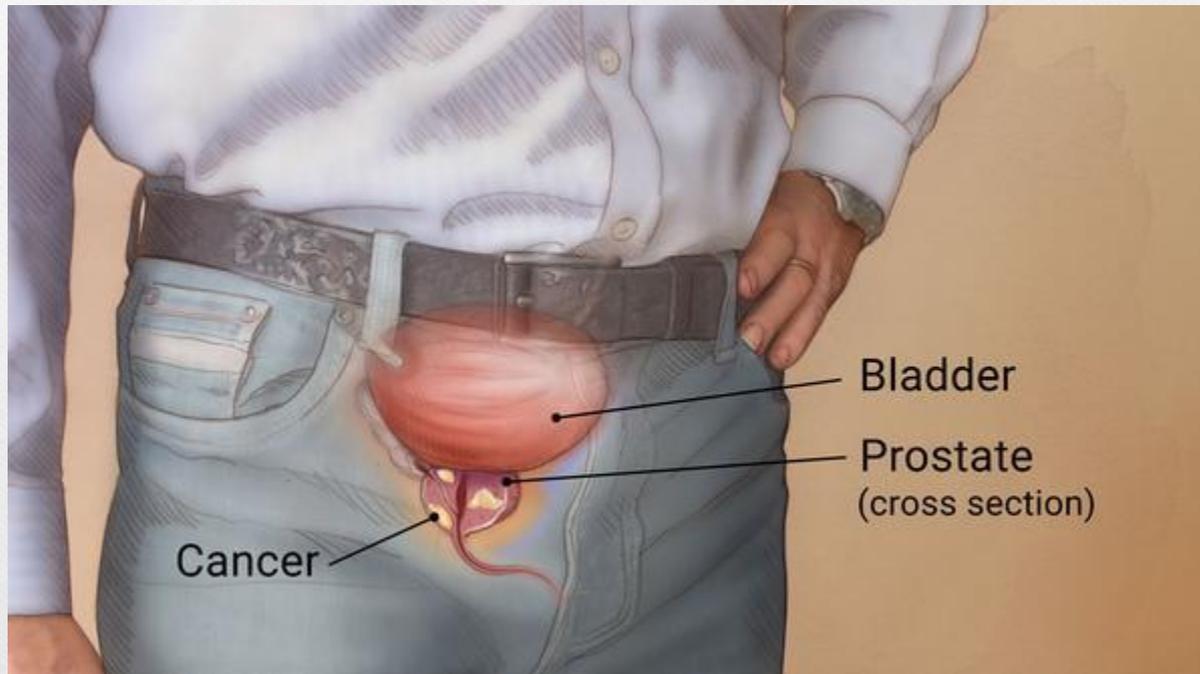


# Arresting Prostate Cancer Development

By Dr. Walker



# Objectives

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The many faces of prostate cancer?

Discuss the pathogenesis of prostate cancer

How does lifestyle impact our risk of prostate cancer?

Arresting prostate cancer development using clinically validated nutrients

Using repurposed drugs to target prostate cancer cells

# Prostate Cancer Key Takeaways

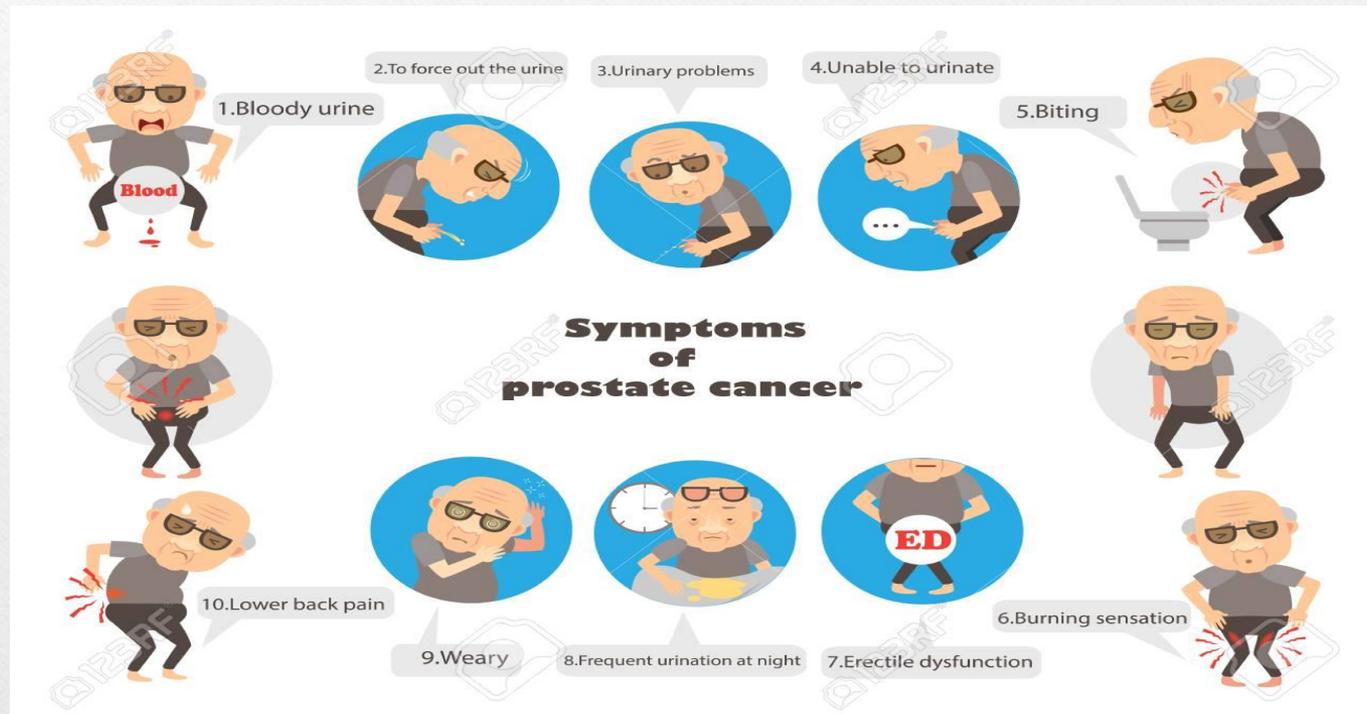
- About 30,000 men will die of prostate cancer
- About 1 in 6 will be diagnosed with prostate cancer during his lifetime.
- Prostate cancer is the second leading cause of cancer death in American men
- About 1 in 36 will die of Prostate cancer.

## Prostate Cancer Facts & Figures

Source: American Cancer Society

	2017	2018
Estimated New Cases	161,360	164,690
Estimated Deaths	26,730	29,430
A man will be diagnosed every...	3.3 minutes	3.2 minutes
A man will die from the disease every...	20 minutes	18 minutes

# Faces of Prostate Cancer

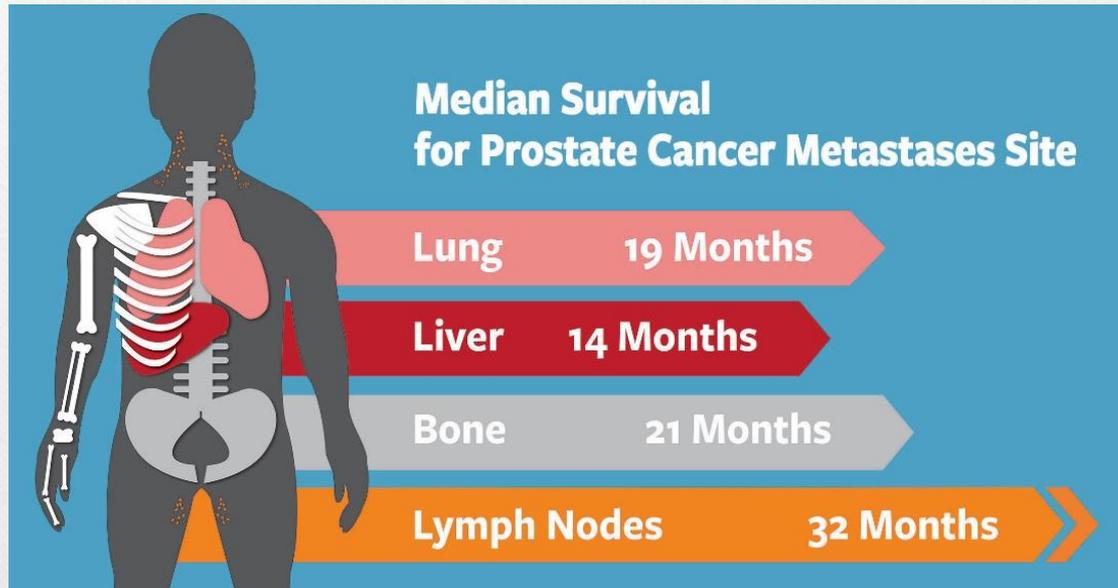


# Personality Matters

**Table 1: Risk of PSA Relapse 5 Years Following Radical Prostatectomy, Based on Various Biopsy Gleason Scores.**

<b>Group 1</b>	<b>Gleason Score 6</b>	<b>5%</b>
<b>Group 2</b>	<b>Gleason Score 3+4=7</b>	<b>17%</b>
<b>Group 3</b>	<b>Gleason Score 4+3=7</b>	<b>35%</b>
<b>Group 4</b>	<b>Gleason Score 4+4=8</b>	<b>37%</b>
<b>Group 5</b>	<b>Gleason Score 9-10</b>	<b>76%</b>

# Location! Location! Location!



# Risk Factors

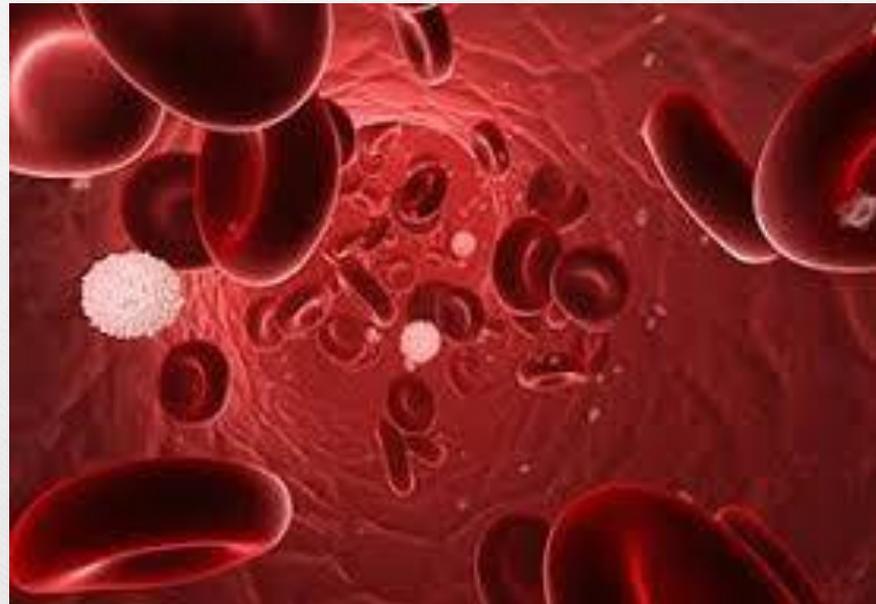
- Age
- Family
- Ethnicity
- Genes
- lifestyle



# Nurture Your Micro-environment

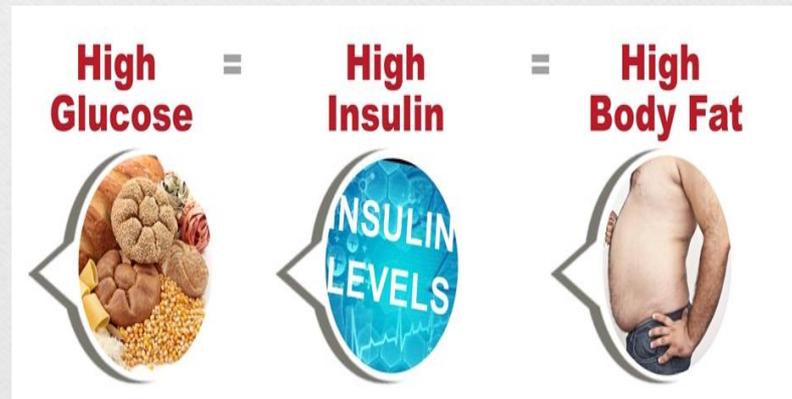
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- Excess  
Insulin/sugar
- Inflammation
- Hormone  
balance
- Hypoxia



# Sugar/ Insulin

- 10 healthy people were assessed for fasting blood-glucose levels and the phagocytic index of neutrophils.
  - Eating 100 g carbohydrates significantly decreased the capacity of neutrophils to engulf bacteria
- Men in the highest tertile (third) of insulin resistance were **almost 3 times more likely to have prostate cancer** than those in the lowest tertile. Conversely, men with the highest insulin sensitivity had a 65% reduced risk of prostate cancer.
- **Standard reference range** 2.6-24.9  $\mu$ IU/mL
- **Ideal insulin level < 5**



# Chronic Inflammation

- Meta-analysis and populations studies have shown a small increase in the relative risk of prostate cancer in men with a history of clinical or symptomatic prostatitis
- Sexually transmitted infections are hypothesized to play a role in the development of prostate cancer, perhaps due to inflammation-induced oncogenesis
- Upregulation of cox 2
- CRP < 0.5 ( men)



# The Heart and Prostate Connection

- Duke researchers analyzed data from 6,390 men in a four-year clinical trial testing a drug's effectiveness in reducing prostate cancer risk
  - **Findings: men with CAD had a 35 percent greater risk of developing PC over time and a 24 percent greater risk of being diagnosed with prostate cancer within the first two years of the study compared to men who did not have heart disease**



# Excess Dihydrotestosterone

- DHT- 4 times more powerful than testosterone
- Androgen stimulation of the androgen receptors
- Studies had shown that men with very low levels of 5-alpha reductase did not develop prostate cancer.
- Standard reference range 30-85ng/dl
- **Optimal range : 30-50 ng/dl**



# The Role of Diet

YOU CAN EAT WHATEVER  
YOU WANT AS LONG AS  
YOU WORKOUT!

TRUE OR FALSE?

# No barbecue!?

- 1.5 servings of pan-fried red meat per week increased the risk of advanced prostate cancer by 30 percent
- Men who consumed 2.5 servings of red meat cooked at high temperatures were 40 percent more likely to have advanced prostate cancer
- A study evaluated almost 1,000 men found that higher consumption of any ground beef was associated with **130%** increased incidence.



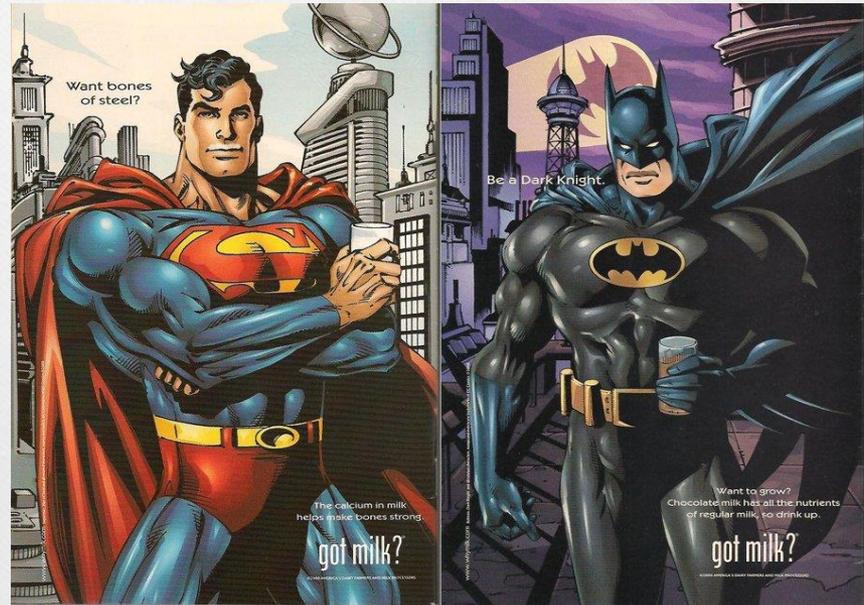
# Love my Eggs!

- A study observed that men with prostate cancer who averaged just under an egg per day had a **two-fold increased** risk of prostate cancer progression compared to men who didn't eat eggs.
- A 2011 study, who consumed more than 2.5 eggs per week showed 81 percent increased risk of fatal prostate cancer compared to 1 egg per week



# Got Milk

- A **2013 Physician's Health Study** 21,660 physicians who were followed for 28 years.
- Skim/low fat milk was associated with increased risk of low grade prostate cancer, whereas
- Whole milk was associated with a **117%** increased risk of progression to fatal disease

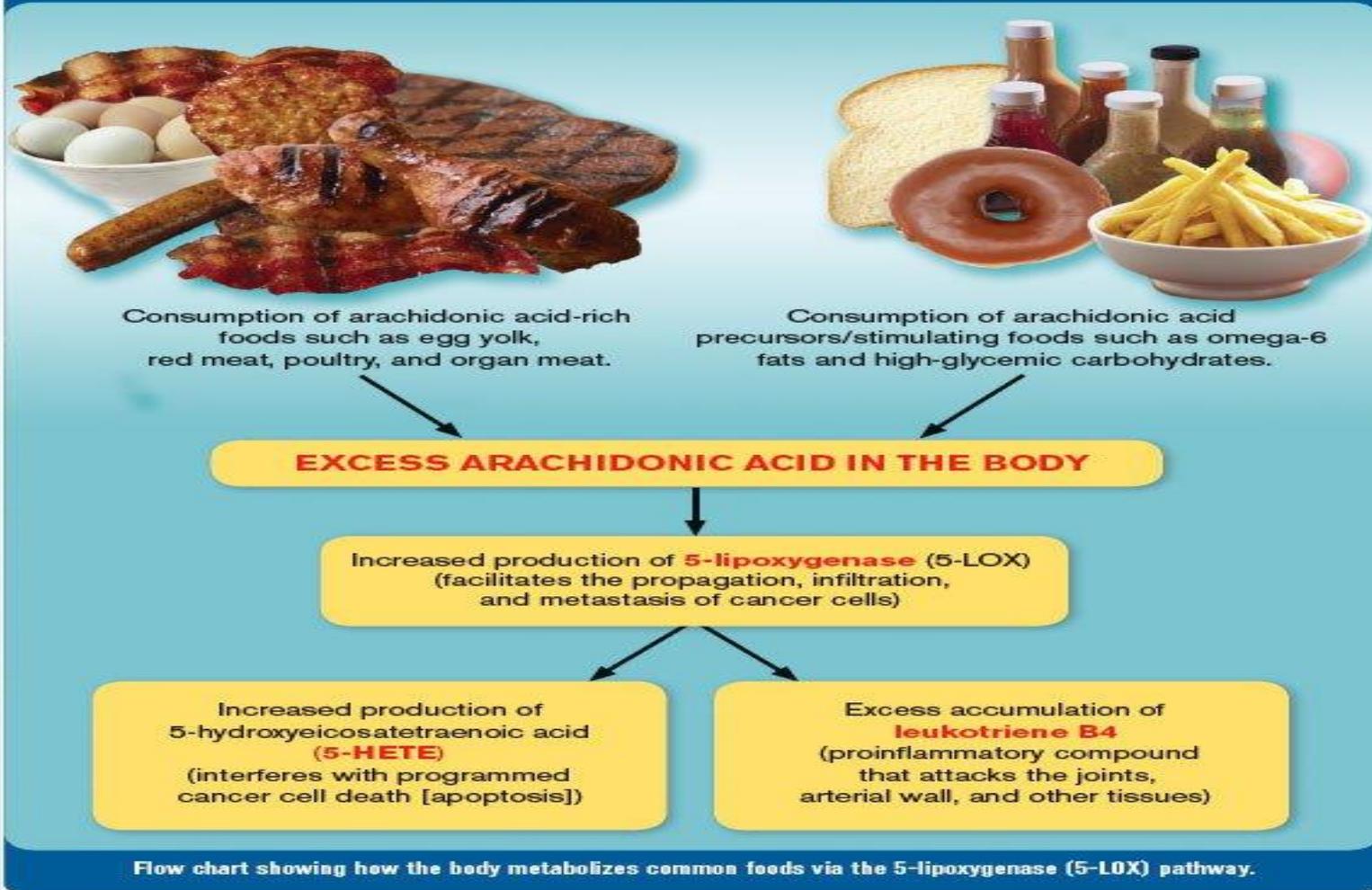


# is Chicken safe ?

- A Harvard report showed men with prostate cancer who consumed a large amount of chicken **quadrupled** the chance of their disease progressing
- Another study of baked poultry was inversely associated with advanced prostate cancer. Meaning, those who ate baked poultry had a lower incidence of aggressive, potentially metastatic disease



**Figure 1: How Common Foods Convert to Deadly Compounds in the Body**



# Can diet Reverse Prostate Cancer Progression or reduce risk?

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# Ornish Study

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- Study of 93 men with biopsy-proven prostate cancer who had elected not to undergo conventional treatment
- Participants were randomly assigned to an experimental group and a control group
- After one year, PSA levels decreased in men in the group who made comprehensive lifestyle changes but increased in the comparison group
- **Serum from the participants inhibited prostate tumor growth in vitro by 70 percent in the lifestyle-change group but only 9 percent in the comparison group**

# Mediterranean Diet

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- Study looked on 733 men with prostate cancer and 1,229 healthy men. The average age 66 years. 5 year duration
- The study collected a range of data such as medical, background information and their eating habits.
- The researchers put the participants into three groups: Western, prudent, and Mediterranean.

# Med Diet

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- Western diet includes: large intakes of fatty dairy foods, processed meats, fast food, refined grains, sweets, sauces, and high-calorie drinks.
- The prudent diet includes low-fat dairy foods, fruits, vegetables, whole grains, and juices.
- **Mediterranean diet high intake of fish, fruits, vegetables, boiled potatoes, legumes, and olive oil, with low levels of juice intake.**
- Each dietary pattern had four categories of adherence, **ranging from low to high.**

# Closing Remarks

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- only a "high adherence to the Mediterranean dietary pattern" was significantly associated with a reduced risk of having prostate cancer with aggressive and extensive tumors.
- No such link was found in the other dietary patterns, either with aggressive or less aggressive tumors



# Mediterranean Diet

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- A prospective study of approximately 50,000 men
- Followed for 24 years
- 22% lower risk of overall mortality

# Ketogenic Diet

- Diet : ketogenic diet is roughly 75% fat, 23% protein, and 2% carbs.
- Body uses ketones instead of sugar as a fuel source
- Strong movement
- No Randomized Controlled Trials



# Good idea: High Fat Diet (animal)?

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- Western diet of processed and high-fat foods had a 2½ times greater risk of dying from prostate cancer and 67% higher risk of death overall.
- Populations studies : adapting a western diet increase PC risk

# Clinical Interventions



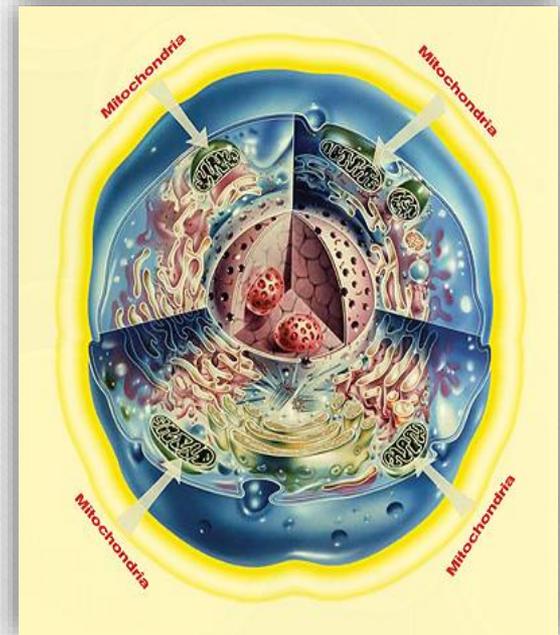
# Vitamin D3

- Nature's sunlight
- The trial included 48 African-American and Caucasian men with low-risk prostate cancer who received 4,000 international units (IU) vitamin D3 for one year
- 19 men diagnosed with prostate cancer who underwent biopsies at a similar interval served as controls
- **Results: 55 percent of the vitamin D-treated subjects had fewer cancerous cores in their biopsied tissue or improved Gleason scores after one year .**
- baseline were **32.8 ng/mL** and increased to **66.2 ng/mL** after vitamin D supplementation
- **Optimal range 50-80 ng/ml**



# Ubiquinol: Coq10

- A total of 504 healthy men with serum PSA level  $\leq 2.5$  ng/ml were randomly assigned to a daily dietary supplement containing CoQ10 (400 mg per day) or a similar regimen of placebo for 12 weeks
- CoQ10 therapy significantly reduced serum PSA level by astounding 33%
- Scavenge free radicals
- Depletion occurs at age 20
- **Dose 200-400 mg of coq10**



# Saw Palmetto

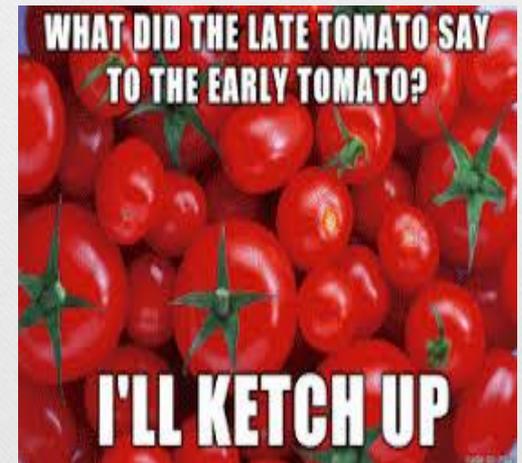
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- Stimulates apoptosis
- Suppress DHT production by as much as 32 % in only 6 months
- Selectively impairs energy production of prostate cancer cells
- **Dose 320mg**



# lycopene

- Cooked or Raw ?
- Heart and prostate health benefits
- Harvard School of Public Health, found that increased dietary intake of lycopene is associated with a decreased risk of PC, especially lethal PC.
- High intakes of tomato or tomato-based products was associated with a 10%-20% decrease in PC
- Lycopene inhibits angiogenesis
- Suggested dosages
- **15-30 milligrams daily** are for prevention
- **45 milligrams daily** existing prostate cancer.



# Curcumin

- Indian Gold
- Both *in vitro* and *in vivo* inhibits
  - angiogenesis
  - metastases
- A suggested dosage : **800-1,200 milligrams daily** with food.



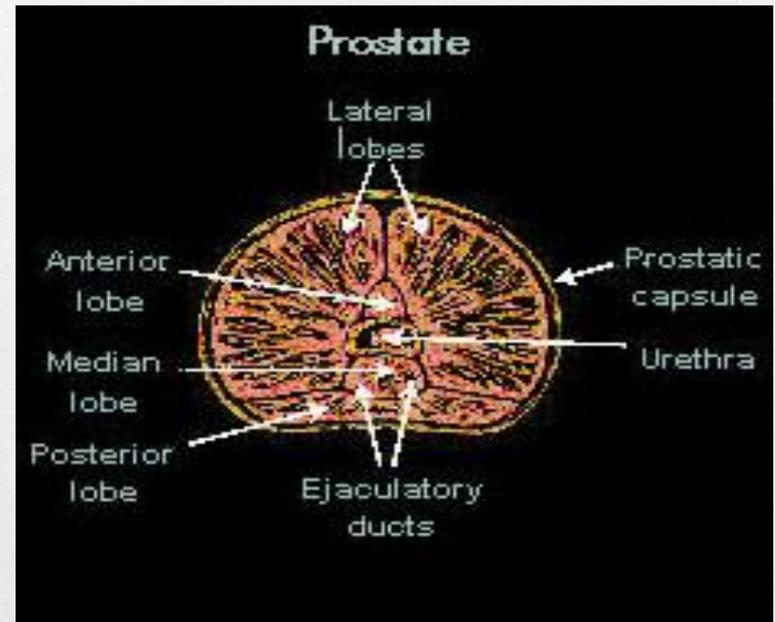
# Pomegranate

- A study involved 92 men with cancer with low grade PC
- Participants were taking 1 gram of pomegranate extract or three pomegranate capsules daily.
- PSA levels were doubling every 12 months
- **After six months of taking the capsules, it took 19 months for their PSA levels to double.**
- **Juice 4- 8 ounces per day**
- **Dose 400mg to 800mg**



# The Doctrine Of Signatures

- Pomegranate



# Broccoli

- Men who were at risk of developing prostate cancer ate either 400g of broccoli or 400g of peas per week in addition to their normal diet over 12 months
- Samples were taken from their prostate gland before the start of the trial and after 6 and 12 months
- **Findings: significant changes in gene expression in the broccoli-rich diet than on the pea diet**
- **Dose : 400mg**



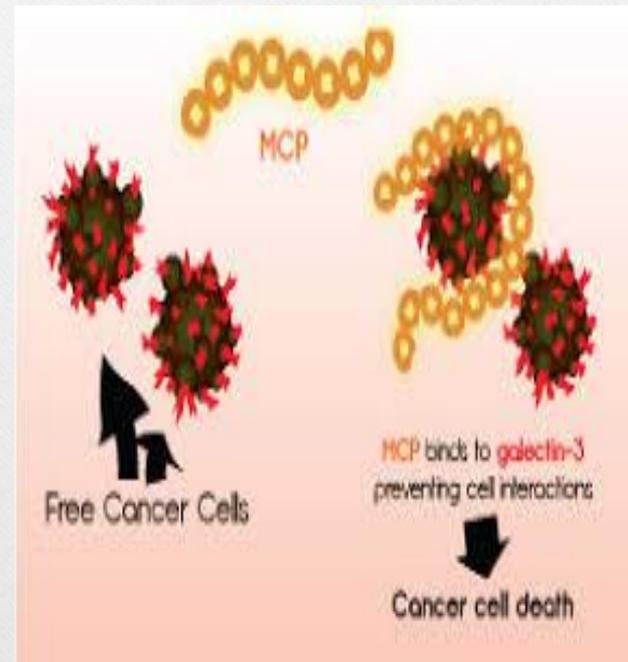
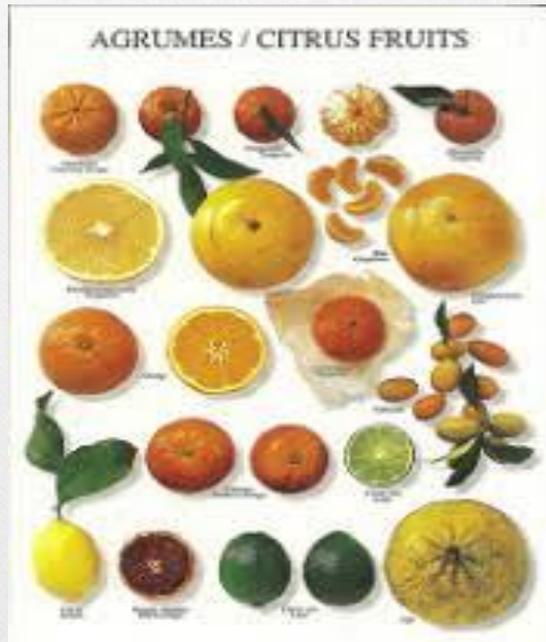
# Modified Citrus Pectin

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- Pilot study of 10 men with biochemical recurrence
- Took 15 grams per day for 12 months
- PSADT increased in eight (80%) of the 10 men after taking MCP
- **Dose : 15 grams per day**



# Mechanism of MCP



# Green tea

- A study recruited 60 men, aged 45-75.
- Dosage :Thirty participants received **200 milligrams** of green tea catechins (**50% EGCG**) **three times daily**, while the other 30 subjects received a placebo.
- Biopsies were conducted at six and 12 months.
- Results: only **one** man in the treatment group was diagnosed with prostate cancer, compared to **nine** men in the control group who developed the disease.
- The lead researcher concluded that “**90%** of chemoprevention effects.



# Green Tea

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- A 2009 study recruited 26 men with positive prostate biopsies prostatectomy whom were given daily doses 1.3 g of tea polyphenols, until time of radical prostatectomy.
- Serum biomarkers: hepatocyte growth factor (HGF), vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF)-I, IGF binding protein-3 (IGFBP-3), and prostate-specific antigen (PSA) were measured
- Liver function enzymes was monitored for toxicity .
- Results showed a significant reduction in serum levels of PSA, HGF, and VEGF in men with prostate cancer after brief treatment with EGCG and no elevation of liver enzymes.
- Suggested dose : 1300mg polyphenols

# Landmark Study: ASCO

- The researchers recruited 199 men with PC with an average age of 74(53 to 89 years)
- The subjects were randomly assigned to receive either a capsule containing a blend of **pomegranate seed, green tea, turmeric, and broccoli** or placebo for 3 to 6 months
- capsule designed to be taken twice daily.
- In the placebo group, PSA levels rose by a median of **78.5%** over the 6-month period
- **supplemented group- PSA rose by a median of only 14.7%**
- **Difference of 63.8%**



# Soy Isoflavones (Genistein)

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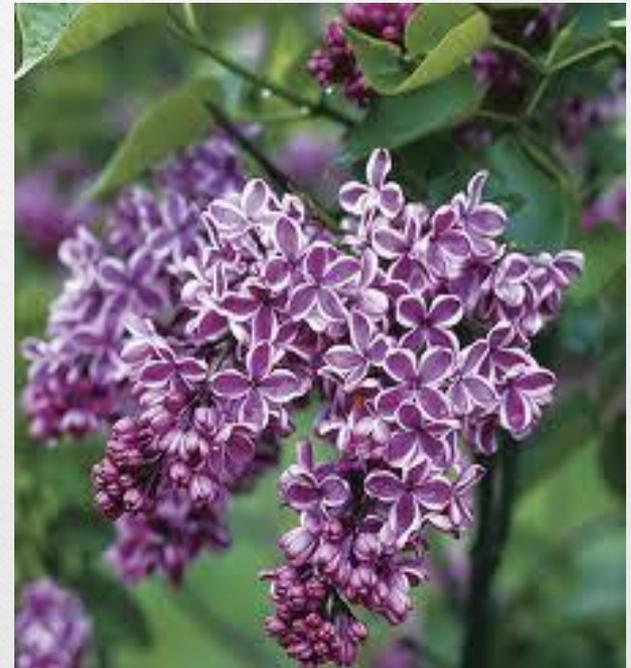
- Pilot Study of 41 men with Prostate cancer were given 100mg isoflavone for 3-6 months
- Three groups: active surveillance, local therapy and refractory hormone
- Results:
- **Group 2** : stabilization of the PSA occurred in 83% of patients in hormone-sensitive
- **Group 3** : 35% in hormone-refractory
- Rate of rise decrease from 31 to 9 percent
- Suggested dose : 200mg isoflavones



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- Repurposed Drugs as Cancer Treatments

# Metformin

- Originally derived from the French lilac
- The study involved a cohort of 3,837 men living in Ontario, Canada, age > 66 years with incident diabetes who subsequently developed prostate cancer.
- Over a median follow-up of 4.64 years, 1,343 participants (35%) died and 291 (7.6%) died as a result of prostate cancer.
- Every additional 6-month interval of metformin use was linked to a 24% decrease in prostate cancer-specific mortality as well as a significant decrease in all-cause mortality that declined over time.
- The longer the men were on the drug, the better they did
- **Dose 1000-2000mg**



# Metformin

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- A study of 87,344 looked on US veterans receiving ADT for advanced Prostate cancer
- Patients receiving metformin for diabetes mellitus had a significant **18% decreased risk of death** compared with men who did not have diabetes mellitus (no metformin)
- 18% decreased risk of skeletal-related events
- 30% decreased risk of cancer-related death.

# Aspirin

- A study of 22000 men were followed from 1982 .
- Those with who took more than three 81mg aspirin tablets a week had a 24 percent lower risk of getting a lethal prostate cancer.
- regular aspirin use after diagnosis was associated with a 39 percent lower risk of dying from prostate cancer.
- Use of aspirin before diagnosis didn't have a measurable benefit



# Avodart

- study involved 302 patients. Men were assigned to receive either Avodart or a placebo for three years.
- All men had prostate biopsies at the mid-point and end of the study, or as needed.
- Results :
  - cancer progression occurred in 38% of men in the Avodart group and 49% of men in the placebo group.
  - Men treated with Avodart were more likely to have a final biopsy that was free of cancer: the biopsy was free of cancer in 36% of men in the Avodart group and 23% of men in the placebo group.
  - Avodart group reported lower levels of prostate cancer-related anxiety.



# Ketoconazole

- At high doses in humans ketoconazole can lower rapidly serum testosterone and maintain it in the castrate range with frequent administration
- Dose 200mg TID with prednisone



# Q and A

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