testing

- CAR – Cortisol Awakening Response
- Mini stress test for HPA Axis function
  - Looking at the rise of cortisol from waking through 30 min post waking



# STRESS RESPONSE – outcomes of longterm stress

Remember this? We don't want this to be a chronic issue

- **Long Term Effect of Cortisol Release:**
  - Insulin dysregulation
  - Blood sugar irregularities/dysglycemia - diabetes
  - Weight gain, specifically around the middle
  - Immune suppression, immune dysregulation
  - Chronic Fatigue
  - Gastrointestinal Issues – parasympathetic nervous system suppression
  - Cardiovascular Concerns – blood vessel constriction, over compensation of the cardiovascular system (high blood pressure)
  - Sex Hormone Imbalances, infertility, irregular periods, heavy periods, low libido/sex drive





# STRESS RESPONSE – treatment and evaluation

- Lifestyle is the major contributing factor
  - Genetics also strongly influence this
  - Always question: HOW did we get here?
  - Remember: you can never out supplement a poor lifestyle!
- Stress Management
  - The way you interpret stress is likely different than the next
- Sleep Hygiene
- Blood Sugar regulation
- Body Movement
- Individual assessment, individual response – customize how you will move forward with stress management





# STRESS RESPONSE - considerations

- Breath work
- Meditation
- HPA Axis support could include:
  - Herbs such as ginkgo, ashwagandha, holy basil, rhodiola
  - Nutrients such as Magnesium, Trace Minerals, Zinc
- Sunshine and circadian balance
- Re-asses and re-evaluate priorities
- Build muscle mass
- Hugs/oxytocin release (pets, partners, family, friends)
- Grounding (feet on the grass/sand/ocean)



# STRESS RESPONSE – Good Luck! 😊

- .....that concludes our talk!
- Any questions, please reach out to:
- [info@dutchtest.com](mailto:info@dutchtest.com)
- Thank you for sharing your time with us today!



Instagram: drrice.Debbie





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# References

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