Casual Friday Presents

BPH: Benign Prostatic Hyperplasia Part 2

A BIOGENETIX CLINICAL PRESENTATION

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Benign prostatic hyperplasia (BPH) refers to the nonmalignant growth or hyperplasia of prostate tissue and is a common cause of lower urinary tract symptoms (LUTS) in older men. Disease prevalence has been shown to increase with advancing age. The histological prevalence of BPH at autopsy is as high as 50% to 60% for males in their 60s, increasing to 80% to 90% of those older than 70 years of age.[1]

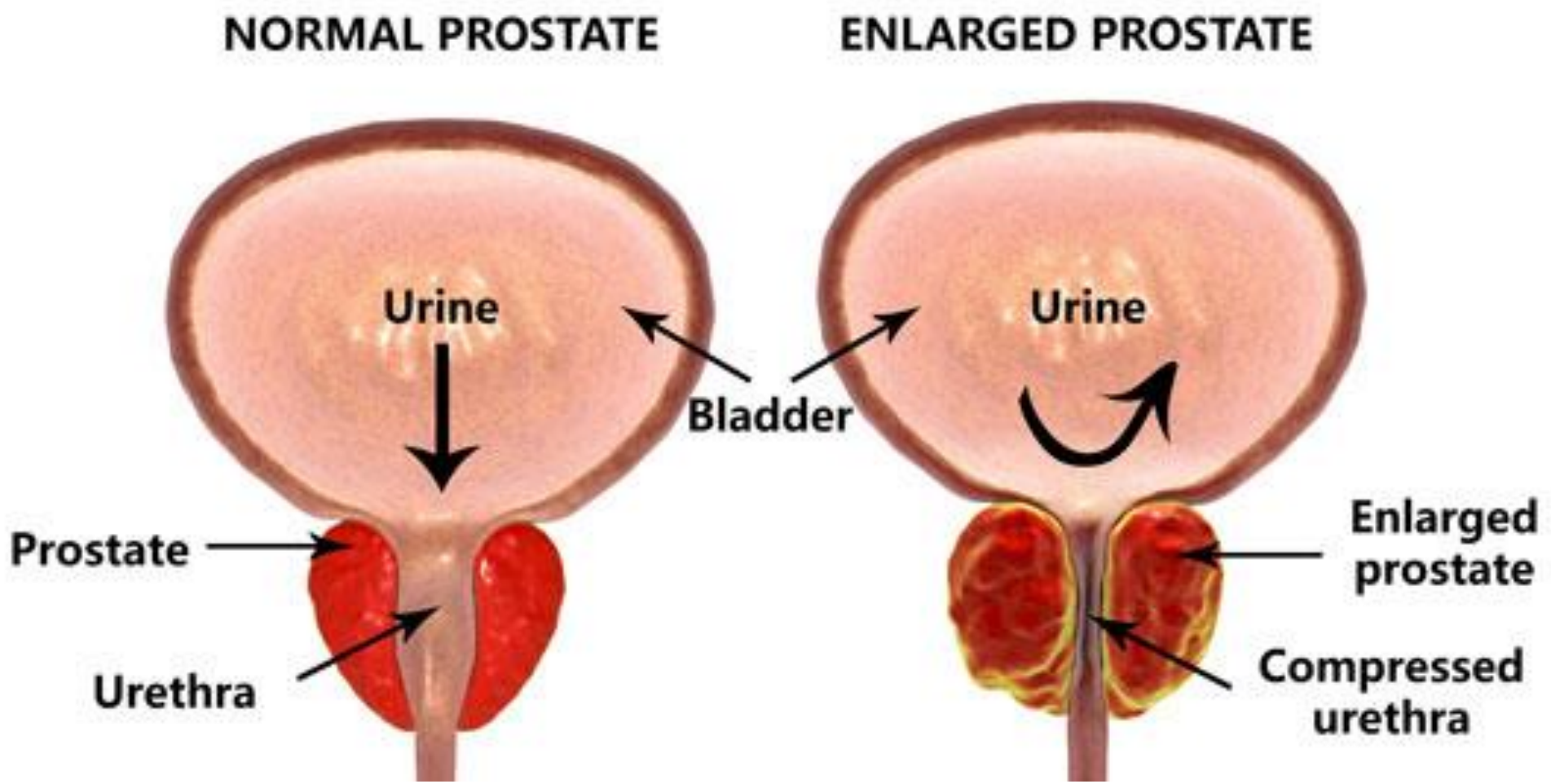
Several definitions exist in the literature when describing BPH. These include bladder outlet obstruction, LUTS, and benign prostatic enlargement (BPE). BPH describes the histological changes, BPE refers to the increased size of the gland (usually secondary to BPH), and bladder outlet obstruction is defined as the blockage to urinary flow.[2][3] Those with BPE who present with bladder outlet obstruction are also termed benign prostatic obstruction.[4]

Lower urinary tract symptoms (LUTS) describe the urinary abnormalities shared by disorders affecting the bladder and prostate, typically caused by BPH. These terms have largely replaced those historically termed "prostatism."

The development of BPH is characterized by stromal and epithelial cell proliferation in the prostate transition zone, which surrounds the urethra. This leads to urethral compression and bladder outflow obstruction, which can result in clinical manifestations of LUTS, urinary retention, or infections due to incomplete bladder emptying.[5] Long-term, untreated disease can lead to the development of chronic high-pressure retention (a potentially life-threatening condition) and long-term or permanent changes to the bladder detrusor muscle.

BPH treatment options range from watchful waiting to various medical and surgical interventions. Risk factors may be divided into non-modifiable and modifiable. Other factors such as age, genetics, geographical location, and obesity have all been shown to influence the development of BPH.[6][7]

BENIGN PROSTATIC HYPERPLASIA



https://auspecialists.com/wp-content/uploads/2019/08/bph.jpg

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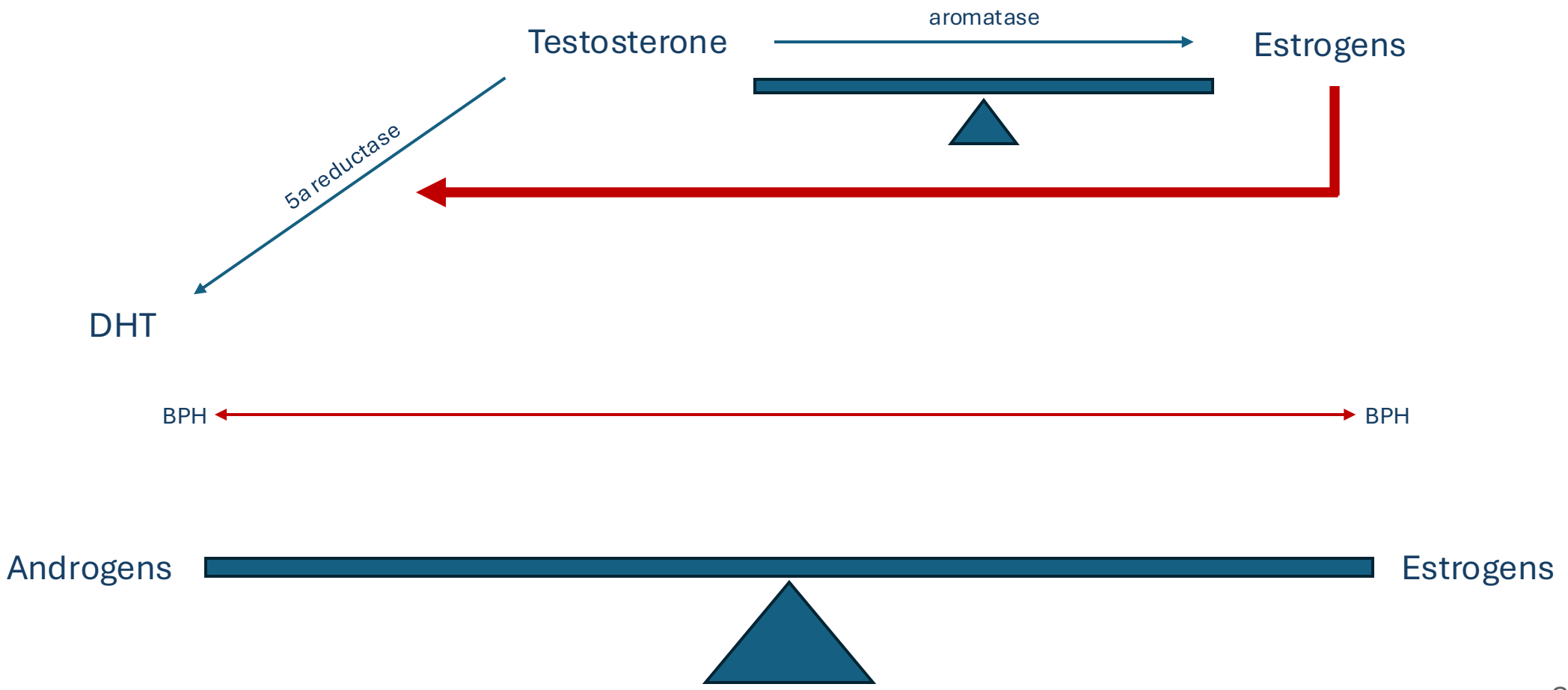
BPH: A hormone balancing act.



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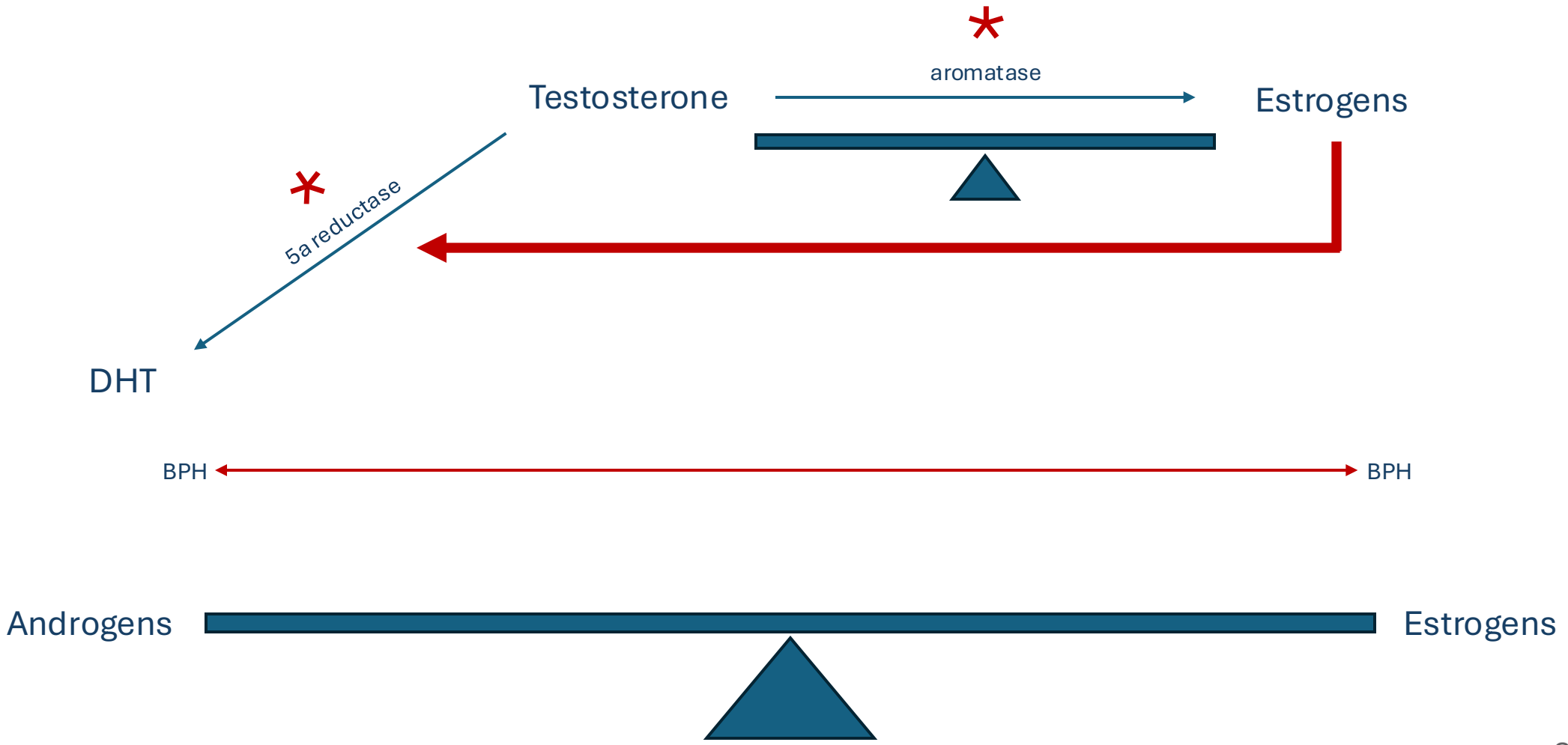
BPH: A hormone balancing act.



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5a reductase

Saw Palmetto
Pygeum
Nettle Root
Cranberry
Green Tea (egcg)
Zinc

*

aromatase

Chrysin
Cruciferous vegetables
Mushrooms
Green Tea (egcg)
Blueberries
Cherries

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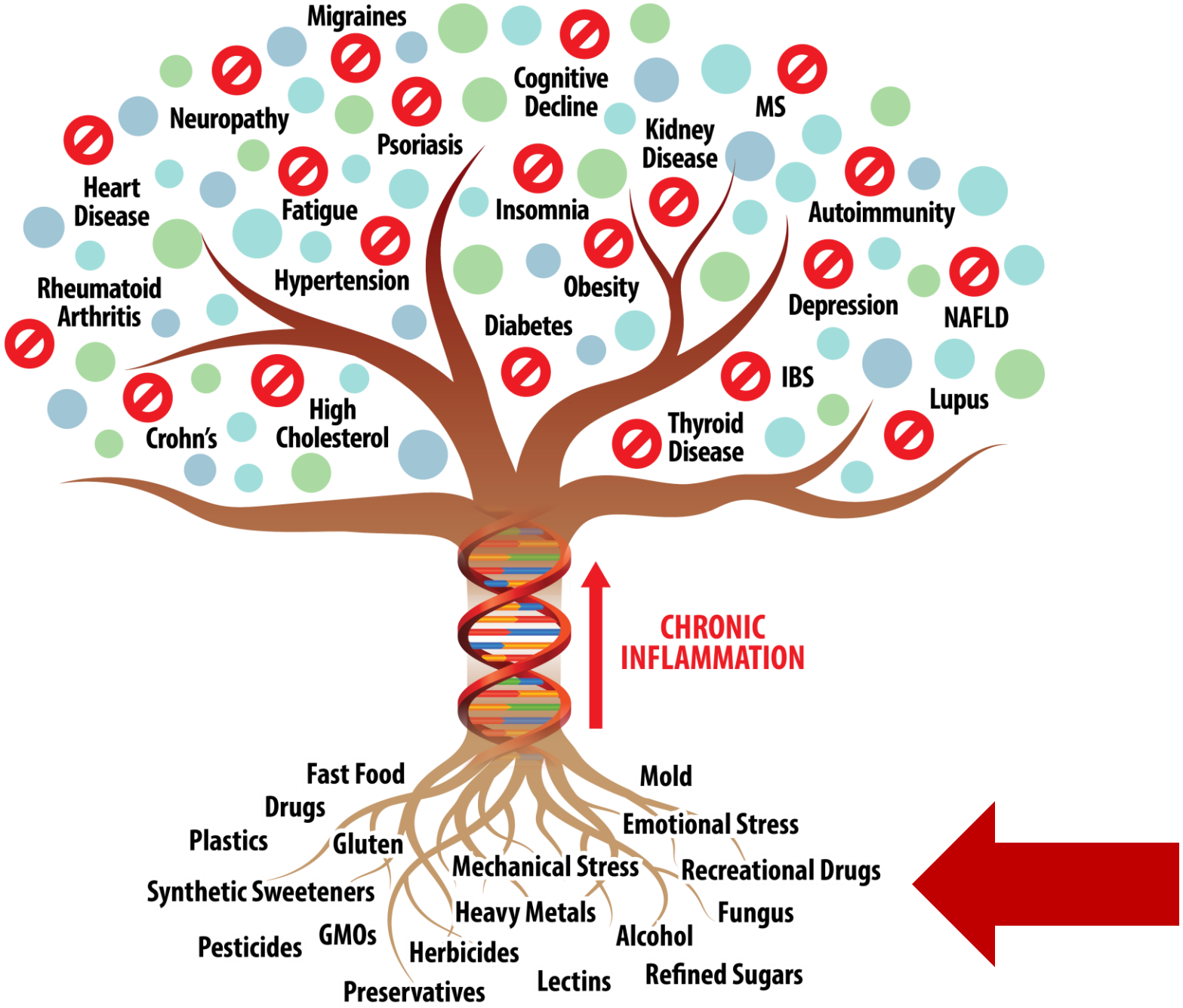
Migraines
Neuropathy
Psoriasis
Cognitive Decline
MS
Kidney Disease
Heart Disease
Fatigue
Insomnia
Autoimmunity
Rheumatoid Arthritis
Hypertension
Obesity
Depression
NAFLD
Diabetes
IBS
Lupus
Crohn's
High Cholesterol
Thyroid Disease
CHRONIC INFLAMMATION
Fast Food
Drugs
Plastics
Gluten
Synthetic Sweeteners
Pesticides
GMOs
Herbicides
Preservatives
Lectins
Refined Sugars
Heavy Metals
Mechanical Stress
Alcohol
Mold
Emotional Stress
Recreational Drugs
Fungus

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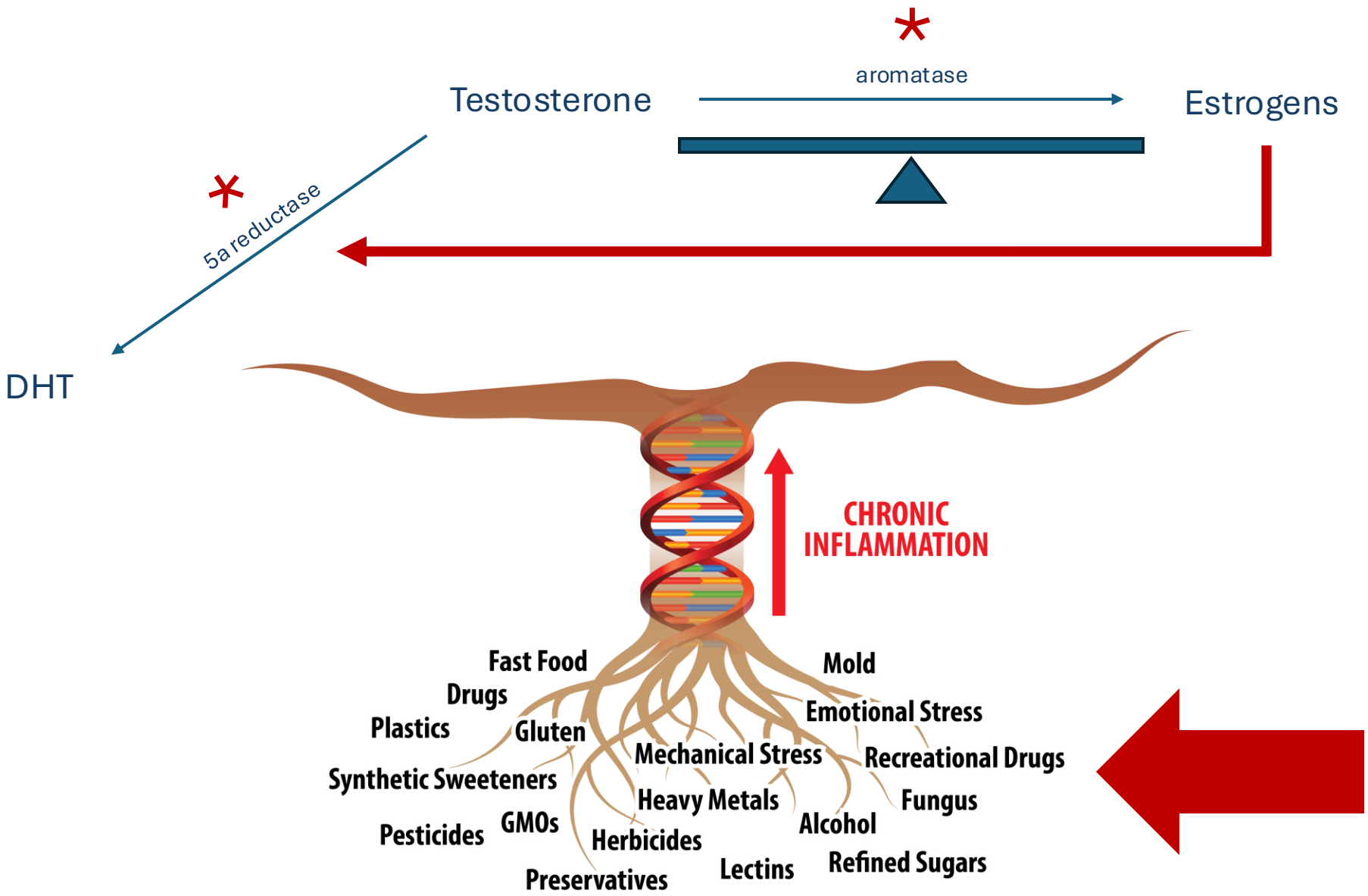
*
aromatase
Testosterone
Estrogens
*
5a reductase
DHT
CHRONIC
INFLAMMATION
Fast Food
Drugs
Plastics
Gluten
Synthetic Sweeteners
Pesticides
GMOs
Herbicides
Preservatives
Lectins
Refined Sugars
Alcohol
Heavy Metals
Mechanical Stress
Mold
Emotional Stress
Recreational Drugs
Fungus

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Risk Factors

Non-modifiable and modifiable risk factors also contribute to the development of BPH. These have been shown to include diabetes, diet, genetic factors, localized inflammation, obesity, and metabolic syndrome.[7]

- **Diabetes and the use of antidiabetic medications**, particularly insulin, appear to increase the risk of BPH, LUTS, and prostatic surgery.[15][16]

- **Dietary factors** also appear to influence the development of BPH. Beta-carotene, carotenoids, and vitamin A seem somewhat protective, while excessive alcohol ingestion, heavy caffeine intake, and high-dose supplemental vitamin C tend to increase BPH risk and symptoms.[17][18][19] No prepared dietary supplement has been proven to help BPH in properly performed, randomized, controlled studies.

- **Genetic predisposition** to BPH has been demonstrated in cohort studies. First-degree relatives in 1 study demonstrated a 4-fold increase in the risk of BPH compared to the control.[20] These findings have demonstrated consistency in twin studies looking at the disease severity of BPH, with higher rates of LUTS seen in monozygotic twins.[21][22]

- **Localized inflammation** is often associated with BPH, at least histologically.[23][24][25] While the exact etiology is unclear, possible causes include increased detrusor voiding pressure, obesity, low-grade or chronic prostatitis, compression of the prostatic ducts, and autoimmune disorders. This would suggest that the use of NSAIDs could be used to treat symptomatic BPH. Three randomized studies have confirmed that NSAIDs can improve BPH symptoms, but the difference was relatively modest at <3 points (International Prostate Symptom Scores [IPSS]) and <1 mL/s improvement in urine peak flow rate.[26]

- **Obesity** is associated with an increased risk of BPH in observational studies.[27][28] The exact cause is unclear but is likely multifactorial, as obesity makes up 1 aspect of metabolic syndrome. Proposed mechanisms include increased levels of systemic inflammation and higher levels of estrogens.[29][30]

- **Metabolic syndrome** refers to conditions that include hypertension, glucose intolerance/insulin resistance, and dyslipidemia. Meta-analysis has demonstrated those with metabolic syndrome and obesity have significantly higher prostate volumes.[31] Further studies looking at men with elevated glycosylated hemoglobin levels (Hba1c) have demonstrated an increased risk of LUTS.[15] Limitations of these studies are that there were no subsequent significant differences in prostate symptom scores, and the effect of diabetes on LUTS has been shown to be multifactorial.[31][32] Further studies are therefore required to establish causation in these individuals.

Roles of Insulin

Insulin Function		
Liver	Adipose Tissue	Muscle
↓ glycogenolysis	↓ lipolysis	↓ protein catabolism
↓ gluconeogenesis	↑ glycerol formation	↓ amino acid oxidation
↓ ketogenesis	↑ fatty acid formation	↑ amino acid uptake
↑ glycogen synthesis	↑ glucose uptake	↑ glucose uptake
↑ fatty acid synthesis		↑ protein synthesis
		↑ glycogen synthesis

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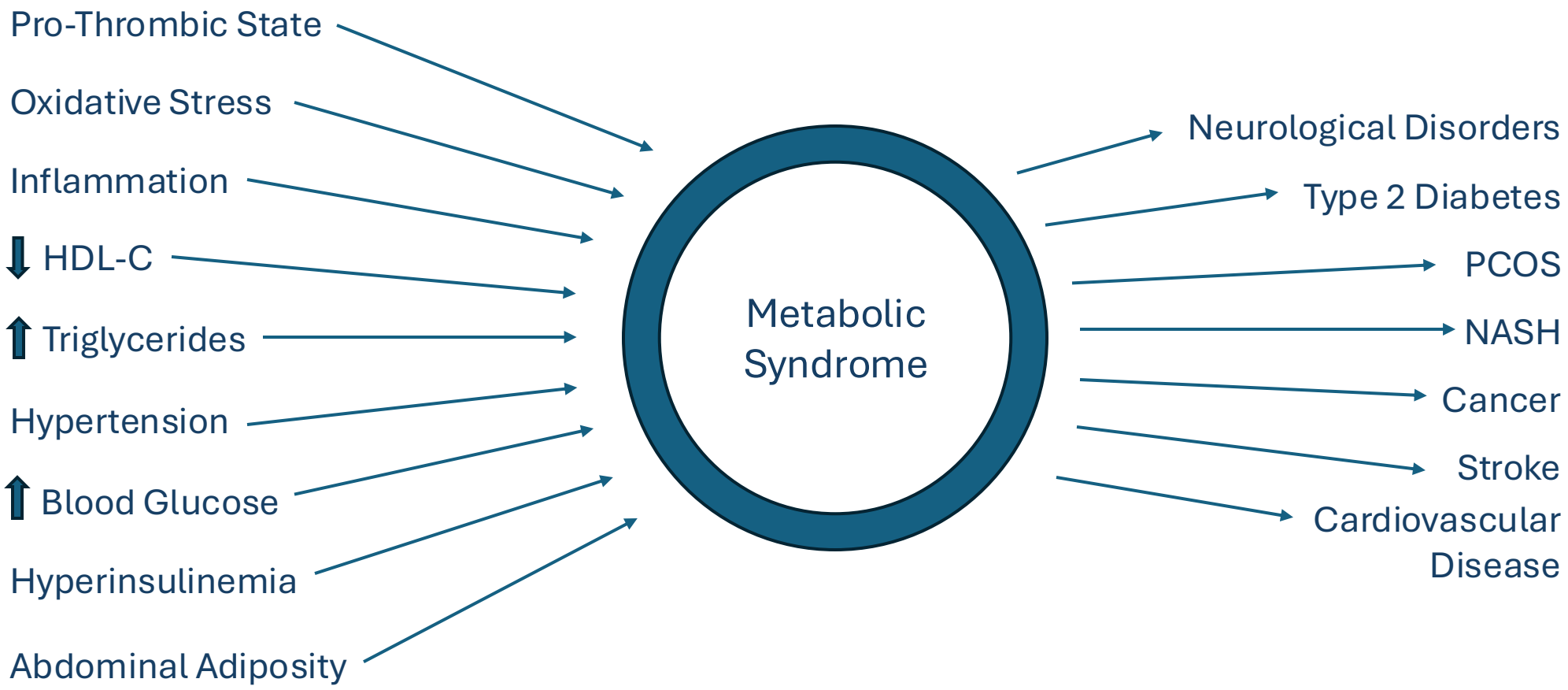
- Metabolic Wind-Up -



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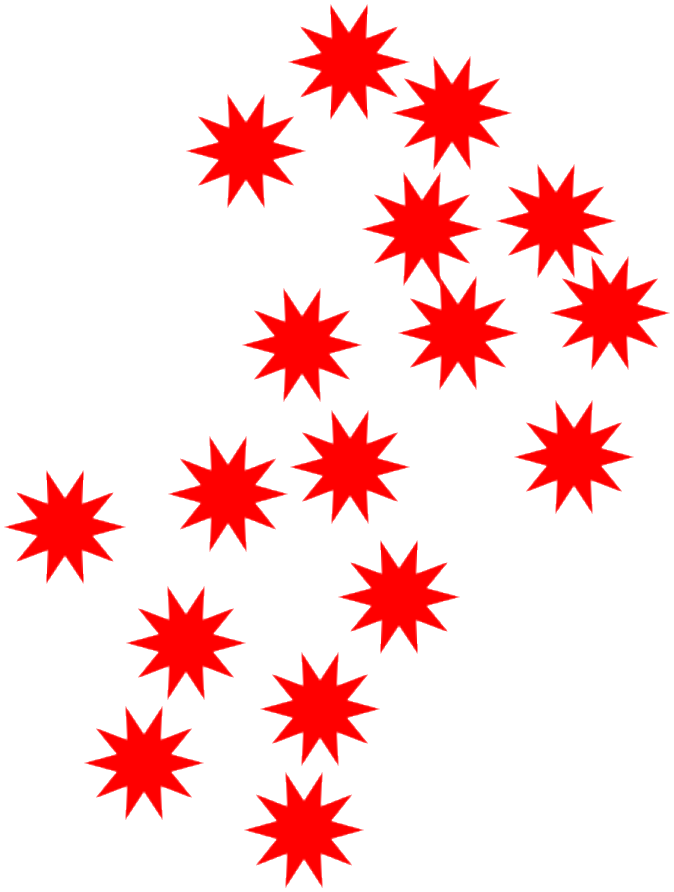
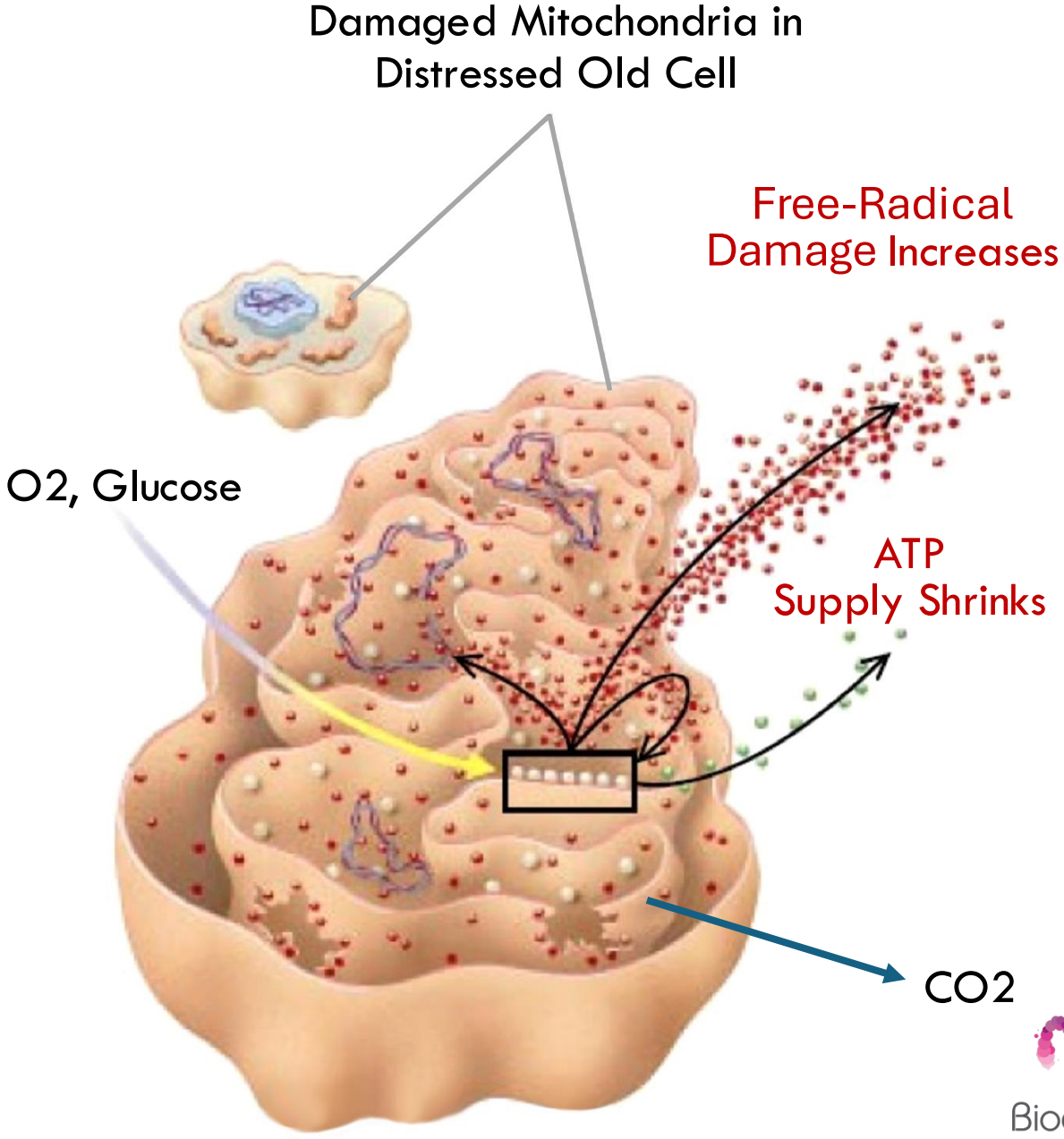
= Glucose Molecule



INSULIN



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Is there a connection between insulin-based therapeutics and BPH (and beyond)?

> Diabetes. 2008 Jun;57(6):1536-43. doi: 10.2337/db08-0094. Epub 2008 Mar 13.

Reduced glucocorticoid production rate, decreased 5alpha-reductase activity, and adipose tissue insulin sensitization after weight loss

Jeremy W Tomlinson [1], Joanne Finney, Beverly A Hughes, Susan V Hughes, Paul M Stewart

Affili

PMID

The changes in 5αR activity are striking. 5αR has 2 isoforms which only share approximately 47% sequence homology (29); the type 1 isoform (5αR1) is located on the short arm of chromosome 5, whilst 5αR2 is located on the short arm of chromosome 2. 5αR1 is expressed in skin and adipose tissue (29;30) and 5αR2 in prostate, epididymis and seminal vesicles; both isozymes are expressed in the liver (29). For cortisol metabolism, studies suggest that the most significant contributor to 5α-reduction of GC metabolites within the liver is 5αR2.

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Reduced glucocorticoid production rate, decreased 5alp… …ulin sens…

Jeremy … …t

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In our study 5αR activity decreased significantly following weight loss. The role of 5αR in the control of body composition and insulin sensitivity has not been investigated in detail. Studies have shown enhanced 5αR activity with obesity (31) and T2DM (32) and sexual dimorphism of expression with increased activity in males (31;33). Dietary macronutrient composition has also been implicated as a regulator of 5αR and 5βR activity; high-fat, low-carbohydrate and moderate-fat, moderate-carbohydrate diets decrease 5αR and 5βR activity (34). The effect was most pronounced in the high-fat, low-carbohydrate diet, but both diets were associated with significant weight loss (34). In rodents, treatment of obese Zücker rats with insulin sensitizers decreases 5αR1 expression in the liver (35). In patients with polycystic cystic ovary syndrome, 5αR activity correlates positively with markers of insulin resistance (36). Specifically with regards to GC metabolism, reduced 5αR activity decreases the inactivation of cortisol to its tetra-hydrometabolites and as a consequence this may relax the drive to the HPA axis and be responsible for the reduction in total GC secretion that we observed after weight loss. Interestingly the converse is probably also true in PCOS where enhanced 5αR activity may drive the HPA axis to maintain circulating cortisol levels at the expense of adrenal androgen excess (37).

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55 yo male
DM2
BPH
HTN

Metformin
Glipizide
Statin
Atenolol

	Test	Current Result and Flag		Previous Result and Date	Units	Reference Interval
	WBC [01]	6.5			x10E3/uL	3.4-10.8
▼	**RBC** [01]	**3.52**	**Low**		x10E6/uL	4.14-5.80
▼	**Hemoglobin** [01]	**10.0**	**Low**		g/dL	13.0-17.7
▼	**Hematocrit** [01]	**31.8**	**Low**		%	37.5-51.0
	MCV [01]	90			fL	79-97
	MCH [01]	28.4			pg	26.6-33.0
▼	**MCHC** [01]	**31.4**	**Low**		g/dL	31.5-35.7
	RDW [01]	13.3			%	11.6-15.4
	Platelets [01]	431			x10E3/uL	150-450
	Neutrophils [01]	65			%	Not Estab.
	Lymphs [01]	22			%	Not Estab.
	Monocytes [01]	6			%	Not Estab.
	Eos [01]	6			%	Not Estab.
	Basos [01]	1			%	Not Estab.
	Neutrophils (Absolute) [01]	4.3			x10E3/uL	1.4-7.0
	Lymphs (Absolute) [01]	1.4			x10E3/uL	0.7-3.1
	Monocytes(Absolute) [01]	0.4			x10E3/uL	0.1-0.9
	Eos (Absolute) [01]	0.4			x10E3/uL	0.0-0.4
	Baso (Absolute) [01]	0.0			x10E3/uL	0.0-0.2
	Immature Granulocytes [01]	0			%	Not Estab.
	Immature Grans (Abs) [01]	0.0			x10E3/uL	0.0-0.1

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	Test	Current Result and Flag		Previous Result and Date	Units	Reference Interval
▲	**Glucose** [01]	**180**	**High**		mg/dL	70-99
▲	**BUN** [01]	**41**	**High**		mg/dL	6-24
▲	**Creatinine** [01]	**1.35**	**High**		mg/dL	0.76-1.27
	eGFR	64			mL/min/1.73	>59
▲	**BUN/Creatinine Ratio**	**30**	**High**			9-20
▼	**Sodium** [01]	**132**	**Low**		mmol/L	134-144
	Potassium [01]	5.2			mmol/L	3.5-5.2
	Chloride [01]	98			mmol/L	96-106
▼	**Carbon Dioxide, Total** [01]	**19**	**Low**		mmol/L	20-29
	Calcium [01]	9.5			mg/dL	8.7-10.2
	Protein, Total [01]	8.3			g/dL	6.0-8.5
▼	**Albumin** [01]	**3.7**	**Low**		g/dL	4.1-5.1
▲	**Globulin, Total**	**4.6**	**High**		g/dL	1.5-4.5
	Bilirubin, Total [01]	0.4			mg/dL	0.0-1.2
▲	**Alkaline Phosphatase** [01]	**128**	**High**		IU/L	44-121
	AST (SGOT) [01]	12			IU/L	0-40
	ALT (SGPT) [01]	14			IU/L	0-44

	Test	Current Result and Flag		Previous Result and Date	Units	Reference Interval
	Lipids [01]					
	Cholesterol, Total [01]	179			mg/dL	100-199
	Triglycerides [01]	135			mg/dL	0-149
	HDL Cholesterol [01]	41			mg/dL	>39
	VLDL Cholesterol Cal	24			mg/dL	5-40
▲	**LDL Chol Calc (NIH)**	**114**	**High**		mg/dL	0-99
	T. Chol/HDL Ratio	4.4			ratio	0.0-5.0

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Thyroid Panel With TSH

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
TSH [01]	3.850		uIU/mL	0.450-4.500
Thyroxine (T4) [01]	6.5		ug/dL	4.5-12.0
T3 Uptake [01]	33		%	24-39
Free Thyroxine Index	2.1			1.2-4.9

Iron and TIBC

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
▼ **Iron Bind.Cap.(TIBC)**	**216 Low**		ug/dL	250-450
UIBC [01]	172		ug/dL	111-343
Iron [01]	44		ug/dL	38-169
Iron Saturation	20		%	15-55

Hgb A1c with eAG Estimation

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
▲ **Hemoglobin A1c** [01]	**10.0 High**		%	4.8-5.6
Please Note: [01]	Prediabetes: 5.7 - 6.4 Diabetes: >6.4 Glycemic control for adults with diabetes: <7.0			
Estim. Avg Glu (eAG)	240		mg/dL	

Thyroxine (T4) Free, Direct

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
T4,Free(Direct) [01]	1.30		ng/dL	0.82-1.77

C-Peptide, Serum

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
C-Peptide, Serum [01]	2.8 C-Peptide reference interval is for fasting patients.		ng/mL	1.1-4.4

Vitamin D, 25-Hydroxy

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
▼ **Vitamin D, 25-Hydroxy** [01]	**19.6 Low**		ng/mL	30.0-100.0

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C-Reactive Protein, Cardiac

Test	Current Result and Flag		Previous Result and Date	Units	Reference Interval
▲ **C-Reactive Protein, Cardiac** [01]	**7.15**	**High**		mg/L	0.00-3.00
			Relative Risk for Future Cardiovascular Event		
			Low		<1.00
			Average		1.00 - 3.00
			High		>3.00

Homocyst(e)ine

Test	Current Result and Flag		Previous Result and Date	Units	Reference Interval
▲ **Homocyst(e)ine** [01]	**20.9**	**High**		umol/L	0.0-14.5

Uric Acid

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
Uric Acid [01]	6.0		mg/dL	3.8-8.4
		Therapeutic target for gout patients: <6.0		

Phosphorus

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
Phosphorus [01]	4.0		mg/dL	2.8-4.1

LDH

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
LDH [01]	146		IU/L	121-224

GGT

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
GGT [01]	61		IU/L	0-65

Triiodothyronine (T3)

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
Triiodothyronine (T3) [01]	78		ng/dL	71-180

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Thyroid Antibodies

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
Thyroid Peroxidase (TPO) Ab [01]	11		IU/mL	0-34
Thyroglobulin Antibody [01]	<1.0		IU/mL	0.0-0.9

Thyroglobulin Antibody measured by Beckman Coulter Methodology
It should be noted that the presence of thyroglobulin antibodies may not be pathogenic nor diagnostic, especially at very low levels. The assay manufacturer has found that four percent of individuals without evidence of thyroid disease or autoimmunity will have positive TgAb levels up to 4 IU/mL.

Magnesium

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
Magnesium [01]	2.1		mg/dL	1.6-2.3

Fibrinogen Activity

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
▲ **Fibrinogen Activity** [01]	**533 High**		mg/dL	193-507

Ferritin

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
▲ **Ferritin** [01]	**496 High**		ng/mL	30-400

Triiodothyronine (T3), Free

Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
Triiodothyronine (T3), Free [01]	2.2		pg/mL	2.0-4.4

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