New Understandings of Polycystic Ovary Disease (PCOS): Skin and Hair

Felice L. Gersh, MD

Medical Director, Integrative Medical Group of Irvine

Consultative Faculty, Fellowship in Integrative Medicine

University of Arizona School of Medicine

Women's Optimal Health (including skin and hair) = Optimized Hormones + Optimized Lifestyle

Prime Directive of Life:

Reproduction and survival

and then to repeat the process …

it's all about the process of making and raising babies!

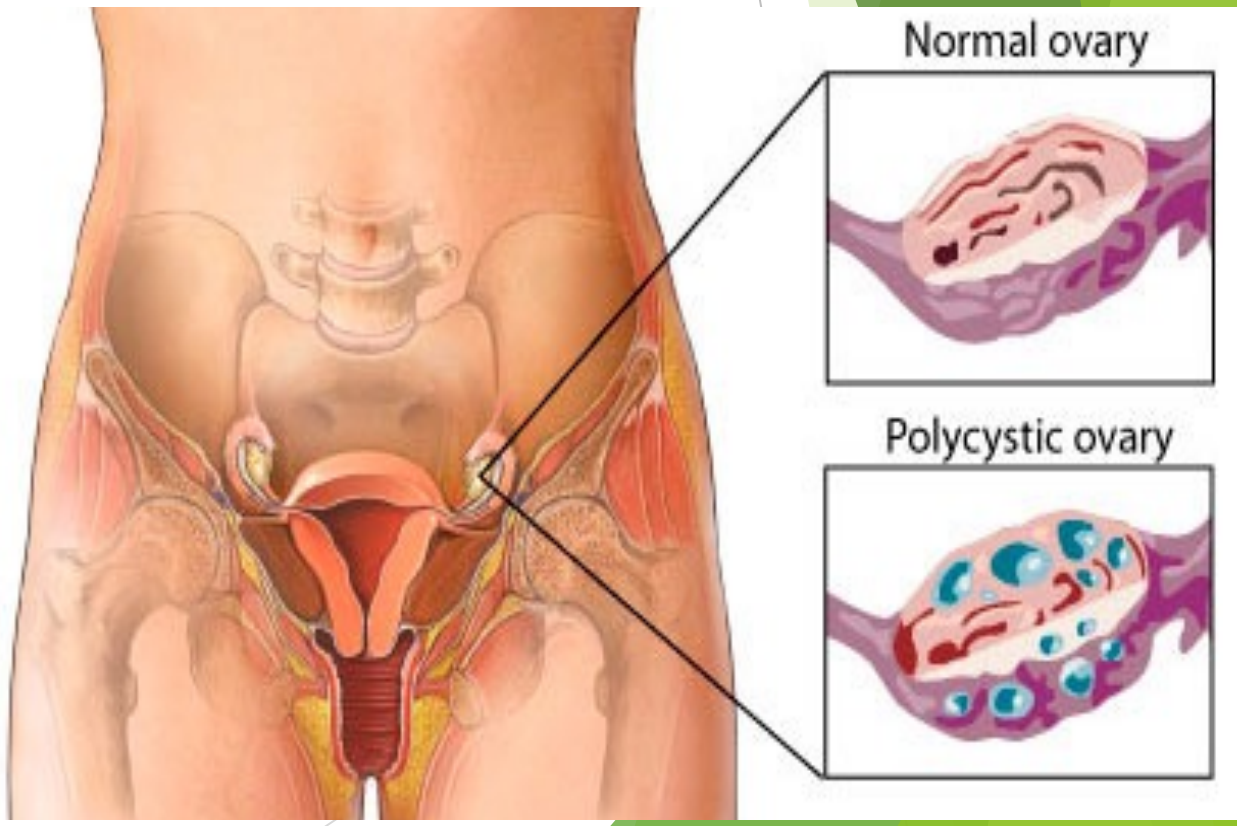
What's Changed?

Nestler JE. *N Engl J Med*. 2008; 358: 47-54.

Polycystic Ovary Syndrome (PCOS)

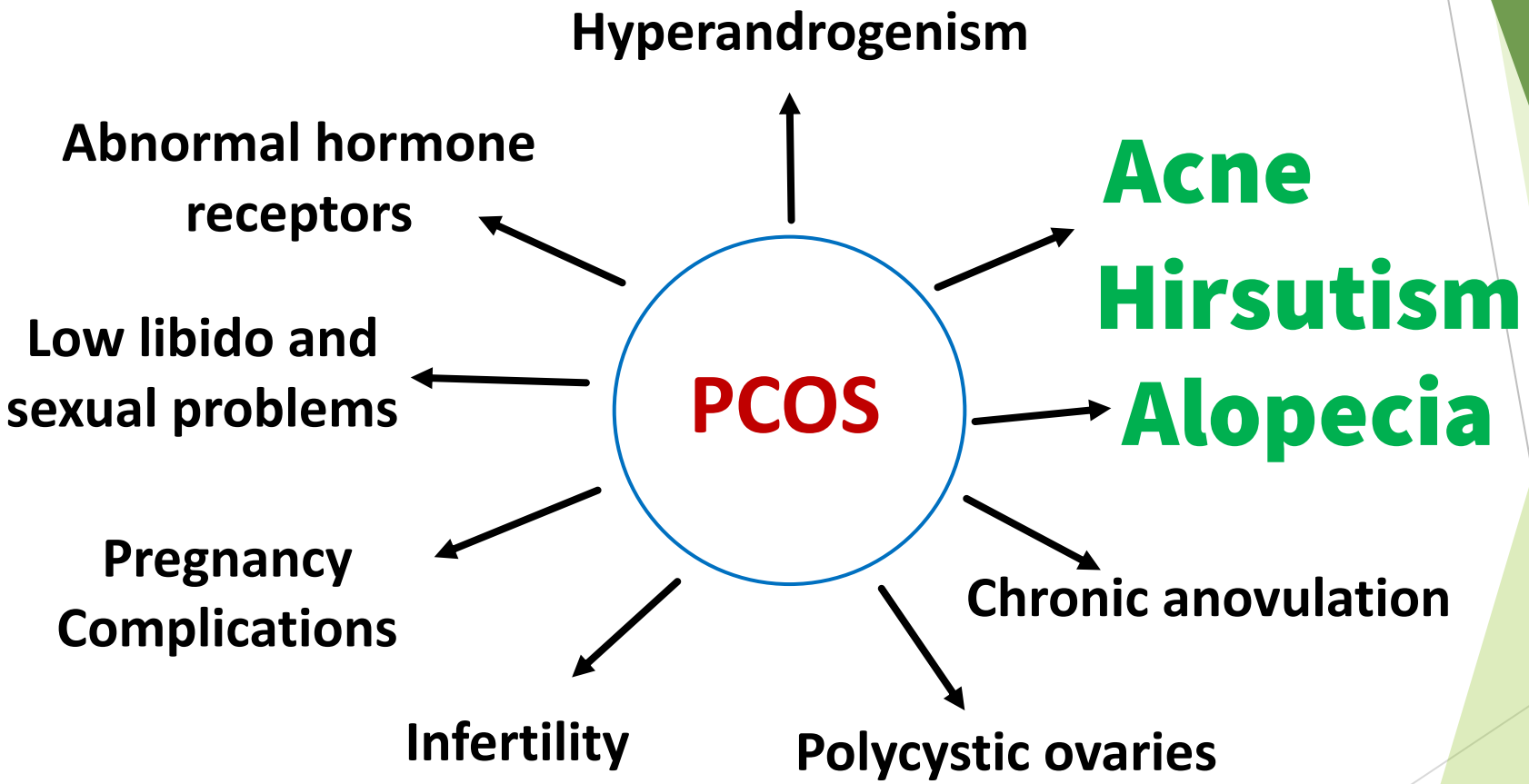
Blending the Role of Hormones, Circadian Rhythm, Environmental Toxicants, and Cardio-Metabolic Health

- A hormonal disorder, becoming obvious after puberty
- Characterized by the proliferation of small cysts in the ovaries
- The most common endocrine dysfunction of women

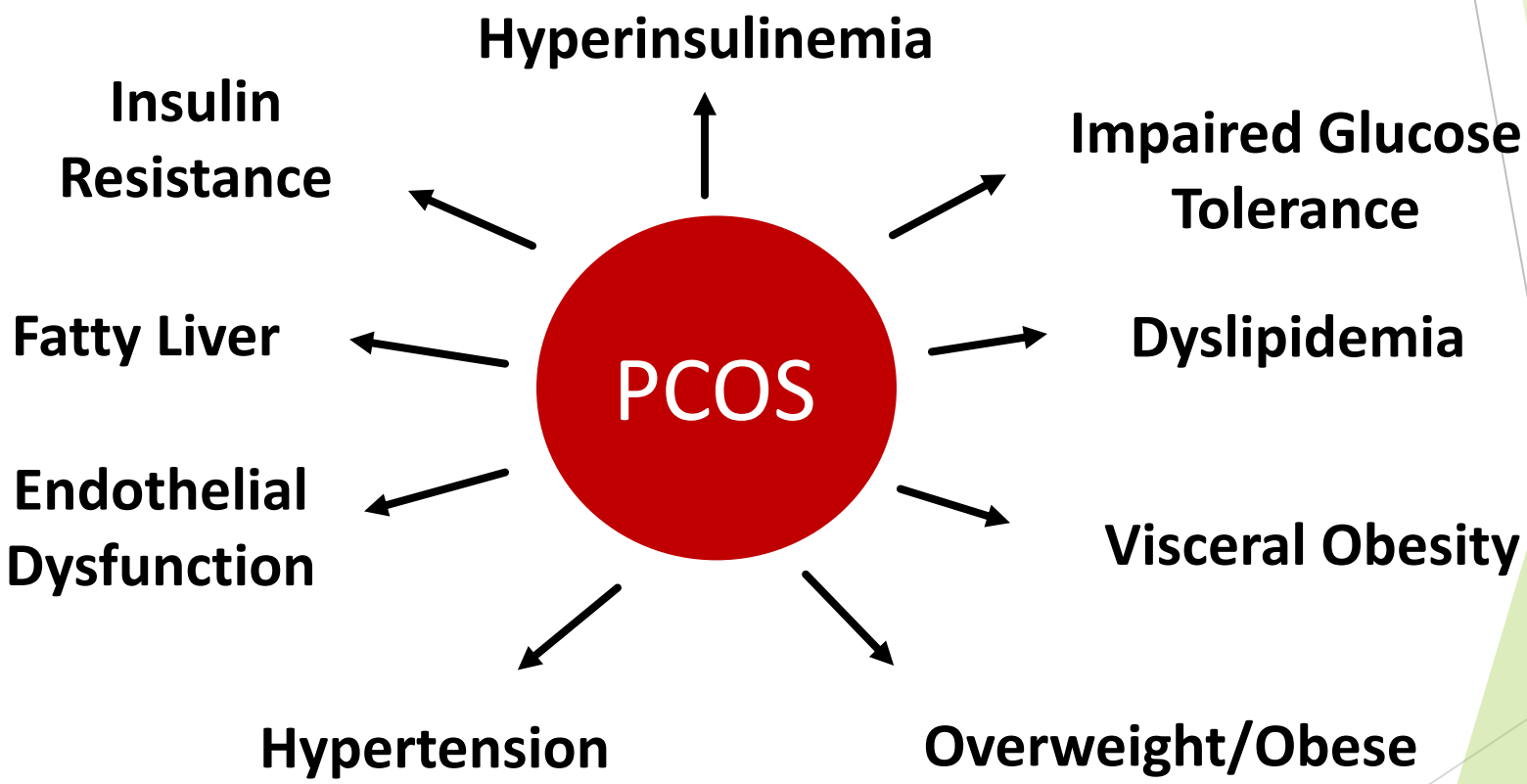


https://www.womenshealth.gov/publications/our-publications/fact-sheet/images/pcos1.jpg

Hormonal/Reproductive Effects of PCOS



Metabolic Effects of PCOS



Use of fasting blood to assess the prevalence of insulin resistance in women with polycystic ovary syndrome. (2004) Fertil. Steril
Prevalence and predictors of dyslipidemia in women with polycystic ovary syndrome. (2001) Am. J. Med.

Other Associated Conditions

- Autoimmune disease (especially thyroid)
- Skin tags and darkened skin (acanthosis nigricans)
- Gastrointestinal problems (IBS, leaky gut)
- Arthritis and tendinitis
- Depression, anxiety, stress
- Vaginal infections
- Sleep dysfunction and OSA
- Cancer

Androgen Excess and Its Effects

- Androgen excess is the most common endocrine disorder of reproductive aged women
- Androgens originate primarily from adrenal and ovaries
- Peripheral tissues (ie: fat, skin) play role converting weak androgens to more potent ones
- Multiple negative effects – cystic acne, hirsutism, androgenic alopecia, virilization, reproductive dysfunction

Lizneva et al. Androgen excess: investigations and management. Best Pract Res Clin Obstet Genaecol. 2016

It's Complicated: Dysregulated Hormones in PCOS

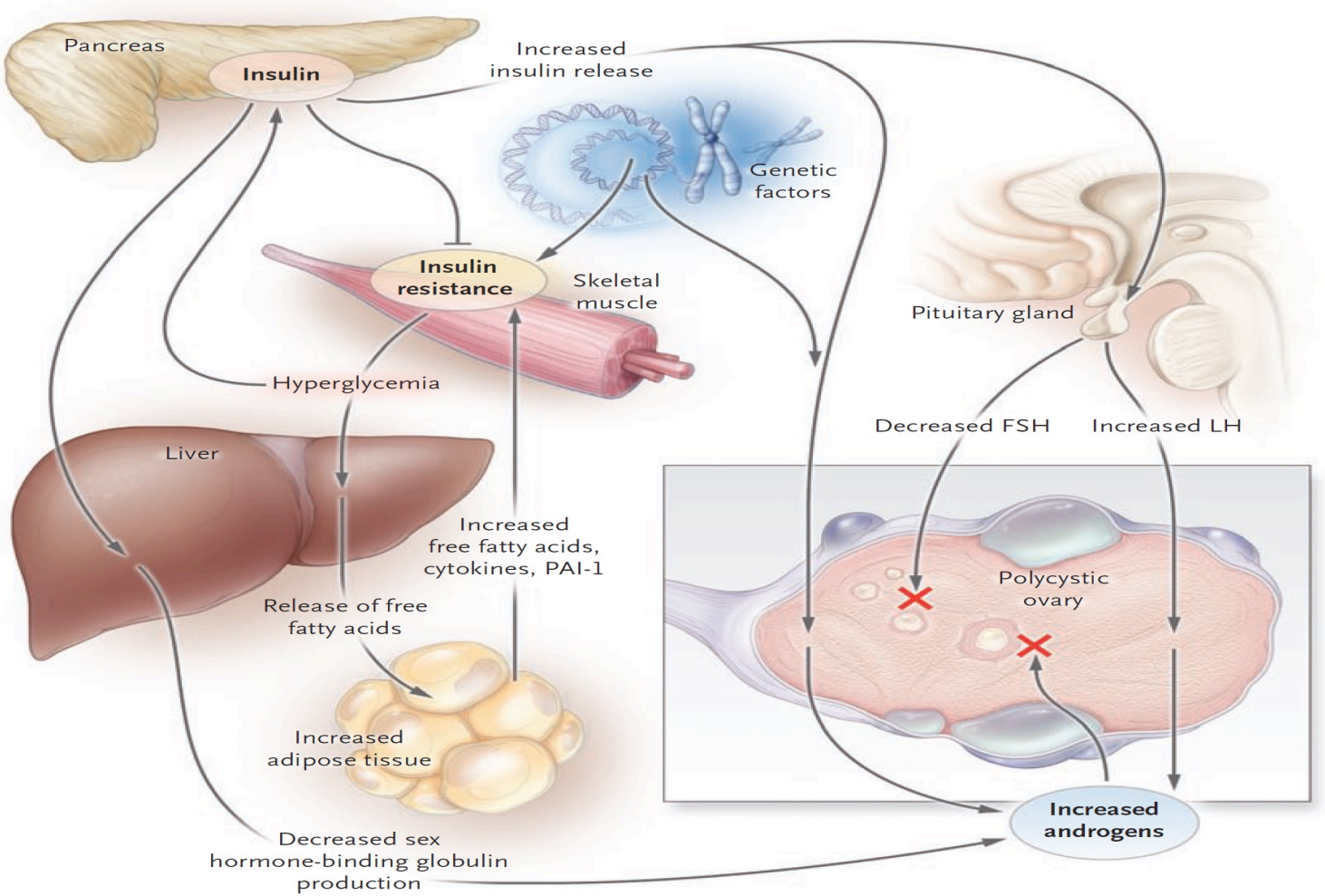
Alteration of estrogen receptor function in women with PCOS

1. **E2 Receptor Beta expression significantly higher than E2 Receptor Alpha**
2. **E2 Receptor Beta is lower compared to levels of controls**
3. **E2 Receptor Alpha is lower than levels found in controls**

Artimani et al. Gynecol Endocrinol. 2015

Dysregulated Hormones & Metabolism

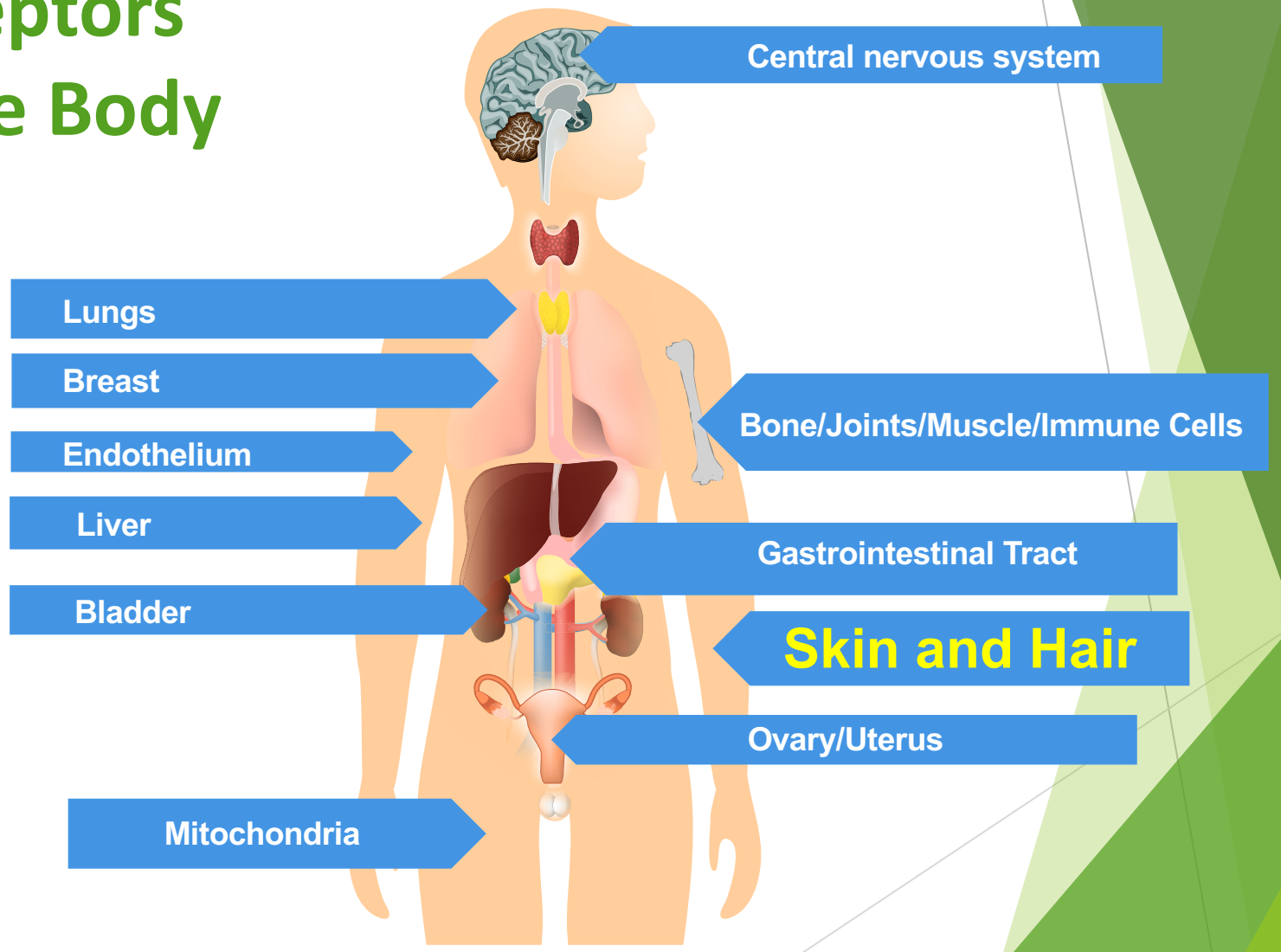
Dysregulation of various hormonal and metabolic processes



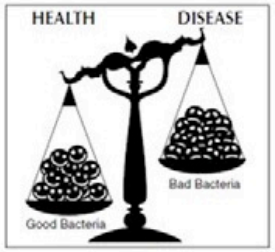
Nestler JE. N Engl J Med. 2008; 358: 47-54

Major Overlooked Factor in PCOS

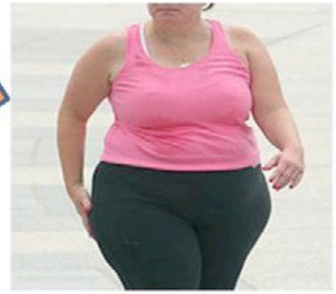
Estrogen Receptors Throughout the Body



High fat/ sugar, low fibre diet causes an imbalance between "good" and bad" gut bacteria

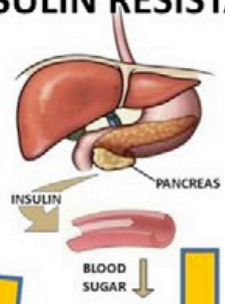


Obesity alters gut micobiota

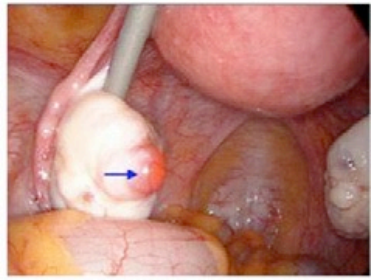


Obesity directly Increases gut permeability

INSULIN RESISTANCE



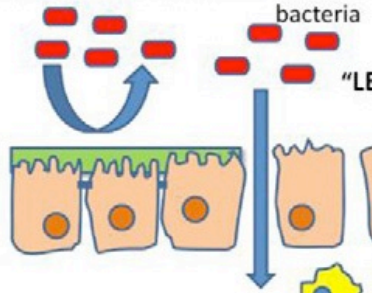
Insulin drives Testosterone Production in ovary, while Impairing follicle development



Gut inflammation initiated State of Insulin resistance

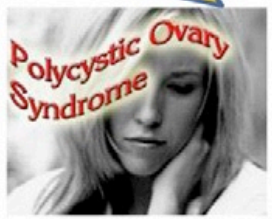
Dysbiosis of colonic microbiota mucous production and epithelial integity- resulting in a "leaky gut"

NORMAL GUT FUNCTION



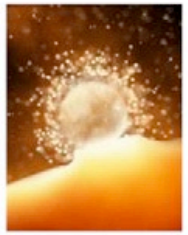
Normal tight junction function and mucous barrier preventing the trans-epithelial passage LPS

Macrophages activated by bacterial LPS that passes through gut wall



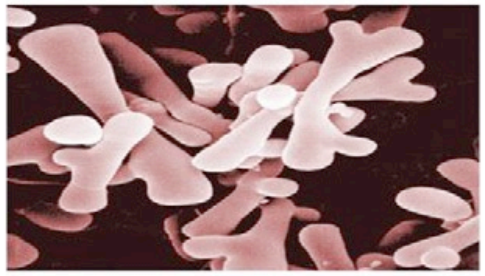
Polycystic morphology On ultrasound

Acne/ hirsuitism

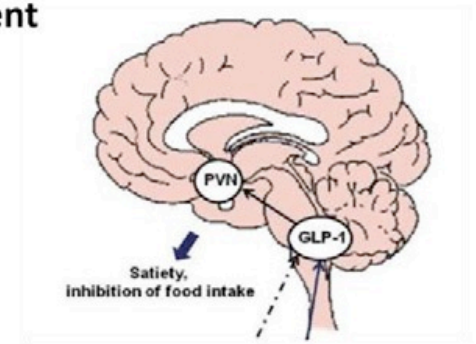


Impaired ovulation

Tremellen et al. Med Hypotheses. 201279(1):104-12



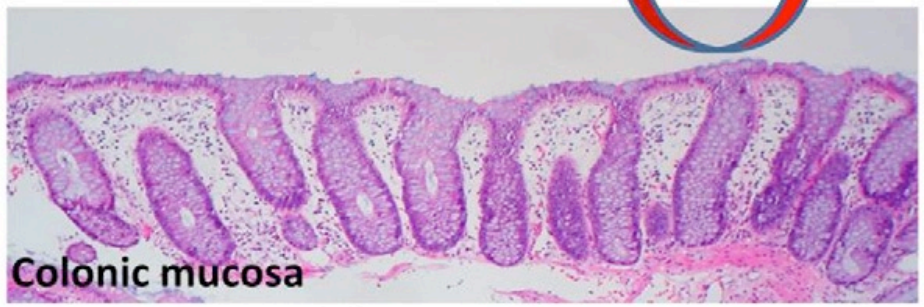
Probiotics and/or prebiotic treatment increases the number of beneficial "good" bacteria in the colon

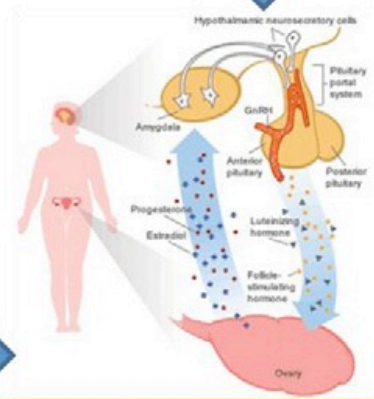


Beneficial "good" bacteria produce Short Chain Fatty Acids (SCFA) that increase colonic mucous production and tight junction function- decreasing the passage of immuno-stimulatory LPS from the colonic lumen into the circulation

Bacterial LPS

Increased production of the satiety hormone GLP-1 by the healthy colon mucosa reduces food intake and results in a Decrease in body fat content



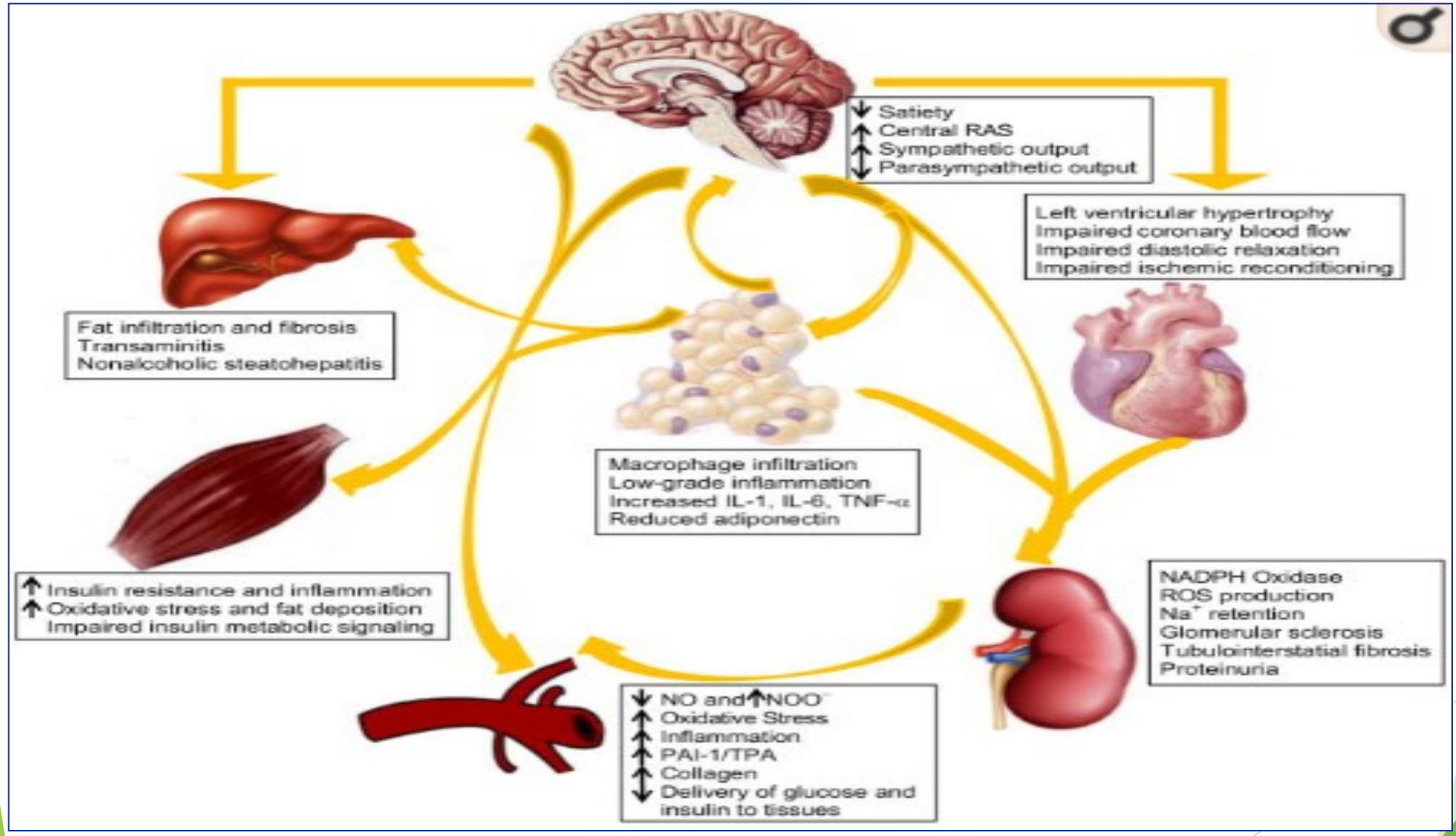


A reduction in inflammation due to reduced passage of LPS across the gut mucosa results in an improvement in insulin sensitivity, with a drop in serum insulin levels

RETURN TO NORMAL OVARIAN FUNCTION

Tremellen et al. Med Hypotheses. 201279(1):104-12

Cardio-Renal-Vascular-Metabolic Syndrome



Guanghong et al. Prog Mol Biol Transl Sci. 2014;127: 229-249

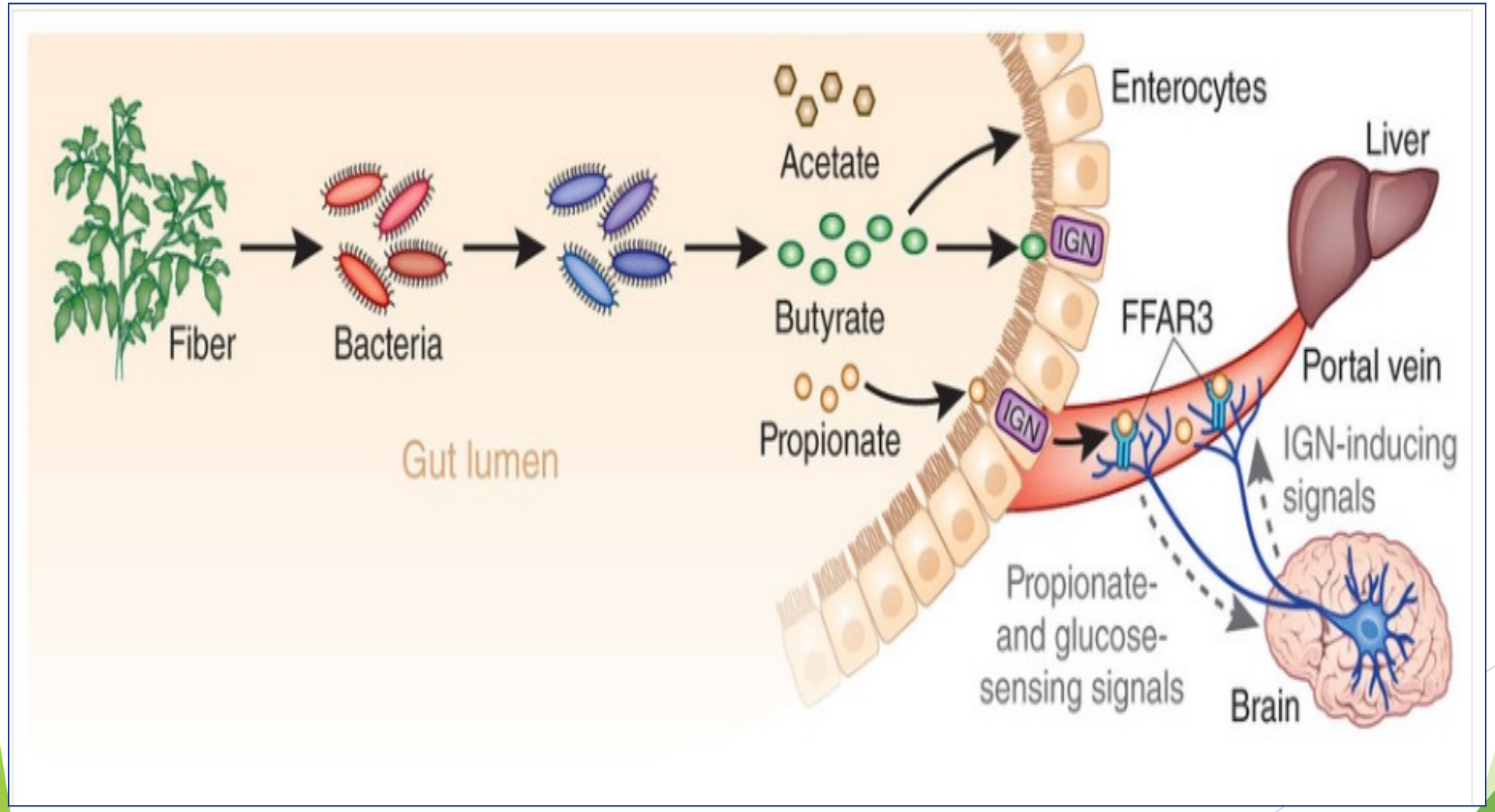
Introducing the Gut Microbiome:
The Unseen Civilization Within Us

Dysbiosis and PCOS

- **Lower microbial diversity and altered phylogenetic composition**
- **Alterations in markers of gut barrier function and endotoxemia**
- **Increase in LPS producing bacteria and serum LBP levels**

Lindheim et al; PLOS One. 2017.12(1)
Guo et al ; PLOS One. 2016
Liu et al. Font. Microbiol. 2017;8,324:1-12

Linking the Microbiome & Short Chain Fatty Acids to Metabolic Health

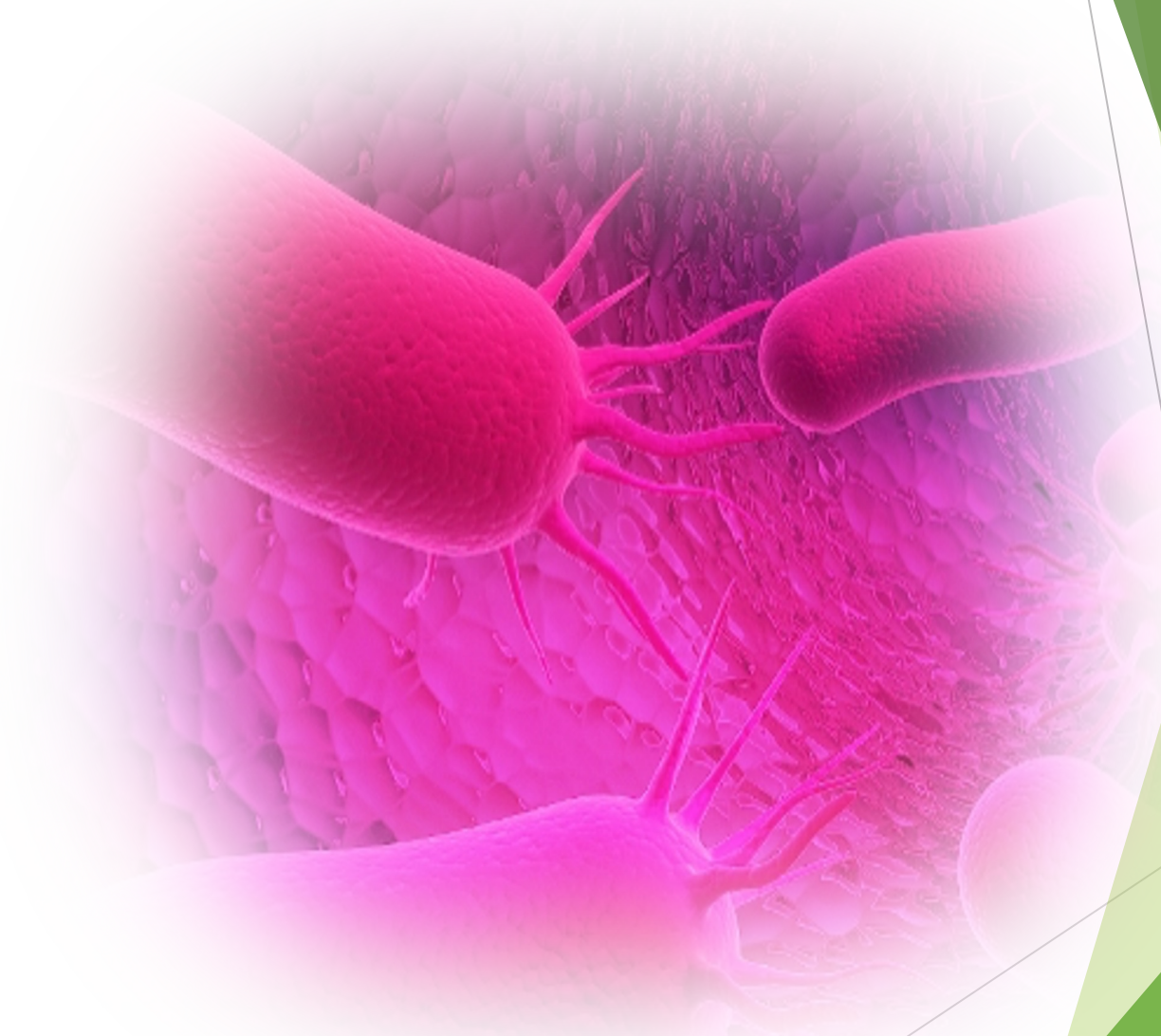


Nature Biotechnology. 2014; **32**, 243–245

Gut Microbiome Clock

Programmed to anticipate food in the daytime only

Bacteria express circadian patterns of swarming & motility



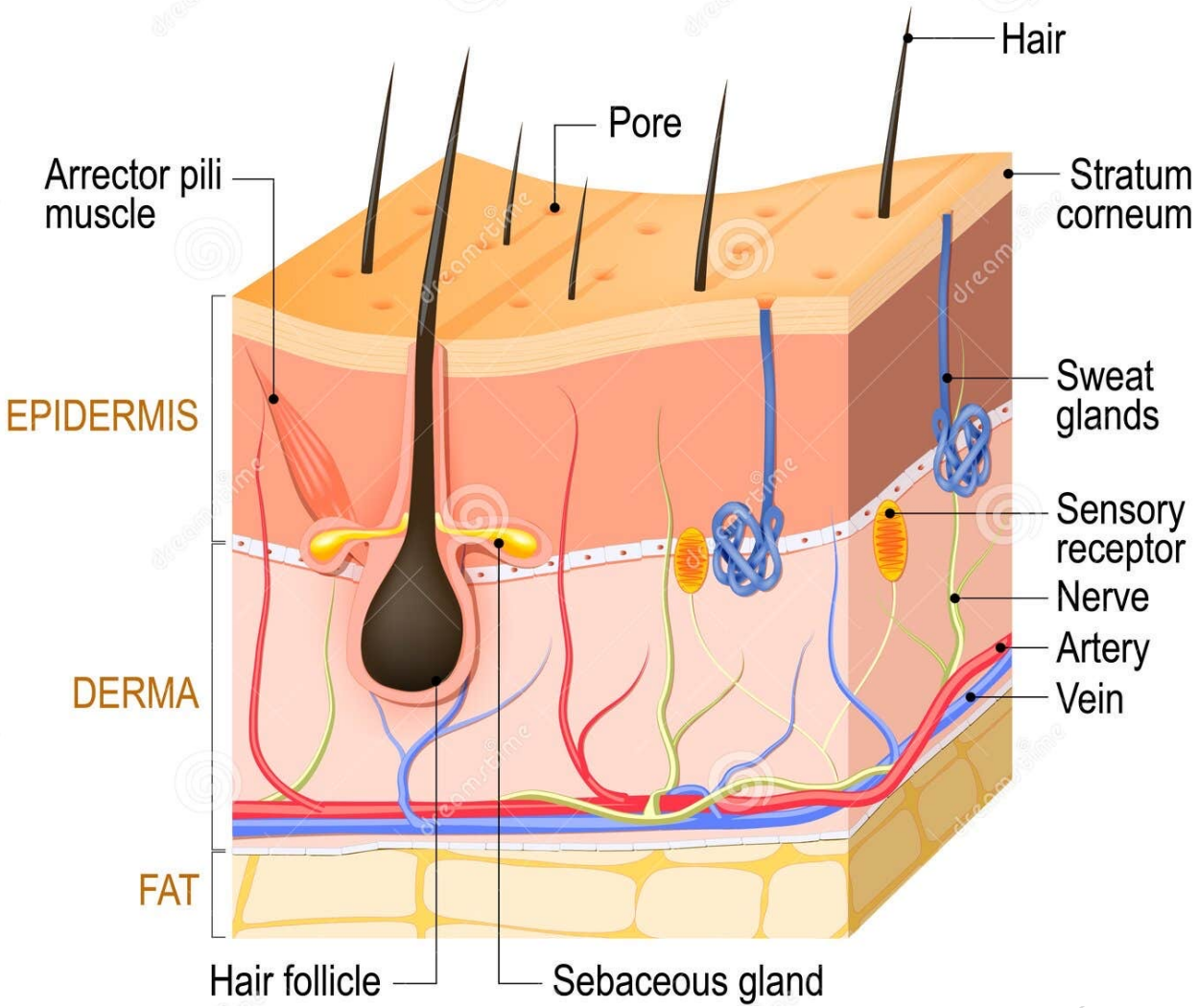
Marquie et al. Occup Environ Med. 2015;72(4):258-64
Castanon-Cervantes et al. 2010. J of Immunol; 185(10)5796-5805
Liang et al. 2015; Proceedings of Nat Acad of Sciences of the USA:112(33);10479-10484
Bechtold et al. 2010; Trends in Phar Scie, 31(5):191-8

PCOS, Hormones, Inflammation & Skin

- The skin - one of most affected organs with PCOS - by oxidative stress

- Skin quality is negatively impacte by hormonal imbalances, systemi inflammation, nutrient deficiencies, gut microbiome dysbiosis

Skin Anatomy



Estrogen Modulates Skin Physiology

Role of Beta Receptor & Beneficial effects on:

- Keratinocytes
- Dermal Fibroblasts
- Melanocytes
- Hair follicles and hair growth
- Sebaceous glands & sebum production
- Apocrine glands
- Angiogenesis
- Wound healing
- Immune responses & skin cancers
- Pigmentation

Inoue et al. The role of estrogen-metabolizing enzymes and estrogen receptors in human epidermis. Mol Cell Endocrinol. 2011;344:35-40.

Estrogen Insufficiency Harms Skin

Negative effects:

- Decreased defense against oxidative stress
- Skin becomes thinner
- Reduced collagen
- Decreased elasticity – noticeable sagging skin – especially around neck, jawline, cheeks
- Increased wrinkling and fine lines - especially “crow’s feet and lines above upper lip
- Increased dryness
- Reduced vascularity
- Compromised protective functions – impaired wound healing, hair loss, pigmentary changes, skin cancers

Inoue et al. The role of estrogen-metabolizing enzymes and estrogen receptors in human epidermis. Mol Cell Endocrinol. 2011;344:35-40.

Estrogen and Wound Healing

- **Estrogen -**
  Role in all phases wound healing - modifying inflammatory response, accelerating re-epithelialization, stimulating granulation tissue formation & regulating proteolysis

- **Acne as a “wound”**

Ashcroft et al. Topical estrogen accelerates cutaneous wound healing in aged humans associated with an altered inflammatory response. Am J Pathol. 1999;155:1137-46
Emmerson et al. The role of estrogen deficiency in skin ageing and wound healing. Biogerontology. 2012;133-20.
Ashcroft et al. Estrogen modulates cutaneous wound healing by downregulating macrophage migration inhibition factor. J Clin Invest. 2003;111:1309-18.

Acne - Presentation

- Comedones – blackheads and whiteheads
- Papules
- Pustules
- Nodules and cysts
- Scars
- Erythema
- Hyperpigmentation

Acne Treatments

- Benzoyl peroxide
- Topical antibiotics
- Systemic antibiotics
- Salicylic acid
- Supplements: Zinc, Vitamin A, Antioxidants, Anti-inflammatories
- Isotretinoin – oral retinoid
- Spironolactone
- Hormone therapy
- Corticosteroids
- Lasers and light therapies
- Chemical peels
- Fillers for scars
- Microneedling, PRP, microdermabrasion
- Surgical procedures

Topical Antimicrobials

- Benzoyl peroxide
- Clindamycin
- Erythromycin
- Azelaic acid

Topical Products for Acne

Topical Retinoids

- Increase skin cell turnover and shedding
- Decrease sebum production
- EXAMPLES: Adapalene, tretinoin, tazarotene, trifarotene

Other Options

- Topical dapsone, sulfur, salicylic acid
- Topical (and oral) niacinamide

Additional Therapeutics

Antibiotics

- Doxycycline
- Minocycline
- Sarecycline
- Clascoterone – topical
- Spironolactone – oral
- Oral contraceptives
- Oral retinoids - Isotretinoin

Estrogen and Skin Pigmentation

Estrogen may directly regulate gene in melanocytes

Hyperpigmentation noted in pregnancy, on oral contraceptives

Thornton MJ. The biological actions of estrogens on skin. Exp Dermatol. 2002;11:487-502.

Estrogen and Hair

Hair density decreases with age and with PCOS

Androgenic alopecia common

- **Estrogen modulates hair growth by influence on other hormones, growth factors, transcription factors, cytokines**

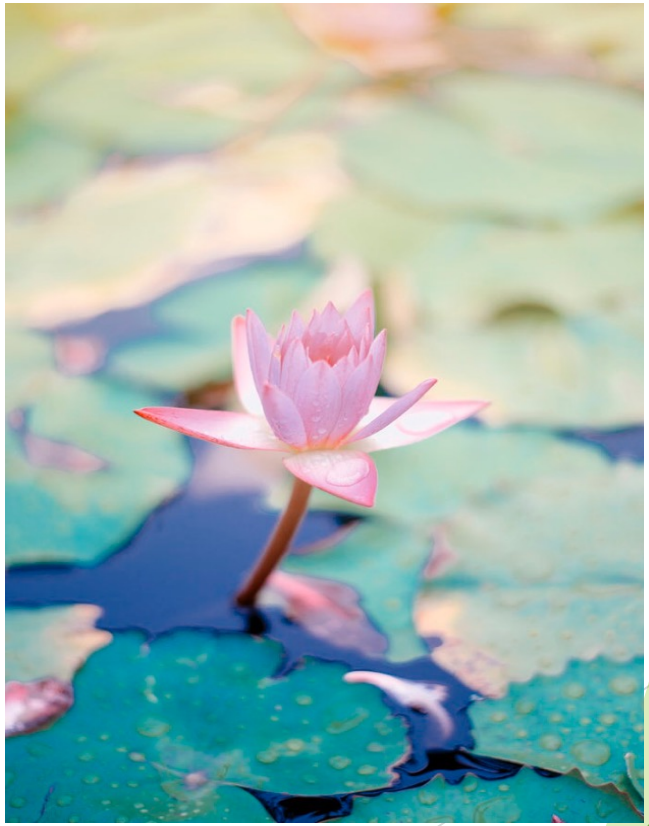
- **Estrogen affects hair growth rate, percent in anagen phase, hair diameter distributions – especially frontal scalp**

Hormonal changes in menopause: do they contribute to a “midlife hair crisis’ in women. British J of Derm. 2011;165(s3):2-11

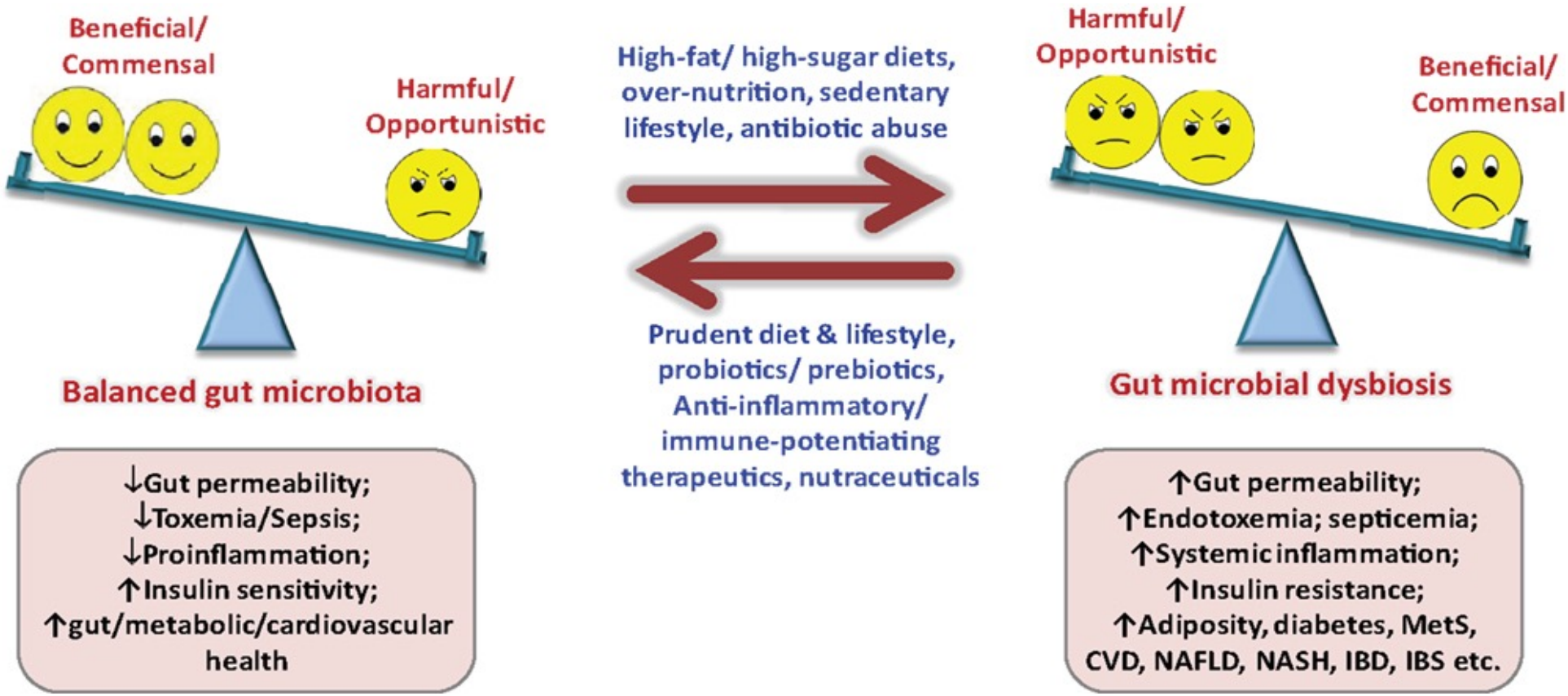
My Integrative 7 Step Program

7 Steps to Optimizing Health for Women: Improving Metabolic and Reproductive Health

1. FEED THE GUT AND PRESCRIBE TARGETED SUPPLEMENTS
2. EAT TO THE BEAT
3. STEP INTO THE LIGHT
4. GET ADEQUATE AND RESTORATIVE SLEEP
5. EXERCISE ANY TIME POSSIBLE
6. LIVE CLEAN AND PURE
7. PERSONALIZE THE PLAN



Work to Achieve a Healthy Gut Microbiome



"Importance of balanced nutrition and gut microbiota, and consequences of gut dysbiosis. MetS, metabolic syndrome; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; CVD, cardiovascular diseases."

Front. Med., 23 June 2014

Feed the Gut

- Eat mostly plants
- Eat lots of fiber
- Eat organic, raw, minimally processed foods – spanning the colors of the rainbow
- Limit sugar, fat, salt
- Avoid alcohol, antibiotics from agriculture, artificial sweeteners, dairy, emulsifiers, gluten
- Recommend targeted supplements
- Reboot – eat vegan for 6 months
- Get some great cookbooks, aligned with the plan

Complex Carbohydrates (70% of diet)

Best Diet to Nourish the Microbiome
EXTREMELY HIGH FIBER

INCLUDE	▶ Complex carbohydrates (70%) whole-grains, all varieties of vegetables, beans, legumes, etc. ▶ Healthy fats from nuts, seeds, olives Add Omega 3 supplement ▶ Natural fiber and prebiotic rich foods ▶ Probiotic rich foods ▶ Green leafy vegetables and root vegetables
LIMIT	• Protein (approximately 12%)
AVOID	• Initially, no protein from animals, dairy, or eggs • NO Sugar and refined carbohydrates • NO Alcohol • AVOID ANY Food intolerances

Fallucca et al. 2014
Candela et al. 2016

Diversity of Microbiome Requires Dietary Diversity

Heiman M et al. *Molecular Metab* 2016;1-4

Phytoestrogens

Phytoestrogens support:

- Gut health
- Menopausal comfort
- Cognitive health
- Cardiovascular & metabolic health
- Cellular health
- Skin & hair!

Rietjens IM, Louisse J, Beekmann K. Br J Pharmacol. 2016 Oct 9.
Singha KK, Mridulaa D, Rehala J, Barnwala P. C Review Food Scie & Nutri. 2011. 51(3); 210-222.

Tips for Beautiful Skin and Hair

Eat phyto-estrogens

- **Isoflavones genistein and S-equol - greater affinity for ER beta – ER beta selective agonists**
- **Reduce UV-induced cell death in cultured keratinocytes, improve skin elasticity, reduce wrinkle depth & increase production of type 1 procollagen**
- **Genistein protects against UV induced senescence in cultured human dermal fibroblasts – upregulates intracellular SOD activity in dose-dependent manner**

Wang et al. Genistein protects against UVB-induced senescence-like characteristics in human dermal fibroblast by p66Shc down-regulation. J Dermatol Sci. 2010;58:19-27.
Jackson et al. Ageing skin: oestrogen receptor beta agonists offer an approach to change the outcome. Exp Dermatol. 2011;20:879-82.

Tips for Beautiful Skin and Hair

- Cleaning skin – use cream-based formula
- Hydrate – use heavier cream – place while skin still wet
- Skip long, hot showers
- Use mineral-based sunscreen on face
- Eat antioxidants
- Eat phyto-estrogens – 3 ounces (85g) unprocessed soy each day
- Control stress
- Exercise
- Targeted skin products – integrative - hyaluronic acid, collagen, antioxidants, protein powders
- Targeted skin products – conventional – retinols, acids
- Procedures – micro-needling, micro-abrasion, lasers, peels, PRP, plastic surgery

Tips for Beautiful Skin and Hair

Include Resveratrol – found in red grapes

- **Can activate ER alpha and ER beta – a potent antioxidant with strong anti-inflammatory properties**

- **Resveratrol upregulates mitochondrial SOD – via ER beta**

Thornton MJ. Estrogens and aging skin. Dermato-endocrinology. 2013;5(2):264-270.
Robb eta l. Resveratrol interacts with estrogen receptor-beta to inhibit cell replicative growth and enhance stress resistance by upregulating mitochondrial superoxide dismutase. Free Radic Biol Med. 2011;50:821-31.

Supplements to Support Skin Health

- Magnesium
- Zinc
- Curcumin
- Omega 3
- Multivitamin and Multimineral

- Hyaluronic Acid
- Probiotic and Prebiotics
- Collagen
- Quercetin
- Vitamin A
- Vitamin C
- Vitamin D

Benefits of Probiotics

- ***Skin***
- **Immune**
- **G.I.**
- **Cardiovascular**
- **Detoxification**
- **Vaginal health**
- **Synthesize essential vitamins**

Probiotics and Skin

- Helps treat and prevent eczema, dry skin, acne, UV-induced damage
- Increase skin's production of ceramides (lipids that trap moisture in skin and keep acne-causing bacteria levels in check
- People with eczema have reduced levels of ceramides
- Reduce oxidative stress in skin – protect against free radical damage
- Reduce effects of sun damage – due to UV light
- Improve skin's moisture barrier
- Enhance hair quality
- May lower risk of skin cancer
- Restore skin's pH – skin pH increases with age

Curcumin and Skin

From Turmeric

- Supports skin health in Psoriasis – suppresses production of TNF alpha by activated macrophages and lowered levels of IL-22 and many other pro-inflammatory cytokines
- Reduced hyperproliferation of keratinocytes in Psoriasis
- Supports skin health in Eczema – lowers pro-inflammatory cytokines
- Lowers systemic inflammation and oxidative stress
- Benefits acne and wound care

Curcumin and Skin

- Benefits aging skin – the “inflammaging” of skin
- Improves signs of photo-aging
- Increase in water content of skin – increased hyaluronan production
- Increases collagen production
- Aid to treat skin cancer – can induce apoptosis in cancer cells
- Upregulated tumor suppressor gene PTEN, prevents activation of NF-Kappa B
- Can help control skin infections – bacterial and fungal

Quercetin: a Flavonoid – and Skin

Sources: apples, onions, garlic, green tea, kale, blueberries, cherries

- Lowers Inflammation
- Dietary scavenger of free radicles
- Potent antioxidant
- Inhibits oxidation
- Stabilizes mast cells

BENEFITS:

Lowers inflammation, reduce redness, itching, water loss, wrinkles and age spots, helps restore skin barrier function, increases hydration, promotes wound healing (acne), provides protection from UV sun damage

Maramaldi et al. Soothing and anti-itch effect of quercetin phytosome in human subjects: a single-blind study. *Clin Cosmet Investig Dermatol*. 2016;9:55-62.

Omega 3 and Skin

- Regulate skin's oil production
- Improve balanced hydration
- Subdue acne breakouts
- Minimize signs of aging
- Soften rough, dry skin
- Soothing effect on irritation and dermatitis
- Boost skins resilience to UV damage and skin cancer

Vitamin C and Skin

- Encourages new collagen growth
- Helps maintain collagen
- Protects skin proteins from damage
- Reduce redness
- Reduce pigmentation
- Protects against sunburn, photoaging, wrinkles, sagging, dryness

Niacinamide and Skin

- Helps lock in moisture to protect from environmental damage
- Helps build keratin to keep skin firm and healthy
- Helps skin grow ceramide (lipid) barrier – retains moisture
- Minimizes redness
- Minimizes pore size and appearance – keeps skin smooth and moisturized
- Regulates oil – for dry and oily skin types

Niacinamide and Skin

- Helps build proteins in skin
- Restorative – restore cellular energy to skin
- Protects against sun damage
- Repair damaged DNA – including from UV rays
- Treats hyperpigmentation
- Minimizes fine lines and wrinkles
- Protects against oxidative stress
- Treats acne

Hyaluronic Acid and Skin

Half of all hyaluronic acid in body in skin

- Helps skin stretch and flex - elasticity
- Reduces skin wrinkles and lines
- Helps skin retain moisture – creates a plumping effect
- Fortifies skin's natural barriers to keep in moisture – helps maintain the lipid barrier – protects and fortifies it
- Aids wound healing
- Reduces scarring – can combine with microneedling

Zinc the Body and the Skin

- Builds collagen via zinc-dependent enzymes – collagenases
- Collagen production, durability, stability
- Builds keratin
- Wound healing
- Fatty acid metabolism
- Immunity
- Hormone Health
- Fertility
- Thyroid function
- Potent antioxidant

Zinc Benefits for Skin:

- Acne

Study comparing minocycline and zinc

- Eczema

Turkish study – low levels zinc, selenium, iron in those with eczema

Study – 73% of eczema patients had total improvement by 1 month with dose 60 mg/day

- Wound healing and infections

Actions on neutrophils and macrophages functions, inflammatory cytokines, natural killer cell/phagocytic activity

Foods Containing Zinc

- Oysters
- Beef, liver, lamb
- Milk and cheese
- Eggs
- Shellfish
- Cereals
- Nuts

Targeted Supplements for Metabolic Support

DIM	Vitamin D	Curcumin	Magnesium
Probiotic	Omega 3	Prenatal Vitamin	Myo-inositol
NAC	Berberine	Chaste Tree	Zinc

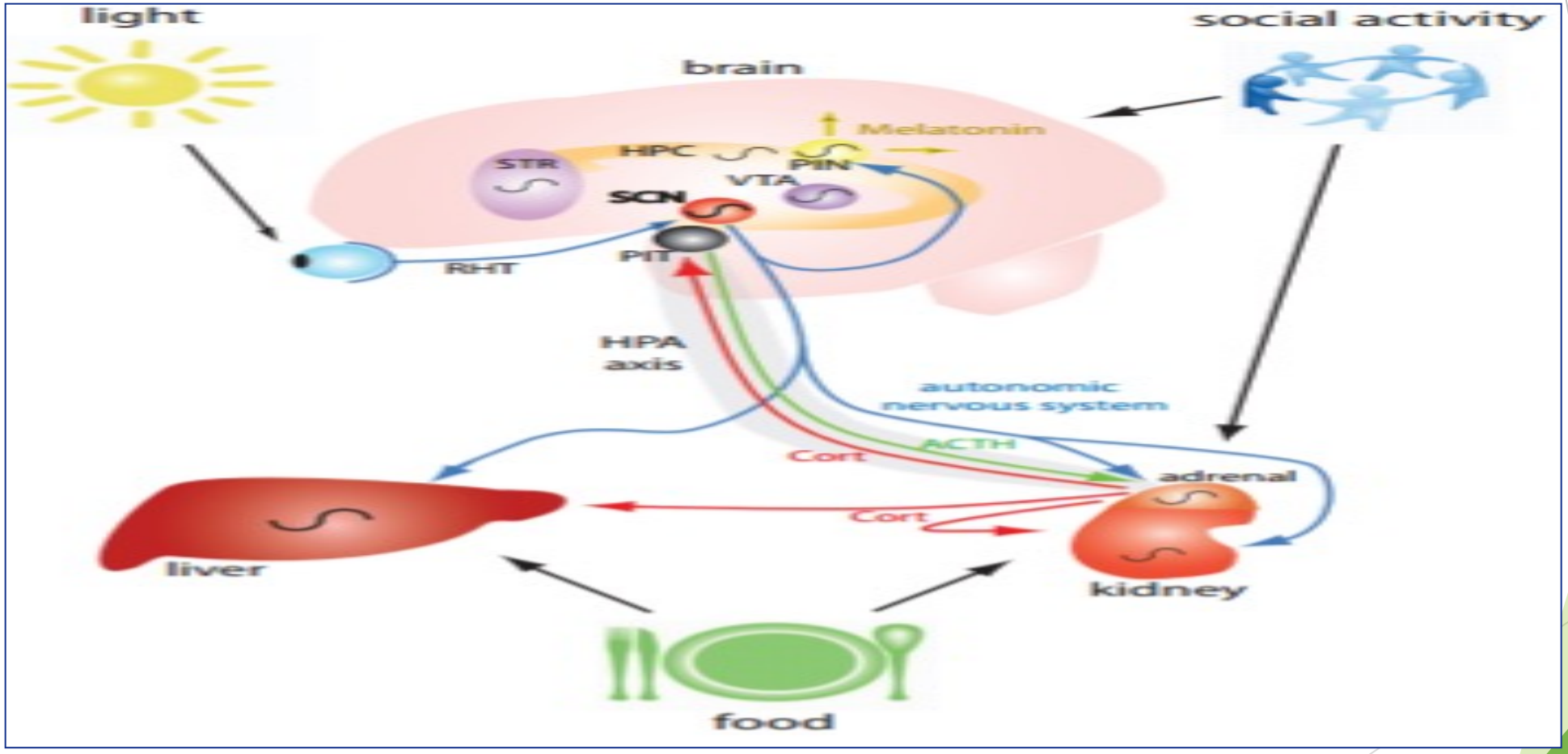
See the Light

- “Watch” the sunrise
- Morning light
- Midday sun
- Watch the sunset
- Dim the lights – reduce blue light exposure
- Sleep in the dark
- Go camping

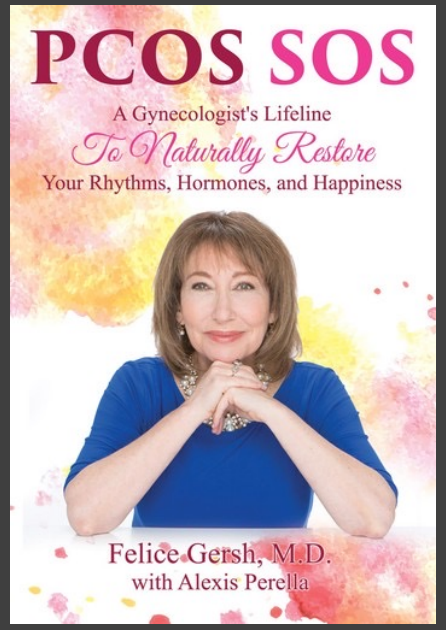
Get Enough Sleep

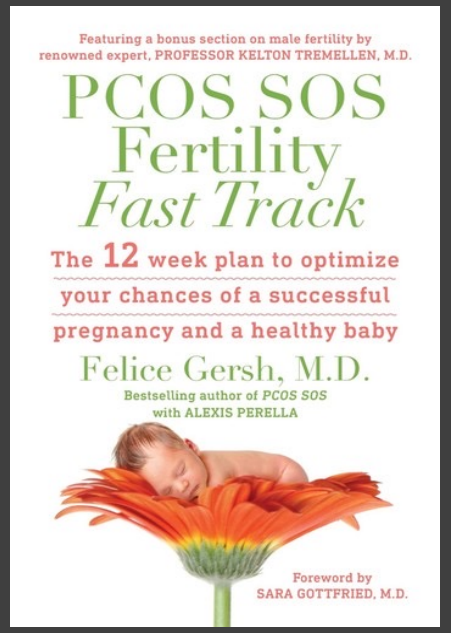
Set up	a sleep routine and stick with it
Make	the bedroom a wonderful place to sleep
Consider	supplements to lower stress and support sleep
Get	a relaxation routine - start 2 hours before bedtime
Limit	caffeine to mornings
Test and treat	sleep apnea
Attend	to heartburn and any other painful condition

Path to Hormonal Health
Metabolic Health – Fertility Optimization



Behav Neurosci 128(3) pg 326-43, 2014.pdf





Thank you!

Felice L. Gersh, MD

- www.integrativemgi.com
- Twitter: @DrFeliceGersh
- Instagram: Dr.FeliceGersh
- Follow my InstagramLive