



## PART II - BENIGN PROSTATIC HYPERPLASIA AND ASSOCIATED LOWER URINARY TRACT SYMPTOMS

*“Life is not living, but living in health”* (Marcus Valerius Martialis, 1st century Roman poet).

In Part I of the series on prostate health, it was contended that BPH/LUTS (benign prostatic hyperplasia with lower urinary tract symptoms) is as serious medical condition with serious adverse health effects. In the spirit of helping men who suffer from BPH/LUTS to live in health, Part II focuses on nonmodifiable and modifiable risk factors. It is important for men to learn about risk factors because BPH/LUTS is a multifactorial condition associated with nonmodifiable and modifiable risk factors, which play an important role in the prevention, prediction and management and of BPH/LUTS.

### Risk Factor Facts

A risk factor is a genetic metabolic diet or lifestyle-related variable that increases the likelihood of contracting a disease such as BPH/LUTS. Risk factors are correlational and not causal in nature. For example, a sedentary lifestyle is correlated with BPH/LUTS but it does not independently cause it. Typically, the more risk factors a man has for BPH/LUTS the greater likelihood he will contract the disease.

### Non-modifiable Risk Factors

Age, gender, race and genetics are among the most studied nonmodifiable risk factors. They are unchangeable, meaning no intervention can change or otherwise control them. However, their deleterious effects can be moderated by making healthy diet and lifestyle changes.

### Modifiable Risk Factors

Unlike their nonmodifiable counterpart, modifiable risk factors are changeable in the sense they can be controlled by diet and lifestyle interventions, thereby, reducing the probability of developing a disease. As with nonmodifiable risk factors, the effects of modifiable risk factors be reduced by interventions. Smoking, sedentary lifestyle, high blood pressure diabetes, dyslipidemia and overweight/obesity are among the most common modifiable risk factors.



## NON-MODIFIABLE DIETARY RISK FACTORS ASSOCIATED WITH BPH/LUTS

### Age

BPH/LUTS is strongly correlated with age. Specifically, it affects 70% of men between 60–69 years of age and 80% of men who are 70 years of age or older. In sum, aging in adult males is highly correlated nonmodifiable risk factor for BPH/LUTS.

### Genetics

Studies show that a family history of the single nucleotide polymorphisms/SNP (most common mutation in the human genome) for BPH is an unmodifiable risk factor for the pathogenesis, progression and prognosis of clinically diagnosed BPH.

## MODIFIABLE METABOLIC RISK FACTORS ASSOCIATED WITH BPH/LUTS

Modifiable risk factors, which are significantly implicated in the pathogenesis of BPH leading to LUTS, can be divided into the categories of lifestyle, metabolic-and diet/nutrition-related factors. It is note worthy that all three categories of modifiable risk factors are associated with a significant increased risk of developing and worsening BPH/LUTS.



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### Physical Exercise/Activity

A sedentary lifestyle is associated with BPH/LUTS. Physical activity compared to a sedentary lifestyle reduces the risk of BPH and LUTS. Thus, regular physical activity would be an appropriate lifestyle intervention to help prevent and treat BPH/LUTS.

### Alcohol Consumption

The effect of alcohol on the BPH/LUTS is too conflicting to report any definitive conclusions or recommendations. Notwithstanding conflicting findings, excessive alcohol intake is reported to be a risk factor for BH/LUTS.

### Smoking

The effect of smoking on BPH and LUTS are too mixed and contradictory to offer any definitive conclusions or recommendations.

### Macronutrients

**Protein intake.** The extent to which protein intake is linked to BPH is unclear. On the one hand, excess intake of protein is positively correlated with the risk of developing of BPH, especially when it is animal protein (i.e., red meat). On the other hand, total protein intake reduces the risk of BPH and its symptoms, while noting that red meat increases the risk of BPH. Thus, it may be more prudent to eat more plant-based protein and leaner meat sources of protein such as fish.

**Carbohydrate intake.** As with protein and fat, the type of carbohydrate is determinative of whether carbohydrate-based foods are associated with the BPH/LUTS. For example, starch-based carbohydrate foods (i.e., bread, pasta and rice) have been found to increase the risk for BPH. Excess starch intake creates a glycemic overload which increases serum insulin and insulin-like growth factor, which in turn stimulate the development of BPH. On the other hand, complex carbohydrates such as fruits and vegetables, which contain inflammation fighting nutrients such as antioxidants, polyphenols, vitamins and minerals and fiber, help prevent BPH.

**Fat intake.** The role of fat in the development of BPH/LUTS is complicated and not fully understood. As with protein, the type of fat is determinative in the development of BPH/LUTS. For example, in a longitudinal study focusing on the risk associated with energy intake and macronutrients on BPH, it was found that the development of BPH differed by the type of fat intake. Specifically, animal fat was not associated with BPH or LUTS, while vegetable fat was positively correlated with BPH and LUTS. In terms of specific fatty acids (the building blocks of fats), the consumption of saturated fatty acids (i.e., palmitic and steric acid) and monounsaturated fatty acids (i.e., oleic acid) are not associated with BPH but polyunsaturated fatty acids (i.e., linoleic acid, alpha-linolenic acid, arachidonic acid, eicosapentaenoic acid/EPA and docosahexaenoic acid/DHA) are positively associated with BPH and LUTS. It is worth noting that fatty acids are prone to lipid peroxidation, which damages them by creating oxidative stress and inflammation, which in turn destroys prostate cells and results in the compensatory cellular proliferation of prostate cells leading to BPH. At the same time, omega-3 fatty acids are reported to confer a protective effect on the prostate by reducing the pro-inflammatory effect of prostaglandins and leukotrienes on the prostate. Since they are vulnerable to oxidation, it might be prudent to take vitamin E and other anti-inflammation nutrients when consuming omega-3 fatty acids either through food or dietary supplements.

#### MACRONUTRIENTS:



CARBOHYDRATES



PROTEINS



FATS



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### Micronutrients

**Vitamin D.** Vitamin D in its bioactive form (1,25-(OH) vitamin D, also called calcitriol or 1,25 dihydroxycholecalciferol) reduces the risk of developing the BPH/LUTS complex. Calcitriol (the active form of vitamin D, 1,25-(OH) vitamin D) binds to vitamin D receptors (VDR) located on and expressed in the cells of the bladder and prostate, which are primary targets of VDR-related agonists such as calcitriol/1,25-(OH) vitamin D, along with the vitamin D homologue ercalcitriol (also called 1-alpha,25-dihydroergocalciferol). It has been shown that VDR agonists, particularly elocalcitol, inhibit prostate growth by targeting the RhoA/Rho-kinase (ROCK) pathway and reduce inflammation by targeting the NF-kappaB pathway in the prostate cells.

**Zinc.** The intake of zinc has a beneficial effect on the prostate and reduce the risk of BPH. However, zinc at elevated concentrations may be a negative effect on prostate health. Specifically, it has been found that when compared to men who did not supplement with zinc, men who took more than 100 mg/day of supplemental zinc had a significant risk for advanced prostate cancer. Also, men who supplemented with zinc for more than 10 years experienced a significant risk of prostate cancer. It should be noted that supplementing with zinc at doses of up to 100 mg/day is not associated with prostate cancer risk. On the other side of the coin, zinc deficiency is associated with oxidative stress which leads to inflammation, a risk factor for the development of BPH/LUTS.

### Sex Steroid Hormones

Androgens and estrogens, generally, testosterone, dihydrotestosterone (DHT) and estrogen, specifically, are heavily implicated with BPH. DHT is an enzyme which converts testosterone into DHT via 5 alpha-reductase in the prostate. Increased production of DHT induces hyperplasia (i.e., an increase in the number of epithelial and stromal cells in the periurethral area of the prostate) causing the prostate to become abnormally large and setting the stage for BPH/LUTS to develop. Testosterone can be converted into estrogen via the enzyme aromatase. Estrogen, estradiol particularly, significantly enlarges the prostate.

### Oxidation and Inflammation

BPH/LUTS is an immune-mediated inflammatory disease caused by tissue-damaging oxidative stress and inflammation directly contributing to BPH. Oxidative stress and inflammation are interdependently related pathophysiological processes that typically appear simultaneously together. In terms of what happens in the prostate, inflammation is a protective immune-driven repair response to cellular injury of prostatic vascular connective tissue that has gone haywire, while oxidative stress is a condition whereby the production of reactive oxygen species (ROS) in the prostate outpaces their detoxification by enzymes such as super oxidized mutase (SOD), glutathione peroxidase, and catalase. Ultimately, prostatic tissue damage caused by oxidative stress and inflammation leads to the compensatory proliferation of epithelial and stromal cells in the transition zone of the prostate resulting in BPH/LUTS.

### Obesity

It is well-established that is associated with an increased risk for the development of BPH, BPH surgery, progression of urinary symptoms, initiation of BPH medical treatment, along with LUTS. Existing evidence suggests that inflammation mediates the relationship between obesity and BPH. It has been confirmed that obesity is a driver of chronic systemic inflammation resulting in "prostate tissue immune cell infiltration, tissue remodeling, hyperplasia, benign prostatic enlargement, increased LUTS severity, and clinical BPH." (p3) Specifically, it was found that centralized/abdominal obesity estimated by waist-to-hip ratio was significantly associated with the severity of inflammation in various regions of prostate tissue as well as with the severity of LUTS among men with inflammation. In short, centralized obesity seems to advance prostate tissue inflammation so as to increase the severity of LUTS.



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### Diabetes and Glucose-Insulin Dysregulation

Diabetes significantly increases the risk of BPH and LUTS. A recent meta-analysis found that LUTS inpatients suffering from BPH and diabetes increased compared to patients with just BPH. It is also reported that systemic inflammation and oxidative stress caused by diabetes can cause BPH. Finally, increased serum insulin and hyperglycemia are associated with clinically diagnosed BPH and LUTS, increased prostate size and an increased risk of prostate enlargement.

### Metabolic Syndrome

Metabolic syndrome (MetS) significantly increases the likelihood of LUTS and BPH/LUTS, with abdominal obesity driving the pathophysiological metabolic changes associated with MetS.

MetS is a constellation of interrelated metabolic risk factors. A diagnosis of MetS requires at least three of the following five clinical criteria: **Elevated waist-circumference**  $\geq 88$  cm for women and  $\geq 102$  cm for men.  $\geq 102$ cm (40 inches), **Elevated triglycerides**  $\geq 150$  mg/dL (1.7 mmol/L), **Reduced HDL**  $< 40$  mg/dL (1.0 mmol/L) in males;  $< 50$  mg/dL (1.3 mmol/L) in females, **Elevated blood pressure Systolic**  $\geq 130$  and/or diastolic  $\geq 85$  mm Hg, **Elevated fasting glucose**  $\geq 100$  mg/dL All of the MetS diagnostic criteria increase the risk of BPH/LUTS.

### Cardiovascular Diseases and Conditions

There is significant correlation between BPH/LUTS and cardiovascular diseases and conditions. For example, men with a history of coronary heart disease, stroke and hypertension are more likely to suffer from BPH/LUTS. Further, there is a significant correlation between moderate and severe LUTS and an increased risk for major adverse cardiac events such as cardiac death, myocardial infarction/heart attack, congestive heart failure and coronary syndrome. Finally, the cardiometabolic conditions of MetS (i.e., low HDL, high triglycerides, high blood pressure and hyperlipidemia) significantly increase the risk of BPH/LUTS.

## STRAUSS NATURALS PROSTATE SUPPORT DROPS, BLADDER SUPPORT DROPS, KIDNEY SUPPORT DROPS & HEARTDROPS FOR BPH/LUTS

**Strauss Naturals Prostate Drops, Bladder Drops, Kidney & Blood Pressure Drops and Heartdrops** is an especially well-suited, effective intervention for BPH/LUTS.

It can help prevent modifiable risk factors associated with BPH/LUTS and moderate their effects, while limiting the effects of nonmodifiable risk factors by reducing the number of modifiable risk factors and the burden they impose on the body.



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