

A4M | MEDICINE REDEFINED

CLINICAL WEIGHT MANAGEMENT Certification Program



THE PREMIER EDUCATIONAL RESOURCE
FOR SAFE & ADVANCED PEPTIDE THERAPY

EDUCATIONALLY
PARTNERED WITH

A4M



NUTRITION, WEIGHT LOSS AND HORMONES

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A4M | MEDICINE
REDEFINED



OCTOBER 23-25
BOSTON, MA

Neither I nor any member of my immediate family have any relevant relationships with a commercial interest to disclose

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Who Am I?

- Prior to Medicine
 - U.S. Air Force, U.S. Army, Sports Medicine and Nutrition
 - Undergrad and Masters work in Molecular Genetics
- University of Arizona College of Medicine
- Emergency Medicine and Trauma
 - Walter Reed Army Medical Center, Penn State Med Center
 - Chief of Baghdad Trauma 2003 (28th CSH)
 - Advanced Training in Obesity Medicine, Nutrition Medicine, Sexual Health and Medicine, Age Management and Regenerative Medicine, and Toxicology
- 2005 I founded Atlantis Medical Wellness Center in MD

Weight Loss and Hormones



- WHY I GIVE THIS LECTURE and The Problem
- Death of the Expert/Everybody is a Weight Loss Doctor
- Nutrition and Hormones In Context:
 - Insulin Resistance/Metabolic Stress/Metabolic Signaling
- Mechanisms Between Sex Hormones and Weight Gain
- Menopause, Hormones, and Weight Gain
- Nutrition's Potential Impact on Hormone Levels and Hormone Sensitivity
- Quick Note/Bonus Slides*
 - Brief Review of non-sex hormone role in wt loss(cortisol/thyroid,etc.)
- Review and Pearls

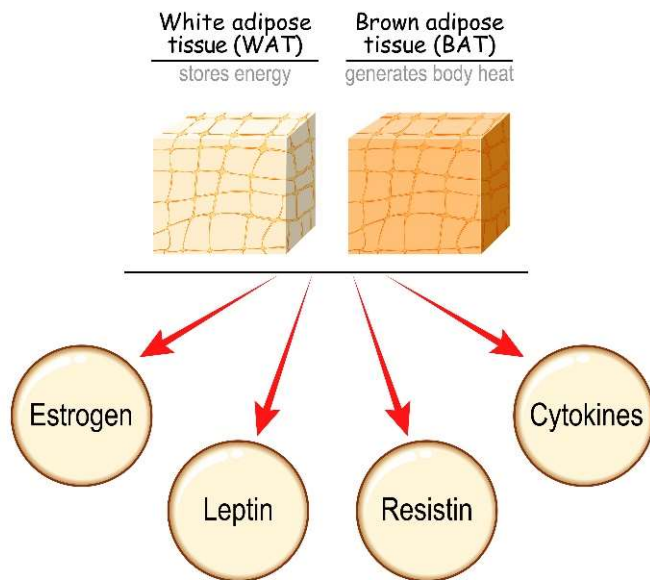
Information Classification: General

Assumptions *In The Interest Of Time*

- Obesity Epidemiology Facts and Necessity to Treat is IMPERATIVE
- You know the Basics of the Endocrine System
- This is not a new discussion.....(1)
- This is based on Literature and Experience.....AND....
- Physicians have Preconceptions and Confirmation Bias, Nutrition Ignorance
- Linear vs Holistic thought processes
- This discussion excludes the role of non sex hormones (cortisol, thyroid, etc.)

Quick Endocrine Review

Hormones produced by an adipose tissue



--Endocrine Glands

--Endocrine Organs

-Liver, kidney, stomach, placenta, skin, intestines(the largest endocrine-related organ system..gherlin/leptin/GLP-1/GIP/etc.)

-Hormones

-a chemical substance that is released into the bloodstream causing an effect on a target organ

-Types

-peptides/protein (TRH/Insulin/GH/LH/TSH/HCG)

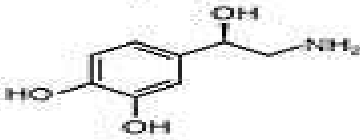
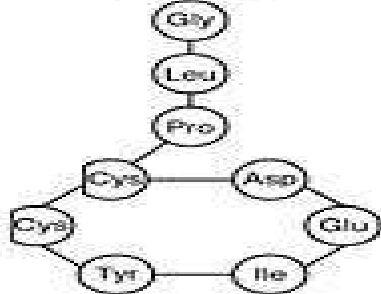

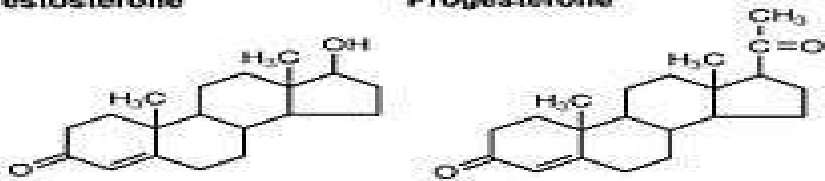
-steroid hormones(E2, T, cortisol, DHEA,VITAMIN D)

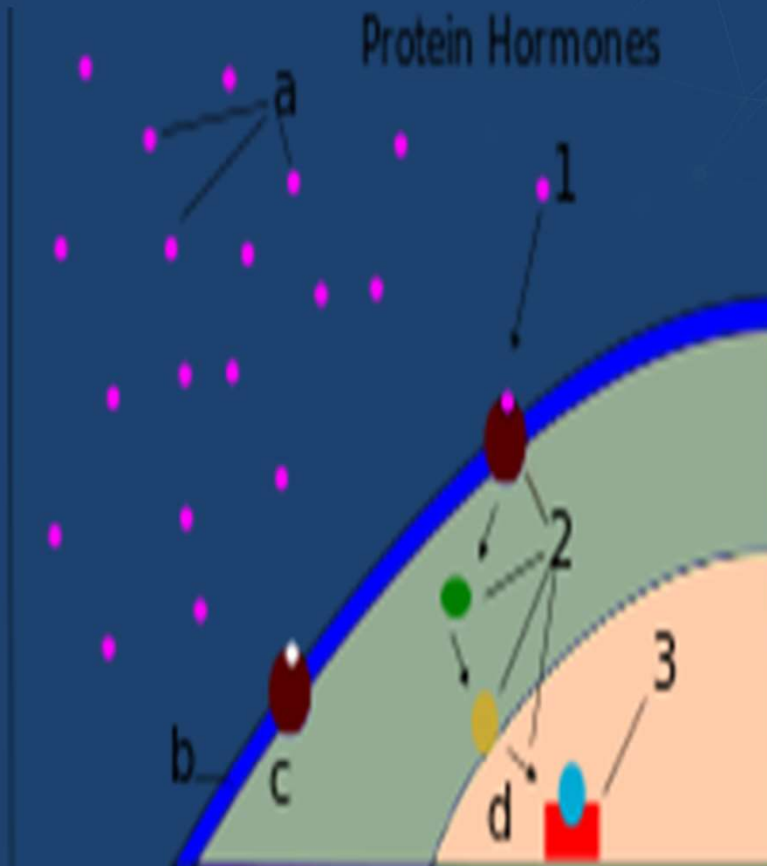
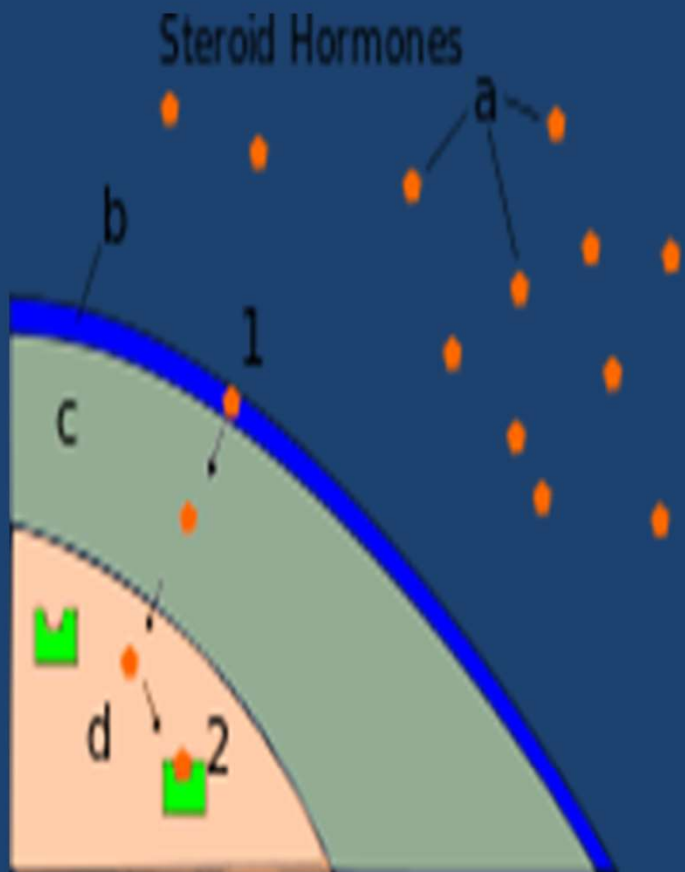
-amino acid (melatonin/thyroxin/)

- *****Don't Forget Adipose Tissue** (look at the 2022 review)***

- Leptin, adiponectin, resistin, estrogens, apelin, visfatin

- Interleukins (are not hormones)

Hormone Class	Components	Example(s)
Amine Hormone	Amino acids with modified groups (e.g. norepinephrine's carboxyl group is replaced with a benzene ring)	<p>Norepinephrine</p> 
Peptide Hormone	Short chains of linked amino acids	<p>Oxytocin</p> 
Protein Hormone	Long chains of linked amino acids	<p>Human Growth Hormone</p> 
Steroid Hormones	Derived from the lipid cholesterol	<p>Testosterone Pregesterone</p> 



THE PROBLEM: U.S. Obesity Rate OVER 40%

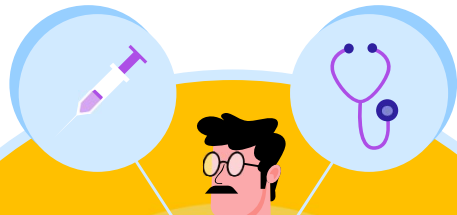


BMI > 30 %: 41.9% Adults >20 y/o
~Total % Population Overweight? 73.6%
~**Since my medical career started, Obesity Rates have tripled....think about that...**



Why I Give This Discussion

We were warned EARLY

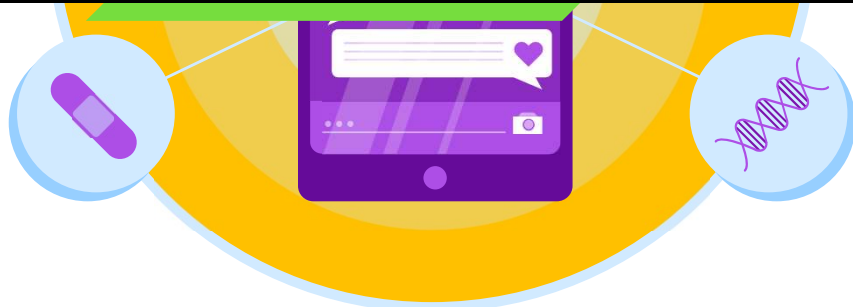


FIRST DECADE of Practice

Less than 13%

Katherine M. Flegal: Obesity Wars and the Education of a Researcher

<https://doi.org/10.1016/j.pcad.2021.06.009>



THIRD DECADE of Practice

>40%

Metabolic Disruptors/Metaflammation

- Patient: My Doctor said: “Everything is Normal”
<https://atlantismedcenter.com/blog/everything-is-normal/>
- Metabolic Disruptors
 - Poor lifestyle choices
 - Obesity, poor sleep, stress
 - Environmental stressors
 - Gut issues (LPS/microbiome)
- Metaflammation
- THE BODY:

Information Classification: General



BASICS FIRST

STEPS TO CHRONIC INFLAMMATION

INSULIN⁽¹⁾

- Chief Inhibitor of Lipolysis
- Inhibits HS-lipase
- Inhibiting FFA Release

EXCESS ADIPOSITY

- Insulin Resistance
- Elevated Plasma FFA
- IR Muscle and Liver
- Decrease B-cell Output
- Increased peripheral storage of triglycerides

LIPOTOXICITY⁽³⁾

- Excess Nutrition
- Visceral Fat Accumulation
- Beta Cell Dysfunction
- Progressive Dyslipidemia

MITOCHONDRIAL DYSFUNCTION

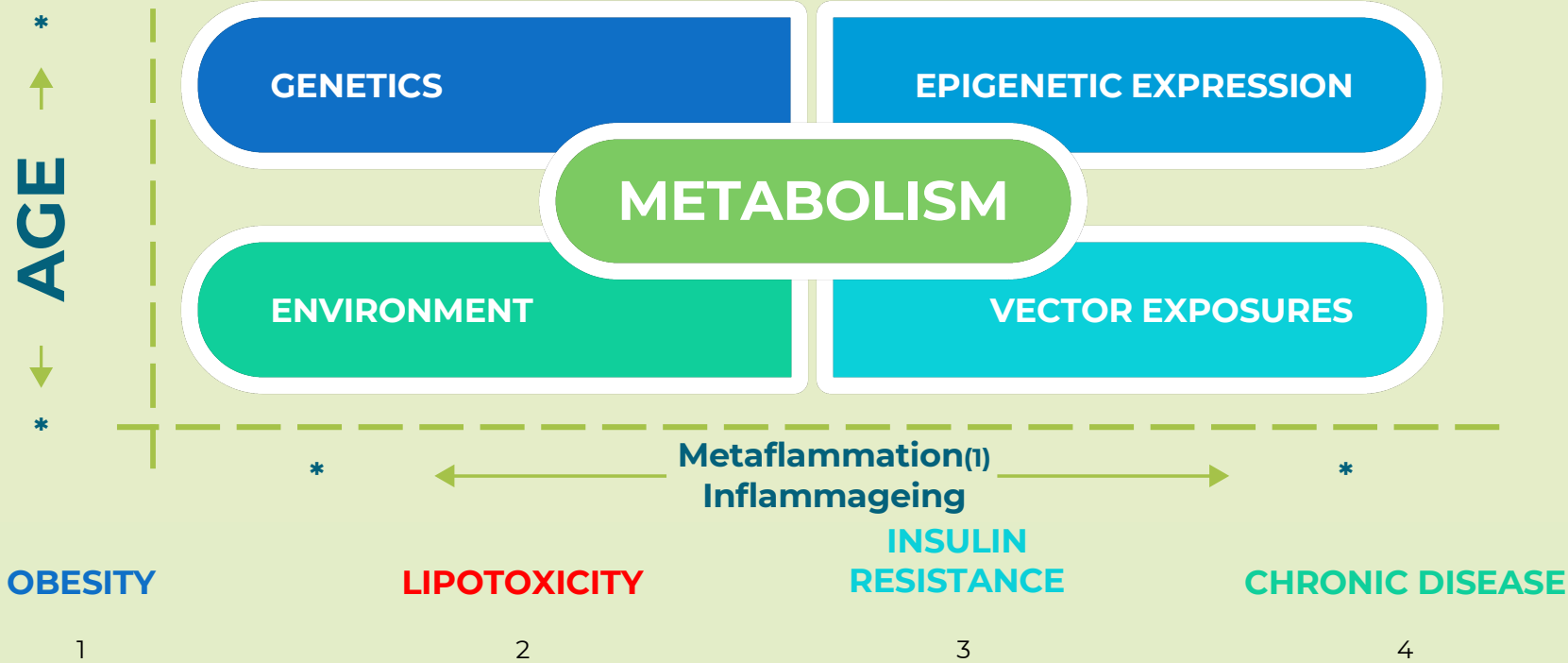
- Metabolic Inflexibility
- ER Stress
- Hypoxia
- Hypertrophy
- Death
- MicroFibrosis

INFLAMMATION

- Macrophage Dysfunction
- RESULT????

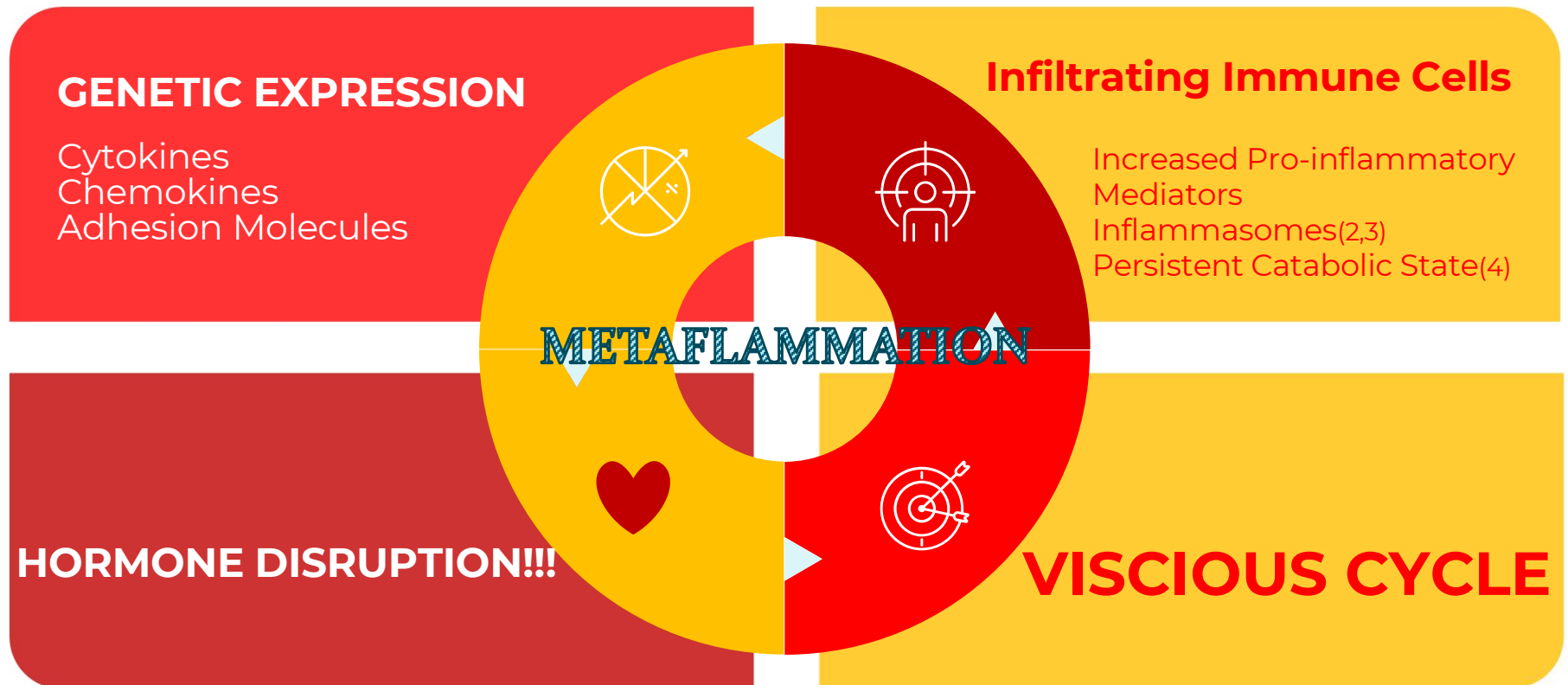
Metaflammation and Accelerated Aging

INFLAMMAGEING



METAFLAMMATION^(1,2)

That Chronic State of Physiologic Inflammation



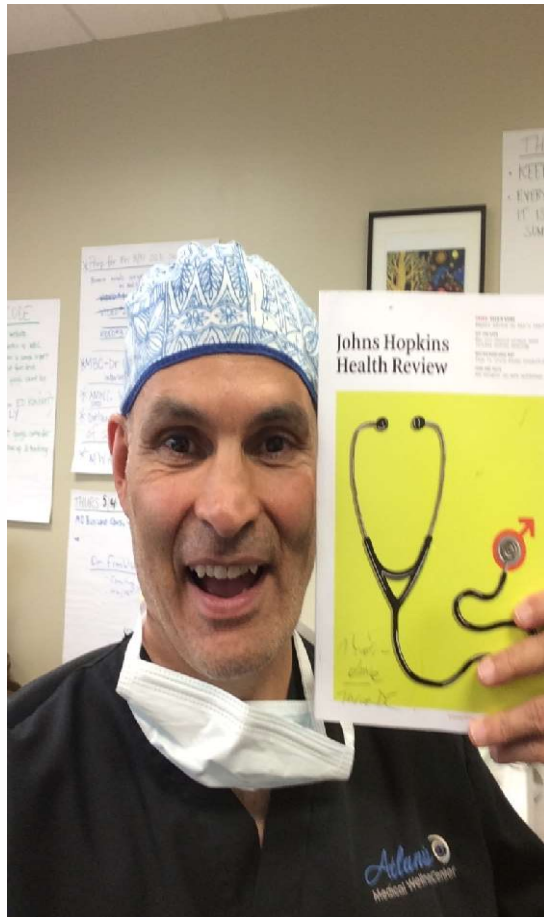
What We Tell Our Patients



- Eat More Fruits and Veggies
- Exercise more...
- Eat Less...
- It is all POOR advice
- Your patients should expect more... Why
- “Biggest Loser” Study*.....
- Why?.....

*Fotheger, E, et al.2016 May 2. doi: 10.1002/oby.21538. **Persistent metabolic adaptation 6 years after "The Biggest Loser" competition.**

What We Tell Our Patients



“Studies show they’re not worth spending money on.”

“I like to recommend to people to just eat well.”

~ “Integrative Gastroenterologist” from Johns Hopkins

~ “How Our Foods Affect Hormones” (1)


~ The Goldilocks Syndrome^(2,3)

~ The Goldilocks Principle of Obesity⁽⁴⁾

Johns Hopkins Health Review. “The Insider’s guide to 5 popular supplements for men.” Vol 4, Issue 1. Summer 2017

Buy a half-gallon of soda (800 calories and 56 spoonfuls of sugar) so KFC can donate a dollar to the Juvenile Diabetes Research Foundation.

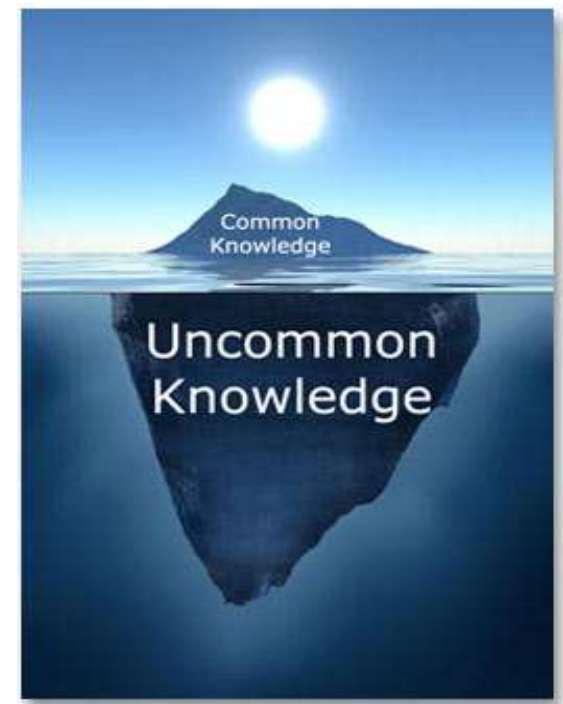
Help find a cure for type 1 diabetes by putting yourself at increased risk of type 2 diabetes.

Who is it that dreams this  up?



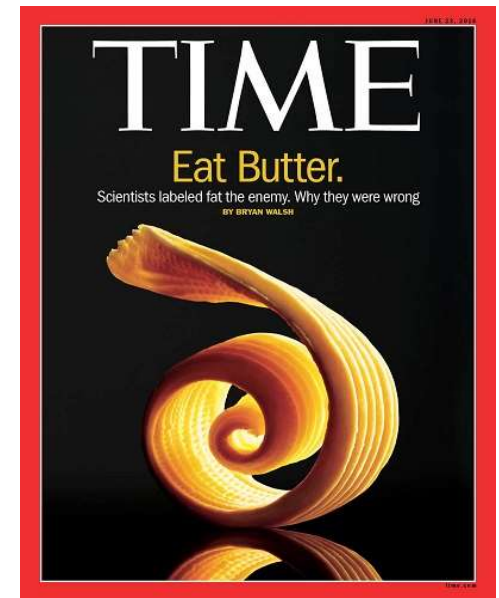
Death of the Expert

- Primary Source of Nutritional and Medical Information?
 - Social Media, Celebrities, Journalist “Specialists”
 - Professional Popular Bloggers/”Influencers”
- They Sound “Smart” (PubMed, Scientific Jargon, etc.)
- They have “Abstract” and confirmation bias knowledge
- Zero Clinical Experience and Application
- Summarized Sensationalism
- Perpetuated as Truth
- Misleading The Public AND.....



Death of the Expert cont'

-YOU!!!!!!
- MD/DO Training Time? Journal Clubs, Research, etc.
- Remember the “Integrative Gastroenterologist?”
- Remember Time Magazine Cover 2014?
- Perpetuated in the media.....
- All based on a Meta-analysis Study_(Annals of IM, Chowdrey et al.)
 - Showed CAD may not be direct relation to FFAs, including butter...NOT that butter is good!
 - Perpetuated by Nutritionists/Dietitians/Docs!
- Non-scientist lack of ability to interpret
- **Read THIS: DEATH OF THE EXPERT: PDF Included in your handouts**



Insulin Resistance/Oxidative Stress

I have a Definition

- 37.6% of US
- Linear Association with

Question...

> Acta Diabetol. 2012 Dec;49(6):421-8. doi: 10.1007/s00592-011-0361-2. Epub 2012 Jan 4.

Insulin resistance/hyperinsulinemia and cancer mortality: the Cremona study at the 15th year of follow-up

risk of gastrointestinal cancer mortality (HR = 2.61 95% CI: 1.73-3.94; P < 0.0001). Age- and sex-adjusted analysis showed that hyperinsulinemia/insulin resistance is associated with cancer mortality independently of diabetes, obesity/visceral obesity and the metabolic syndrome.

- IR negative effects on hormone production and receptor function

Abstract

Type 2 diabetes is associated with risk of cancer. Hyperinsulinemia and insulin resistance may be the link with cancer, but whether this is independent of the diabetes status, obesity/visceral obesity and metabolic syndrome is uncertain and the present study wanted to address this issue. Fifteen-year all-cause, CVD and cancer mortality data were obtained through the Regional Health Registry in 2,011 out of 2,074 Caucasian middle-aged individuals of the Cremona Study, a population study on the prevalence of diabetes mellitus in Italy in which anthropometric and metabolic characteristics were collected. During the 15-year observation period, 495 deaths were registered: 221 CVD related and 180 cancer related. Age and sex were independently associated with all-cause, cancer and CVD

"PREDIABETES"HAHAHAHAHA!!!

DukeHealth FaxServer 4/17/2019 8:00:57 AM PAGE 3/010 Fax Server

Name: [REDACTED] | [REDACTED] | [REDACTED] | PCP: VAIDIA [REDACTED], MD

POC DPC HEMOGLOBIN A1C - Details

Comments from the Doctor's Office

Hba1c is in the pre-diabetes range-please work on low carb diet and exercise. Please return to clinic in 6 months.

NO
This is Diabetes

Study Result

Narrative

POC TEST(S) ABOVE PERFORMED AT THE PATIENT CARE LOCATION AND OVERSEEN BY THE DPC POCT PROGRAM.

Component Results

Component	Your Value	Standard Range
Hemoglobin A1C	<u>Your Value</u> 6.3%	Standard Range <6.5%
Average Blood Glucose (Calculated From HgBA1c Level)	Your Value 134 mg/dL	Standard Range mg/dL

General Information

Collected

10/17/2018 4:15 PM

Resulted

10/17/2018 4:22 PM

Ordered By

V [REDACTED], MD

Result Status

Final result

Nutrition-Hormone Relationship

Multiple Hormonal Shifts

Intake Patterns

Fasting
 Excess Calories
 High Glycemic Load
 i.e. thyroid, cortisol function



"PRE-DIABETES"

Waiting to Fall Off The Cliff

49%-52% in U.S.(1)**

The Definition Mistake:
 Prediabetic~DM~IR~Hyperinsulinemic
 Beginning the diet discussion EARLY



Impact on Hormone Sensitivity

Direct and Indirect
 NOT Linear
 High Processed Carb Diet

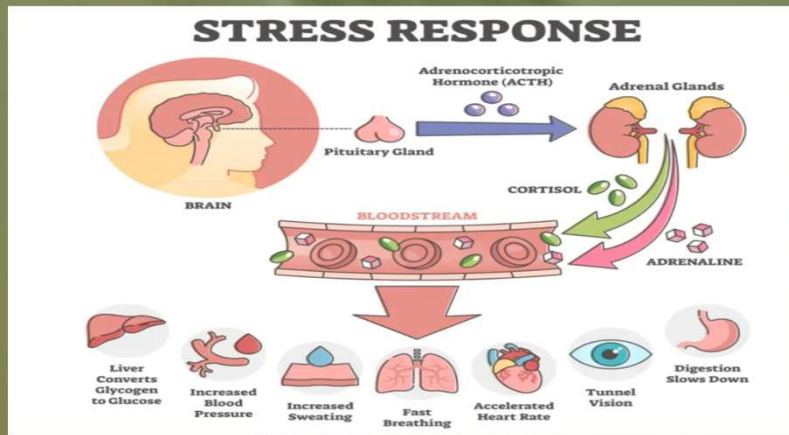
Western Diet

Upregulation of cortisol release
 Pancreatic beta-cell responsiveness
 Leptin Resistance

Hormone Dysfunction is Multifactorial

Obesity the Real Epidemic?
 Diet Approach Must be Individualized
 Imagine Epigenetic Changes
 Nutrigenomics

Information Classification: Genetic ****Highly Underestimated****



1

Western Diet

2

↑ Cortisol(1,2,3)

3

IR and Fertility(4,5,6)

4

Appetite/Obesity(7,8,9)

The Obesogenic Rat Diet

Low Fiber
Refined Carbs
Saturated Fats

Chronic Cortisol Stress
Flattening of Diurnal Curve

Negative Effects on
Peripheral and Central
Response

Increased AD Risk

Negative impact on Sex
Hormones

Endocrine Disruptors in Foods

CLEAR Relationship with IR,
Infertility, and Obesity

Leptin Release/Resistance

Estrogen/Testosterone
Balance

Hypogonadism Obesity
Cycle

Information Classification: General

BENJAMIN
GONZÁLEZ
MD

Hypogonadism-Obesity Cycle⁽¹⁾

- Adipocytes have high expression of aromatase⁽¹⁾
- Estrogens cause negative feedback on HPG
- Obesity and Testosterone Levels directly related
- Lowered T further increases adiposity⁽¹⁾
- Excess adiposity increases inflammatory cytokines (IL-6, IL-1beta, TNF α , etc.)
 - Suppresses GnRH
- Increased adiposity, increased leptin levels lead to Leydig Cell dysfunction
- Excessive HPA Activation, IR/Diabetes, Micro and Metaflammation.....?

Clinic

e Stress



Information Classification:

BENJAMIN
NZÁLEZ
M.D.

WHAT HAPPENS?^(1,2)

Dyslipidemia^(1,7)

- Increased LDL-P # and Decrease Size
- Increased ApoB
- LDL Oxidation

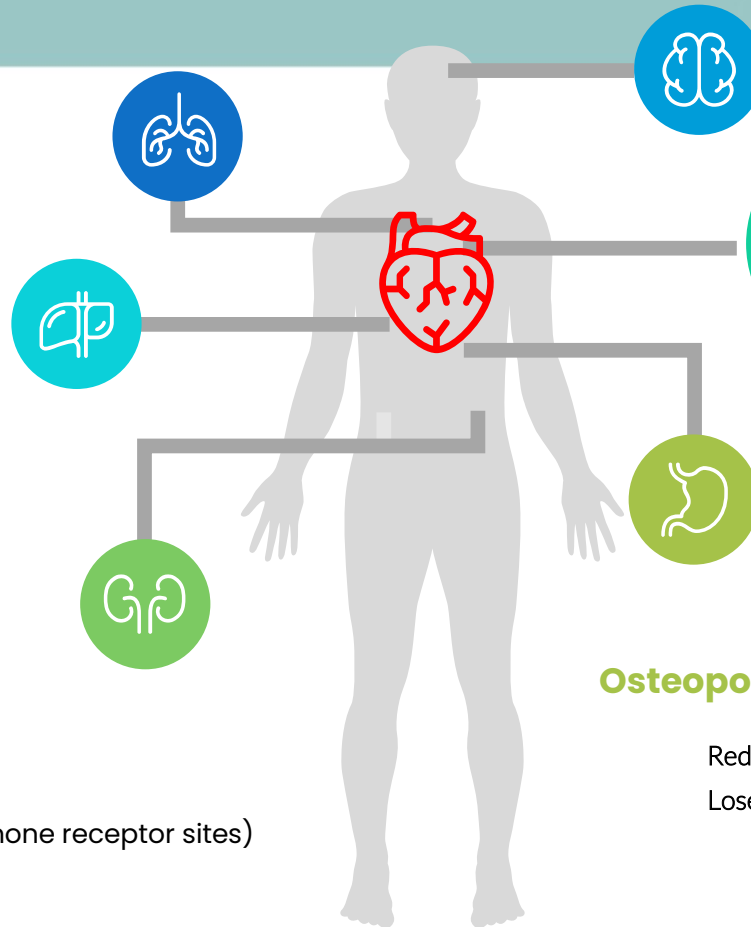
Endothelial Dysfunction^(3,4,5,6)

- Glycocalyx degradation
- Increased permeability
- Increased inflammation
- Persistent inflammation
- Increased risk of thrombosis

Hormone Disruption

- Decreased Production
- Decreased Receptor Effectiveness
- PGC-1 α downregulation (co-regulator of hormone receptor sites)

Information Classification: General



Insulin Resistance⁽²⁾

- Insulin Receptor Retract and Downregulate
- Glucose Goes Up
- Inefficient Energy Production
- "High Level" Glycolysis⁽²⁾

Lose Neuroplasticity

- Accelerated Neurodegeneration
- Centrally and Peripherally

Osteoporosis/Sarcopenia/Neurodegeneration

- Reduced Bone Turnover
- Lose GH Production and hormone signaling

Sex Hormones and Weight Loss

Basics

Estrogen(1,2)

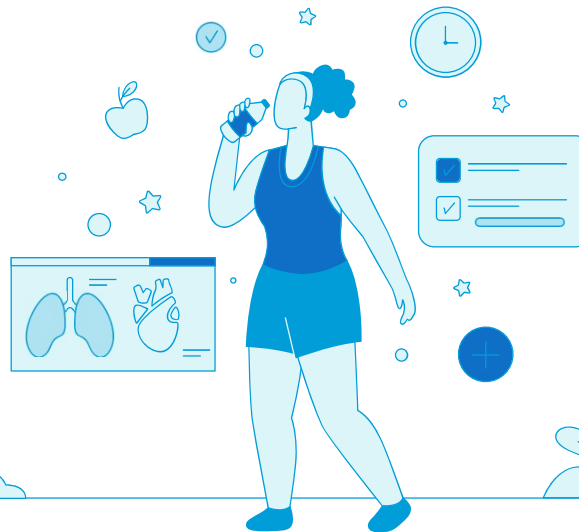
- Control distribution of adipose
- Influences IR
- Controls appetite centrally
- Regulates thermogenic potential in BAT
- ERs are EVERYWHERE
- Arcuate Nucleus to regulate feeding
- ESTRONE.....(3)

Testosterone Estrogen

Not just for Men
Not just for Women

Testosterone(4,5)

- What is the key to aging well and weight management?
- LowT leads to increased adiposity
- Obesity leads to LowT
- Severe obesity leads to LowFT
- Vicious cycle the longer in.....
- Reversible
- Obesity leads to sarcopenia
- Traditional approach to wt loss promotes sarcopenia
- Another vicious cycle



Estrogens And Breast Cancer

- “Fear of breast cancer is the strongest factor limiting postmenopausal hormone use. The most powerful study to date definitively demonstrated that estrogen does not cause an increased risk for cancer. The increased risk was associated only with taking the progestin/Provera and not estrogen.”
 - ~JAMA 2004;291(24):2947-2958
- Getting Rid of The Black Box: The FDA Panel ⁽¹⁾
- What is the second biggest fear women have with HRT?

Estrogen Metabolites

- 2-hydroxyestrogen(2OH)
 - Kills breast cancer cells. Progestins reduce formation of 2OH
- 4-hydroxyestrogen(4OH)
 - Initiates breast cancer by DNA damage
- 16-hydroxyestrogen(16OH)
 - Promotes proliferation of breast cancer by interacting with the estrogen receptor

Estrogen Metabolism

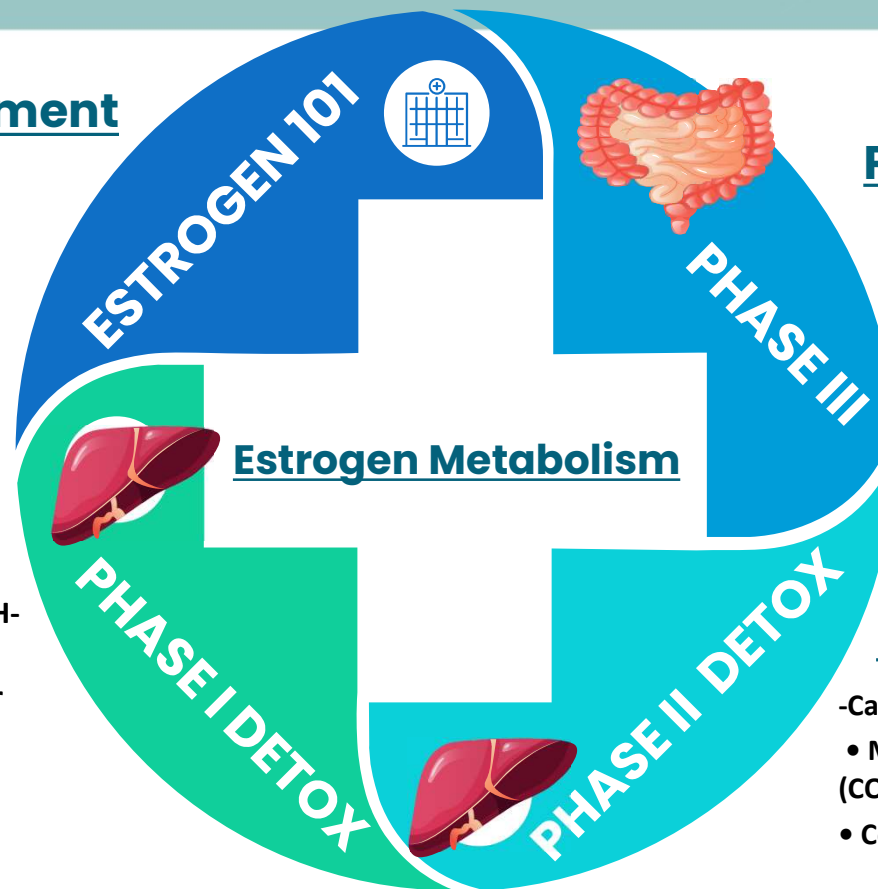
Estrogen Passive Movement

- Requires transformation for movement: DETOX

PHASE I: CYP450 enzymes

- HYDROXYLATION
- CYP1A1, CYP1A2 → 2-OH-E1 and 2-OH-E2 (catechol)
- CYP3A4 → 16-OH-E1 and 16-OH-E2 (or Estriol, E3)
- CYP1B1 → 4-OH-E1 and 4-OH-E2 (catechol)

Information Classification: General

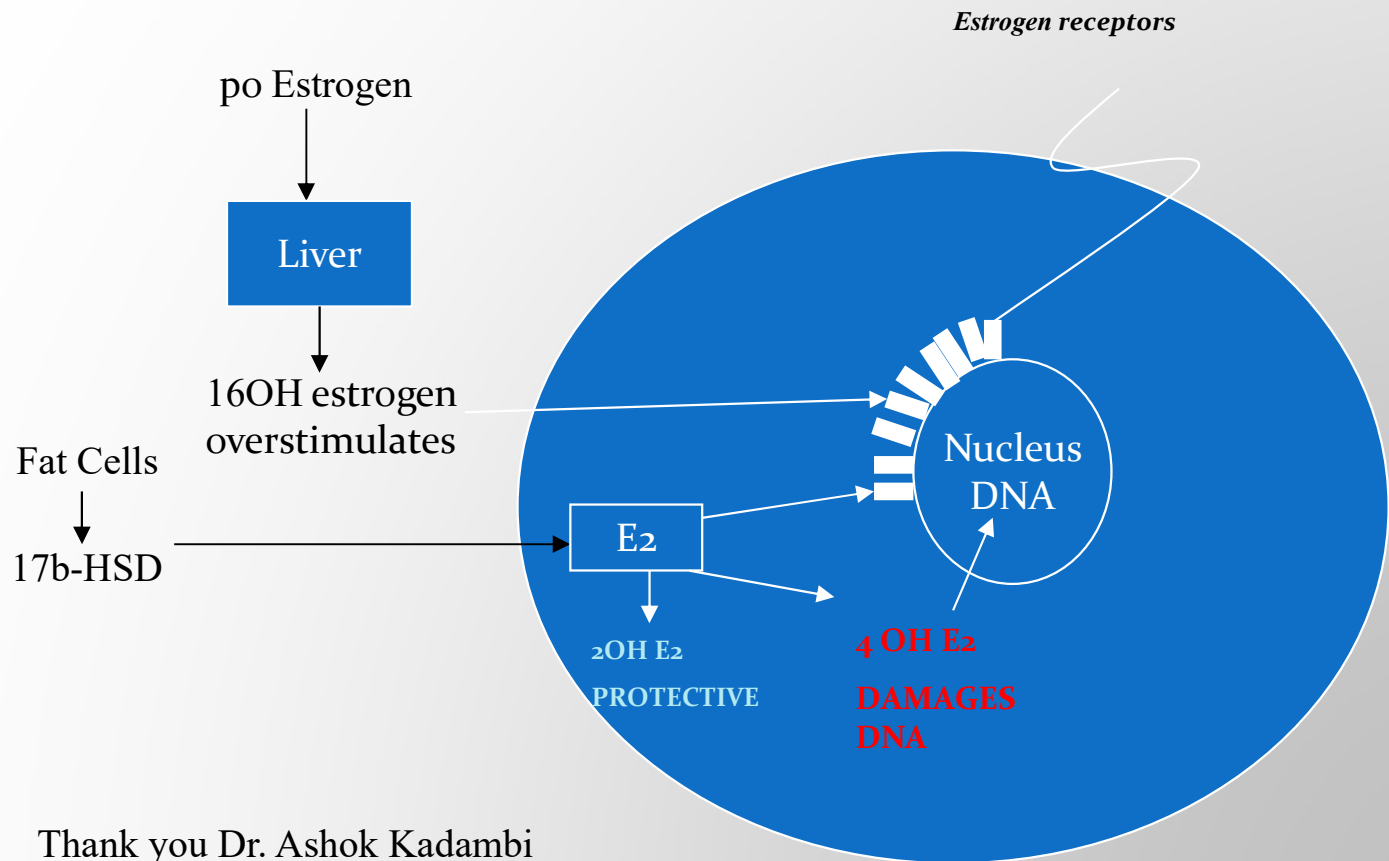


PHASE III: Elimination/recycle

- Renal Secretion
- Gut Secretion and Recycle: Estrobolome

PHASE II: Methylation/conjugation

- Catechol-O-Methyltransferase (COMT)
- Methylation → Catechol-O-Methyltransferase (COMT) → 2Me-E1, 2Me-E2, 4Me-E1, 4Me-E2
- Conjugation (glucuronidation, sulfation)



Thank you Dr. Ashok Kadambi
 Medical Director Ft Wayne Endocrinology

Breast Cancer Risk

- Keep the ratio of 2-OH/16-OH close to 0.9
- **The 2-OH is THE protective estrogen metabolite**
- Vitamin D increases 2-OH and reduces 16-OH
- Measure 25 hydroxyVit D levels and keep this in the high end (50 – 100 ng/ml).....however.....

- Fear and Misinformation Discussion 2024 pdf ⁽¹⁾
- NEED MORE STUDIES ^(2,3,4,5)
- Safety and Efficacy of Bioidentical Hormone Therapy in Menopause: A Literature Review 2021 pdf: ^(6,7)

Premarin Risk

- Premarin (equine derived) contains at least 10 estrogens that leave behind different metabolic footprints. These abnormal metabolites may be oncogenic
 - Proc Soc Exp Bio Med 1998, Jan;217(1):6-16
- A metabolite of Premarin--Equilenin is metabolized to highly cytotoxic quinoids. These metabolites caused redox damage in vivo utilizing human breast cancer cell line
 - Chem Res Toxicol. 1999 Feb;12(2):204-13
- Premarin's major metabolites: Quinones (equilin and equilenin) cause breaks in DNA and may be oncogenic
 - Chem Res Toxicol. 1998, Sept;11(9):1105-1111
- A Healthy Gut Microbiome/Estrobolome excretes conjugated estrogens and promotes reabsorption of deconjugated estrogens
 - The Intestinal Microbiome and Estrogen Receptor-Positive Female Breast Cancer
 - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5017946/>

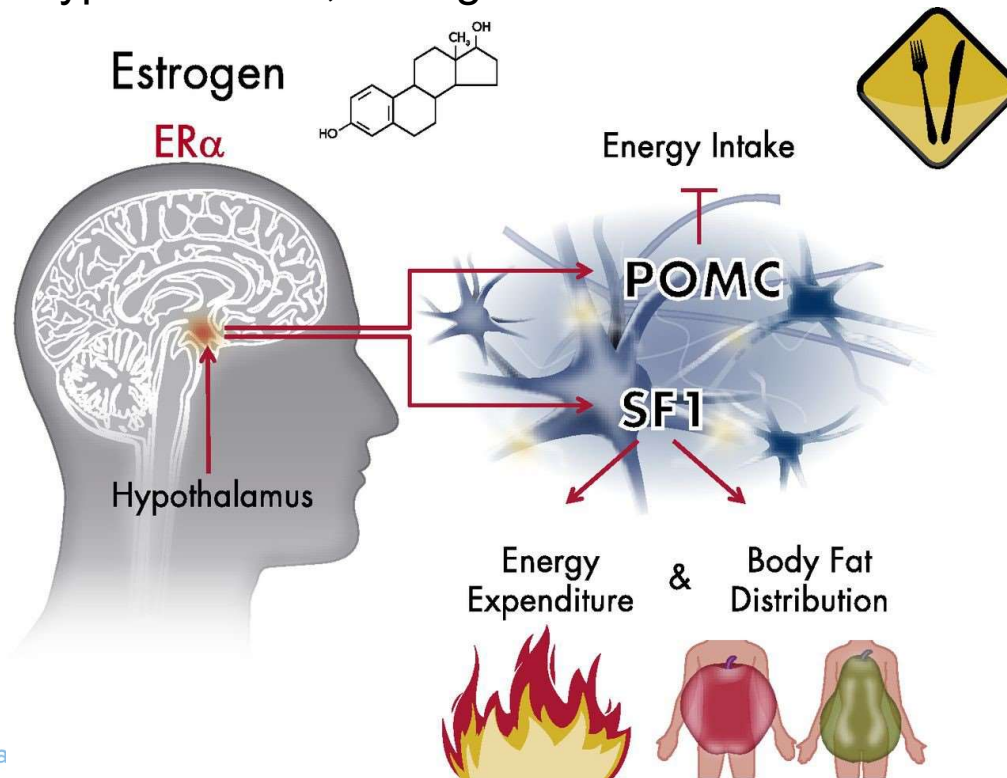
Estrogen and Energy Balance

- Estrogen acts on Ventral Medial Hypothalamus to control Energy Expenditure
- Estrogen Effects on FFA Oxidation
- Estrogens regulate the thermogenic potential of BAT
- E2 receptors alpha and beta are expressed in human VAT
- SNPs of the ER's are associated with increased risk for obesity in humans
- E2 facilitates uptake of glucose in skeletal muscle
- E2 via ER α and ER β in pancreas facilitates synthesis and release of insulin



Estrogen and Energy Balance

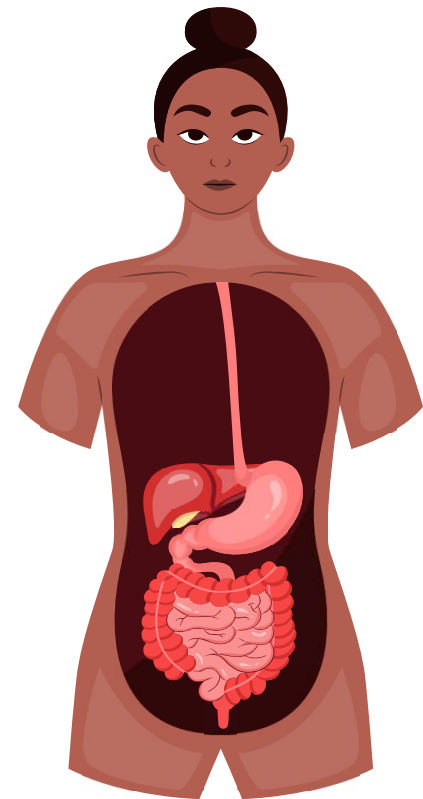
Summary of hypothalamic ER α actions regulating energy balance. In the hypothalamus, estrogen action through ...



Estrogen and Energy Balance

- Estrogen facilitates anorexigenic signals, inhibits action of orexigenic NPY (neuropeptide Y), ghrelin, and MCH (melanin concentrating hormone)
- Increases anorectic actions of leptin with direct effects on leptin sensitivity
- Increases expression of insulin receptors in adipose tissue
- Chronic stress leads to loss of protective effects of estrogen on metabolism and appetite regulation
- Gut Microbiome plays a direct role in Estrogen metabolism

Information Classification: General



Progesterone and Energy Balance

D. Rochester, A. Jain, A.J. Polotsky, H. Polotsky, K. Gibbs, B. Isaac, *et al.*

Partial recovery of luteal function after bariatric surgery

Nonpregnant women with obesity have been shown to have luteal progesterone levels in approximately 75%–80% lower than those of normal-weight women (18). Pregnant Fe women with obesity have serum progesterone levels inversely related to their BMI, and it has been postulated that this may influence the increased miscarriage rate noted among

Progesterone and Energy Balance

- In males, obesity is associated with low progesterone levels likely due to lower adrenal progesterone secretion⁽¹⁾
- Allopregnanolone^(2,3)
 - Neurosteroid progesterone metabolite
 - GABAergic effect, brain plasticity, increased depression and anxiety, feeding/hunger
 - Higher levels noted in overweight girls



Testosterone and Energy Balance

- Key hormone in the pathology of obesity⁽¹⁾
- Low T leads to
 - Increased central adiposity and sarcopenia
 - A vicious circle with exercise/motivation
 - Impaired glucose control and insulin insensitivity
 - Dyslipidemia
- Obesity leads to LowT, LowT leads to Obesity.....an unfortunate cycle
- Final outcome is disability
- REMINDER: DO NOT THINK LINEARLY.....



Testosterone and Energy Balance

- Bidirectional relationship between testosterone and obesity⁽¹⁾
- 52.4% of overweight and obese men were hypogonadal
- 75% of bariatric surgical pt men were hypogonadal⁽³⁾
- SWAN Study(pdf attchd-5):
- Negative Hypogonadal-Obesity Cycle
- The longer the cycle is present, the harder it is to reverse
- Testosterone Replacement may begin the Metabolic Repair
- That feeling of improved well being leads to.....



- Quick Note: Supraphysiologic dosing, anabolic steroid abuse decreases insulin sensitivity

Information Classification: General

Testosterone and Energy Balance

- **Testosterone and Obesity**⁽¹⁾

- Androgenic effects on enzymatic pathways of fatty acid metabolism, glucose control and energy utilization are apparent and often tissue specific with differential effects noted in different regional fat depots, muscle and liver to potentially explain the mechanisms of testosterone action.

- **Testosterone and Weight Loss in Men, 2014 Endocrinology literature**⁽²⁾

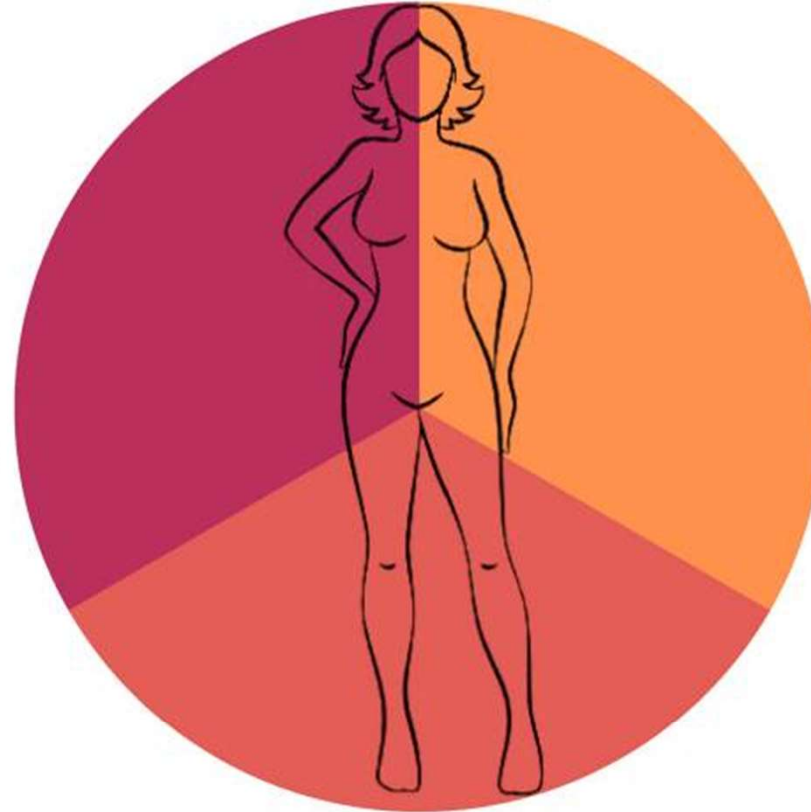
- Long term TRT in men with deficiency improves body comp/quality of life/healthspan
- Ameliorates ALL Metabolic Syndrome (MetS) components
- “TRT with or without lifestyle modifications may prove very effective and useful in the management of obesity”
- Testosterone replacement may therefore potentially be an effective adjunctive treatment for weight management in obese men with concomitant hypogonadism.

- **TRT in women: Myths and Misconceptions pdf**⁽³⁾

Weight Gain during Menopausal Transition

Hormonal Factors

- Decrease in Estradiol and Estrogen (E2)
- Increase in Visceral Adipose Tissue
- Increase in Ghrelin
- Decrease in Testosterone
- Decrease in Progesterone



Age-Related Factors

- Subcutaneous Adipose Tissue
- Decrease in RMR
- Decrease in Energy Expenditure
- Earlier Final Menstruation Period
- Early Onset Menopause
- Decrease in Lean Muscle Mass

Lifestyle Factors

- Physical Activity
 - Diet
 - Evening Chronotype
 - Smoking
 - Alcohol Intake
-

Menopause and Energy Balance

- It is NOT just about the hormone levels!
- Androgen excess and higher Test/E2 ratios promotes VAT distribution^(1,2)
- Androgen replacement in obese women produces greater weight loss and maintenance of lean mass⁽³⁾
- Testosterone is Breast Protective in post menopausal women

C. Dimitrakakis, R.A. Jones, A. Liu, C.A. Bondy

Breast cancer incidence in postmenopausal women using testosterone in addition to usual hormone therapy

Menopause, 11 (2004), pp. 531-535

Menopause and Energy Balance

- Low free or low bioavailable testosterone is associated with loss of lean mass in women⁽¹⁾
- Levels of T are inversely associated with.....
 - VAT, Subcutaneous and Pericardial, Skeletal Muscle Fat
 - Hepatic Fat Creep.....




COMMENTARY |

 Open Access




Weight gain during the menopause transition: Evidence for a mechanism dependent on protein leverage

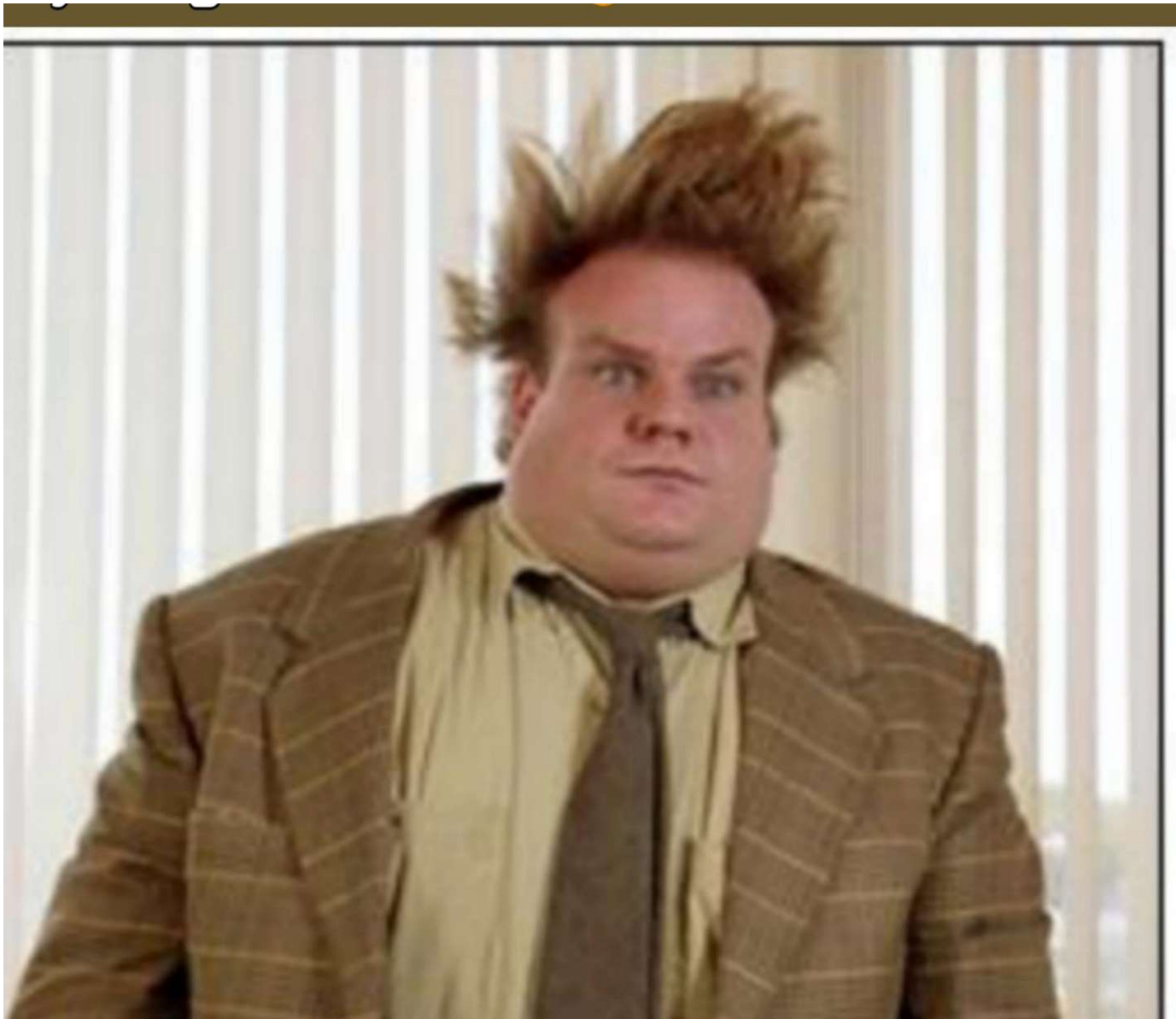
Stephen J. Simpson, David Raubenheimer, Kirsten I. Black, Arthur D. Conigrave 

First published: 08 September 2022 | <https://doi.org/10.1111/1471-0528.17290> | Citations: 2

YOU CAN'T
OUT-EXERCISE



A BAD  DIET.



Nutrition and Hormones

- Diet changes Hormone Production and Response, supplement effects⁽¹⁾
- Epigenetic change takes time.....Both Ways



Things I Did Not Talk About



- A Lot.... Starting with Menopause and Weight/Obesity, HRT details
- Supplements/micronutrients/herbs affecting hormones (i.e ashwagandha, etc.) ⁽⁷⁾
- Endocrine Disruptors found in diet and effects on hormone production and response^(1,2)
- Gut Health and Hormones^(6,7)
- Metabolic Flexibility
- **Hormone Lab Values Optimal vs Reference range: HANDOUT Included**
- Hormones found in foods and potential health effects⁽⁴⁾
- **“Food as a Hormone”** ⁽⁵⁾
- **ASK YOUR QUESTIONS AT THE PANEL DISCUSSION**

Information Classification: General

WHY I GIVE THIS LECTURE



- Every mistake the system and providers could make was made with her.

WHY I GIVE THIS LECTURE



Summary, Pearls, Takeaways

- Focus on EARLY ID and Aggressive Management of IR
- Estrogen and Testosterone play a direct and powerful role in weight loss/METABOLIC REPAIR
- Testosterone plays a direct role in metabolic Repair/Wt Loss in women
- Introduce Diet, Nutrition, Purposeful Supplementation EARLY in Hormone Discussion
- Manage HPA Axis Allostatic Load via DIET first then.....
- The Need for Sex/Gender/Age-Specific Studies in Nutrition and Hormones
- LOOK AT BONUS SLIDES IN SLIDE DECK!!!!



AFTER LECTURE IS DONE>>>>>.....



Thank You!!



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Focused Pearls: GET ONE NOW @BenGonzalez_MD

- Practical Testing: More than just fasting glucose and HbA1c
- HOMA-IR
- LabCorp: NMR LipoProfile with Lipids (123638) has IR score*
- Quest: Cardio IQ IR Panel w/Score(36509)
- Fasting Insulin, Triglycerides, Apolipoprotein B, Homocysteine
- **Antioxidant Screening**: The Most Efficient Way to Bring the Conversation of Nutrition to the Patient
- **Critique This Study**:
<https://jamanetwork.com/journals/jama/article-abstract/195531>



There is a Difference!

Same Diets Given to Men and Women

BODY FAT

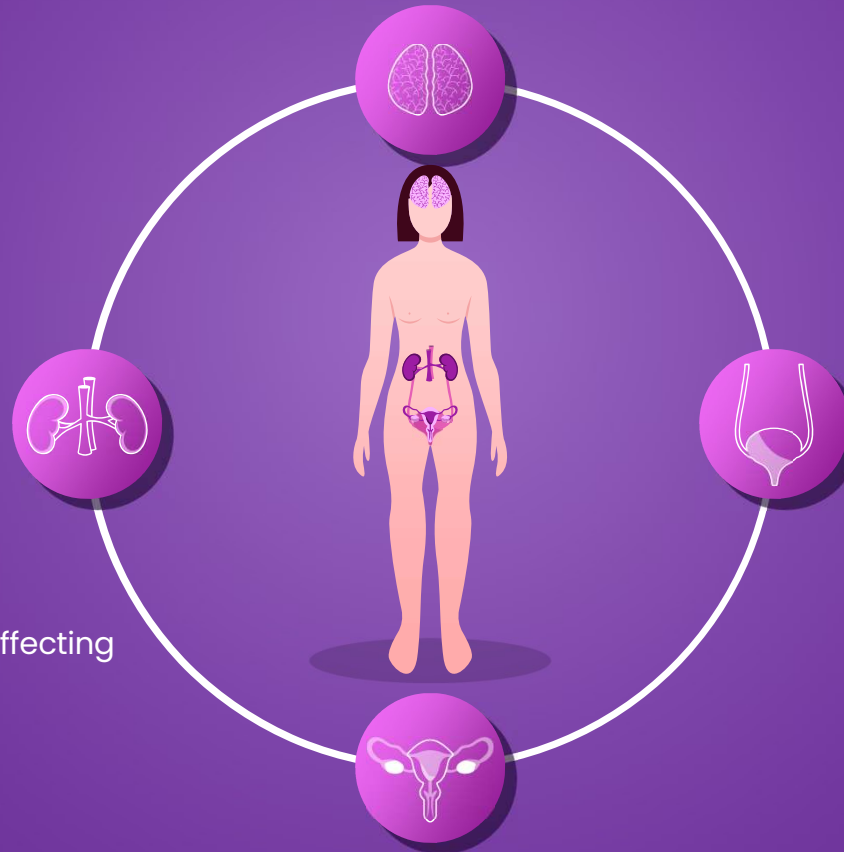
- ~Inflammatory and Hormonal Response
- ~Body Heat Dissipation
- ~Women consume fewer kJ/kg and IR and leptin response differences

Postprandial Metabolism

- ~Glucose and fat oxidation
- ~Exogenous Estrogens induces reduction of postprandial FFA oxidation

DIETS

- ~Gender Differences Not Well Studied
- ~Early Overnutrition Sensitizes GH Axis affecting long-term obesity
- ~Weight Loss Studied, Maintenance Not
- ~HLC vs HLF Diets Gender Differences (Men Lose more BF on HLC) (3)



EXERCISE

- ~Burn more fat during exercise
- ~Higher Fat:Glucose Burn Rate Yet.....
- ~YET..Women lose less fat than Men with same energy deficit
- ~More efficient fat storage in non-exercise periods
- ~Higher Fat Mass allows for preferential use while exercising
- ~METABOLIC FLEXIBILITY

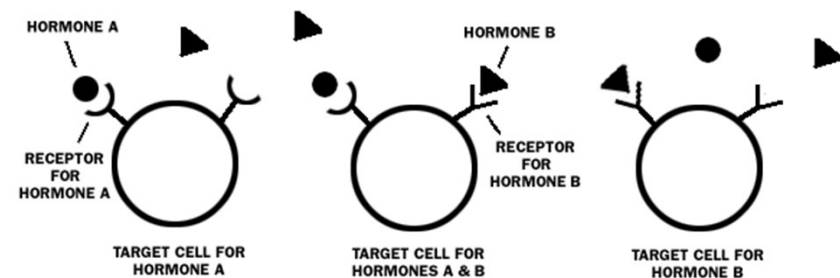
SEX HORMONES

- ~Estrogen Effects on FFA Oxidation
- ~Exogenous vs Endogenous E2 Effects
- ~Hormonal Disruption of liberal statin use
- ~Gender Differences in Metabolism: Nutrition and Supplements*****

Hormones and Metabolism

□ GOOD REVIEW SLIDE FOR OBESITY BOARDS

- **GI peptides** relay short term signals triggering meal termination
 - Cholecystokinin(CCK), peptide YY(PYY), pancreatic polypeptide(PP)
 - Oxyntomodulin(OXM)
 - Incretins: Gastric inhib polypeptide/glucose-dependent insulinotropic polypeptide (GIP)
 - Glucagon-like peptide 1 (GLP-1)
 - Ghrelin –appetite stim hormone in gastric fundus
 - Acts primarily on NPY and AgRP/ARC
- Insulin and leptin primarily deliver long term info to CNS
- Insulin-CNS vs Insulin-Arcuate Nucleus: READ THE NOTES



WHAT IS HAPPENING?

• Antioxidants and Hormones

- Testosterone production
- Infertility

Conclusion

The research draws attention to the alternate treatment approaches in infertile men. Antioxidant treatment can increase the serum sex hormone levels.

Conclusions: These findings shed new light on the intricate associations between serum antioxidants and endogenous hormones in healthy premenopausal women and support the hypothesis that concentrations of serum vitamins affect steroidogenesis even after adjustment for oxidative stress.

Do antioxidants improve serum sex hormones and total motile sperm count in idiopathic infertile men?

[Barış Saylam^{#1}](#) and [Selahittin Çayan²](#)

[▶ Author information](#) [▶ Article notes](#) [▶ Copyright and License information](#) [▶ Disclaimer](#)



Go to:

lance that
: This study
erm parameters

WHY???

- The Body is TRAINED to be Efficient in Burning Glucose
- Mitochondrial Dysfunction: Reduced FFA Oxidation
- The SHIFT is towards Oxidizing Carbs
- RESULT?
 - The accumulation of IM lipids
 - Diacylglycerols (DAG), ceramides (Cer), long-chain acyl-CoAs
- Mitochondrial mass, structure, function altered by IR
- IR Begins Years Prior to the Dx of T2DM
 - If you are IR you have a higher RQ
 - Long term higher RQ = persistently sick mitochondria
- Metabolic Inflexibility:

Information Classification: General

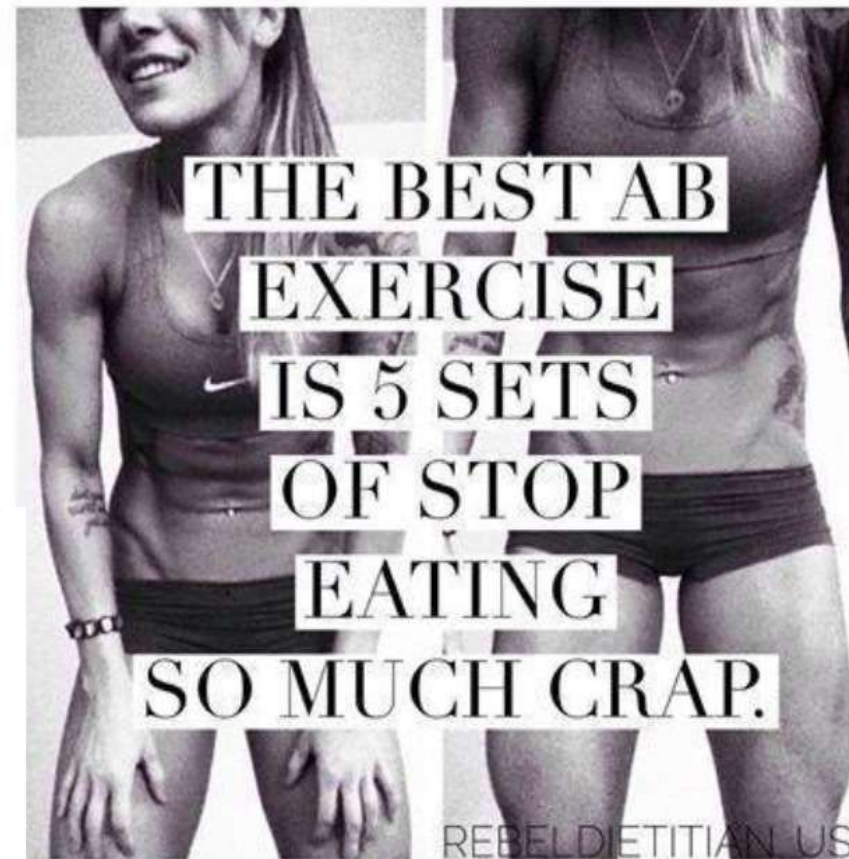


METABOLIC FLEXIBILITY

- **Ability to Adapt to Different Fuel Selections**
- **Physically Active with Healthy Mitochondria**
 - Increased Fat Intake, Body RQ Drops
 - Fasting?...You burn more fat
- **Overweight/Obese or Inactive?**
 - More Fat Intake, More Fat Storage
- **Metabolic Flexibility and IR**

Acute lipid oversupply during hyperinsulinemia reveals metabolic flexibility in trained compared to untrained subjects

During a hyperinsulinemic-euglycemic "glucose" clamp without (light bars) or with (dark bars) co-infusion of intralipid, trained subjects decrease glucose oxidation (green bars), increase fatty acid oxidation (yellow bars) and preserve muscle glycogen storage (red bars) relative to untrained subjects, who exhibit metabolic *inflexibility*. In other words, untrained subjects do not effectively decrease glucose oxidation or increase fatty acid oxidation, and they have diminished glycogen storage in the face of lipid overload. Data were obtained from (Dube et al., 2014).



What the Patient is Fighting

□ Hedonic Override⁽¹⁾

- The drive to eat highly palatable foods distinct from homeostatic hunger
- Our brain is positively stimulated by availability of food, fast, calorie dense, easily absorbed and stored food



Obesogenic Rat Food

Protein: 16%
Fat: 44%
Carbs: 40%



Average U.S. Diet

Protein: 15%
Fat: 35%
Carbs: 50%

Rising Sea Levels – An Alternative Theory

Antioxidants and Hormones

- Antioxidants play a powerful role in IR
- You Must MEASURE and be PURPOSEFUL
- Full pdf 2015 Review of Antioxidant Supplementation in Obesity and Diabetes
- Research-to-Date Does not support the consensus that antioxidant treatment is primary solution.....HOWEVER

[Redox Biol.](#) 2021 Aug; 44: 102005.

Published online 2021 May 18. doi: [10.1016/j.redox.2021.102005](https://doi.org/10.1016/j.redox.2021.102005)



PMCID: [PMC8167146](#)

PMID: [34049222](#)

Reactive oxygen species in exercise and insulin resistance: Working towards personalized antioxidant treatment

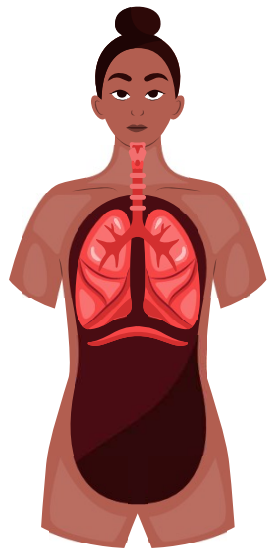
[Kathryn McKeegan](#)^a, [Shaun A. Mason](#)^a, [Adam J. Trewin](#)^a, [Michelle A. Keske](#)^a, [Glenn D. Wadley](#)^a,
[Paul A. Della Gatta](#)^a, [Michalis G. Nikolaidis](#)^b and [Lewan Parker](#)^{a,*}



[Information on this section of the site](#) **You MUST MEASURE!!!**

Gender Bias in Medicine

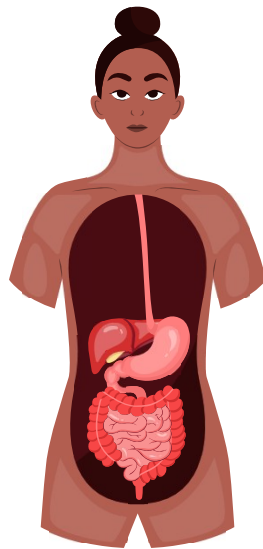
There Is a Difference!



Reduced O₂ Carrying Capacity

No difference in CV Adaptations to Aerobic Training

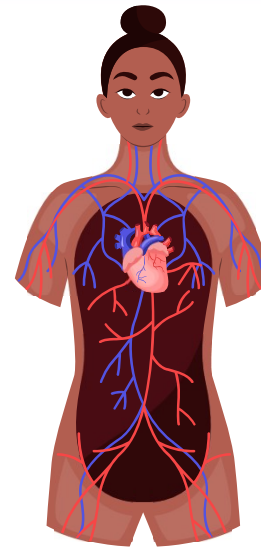
Information Classification: General



Pharmacokinetics

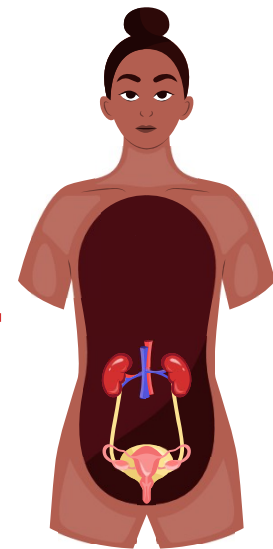
"Standard" Drug Dosage

↑ Blood Concentrations
↑ Elimination Times
i.e. MTX clears 13-17% slower



Ion Channels

Heart/kidney react differently to renal/cardia specific medications (digitalis/ACE inhibitors/anti-arrhythmics)
(ACC 2015 Discussion)



Hormonal Response

Estrogen effects on liver

Summary and Pearls

- **Related and Referenced Subject pdfs**

- **ASA Use** <https://heart.bmj.com/content/heartjnl/101/5/369.full.pdf>
- **Gender and CV Pharmacotherapeutics:** <https://onlinelibrary.wiley.com/doi/epdf/10.1111/j.1527-5299.2005.04171.x>
- **Gender Differences in Energy Metabolism/Lifestyle Modifications:** <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3136178/pdf/JNUME2011-391809.pdf>
- **Participation to Prevalence Ratio (PPR) reference:** <https://reader.elsevier.com/reader/sd/pii/S0735109718336258?token=E3039940D41346006EFF0F0C4D57E370EC53AA0A55D4845A555FC2D2AA24FD1178AC5075ECEE7BD5E074CE6B3CD84801&originRegion=us-east-1&originCreation=20211009185304>
- **Gender Differences in Weight Loss Studies:** <https://www.nature.com/articles/s41366-020-00708-y.pdf>
- **JUPITER: a Few Words of Caution (2009):** <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2798141/pdf/nihms126612.pdf>
- **Gender differences in coronary heart disease (2010):** <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3018605/pdf/nhj1859800.pdf>
- **Estrogen Replacement Therapy Induces Antioxidant and Longevity-Related Genes in Women after Medically Induced Menopause**
<https://jamanetwork.com/journals/jama/article-abstract/195531>

Information Classification: General



Cholesterol Based Hormones: A Word

□ Reminders:

□ Sex Hormones

- Steroid Hormones (cholesterol based thus lipid soluble)
 - Effects are primarily intercellular
 - Androgens, estrogens, progestogens (progesterone)
 - Dehydroepiandrosterone (DHEA-S)
 - Vitamin D (sterol converted in body to steroid))

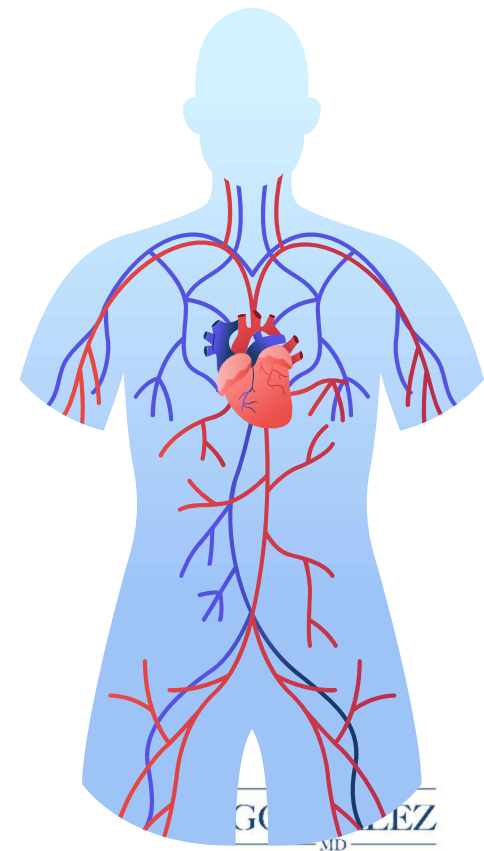
□ Liberal use of statins affects sex hormones

- JUPITER Study did not really show benefit of statins for women yet “highly recommended”
- Think about sex hormone disruption
- May help with PCOS.....

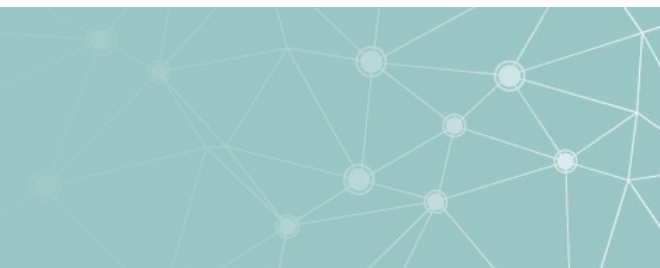
Gender Bias in Medicine

CVD

- CVD diagnostic tools Designed, Developed, and Researched for Male Patients
- **Women under age 55 are 7 times more likely to be misdiagnosed in mid-heart attack in ER**
- JUPITER “pro-statin” 2008 Study showed NO Benefit for Women
 - YET...The authors know this they still recommend that HEALTHY Women with no hx of heart disease should still take statins for primary prevention
- AHA Did not formally acknowledge gender differences until 2016



Gender Bias in Medicine



• Sex Differences in Disease Management

Sex and gender differences in health(2017): <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3388783/>

- Women with myocardial infarction receive less guideline-based diagnosis and less-invasive treatment than men [3].
- Women with heart failure receive fewer guideline-based diagnostic procedures and treatments, and fewer implantations and heart transplantations. Women have a better outcome than men [54].
- Women with atrial fibrillation receive less anticoagulation treatment with warfarin. Even so, they have a greater risk for stroke than men [51].
- Women obtain dialysis later than men, and undergo fewer kidney transplants, both from living and deceased donors [52,53].
- There is a significant delay in referral of female patients with rheumatoid arthritis to an early arthritis clinic in comparison with male patients [15].
- Osteoporosis and depression are considered female diseases. Both might be under-diagnosed in men [16].

Information Classification: General

BENJAMIN
GONZÁLEZ
MD

Discussions/Resources

- **Justice and the Inclusion of Women in Clinical Studies: A Conceptual Framework:**
<https://www.ncbi.nlm.nih.gov/books/NBK236575/> (SADLY: A 1999 Publication)
- **Applying a Women's Health Lens to the Study of the Aging Brain:**
<https://www.frontiersin.org/articles/10.3389/fnhum.2019.00224/full> (2019)
- ***Sex Matters***: Alyson McGregor, MD
- ***Invisible Women***: Caroline Criado Perez
- **NIH Office of Research on Women's Health:** <https://orwh.od.nih.gov/>

Top DrG Tips

- ❑ **Simply Ask EXACTLY what your patient eats**
- ❑ **Encourage Plant Based in the beginning**
- ❑ **Encourage Mindfulness**
- ❑ **Establish Rescue and Panic Weight**
- ❑ **Choose ONE Thing at a Time to change**
- ❑ **Eliminate “The Biggest Loser” Mentality**
- ❑ **Change Snacks**
- ❑ **Have A Rescue Plan**
- ❑ **Follow up, Follow up, Follow up, Follow up**

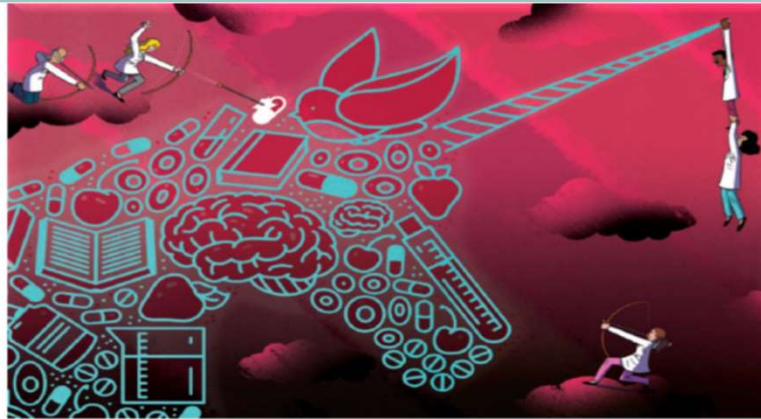
**“Research is to see what
everybody else has seen,
and to think what nobody
else has thought”**

***Albert Szent-Gyorgyi
1937 Nobel Prize for Medicine***

21 Day Healthy Challenge



Science Myths that JUST WON'T DIE



Myths *that will not die*

False beliefs and wishful thinking about the human experience are common. They are hurting people — and holding back science.

BY MEGAN SCUDELLARI

In 1997, physicians in southwest Korea began to offer ultrasound screening for early detection of thyroid cancer. News of the programme spread, and soon physicians around the region began to offer the service. Eventually it went nationwide, piggybacking on a government initiative to screen for other cancers. Hundreds of thousands took the test for just US\$30–50.

Across the country, detection of thyroid cancer soared, from 5 cases per 100,000 people in 1999 to 70 per 100,000 in 2011. Two-thirds

of those diagnosed had their thyroid glands removed and were placed on lifelong drug regimens, both of which carry risks.

Such a costly and extensive public-health programme might be expected to save lives. But this one did not. Thyroid cancer is now the most common type of cancer diagnosed in South Korea, but the number of people who die from it has remained exactly the same — about 1 per 100,000. Even when some physicians in Korea realized this, and suggested that thyroid screening be stopped in 2014, the Korean

322 | NATURE | VOL 528 | 17 DECEMBER 2015

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Information Classification: General

Nature 528, 322–325 (17 December 2015)

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GONZÁLEZ
MD

Targeted Supplements for hormonal-based Approach to IMPROVED METABOLISM and SUSTAINED WEIGHT LOSS

- Glucose Regulation, Dopamine and Serotonin support, Improving thermogenesis and lipolysis (fat burning), Cortisol/Stress management, Thyroid support, Sex hormone support
- Misc. Metabolic Management – detoxification, gut support, sleep improvement, inflammatory control, improved lipid profile
- **The following information/ 18 slides are updated from lectures on supplements and nutraceuticals in metabolism management given by James B. LaValle R.Ph, CCN, Co-Chair A4M/MMI**

Dopamine and Serotonin Support

- **THEACRINE:**
- Binds to Adenosine receptors – decreased adenosine levels
- Improves Focus and Concentration
- Does not habituate in doses up to 300mg/day
- Reported to improve dopamine levels
- Modulates other neurotransmitters
- Decreases ROS and Inflammatory Cytokines centrally
 - Journal of the International Society of Sports Nutrition 2014, 11(Suppl 1):P49
 - Zheng et al. Phytochemistry. 2002;60:129-134

Dopamine and Serotonin Support

- **MUCUNA:**

- From the seed of *Mucuna pruriens*

- Velvet Bean

- Contains high amount of L-DOPA

- Improves dopamine pool

- Helps improve the reward cascade

- Helps improve satiety

- - Shukla KK, Mahdi AA, Ahmad MK, et al. Mucuna pruriens improves male fertility by its action on the hypothalamus-pituitary-gonadal axis. Fertil Steril. 2009;92(6):1934-40.

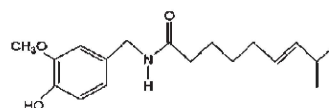
- - Katzenschlager R, Evans A, Manson A, et al. Mucuna pruriens in parkinson's disease: a double-blind clinical and pharmacological study. J Neurol Neurosurg Psychiatry. 2004;75(12):1672-7.

Dopamine and Serotonin Support

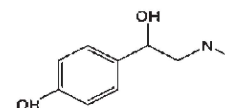
- **5-hydroxytryptophan:**

- Amino acid precursor for serotonin
 - Manufactured from L-tryptophan
 - Supports serotonin pools
 - Reported to reduce carbohydrate cravings and improve weight loss
 - Helps with mood stabilization
 - 50-100mg tid
-
- Birdsall, T. C. 1998. 5-Hydroxytryptophan: a clinically-effective serotonin precursor. *Alternative Medicine Review* 3: 271-280
 - Cangiano C, et al 1991. Effects of 5-hydroxytryptophan on eating behavior and adherence to dietary prescriptions in obese adult subjects. *Adv Exp Biol Med* 294 ("Kynurenine and Serotonin Pathways"): 591-593

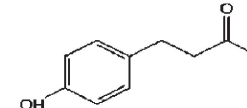
Metabolic and Weight Management Support



Capsaicin



Synephrine



Raspberry ketone (RK)

- **Raspberry Ketones:**

- RK lab studies report thermogenics properties and improved lipid metabolism of adipocytes
- In-vitro inhibition of adipogenic and lipogenic gene expression
- Also may decrease fat absorption from small intestine
- Increases Norepinephrine
- Dosage 100 to 150 mg bid-tid

- **POOR STUDY..GOOD REVIEW2015:** https://etd.ohiolink.edu/apexprod/rws_etd/send_file/send?accession=oduhonors1430845300&disposition=inline
- **UPDATE - GREAT DISCUSSION..GREAT REVIEW:** Pharmacological Exploration of Phenolic Compound: Raspberry Ketone—Update 2020
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8309185/>
- Morimoto C, Satoh Y, Hara M, et al. Anti-obese action of raspberry ketone. Life Sci. 2005 May 27;77(2):194-204. Epub 2005 Feb 25.
- Park KS. Raspberry ketone increases both lipolysis and fatty acid oxidation in 3T3-L1 adipocytes. Planta Med. 2010;76:1654-58.
- Park KS. Raspberry ketone, a naturally occurring phenolic compound, inhibits adipogenic and lipogenic gene expression in 3T3-L1 adipocytes. Pharm Biol. 2015;53(6):870-5

Glucose Regulation and Support

- **Chromium:**

- Important in insulin regulation and blood sugar control
- Metabolism of carbs and fats
- High sugar diet (>35% of calories) can increase chromium excretion in the urine
- Low chromium levels = increased risk for insulin resistance **and** Type 2 diabetes
- A 2007 systematic review of 41 human trials reported Chromium supplementation significantly improved glycemic response among patients with diabetes

Docherty JP, et al. A double-blind, placebo-controlled, exploratory trial of chromium picolinate in atypical depression: effect on carbohydrate craving. J Psychiatr Pract. 2005 Sep;11(5):302-14.

Lau FC, et al. Nutrigenomic basis of beneficial effects of chromium(III) on obesity and diabetes. Mol Cell Biochem. 2008 Oct; 317(1-2):1-10. Epub 2008 Jul 18. Review.

Lau FC, et al. [Nutrigenomic basis of beneficial effects of chromium\(III\) on obesity and diabetes](#). Mol Cell Biochem. 2008 Oct;317(1-2):1-10. Epub 2008 Jul 18. Review.

Vincent J. The biochemistry of chromium. Journal of Nutrition. 2000;130:715-718.

Glucose regulation and support

- **Chromium:**
- Randomized, double-blind, placebo-controlled study in 447 poorly managed, overweight/obese Type 2 diabetics
- Pts. administered chromium (600mcg, picolinate) + biotin (2mg) + oral hypoglycemic meds x 90 days
- Pts. using supplements reported:
 - ↓ HbA(1c)
 - ↓ FBS
 - ↑ Glycemic control

Albarracin CA, et al. Chromium picolinate and biotin combination improves glucose metabolism in treated, uncontrolled overweight to obese patients with type 2 diabetes. *Diabetes Metab Res Rev.* 2008 Jan-Feb;24(1):41-51.

Glucose regulation and support

- **Alpha Lipoic Acid (ALA):**
- Mixed racemic, Antioxidant, Improves Detoxification (including heavy metals)
- Improve insulin sensitivity, glycemic control, Reduce incidence/symptoms of neuropathies
- Affects beta cell function
- ↑cAMP-activated protein kinase (AMPK)
- ↑ PGC-1 alpha, ↑ PPAR alpha
- Improves glucose utilization and mitochondrial biogenesis
- Studies report exercise and ALA therapy improves IRS-1 dependent insulin signaling

Henriksen EJ. Exercise training and the antioxidant alpha-lipoic acid in the treatment of insulin resistance and type 2 diabetes. *Free Radic Biol Med.* 2006 Jan 1;40(1):3-12. Review.

Padmalayam I, Hasham S, Saxena U, Pillarisetti S. Lipoic acid synthase (LASY): a novel role in inflammation, mitochondrial function, and insulin resistance. *Informa Diabetes.* 2009 Mar;58(3):600-8.

Glucose regulation and support

- **Alpha Lipoic Acid (ALA) - 2020 UPDATE:** Improved insulin sensitivity, glycemic control in women with PCOS
 - “.....the combination of ALA and MI showed to be useful as long-term therapy in PCOS women, providing a normalization of the menstrual cycle and an amelioration of insulin levels with a high tolerability.”
-
- Clinical and Metabolic Effects of Alpha-Lipoic Acid Associated with Two Different Doses of Myo-Inositol in Women with Polycystic Ovary Syndrome: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7106925/>
 - Long-term treatment with α -lipoic acid and myo-inositol positively affects clinical and metabolic features of polycystic ovary syndrome: <https://pubmed.ncbi.nlm.nih.gov/31317814/>

Glucose regulation and support

- **OTHER:**

- **Benfotiamine:** Lipid soluble form of vitamin B1 (thiamin), helps improve glucose regulation and insulin sensitivity

Alkhalaf A, Kleefstra N, Groenier KH, et al. Effect of benfotiamine on advanced glycation endproducts and markers of endothelial dysfunction and inflammation in diabetic nephropathy. *PLoS One*. 2012;7(7):e40427.

Stirban A, Negrean M, Stratmann B, et al. Benfotiamine prevents macro- and microvascular endothelial dysfunction and oxidative stress following a meal rich in advanced glycation end products in individuals with type 2 diabetes. *Diabetes Care*. 2006;29(9):2064-71.

- **Pyroloquinoline quinone:** Antioxidant and redox cofactor, improves insulin signaling and glucose tolerance

Misra HS, Raipurohit YS, Khairnar NP. Pyrroloquinoline-quinone and its versatile roles in biological processes. *J Biosci*. 2012;37(2):313-25.


- Contains isoflavone compounds
 - Puerarin – major constituent
 - Formononetin
 - Genistin
 - Genistein
 - Daidzin
 - Daidzein
- Constituents similar to those found in red clover, soy and black cohosh
- Estrogen receptor modulation



Kudzu (*Pueraria lobata*) root

- Zhang Z, Lam TN, Zuo Z. Radix Puerariae: an overview of its chemistry, pharmacology, pharmacokinetics and clinical use. J Clin Pharmacol. 2013;53(8):787-811.

Information Classification: G Zhang YB, Chen WH, Guo JJ, et al. Soy isoflavone supplementation could reduce body weight and improve glucose metabolism in non-Asian postmenopausal women – a meta-analysis. Nutrition. 2013;29(1):8-14.

- 
- Studies support improvement in cycle
 - Reduced cardiovascular risk
 - Reduced estradiol
 - **Decrease aromatization of estradiol**
 - Increased SHBG in low SHBG women
 - Decreased cancer risk
 - Improved bone density

Isoflavones in Kudzu

- Kumar NB, Cantor A, Allen K, et al. The specific role of isoflavones on estrogen metabolism in premenopausal women. *Cancer*. 2002;94(4):1166-1174.
- Alekel DL, van Loan MD, Koehler KJ, et al. The soy isoflavones for reducing bone loss (SIRBL) study: A 3-y randomized controlled trial in postmenopausal women. *Am. J. Clin. Nutr.* 2010;91:218-230.

Kudzu root

- Reported to interact with PPAR- γ and PPAR- α

Jungbauer A, Medjakovic S. Phytoestrogens and the metabolic syndrome. *J Steroid Biochem Mol Biol*. 2013;[Epub ahead of print].

- May help improve symptoms of metabolic syndrome

- Antioxidant/antiinflammatory (COX-2)

Bebrevska L, Foubert K, Hermans N, et al. In vivo antioxidative activity of a quantified lobata root extract. *J Ethnopharmacol*. 2010;127(1):112-7.

Pueraria

DIM (diindolylmethane)

- Found in cruciferous veggies
- Helps convert active estrogens into 2-hydroxyestrone
- May act as weak estrogen



Wang TT, Milner MJ, Milner JA, Kim YS. Estrogen receptor alpha as a target for indole-3-carbinol. *J Nutr Biochem.* 2006;17(10):659-64.

DIM (diindolylmethane)

- May also help improve free testosterone levels

Garikapaty VP, Ashok BT, Tadi K, et al. 3,3'-diindolylmethane downregulates pro-survival pathway hormone independent prostate cancer. *Biochem Biophys Res Commun.* 2006;340(2):718-25.

- Decreased risk of hormonally related cancers, including breast, prostate and thyroid

Eurycoma (*Eurycoma longifolia*) root

- Tongkat ali or “Malaysian ginseng” - used in SE Asian cultures for improved testosterone levels, libido
- Reported to improve testosterone levels (free and total) in men and women
- Also improves testosterone/cortisol ratio



Eurycoma (*Eurycoma longifolia*) root

- Quassinoids - major phytochemical compounds
- Laboratory studies:
 - Aromatase inhibition
 - At high concentration may also have phosphodiesterase inhibiting properties
- Helps stimulate osteoblast proliferation and osteoclast apoptosis

Eurycoma (*Eurycoma longifolia*) root

- 2013 study (n=25; 13 men, 12 women; ages 52-72)
- 400mg standardized water extract of Eurycoma QD x 5 weeks
- Significant increases in total and free testosterone
- Significant declines in SHBG
- Improved muscular force

Henkel RR, Wang R, Bassett SH, et al. Tongkat ali as a potential herbal supplement for physically active male and female seniors-A pilot study. *Phytother Res.* 2013;[Epub ahead of print].

Eurycoma (*Eurycoma longifolia*) root

- 2013 clinical trial
- N=63 men and women
- 200 mg QD standardized water extract for 4 weeks
- 37 % decrease in cortisol levels
- 16% increase in testosterone levels
- Reduced symptoms:
 - -11% stress
 - -15% confusion
 - -12% anger

Talbott SM, Talbott JA, George A, et al. Effect of Tongkat Ali on stress hormones and psychological mood state in moderately stressed subjects. J Int Soc Sports Nutr. 2013;10(1):28.

Eurycoma (*Eurycoma longifolia*) root

- 2012 randomized, double-blind, placebo controlled parallel group study (n=109 men; ages 30-55)
- 300 mg QD *Eurycoma* root standardized water extract for 12 weeks
- Reported improvements in erection, sexual libido, sperm motility and semen volume
- A significant improvement in fat mass was also reported in subjects with a BMI ≥ 25 .

Ismail SB, Wan Mohammad WM, George A, et al. Randomized Clinical Trial on the Use of Physta Freeze-dried Water Extract of Eurycoma longifolia for the Improvement of Quality of Life and Sexual Well-Being in Men. Evid Based Complement Alternat Med. 2012;2012:429268.