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Editorial

A Pharmaconutritional Strategy to Reverse BPH

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Benign prostatic hyperplasia (BPH) has become very common in ageing males. Like so many other chronic disorders it is increasing, with a near-doubling in the last 2 decades [1,2]. And as with the case of so many other chronic disorders, that increase is obviously due to our unhealthy diet and lifestyle because BPH hardly occurs in vestigial groups [3].

The prostate grows rapidly during puberty (which is occurring at progressively earlier ages [4]), and remains at a fighting weight of circa 20g for a decade or two before - in the industrialised nations - it starts growing again. These two phases of growth are quite different. The first is driven by endocrine changes, and is a natural part of the journey to sexual maturity. The second is unnatural, unnecessary and largely driven by chronic inflammation [5,6], with insulin resistance as a possible ancillary driver [7].

While risk-enhancing genes have been provisionally identified [8], lifestyle factors appear to be far more important. These include diabetes and obesity (both of which are pro-inflammatory and involve insulin resistance) and heart disease, which is often the end result of chronic inflammation and insulin resistance.

Patients with these lifestyle diseases are also typically dysbiotic.

In pre-clinical models endotoxemia, a pro-inflammatory condition caused by dysbiosis and which in turn causes generalised chronic inflammation [9] and insulin resistance [10], triggers BPH [11]. This likely explains why NAFLD, another disease driven by endotoxemia [12] and insulin resistance [13], and which currently affects 1 in 3 globally [14], is associated with an increased risk of BPH [15].

Insulin resistance, chronic inflammation, dysbiosis and endotoxemia are all caused by the modern diet and lifestyle via a limited number of mechanisms, which are quite well understood and have been covered in many previous blog posts (See www.drpaulclayton.eu). So already we can start to see how a dietary regime designed to restore an anti-inflammatory environment, eubiosis and insulin sensitivity should reduce the risk of BPH, and might even persuade an expanding prostate to go into reverse.

Reversal is possible, of course, because the prostate is plastic. It is a living organ, and like all living tissue is constantly remaking itself.

Cells are constantly proliferating on one side of the equation, and entering apoptosis (programmed cell death) on the other. If these two processes are in balance, the organ maintains normal size and function. If proliferation rates increase and/or apoptotic rates decline, the total number of cells in the prostate must increase over time. The prostate is compelled to grow until the urethra is compromised and symptoms emerge.

Inflammation is important on both sides of this equation

Whether it is caused by local microbiota shift (aka 'infection') or by diet-related pro-inflammatory issues, inflammation in the prostate boosts rate of cell proliferation via mechanisms which probably include oxidative stress [16]. On the apoptosis side, there is persuasive evidence that programmed cell death rates are reduced by up to 75% in the enlarged prostate [17], likely due to raised levels of the control protein bcl-2 [17].

TGF-beta1 and bcl-2 have multiple functions but in the non-cancerous prostate they regulate apoptosis, with TGF-beta1 increasing apoptosis and bcl-2 reducing it. Levels of both are elevated in the enlarged prostate [17]. The slowed rate of apoptosis in BPH demonstrates that the bcl-2 effect is dominant, and bcl-2 expression is increased in various models of chronic inflammatory stress [18,19].

As chronic inflammation increases cell proliferation and reduces programmed cell death in the prostate it is an obvious potential cause of BPH; and as the modern diet and lifestyle encourages chronic inflammation [20-22], thinking of BPH as an inflammatory complication seems not only plausible but also potentially productive.

Well-known herbal remedies such as saw palmetto are able to reduce prostate size by inhibiting 5-alpha-reductase and thus reducing levels of DHT, a testosterone metabolite which exerts local anabolic effects. Saw palmetto may also have directly anti-inflammatory effects [23], but these only emerge at high doses [24] and are probably not relevant to common usage.

A broad-spectrum anti-inflammatory/prebiotic program will confer a wider range of benefits, and can be used prophylactically. Unsurprisingly, the three main anti-inflammatory dietary components are the omega 3 HUFA's, polyphenols and prebiotic fibers.

There is not much data on the role of fish oil in BPH, other than a 2017 combinatorial clinical trial in which fish oil may have slightly enhanced the effects of the BPH drugs tamsulosin and finasteride [25]. The fish oil used in this study was the usual badly formulated commercial product stabilized with vitamin E. Such products have poor secondary bioavailability, and would not be expected to be particularly effective.

With regard to polyphenols, the case is stronger. In preclinical models of BPH curcumin down-regulates inflammatory mediators in the prostate, slows cell growth and shrinks the prostate [26,27]. Other polyphenols have generated similar results [5,28-30].

With prebiotics the case is more complicated.

The dysbiotic gut appears to drive BPH via two distinct mechanisms, one humoral and one cellular. It leaks LPS into the portal circulation, generating chronic systemic inflammation which drives prostate cell proliferation [11,16]. It also facilitates the translocation of gut bacteria to other sites, including the genitourinary tract [30] and likely including the prostate. Bacterial and non-bacterial prostatitis are reported to double the risk of developing BPH [32].

When a dysbiotic gut is made eubiotic by using prebiotics, the reduction in endotoxemia and systemic inflammatory stress would be expected to reduce proliferative drive in the prostate [11]. The reduced translocation of enteric bacteria would be expected to lower but not eliminate the incidence of bacterial prostatitis, as many of the bacterial species involved in this condition derive not from the gut but from the urinary tract [31].

The data linking prebiotics to BPH are scant. I am aware of one paper which showed that the human milk prebiotic sialyllactose could reduce certain aspects of BPH [33], but sialyllactose has multiple properties and it is not clear whether the prebiotic function was in play here.

Given the enormous therapeutic indices of omega 3's, polyphenols and prebiotic fibers, these three actives can be easily combined on the plate and in a supplemental program. In the context of today's rapidly rising rates of BPH a restoration of pre-transitional nutritional values should significantly cut the numbers of prostate patients, and make old men's lives a little easier.

There is little evidence to support this hypothesis, yet. A few sets of epidemiological data hint (no more than that) that the Mediterranean diet may be associated with a reduced risk of BPH [34], but there is no proof. Going forward, a simple prospective clinical trial could provide this.

In my own case, at least, the regime appears to have been entirely successful.

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