The Urinary System
Men’s Health and Fertility
Naturopathic Nutrition 2
Learning Outcomes:

On successful completion you will be able to:

• Explain the structure and function of the urinary and male reproductive systems.
• Identify a range of common pathologies affecting the urinary and male reproductive systems.
• Evaluate orthodox medical approaches to a range of male reproductive and urinary pathologies.
• Outline nutritional therapy approaches to support a healthy urinary system and the male reproductive system.
• Discuss factors affecting fertility.
• Discuss preconception care and natural fertility management.
• Show awareness of the importance of referral with ‘Red Flag’ symptoms.
Urinary System

- Produces, stores and eliminates urine.

- **2 Kidneys** – Size of a clenched fist; 150g in weight; posterior or to the organs of digestion, around or just below the ribcage and close to the lumbar spine.

- **2 Ureters** – Propel urine from the kidneys to the bladder; 25-30cms long.

- **Bladder** – Hollow muscular organ; hold up to 500ml for 2-5 hrs; sphincters control release which is a conscious process.

- **Urethra** - Emerges from the end of the penis in males and between the clitoris and the vagina in females.
Function of the Urinary Tract

• Kidneys:
  – Excretion of metabolic waste and foreign chemicals.
  – Primary means for excretion of metabolic waste.
    • e.g. Urea – Amino acids
      Creatinine – Muscle Creatine
      Uric acid – Nucleic acid
      Bilirubin – Haemaglobin
  – As fast as it is created, it must be excreted.
  – Regulation of water and electrolyte balance.
  – Kidneys adjust excretion rated to match intake.
  – The ability to adjust excretion rates of electrolytes is vast.
    • e.g. Increase in dietary Na > 10 or
    • < 1/10 normal – has little affect on extracellular water (ECW)
Function of the Urinary Tract

- Kidneys:
  - Regulation of acid-base balance:
    - Excreting acids
    - Regulating body fluid buffer stores
    - Only means for eliminating some acid by products e.g. Sulfuric acid and phosphoric acid.
  - Regulation of hormones:
    - 1,25-dihydroxy vitamin D3, renin, erythropoietin
  - Regulation of arterial pressure:
    - Long term - Excretion of sodium and water
    - Short term – Secreting vasoactive factors
  - Gluconeogenesis:
    - Synthesis of glucose from amino acids
Cystitis

- Bladder cystitis is defined as inflammation of the urinary bladder from any cause.

- It is a relatively common condition affecting both sexes and all ages.

- It has no racial predisposition, but female individuals, especially those younger than 50 years, are affected more often than male individuals.
Cystitis

• 10% to 20% of all women have urinary tract discomfort at least once a year.

• 37.5% of women with no history of urinary tract infection (UTI) will have one within 10 years.

• 2% to 4% of apparently healthy women have elevated levels of bacteria in their urine, indicative of an unrecognised UTI.

• The incidence of cystitis is high in women because of the short length of the urethra and because of the proximity of the urethra to the anus.
  – This anatomy makes the female urinary bladder relatively easily accessible to intestinal pathogens.
Cystitis

• Urinary tract infections are rare in healthy men.

• When they do occur in a man, it's most often the result of an underlying condition such as prostate disease, incontinence, or some other condition.

• Since there is almost always some other condition involved, urinary tract infections in men are almost always considered complicated.
Cystitis – Risk Factors

• Sexual activity
• Incontinence
• Diaphragm or spermicide use
• Incomplete voiding of the bladder results in stasis of urine and, hence, the concentration of bladder bacteria.
• Taking baths
• Douching
• Recent bacterial infection
• Foreign body or a neoplasm in the bladder
• Abnormal communication between the bladder and nearby structures (fistulae)
Cystitis

• Cystitis may be symptomatic or asymptomatic.

• Patients with cystitis may present with symptoms of **urgency**, **frequency**, **dysuria**, **hematuria**, **cloudy and offensive-smelling urine**, or **suprapubic discomfort**.
  – These symptoms may occur singly or in combination.
  – The symptom of urgency results from the stimulation of the afferent arc of the micturition reflex.
  – The offensive smell results from the bacterial conversion of urea to ammonia.
Cystitis - Symptoms

• Burning pain on urination.
• Increased urinary frequency, nocturia.
• Turbid, foul-smelling, or dark urine.
• Lower abdominal pain.
• Urinalysis shows significant pyuria and bacteriuria.

Accessed: (18/01/2010)
The diagnosis of bladder infection is imprecise because clinical symptoms and the presence of significant amounts of bacteria in the urine do not correlate well.

As indicated in the below table, only 60% of women with the typical symptoms of UTI actually have significant levels of bacteria in their urine.

Equally important, however, is the fact that 20% have the more potentially serious involvement of the upper tract.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Percentage of subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper urinary tract infection</td>
<td>20</td>
</tr>
<tr>
<td>Bladder infection</td>
<td>40</td>
</tr>
<tr>
<td>Low levels of bacteria in urethra</td>
<td>16</td>
</tr>
<tr>
<td>Urethral chlamydia</td>
<td>8</td>
</tr>
<tr>
<td>Unsuspected vaginitis</td>
<td>4</td>
</tr>
<tr>
<td>Other (e.g., herpes, gonorrhea, pelvic inflammatory disease)</td>
<td>12</td>
</tr>
</tbody>
</table>

Cystitis - Diagnosis

- Diagnosis is made according to signs and symptoms and urinary findings.

- Microscopic examination of the infected urine shows high levels of white blood cells (WBCs) and bacteria.

- Culturing the urine determines the quantity and type of bacteria involved.
  - *Escherichia coli* (from the colon) is by far the most common.

- The presence of fever, chills, and low back pain can indicate involvement of the kidneys.

- Those with recurrent infections should be examined by intravenous urogram to determine if a structural abnormality is present.

Cystitis

The patient MUST present to a medical practitioner if there is:

- Fever
- Nausea
- Low back pain
- Vomiting
Cystitis - Orthodox Treatment

- The selected antimicrobial should be active against the most common causative organism.

- A patient who has undergone previous episodes will usually know which antimicrobial works best.

- The treatment would be given for 5-7 days.

- Broad-spectrum antimicrobials should be reserved for cases in which the bacterial culture results and sensitivity are known.
Cystitis - Treatment Overview

- Enhancing the flow of urine by achieving and maintaining proper hydration.

- Promoting a pH that inhibits the growth of the organism.

- Preventing bacterial adherence to the endothelial cells of the bladder.

- Enhancing the immune system.

Accessed: (18/01/2010)
Cystitis - Acidify or Alkalise?

- Many practitioners believe acidifying the urine is the best approach in addressing cystitis, yet several arguments can be made for alkalinising the urine including that it is often difficult to acidify the urine.

- Many popular methods of attempting to acidify the urine, such as ascorbic acid supplementation and the drinking of cranberry juice, have little effect on pH at commonly prescribed doses.

Cystitis - Acidify or Alkalise?

• The best argument for alkalinising the urine is that it appears to be more effective, especially in women without pathogenic bacteria in their urine.

• The best method for alkalinising the urine appears to be the use of citrate salts
  – e.g. potassium citrate or sodium citrate.
  – These salts are rapidly absorbed and metabolised without affecting gastric pH or producing a laxative effect. They are excreted partly as carbonate, thus raising the pH of the urine.
  – Potassium citrate or sodium citrate, or both, have long been employed in the treatment of lower UTIs.

Accessed: (18/01/2010)
Cystitis - Nutritional Therapy

• Eliminate refined foods, fruit juices, caffeine, alcohol, and sugar which may compromise immune function.

• Avoid sexual activity until infection is resolved.

• Drink plenty of fluids, such as water and herbal teas.

• Reduce pro-inflammatory foods and emphasise foods high in anti-inflammatory essential fatty acids such as oily fish and nuts / seeds.

• Eat a minimally processed diet rich in antioxidants, phytonutrients and bioflavonoids.

• Stress management techniques should be implemented.

• Address contraceptive use – condoms, diaphragms, lubricant
Cystitis - *Vaccinium macrocarpon* (Cranberry)

- Used in the prevention and treatment of cystitis, bacteriuria and pyuria.

- Benzoic acid and quinic acid metabolise to **hippuric acid** which may prevent bacteria from adhering to the epithelial cells of the bladder.
  - The adhesion is required to initiate many infectious diseases.

- **Proanthocyanidins** in cranberry seem to envelop *E. coli* and prevents it from binding to epithelial cells.

- In one study, **0.5 litre/day** of cranberry juice was shown to produce beneficial effects in 73% of the subjects (44 females and 16 males) with active UTIs. Withdrawal of cranberry juice in the people who benefited resulted in recurrence of bladder infection in 61%.

Accessed: (18/01/2010)
Cystitis - *Vaccinium macrocarpon* (Cranberry)

• Blueberry juice is a suitable alternative to cranberry juice.

• Most cranberry juices on the market contain one third cranberry juice mixed with water and sugar.
  – Fresh cranberry (unsweetened or sweetened with apple or grape juice) or blueberry juice is preferred.

• There is a theoretic concern regarding the use of cranberry juice and kidney stone formation.
  – Cranberries are considered an oxalate-containing food, the thinking is that this may encourage oxalate-rich kidney stone formation. However, urinary oxalate excretion does not increase after drinking cranberry juice and none of the studies using cranberries have reported increased kidney stone incidence.

• Consumption of cranberry should be **avoided** in patients with renal insufficiency.

Cystitis and D-Mannose

- D-mannose is a sugar that is found in a variety of food sources, including blackcurrants and redcurrants, gooseberries, aloe vera, soy beans and vegetables including cabbage, eggplant and tomatoes.

- A simple sugar that acts similarly to cranberry juice in that it helps to prevent the pili of *E. coli* and other bacteria from adhering to the bladder wall.
  - Bacteria produce lectins, which bind the organism to sugar residues, such as mannose, on host cells. Theoretically, giving supplemental mannose can bind the bacteria and prevent attachment to the urinary tract lining.
Cystitis and D-Mannose

• Of 73 E. Coli strains studied in a trial, 90% demonstrated adherence to epithelial cells in women. D-mannose inhibited completely the adherence of 25 strains (42 %) and inhibited an additional 11 strains (18 %) by at least 50%.

• 2,500 - 5,000 mg every four to six hours or more.

• Some research suggests that d-mannose can increase glycosylated hemoglobin (HbA1c)


Interstitial Cystitis

- Interstitial cystitis (IC) is a chronic inflammatory condition of the lamina propria of the bladder.

- IC has continued to be an unresolved problem despite intense investigation over the past 40 years.

- Its cause and pathogenesis are still undetermined, one of exclusion although many theories exist.

- Diagnosis is essentially one of exclusion - like irritable bowel syndrome.

- IC may in fact be one or many diseases and probably has a pluricausal aetiology and a multifactorial pathogenesis.
The diagnosis of IC is based on the following clinical tetrad:

1. Chronic irritative voiding.
2. Sterile, normal urine.
3. Characteristic findings on cystoscopy including Hunner’s patch or other findings such as "glomerulations".
   - Glomerulations are small haemorrhages observed after bladder distension.
4. Lack of any other cause for the symptoms and clear evidence of compromised bladder function.
Interstitial Cystitis

• Pain is the most common presenting complaint, being present in over 70% of patients.
  – Pain is usually suprapubic, although urethritis, loin pain and dyspareunia are also common.

• A long history of frequency, dysuria and urgency in the absence of proven infection is often present.

• Bladder capacity is usually reduced and there may be substantial fibrosis.
Interstitial Cystitis

- Caucasian women account for 90 to 95% of cases.

- Incidence is greatest between the ages of 40 and 60 years.

- The prevalence is about 1 to 3 cases in every 10,000.

- There is an association with systemic lupus erythematosus, irritable bowel syndrome, and fibromyalgia.

- There is no established drug treatment for IC but surgical treatments may have some success.
Factors which may be involved in the pathogenesis of IC include:

- Infection
- Lymphatic/vascular obstruction
- Autoimmunity
- Leaky urothelium
- Irritant chemicals in urine (from micro-organisms, metabolites or food intolerance)
- Reduced nitric oxide synthase (NOS) activity
- Epithelial growth factors
- Neurogenic inflammation involving mast cells.
Interstitial Cystitis

- The "leaky bladder urothelium" theory postulates that there is a problem with the glycosaminoglycan layer of the bladder epithelium, which results in increased permeability to potassium into the bladder wall, causing inflammation and pain.

- Eliminating food sensitivities to reduce inflammation appears to be a valid goal.

- Repeated ingestion of a food allergen could easily explain the chronic nature of interstitial cystitis
Interstitial Cystitis

• Suspected allergens/sensitivities:
  – Benzol alcohol, citric acid, monosodium glutamate, aspartame, saccharine and foods containing preservatives and artificial ingredients and colours.
  – Apples, apricots, avocados, bananas, cantaloupes, citrus fruits, cranberries, grapes, nectarines, peaches, pineapples, plums, pomegranates, strawberries and juices made from these fruits.
  – Aged cheeses, sour cream, eggs, yogurt and chocolate.
  – Fava beans, lima beans, onions, rhubarb, tofu and tomatoes.
  – Rye and sourdough bread.
  – Aged, canned, cured, processed or smoked meats and fish, anchovies, caviar, chicken livers, corned beef and meats that contain nitrates or nitrites.
Interstitial Cystitis

• Suspected allergens/sensitivities:
  – Most nuts
  – Alcoholic beverages, beer, wine, carbonated drinks, coffee, tea and cranberry juice.
  – Mayonnaise, miso, spicy foods (especially Chinese, Indian, Mexican and Thai foods), soy sauce, salad dressing and vinegar.
  – Tobacco, caffeine, diet pills, junk foods, recreational drugs, cold and allergy medications containing ephedrine or pseudoephedrine.

• Many IC patients find that they have the **least problems** with rice, chicken, potatoes, pasta, vegetables and meat.
Interstitial Cystitis

• Pelvic Floor:
  – Pain in the bladder and/or pelvis can trigger long term, chronic pelvic floor tension which is often described by women as a burning sensation, particularly in the vagina.
  – Men with pelvic floor tension experience referred pain, particularly at the tip of their penis.
  – 9 out 10 with painful sexual intercourse have muscle tension is the primary cause.

• Kegel exercise:
  – Fortify muscle tone by strengthening the muscles of the pelvic floor.
  – Stop and restart flow mid stream urination then ‘practice makes perfect’ – not recommended whilst infection is present. Be sure to void completely with each trip to the toilet.
Interstitial Cystitis - Nutrients

• Arginine – source of nitrogen for nitric oxide (NO) production; NO important determinant of the symptoms and immunological responses associated.
  – 1500mg per day

• Chondrotin sulphate – repair mucosal damage
  – 1200mg per day

• Glucosamine – repair mucosal damage.
  – 1500mg per day

• Methylsulfonylmethane (MSM) – anti-inflammatory.
  – Start at 1000mg per day up to 18 grams.
Kidney Stones / Urolithiasis

- During the last few decades the pattern and incidence of the disease have changed markedly. In the past, stone formation was almost exclusively in the bladder, but today most stones form in the upper urinary tract.

- More than 10% of all men experience a renal stone during their lifetimes, with an annual incidence of 0.1% to 6% of the general population.

- Once a kidney stone does occur, there is a 50% chance of recurrence within 5 to 7 years if there is no treatment.

- May be due to renal, urologic, endocrine, and metabolic disorders.
Kidney Stones - Diagnostic Summary

• Usually asymptomatic.

• Diagnosed adventitiously or from acute symptoms of urinary tract obstruction.

• The pain may be some of the most severe pain that humans experience, and complications of stone disease may result in severe infection, renal failure, or, in rare cases, death.

• Excruciating intermittent radiating pain originating in the flank or kidney.

• Nausea, vomiting, abdominal distension.

• Chills, fever, and urinary frequency if infection present.
Kidney Stones

The following primary and secondary metabolic diseases cause kidney stones must be ruled out early in the clinical process:

- Hyperparathyroidism
- Cystinuria
- Vitamin D excess
- Milk-alkali syndrome
- Destructive bone disease
- Primary oxaluria
- Cushing syndrome
- Sarcoidosis
Kidney Stones - Stone Formation

More than 1 of 3 general mechanisms is likely to be active.

(1) The possible presence or abundance of substances that promote crystal and stone formation.
   • Including reduction in urine volume (dehydration) and an increased rate of excretion of stone constituents.

(2) A possible relative lack of substances to inhibit crystal formation.
   • Including urinary stasis, pH changes, foreign bodies, and reduction of abnormal substances which solubilise stone constituents.

(3) A possible excessive excretion or concentration of salts in the urine, which leads to supersaturation of the crystallising salt.
   • The greater the degree of supersaturation, the greater the rate of growth of the calculi.
Kidney Stones

• Diagnosing type of stone is critical to treatment:
  – Amino Acids
  – Cysteine: 2%

• Minerals:
  – Calcium: 75-85%; oxalate, phosphate or urate; 50% a mix of oxalate and phosphate.
  – Magnesium: 15%
    • Struvite = Magnesium ammonium phosphate.
    • Struvite are associated with chronic bacterial UTIs capable of splitting urea into ammonium, which combines with phosphate and magnesium.
  – Phosphorus: Struvite and calcium phosphate

Kidney Stones - Calcium

• Most causes of hypercalciuria are absorptive.
  – Increased absorption in individuals after a normal diet causes an elevation of serum calcium levels and a suppression of parathyroid function as an abnormal response to vitamin D.
  – Approximately 10% of cases of primary hypercalciuria are renal in origin.

• The inability of the kidney to conserve calcium results in low serum calcium concentrations, which stimulate parathyroid hormone secretion.
  – Hyperparathyroidism is found in 5-10% of patients with calcium stones.

• Calcium stones can also occur in approximately 15% of patients with sarcoidosis in whom the production of activated vitamin D by macrophages is abnormal.

Kidney Stones

Organic Acids:

• Oxalic Acid: Calcium oxalate
  – Calcium stones can also occur in approximately 15% of patients with sarcoidosis in whom the production of activated vitamin D by macrophages is abnormal.

• Uric Acid: 6% - usually in the form of calcium urate.
  – Approximately 25% of persons with uric acid kidney stones also have gout.

Kidney Stones

- Chemical and physical characteristics of urinary stones:

<table>
<thead>
<tr>
<th>Composition</th>
<th>Crystal name</th>
<th>Frequency (%)</th>
<th>X-ray appearance</th>
<th>Urine characteristics</th>
<th>Crystal characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium oxalate</td>
<td>Whewellite</td>
<td>30-35</td>
<td>Opaque</td>
<td>Nonspecific</td>
<td>Small, hempseed or mulberry-shaped, brown or black</td>
</tr>
<tr>
<td>Calcium oxalate + calcium phosphate</td>
<td></td>
<td>30-35</td>
<td>Opaque</td>
<td>pH&gt;5.5</td>
<td>Small, hempseed or mulberry-shaped, brown or black</td>
</tr>
<tr>
<td>Calcium phosphate</td>
<td>Apatite</td>
<td>6-8</td>
<td>Opaque</td>
<td>pH&gt;5.5</td>
<td>Staghorn configuration, light in color</td>
</tr>
<tr>
<td>Magnesium ammonium phosphate</td>
<td>Struvite</td>
<td>15-20</td>
<td>Opaque</td>
<td>pH&gt;6.2</td>
<td>Staghorn configuration, light in color</td>
</tr>
<tr>
<td></td>
<td>Triple phosphate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uric acid</td>
<td></td>
<td>6-10</td>
<td>Translucent</td>
<td>pH&lt;6.0</td>
<td>Ellipsoid, tan or red-brown</td>
</tr>
<tr>
<td>Cystine</td>
<td></td>
<td>2-3</td>
<td>Opaque</td>
<td>pH&lt;7.2</td>
<td>Multiple, faceted, maple syrup color</td>
</tr>
</tbody>
</table>
Kidney Stones

- Causes of excessive excretion of relatively insoluble urinary constituents:

<table>
<thead>
<tr>
<th>Constituent</th>
<th>Cause of excess excretion</th>
<th>Laboratory findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>(&gt;250 mg/day excreted)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Absorptive hypercalciuria</td>
<td>Low serum PO₄</td>
</tr>
<tr>
<td></td>
<td>Renal hypercalciuria (renal tubular acidosis)</td>
<td>30%-40% of all stone formers</td>
</tr>
<tr>
<td></td>
<td>Primary hyperparathyroidism</td>
<td>High serum calcium</td>
</tr>
<tr>
<td></td>
<td>Hyperthyroidism</td>
<td>High 1,25(OH)₂D₃</td>
</tr>
<tr>
<td></td>
<td>High vitamin D intake</td>
<td>High serum calcium</td>
</tr>
<tr>
<td></td>
<td>Excess intake of milk and alkali</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Aluminum salt intake</td>
<td>Low serum phosphate</td>
</tr>
<tr>
<td></td>
<td>Destructive bone disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sarcoïdosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prolonged immobility</td>
<td></td>
</tr>
</tbody>
</table>
### Kidney Stones

- **Causes of excessive excretion of relatively insoluble urinary constituents:**

<table>
<thead>
<tr>
<th>Component</th>
<th>Condition/Intervention</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxalate</td>
<td>Familial oxaluria</td>
<td>Rare</td>
</tr>
<tr>
<td></td>
<td>Ileal disease, resection, or bypass</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Steatorrhea</td>
<td></td>
</tr>
<tr>
<td></td>
<td>High oxalate intake</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ethylene glycol poisoning</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vitamin C excess (extremely unlikely)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Methoxyflurane® anesthesia</td>
<td></td>
</tr>
<tr>
<td>Uric acid</td>
<td>(&gt;750 mg/day excreted)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gout</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Idiopathic hyperuricosuria</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Excess purine intake</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anticancer drugs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Myeloproliferative disease</td>
<td></td>
</tr>
<tr>
<td>Cystine</td>
<td>Hereditary cystinuria</td>
<td></td>
</tr>
</tbody>
</table>
Kidney Stones - Nutritional Treatment

• Diagnosing the type of kidney stone is **critical** to identifying the appropriate therapy.

• Careful evaluation of the following criteria usually determines the composition of the stone, if one is not available for chemical analysis:
  – Food intake
  – Underlying metabolic or disease factors
  – Serum and urinary calcium, uric acid, creatinine, and electrolyte levels
  – Urinalysis
  – Urine culture.
Kidney Stones - Fluids

- In a review and meta-analysis of trials published during 1950-2008, investigators examined the efficacy and safety of diet, fluid, or supplement interventions for secondary prevention of nephrolithiasis. Of the eight trials the investigators found to be eligible, two reported that a water intake >2 L/day or fluids to achieve urine output >2.5 L/day reduced stone recurrence (RR 0.39, 95% CI 0.19-0.80).

- In another trial, fewer consumers of high amounts of soft drinks assigned to reduced soft drink intake had renal colic than controls (34% vs. 41%; \( P = .023 \)).

- Findings from trials that examined dietary calcium, sodium, animal protein, fruit, and fibre were mixed, although no trial examined the effects of one of these components at a time.

Kidney Stones - Urinary pH

- In one study, 12 healthy men were given a standardised diet plus cranberry, black currant, or plum juice. These subjects then provided 24-hour urine collections for evaluation.
- The researchers found that:
  - **Cranberry juice decreased** the urinary pH and significantly increased the excretion of oxalic acid and the relative supersaturation for uric acid.
  - **Black currant juice increased** urinary pH, excretion of citric acid, and loss of oxalic acid.
- The researchers concluded that black currant juice could support the treatment and prevention of uric acid stones through its alkalisising effect.
- Conversely, because cranberry juice acidifies urine, it could be useful in the treatment of brushite and struvite stones as well as for urinary tract infections.
Kidney Stones - Nutritional Treatment

• Calcium stones
  – The high incidence of calcium-containing stones in affluent societies is directly associated with the following dietary patterns:
    • Low amounts of fibre
    • Intake of highly refined carbohydrates
    • High alcohol consumption
    • Large amounts of animal protein
    • High intake of fat
    • High intake of calcium-containing food
    • High intake of vitamin D-enriched food
Kidney Stones - Low Oxalate Food Intake

- A low oxalate diet is a common prescription for recurrent calcium oxalate kidney stones.
  - Oxalic acid is able to pass through the intestinal wall into the blood and enter the kidneys where it has a chance to combine with calcium.
  - Excessive oxalate in the urine cannot be dissolved, crystals settle out, and stones form.

- A low oxalate diet is usually defined as less than 50 mg oxalate per day.
Kidney Stones - Oxalate Containing Foods

- Note that the **leaves** of a plant almost always contain higher oxalate levels than the roots, stems, and stalks.
- Fruits: Blackberries, blueberries, raspberries, strawberries, currants, kiwifruit, purple grapes, figs, tangerines, and plums.
- Vegetables: *High* - spinach, Swiss chard, beet greens, collards, okra, parsley, leeks; *Moderate* – celery, green beans, rutabagas, and squash.
- Nuts and seeds: Almonds, cashews, and peanuts.
- Legumes: Soybeans, tofu and other soy products.
- Grains: Wheat bran, wheat germ, quinoa.
- Other: Cocoa, chocolate, and black tea.
Kidney Stones - Low Purine Food Intake

• The level of dietary purine consumption is linearly related to the rate of urinary uric acid excretion.

• Hyperuricosuria is a causative factor in recurrent calcium oxalate stones.

• These foods should be eliminated:
  – Organ meats, meats, shellfish, yeast (brewer's and baker's), herring, sardines, mackerel, and anchovies.

• Foods with moderate levels of protein should be curtailed as well.
  – These include dried legumes, spinach, asparagus, fish, poultry, and mushrooms.
• Although most doctors still tell their patients with kidney stone to avoid calcium supplements, this advice is outdated. A strong body of evidence has emerged refuting the general trend to restrict calcium supplementation in patients with kidney stone.

• One study evaluated calcium intake and the dietary profile in 37 outpatients with kidney stones and 45 control subjects. Dietary calcium, assessed from 4-day dietary records, was significantly lower for patients with urinary calculi.

• Another study further supporting the benefits of calcium intake is a 5-year randomised trial comparing the effect of two diets in 120 men with recurrent calcium oxalate stones and hypercalciuria. Upon completion, the men consuming the normal calcium diet experienced a 51% reduction in the risk of stone recurrence. During follow-up, urinary calcium levels dropped significantly in both groups, but urinary oxalate was reduced in the normal calcium intake group and increased in the low calcium intake group.

• **300 to 1000 mg** daily may prove to be an effective preventive measure against calcium oxalate kidney stones.
Kidney Stones - Treatment

- **Weight** control and correction of **carbohydrate** metabolism are important, because excess weight and insulin insensitivity lead to hypercalciuria.

- **Magnesium** - Has been shown to increase the solubility of calcium oxalate and inhibit the precipitation of both calcium phosphate and calcium oxalate - 600 mg per day.

- **Pyridoxine** - known to reduce the endogenous production and urinary excretion of oxalates – 25 mg per day.
  - The combination of magnesium and pyridoxine shows greater results.

- A higher concentration of **glutamic acid** in the urine induces precipitation of calcium oxalate.
Kidney Stones - Treatment

- **Folic acid** – High dose supplemental folic acid promotes purine scavenging and xanthine oxidase inhibition, resulting in decreased excretion of uric acid – 5 mg per day.

- **Citrate** - Reduce urinary saturation of calcium oxalate and calcium phosphate and to retard the nucleation and crystal growth of calcium salts.
  - Magnesium or potassium citrate

- **Vitamin C** - Often cited as a potential factor in the development of calcium oxalate kidney stones. However, numerous studies have shown that in persons not undergoing hemodialysis or suffering from recurrent kidney stones, severe kidney disease, or gout, high-dosage vitamin C therapy does not cause kidney stones. Vitamin C ingestion of up to 10 g/day has not had any effect on urinary oxalate levels.
Prostate Gland

- The prostate is an exocrine gland of the male mammalian reproductive system.

- Its main function is to store and secrete a clear, slightly basic fluid that constitutes up to one-third of the volume of semen.

- A healthy human prostate is slightly larger than a walnut and surrounds the urethra just below the urinary bladder.

- The most common disorders of the prostate are prostatitis and benign prostatic hyperplasia.
Male Reproductive Anatomy

Male Reproductive Tract

- Bladder
- Seminal Vesicles
- Prostate
- Urethra
- Penis
- Rectum
- Vas Deferens
- Testis
- Scrotum
- Epididymis
- Tunica Vaginalis
- Anus
Prostatitis

• An infection or inflammation of the prostate gland.
  – Microscopic inflammation of the tissue of the prostate gland, which spans a broad range of clinical conditions.

• Approximately 8.2% of men have prostatitis at some point in their lives.

• The most common urological disorder in men less than 50 years of age.

• Commonly causes pain in the testicles and may sometimes cause problems with ejaculation, urination, or defecation.

Accessed: 24 January 2010
Prostatitis

• **Chronic nonbacterial:**
  – Abnormally high number of inflammatory cells in secretions from the prostate but it occurs without infection of the urinary tract; approximately 64%.

• **Prostadynia:**
  – Similar to non-bacterial except that secretions from the prostate does not contain inflammatory cells; approximately 31%.

• **Acute bacterial:**
  – Detrimental bacteria (usually E. Coli). May progress to chronic bacterial prostatitis; approximately 3%; life threatening and requires immediate medical care.

• **Chronic bacterial:**
  – Differs from acute bacterial in that it is more difficult to cure and frequently recurs; approximately 2%. 
Prostatitis Signs and Symptoms

- Recurrent urinary tract infections.
- Difficulty starting urine stream.
- Decreased strength and force of the stream.
- Dribbling after urination.
- Urinary frequency.
- Nocturia
- Incomplete bladder emptying.
- Urinary urgency.
- Dysuria
- Fever with chills.
- Generalised malaise.
- Bladder outlet obstruction, complete inability to urinate.
- Painful ejaculation, bloody semen, or sexual dysfunction.
- Pain localised to lower back (sacral), pelvis, or perineum.
- Blood in the urine, caused by bursting of small veins in the urethra and bladder.
Prostatitis - Quercetin

- Objectives:
  - The National Institutes of Health (NIH) category III chronic prostatitis syndromes (nonbacterial chronic prostatitis and prostatodynia) are common disorders with few effective therapies. Bioflavonoids have recently been shown in an open-label study to improve the symptoms of these disorders in a significant proportion of men. The aim of this study was to confirm these findings in a prospective randomized, double-blind, placebo-controlled trial.

Prostatitis - Quercetin

• Methods:
  – Thirty men with category IIIa and IIIb chronic pelvic pain syndrome were randomised in a double-blind fashion to receive either placebo or the bioflavonoid quercetin 500 mg twice daily for 1 month. The NIH chronic prostatitis symptom score was used to grade symptoms and the quality-of-life impact at the start and conclusion of the study. In a follow-up unblind, open-label study, 17 additional men received 1 month of a supplement containing quercetin, as well as bromelain and papain (Prosta-O), which enhance bioflavonoid absorption.

• **Results:**
  – Two patients in the placebo group refused to complete the study because of worsening symptoms, leaving 13 placebo and 15 bioflavonoid patients for evaluation in the blind study. Both the quercetin and placebo groups were similar in age, symptom duration, and initial symptom score. Patients taking placebo had a mean improvement in NIH symptom score from 20.2 to 18.8 (not significant), while those taking the bioflavonoid had a mean improvement from 21.0 to 13.1 (P = 0.003). Twenty percent of patients taking placebo and 67% of patients taking the bioflavonoid had an improvement of symptoms of at least 25%. In the 17 patients who received Prosta-Q in the open-label study, 82% had at least a 25% improvement in symptom score.

• **Conclusions:**
  – Therapy with the bioflavonoid quercetin is well tolerated and provides significant symptomatic improvement in most men with chronic pelvic pain syndrome.

Prostatitis - Zinc

• Objective:
  – To investigate the seminal parameters, zinc concentration and antibacterial activity in patients with non-inflammatory chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS).

• Methods:
  – Seminal parameters, zinc concentration and antibacterial activity of seminal plasma were detected in 60 CP/CPPS patients and 20 normal men.

Prostatitis - Zinc

• Results:
  – Statistically significant differences were found in the duration of semen liquefaction, sperm vitality, sperm motility, zinc concentration and antibacterial activity of the seminal plasma between the CP/CPPS and the control males (P < 0.01). **Zinc concentration** was significantly correlated with the duration of sperm motility (r = 0.272, P = 0.015) and antibacterial activity of the seminal plasma (r = 0.449, P < 0.01) in the CP/CPPS patients.

• Conclusion:
  – CP/CPPS has a **significant negative impact** on semen liquefaction, sperm motility and vitality, zinc concentration and antibacterial activity of seminal plasma. The **antibacterial activity of seminal plasma is positively correlated with zinc concentration and sperm motility.**

The prostate is a gland that surrounds the posterior urethra in man and, along with seminal vesicles, produces prostatic and seminal fluids. Prostatitis, benign prostatic hyperplasia (BPH), and prostate cancer are the most frequent pathologies of this gland. Zinc is an important element in the makeup of prostatic fluid and plays an important role in the immunology of the infectious and neoplastic pathologies of the prostate. The aim of this study was to determine zinc concentrations in prostatic fluid of patients with prostate pathologies and to use this measurement as a diagnostic parameter. Thirty patients with prostatic pathologies and ten healthy controls were studied. Prostatic fluid samples were collected using prostatic massage. Zinc concentration was determined using electrothermal atomizer atomic absorption spectrometry (ETA-AAS).

Prostate Health - Zinc

- The mean zinc concentrations obtained in the studied population were as follows: 11 patients with BPH: 15.087,78 micromol/dL, 10 patients with prostatitis: 863,33 micromol/dL, 9 patients with prostate cancer: 1.027,60 micromol/dL and 10 healthy subjects: 7.467,52 micromol/dL. The low zinc concentrations obtained in patients with prostatitis and prostate cancer, in contrast to the control group, led us to consider the possibility of recommending zinc supplements as a coadjuvant therapy in patients with prostatitis and also, to use zinc measurements as another diagnostic tool, for cases in which it is necessary to differentiate benign prostatic hyperplasia from prostate cancer.

Benign Prostatic Hyperplasia

- BPH is the result of non-malignant neoplasms of epithelial glandular tissue, which causes hypertrophy of the prostate gland.

- The resulting enlargement of the fibromusculature of the prostate gland causes difficulty in urination and sexual function.

- Very common problem in older men.
  - The chance of prostate problems increases dramatically with age.
    - By age 60 - > 50% of men have some prostate enlargement.
    - By age 70 - 90% have prostate enlargement.
    - About 33% over age 50 develop symptoms due to prostate enlargement.

Benign Prostatic Hyperplasia

- As men age, testosterone levels decrease and prolactin, oestradiol, sex hormone-binding ligand, luteinising hormone (LH), and follicle-stimulating hormone (FSH) levels all increase.

- The prostate is affected by testosterone and oestrogen.

- Both these hormones contribute to increased levels of dihydrotestosterone (DHT).
  - DHT increases prostatic cell proliferation and glandular size.

http://www.naturaldatabase.com/(S(c4rmokbt3rje44ecve0dxx45))/ce/CECourse.aspx?cs=&pm=5&s=nd&pc=07-23&searchid=18790707#keywordanchor
Accessed: 24 January 2010
Benign Prostatic Hyperplasia - DHT

- The increase in DHT is largely due to:
  - A decreased rate of removal
  - An increase in the activity of the enzyme 5-alpha-reductase, the enzyme that converts testosterone to DHT.

Modern Phytotherapist
Benign Prostatic Hyperplasia - Oestrogens

- Prostate size correlates with oestradiol levels and with the ratio of oestradiol to free testosterone.

- Oestrogens increase the number of DHT receptors in the prostate and also inhibits DHT metabolism. These changes can lead to further enlargement of the prostate.

- Testosterone and DHT are extensively metabolised by hydroxylation, which decreases the normally high affinity of the cytosolic receptor proteins for these hormones, thereby allowing their excretion.
  - Oestrogens inhibit this hydroxylation.

Benign Prostatic Hyperplasia - Oestrogens

- Oestrogens originate from testosterone and the adrenal androgen androstenedione through conversion by the **aromatase** enzyme system.

- Aromatase levels increase due to:
  - Increased age
  - Increased fat mass
  - Increased insulin
  - Increased alcohol intake
  - Increased prostaglandin levels
  - Increased cytokines
  - Increased growth factors

DHT = dihydroepiandrosterone; DHEA = dehydroepiandrosterone
5α-R = 5-alpha reductase; 17β-HD = 17-Beta hydroxysteroid dehydrogenase

http://bestpractice.bmj.com/best-practice/images/bp/869-2-iline-bp_default.gif
Benign Prostatic Hyperplasia – SHBG

- SHBG increases with age and can act like an additional androgen receptor in the prostate cell.

- It is suggested that when oestrogen binds to SHBG in the cell membrane, insulin-like growth factor 1 (IGF-1) is synthesised causing proliferation of prostatic epithelial cells.

Benign Prostatic Hyperplasia
Symptoms

• The symptoms due to BPH can be divided into:
  – **Voiding** symptoms which include decreased force of stream, hesitancy, intermittency, straining to void, incomplete emptying and urinary retention.
  – **Storage** symptoms which include urgency, frequency, nocturia, dysuria and urge incontinence.

• These symptoms are collectively referred to as lower urinary tract symptoms.

Symptoms

• Urinary frequency:
  – The need to urinate frequently during the day or night (nocturia), usually voiding only small amounts of urine with each episode.
  – Interrupted sleep to urinate at night.

• Urinary urgency:
  – The sudden urgent need to urinate quickly.
  – The sensation of imminent loss of urine without control.

Accessed: 24/01/2010
Symptoms

• Hesitancy:
  – Difficulty initiating the urinary stream.
  – Having to stand at or sit on the toilet for some time prior to producing a urinary stream.

• Incomplete bladder emptying:
  – The sensation of incomplete evacuation of urine from the bladder.
  – The feeling of persistent residual urine regardless of the frequency of urination.

Symptoms

• Straining:
  – The need strain or push (Valsalva maneuver) to initiate and maintain urination in order to more fully evacuate the bladder.

• Decreased force of stream:
  – The subjective loss of force of the urinary stream over time.

• Dribbling or dripping:
  – The loss of small amounts of urine due to a poor urinary stream.

Accessed: 24/01/2010
Diagnosis - Digital Rectal Examination (DRE)

• The is an integral part of the evaluation for men with presumed BPH.

• The prostate size and contour can be assessed, nodules can be evaluated, and areas suggestive of malignancy can be detected.

• A more precise volumetric determination can be made using transrectal ultrasonography (TRUS).
Diagnosis - Digital Rectal Examination (DRE)

- In general, an estimation of the number of index finger pads that one can sweep over the rectal surface of the prostate during a DRE is a useful way for estimating gland size.

- A normal size prostate is approximately 20g.

- Each fingerbreadth correlates to approximately 15-20 g of tissue.
  - For example, one can report the prostate size as "2-3 fingerbreadths wide" when charting or communicating.
  - Most asymptomatic men have glands less than or equal to 2 fingerbreadths.
Diagnosis - Prostate Specific Antigen

- Although benign prostatic hyperplasia (BPH) does not cause prostate cancer, men at risk for BPH are also at risk for prostate cancer and should be screened accordingly.

- A physician should discuss the risks and benefits of PSA screening with the patient.
  - Using the PSA test to screen healthy men for prostate cancer is somewhat controversial and is not recommended at present in the UK. This is because in many cases PSA testing detects early cancers that are extremely slow-growing and may never cause life-threatening disease - this may cause further unnecessary testing and treatment. However, men who have an increased risk for prostate cancer (such as Afro-Carribean or African-American men, and those with a family history of the disease) may wish to be screened for prostate cancer.

Lab tests online UK.  [http://www.labtestsonline.org.uk/understanding/analytes/psa/test.html](http://www.labtestsonline.org.uk/understanding/analytes/psa/test.html)
Accessed: 25/01/2010
Diagnosis - Prostate Specific Antigen

• Serum PSA may increase due to:
  – BPH, diagnostic examinations, physical exercise, ejaculation, acute and chronic prostatitis, and ductal obstruction.
  – It is also related to the volume of the prostate and to age of the individual.

• The normal value for PSA is less than 4 ng/ml.

• Levels between 4.0 ng/mL and 10.0 ng/mL may indicate BPH
  – PSA levels greater than 4 should be referred to a urologist for further evaluation.

• An elevation greater than 10 is highly indicative of prostate cancer.

Diagnosis - Prostate Specific Antigen

- PSA testing should be offered to any patient with a 10-year life expectancy in whom the diagnosis of prostate cancer would change management.

- The American Cancer Society recommends that annual prostate-specific antigen (PSA) testing and DRE for prostate cancer screening be offered at the following ages:
  - Starting at age 50 years in men who are expected to live at least 10 more years.
  - Starting at age 45 years in men at high risk for prostate cancer - African-Americans and men with a close relative with prostate cancer.
  - Starting at age 40 years in men with multiple close relatives with prostate cancer.

Accessed: 25/01/2010
Pathology Tests

• Bacterial culture (Prostatitis):
  – A bacterial culture may determine what bacterium is causing the infection.
  – First void and mid-stream urine samples and possibly expressed prostatic secretions may be collected and subjected to microscopy and culture.
Orthodox Treatment

• Treatment options for BPH consist of:
  – Doing nothing,
  – Drug treatment with alpha-blockers and/or 5-alpha reductase inhibitors, or
  – Surgical treatment.

• Treatment decisions are based on the severity of symptoms and their effect on quality of life.

• Antibiotics:
  – Depending on the severity of the infection, antibiotics may be given by mouth or by intravenous injection.

• NSAID’s:
  – Nonsteroidal anti-inflammatory drugs are often used for analgesic, anti-inflammatory and anti-pyretic effects.

http://www.naturaldatabase.com/(S(c4rmokbt3rje44ecve0dxx45))/ce/CECourse.aspx?cs=&pm=5&s=nd&pc=07-23&searchid=18790707#keywordanchor0
Orthodox Treatment

• 5-alpha-reductase inhibitors:
  – Inhibit the conversion of testosterone to DHT. This drop in DHT levels may reduce prostate size.
  – For example, Dutasteride and Finasteride.

• Alpha-adrenergic drugs:
  – May relieve symptoms by blocking alpha-1 adrenoceptors in the prostate and bladder neck, relaxing smooth muscle and improving urine flow.
  – For example, Terazosin, Alfuzosin, Doxazosin.
Orthodox treatment

• Close monitoring by physician:
  – Severity of symptoms is associated with a greater likelihood of the need for surgery.

• Transurethral microwave thermotheraphy (TUMT):
  – An alternative to surgery
  – Catheter tipped with a special antenna that delivers microwave energy to the prostate to selectively heat and kill prostate tissue.

• Surgery:
  – 90% of all surgeries performed are endoscopic device inserted into the urethra (TURP).
Nutritional Therapy

• A positive association exists between abdominal obesity and BPH.

• Increased sympathetic activity may cause the prostate smooth muscle to contract, resulting in a worsening of lower urinary tract symptoms.

• An inverse association exists between physical activity and BPH.
  – Physical activity may serve a threefold purpose:
    1. It may increase blood flow to the area, allowing the body to remove wastes efficiently;
    2. It can decrease sympathetic stress responses, thus relaxing prostatic tissue; and
    3. It can reduce excess abdominal weight, which increases overall lower body pressure, thus relaxing the prostate/rectal region and improving blood flow into and out of the area.

Nutritional Therapy

• Avoid pesticides:
  – e.g., dioxin, polyhalogenated biphenyls, hexachlorobenzene, and dibenzofurans
  
• Increase 5-alpha reduction of steroids.

• Increase fruit and vegetable consumption.

• Increase the intake of zinc.

• Increasing omega 3 essential fatty acids was previously recommended, new research highlights fish oils as a possible hazard.
  – Read more: http://jnci.oxfordjournals.org/content/105/15/1132

Nutritional Therapy

• Decrease coffee consumption and butter consumption.

• Avoid margarine.

• Cholesterol levels below 5.4 mmol/L.

• The Budwig diet is a popular cancer therapy diet, with preliminary research supporting its inclusion of flaxseeds and reduction of sugar, meat, butter and margarine.

Nutritional Therapy - Protein

• An 8-year study of 3523 men with BPH cited that total protein intake is positively associated with BPH, with the association being slightly stronger for *animal* protein intake than for vegetable protein intake.

• Interesting some evidence suggests that a high-protein diet (total calories: 44% protein, 35% carbohydrate, 21% fat) can inhibit 5-alpha-reductase, while a low-protein diet (10% protein, 70% carbohydrate, and 20% fat) may stimulate the enzyme.

Nutritional Therapy - Protein

• A theoretical reason as to why high protein intake may not be helpful in BPH relates to a greater osmolar load, which may influence urinary output, imposing extra burden on an already taxed system.

• Recommend against excess animal protein as a means to increase total protein intake.

• Recommend a high-quality, plant-derived and coldwater fish-based protein sources in moderate amounts.
Nutritional Therapy

• Low-fat, high-vegetable, and high-protein diet reduces the risk of benign prostatic hyperplasia.

• Researchers examined dietary risk factors for incident benign prostatic hyperplasia (BPH) in 4770 participants in the Prostate Cancer Prevention Trial (1994-2003) over a 7-year period, during which 876 men developed BPH.

• Men with the highest intake of total fat had a 31% increased risk for developing BPH compared with men with the lowest, and men with the highest polyunsaturated fat intake had a 27% higher risk.

Nutritional Therapy

• Higher protein consumption reduced the risk by 15% (all $P < .05$). Additionally, the risk was significantly lower in high consumers of alcoholic beverages (0 versus ≥2/day, hazard ratio [HR] = 0.67) and vegetables (<1 versus ≥4/day, HR = 0.68) and higher in daily (versus <1/wk) consumers of red meat (HR = 1.38).

• There were no associations of supplemental antioxidants with risk, and there was weak evidence for associations of lycopene, zinc, and supplemental vitamin D with reduced risk. A diet low in fat and red meat and high in protein and vegetables and regular alcohol consumption may reduce the risk of symptomatic BPH.

Nutritional Therapy - Alcohol

- Higher alcohol intake may be associated with BPH.
- In a 17-year study of 6581 men in Hawaii, it was noted that an alcohol intake of at least 700 ml/month was directly correlated with the diagnosis of BPH. The association was most significant for beer, wine, and sake and less for distilled spirits.
- A smaller study of 889 men described an inverse association between alcohol intake and men treated surgically for BPH or in "watchful waiting" for surgical intervention. This study also mentioned the correlation of higher rates of BPH in men with coronary disease.
- Although these studies are apparently contradictory in relationship to alcohol, it is possible that in men at higher risk for coronary artery disease due to higher levels of low-density lipoproteins, alcohol may play an overall protective role by reducing these lipoproteins.

• Shown to reduce the size as noted by rectal palpation, radiograph, and endoscopy and reduced symptomatology.
  – May inhibit the activity of 5-alpha-reductase.
  – May block testosterone’s aromatisation to oestradiol.
  – May inhibit specific binding of androgens to the cytosol and nuclear androgen receptors.
  – May inhibit prolactin secretion.
  • Prolactin has been shown to increase the uptake of testosterone by the prostate, thereby leading to increased levels of DHT by providing more substrate.

Nutritional Therapy - Zinc

• Zinc concentrations in the prostate are uniquely high but are dramatically decreased with prostate cancer. Studies have suggested that increasing zinc in the prostate may be a potential therapeutic strategy.

• The goal of this study was to evaluate the antiproliferative effects of zinc in prostate cancer cells (PC-3) and noncancerous benign prostate hyperplasia (BPH) cells (BPH-1) and to define possible mechanisms. PC-3 and BPH-1 cells were treated with zinc (0 -250 μM) for 24 and 48 h, and cell growth and viability were examined.

Nutritional Therapy - Zinc

• Apoptosis was assessed by phosphatidylserine externalization, caspase activation and protein expression of B-cell CLL/lymphoma 2 (Bcl-2)-associated X protein (BAX): Bcl-2.

• **BPH-1 cells were more sensitive to the antiproliferative effects of zinc compared to PC-3.** The response to zinc in PC-3 and BPH-1 cells differed as evidenced by opposing effects on Bcl-2:BAX expression.

• Additionally, different effects on the nuclear expression and activity of the p65 subunit of nuclear factor kappa B were observed in response to zinc between the two cell types. **The differential response to zinc in PC-3 and BPH-1 cells suggests that zinc may serve an important role in regulating cell growth and apoptosis in prostate cancer and hyperplasia cells.**

Nutritional Therapy - Beta-Sitosterol

• Phytosterols have been shown to improve BPH.

• A double-blind study consisted of 200 men receiving beta-sitosterol (20 mg) or placebo three times daily.
  – The beta-sitosterol produced an increase in maximum urine flow rate from a baseline of 9.9 ml/s to 15.2 ml/s and a decrease in mean residual urinary volume of 30.4 ml from 65.8 ml.
  – No changes were observed in the placebo group.

• A 100mg serving of soybeans, tofu, or other soyfood provides approximately 90 mg of beta-sitosterol.

Nutritional Therapy - Lycopene

- A carotenoid pigment of tomatoes and other red or pink fruits and vegetables.

- May inhibit 5-alpha reductase and interleukin-6 signalling, and its antioxidant properties may help prevent cell proliferation and remodelling in the prostate.

- Scientists enrolled 40 cancer-free men with BPH and serum prostate-specific antigen (PSA) levels of greater than 4.0 mcg/L. The men were randomised to receive 15 mg lycopene or placebo daily for six months.
A possibly beneficial role of lycopene in patients diagnosed with benign prostate hyperplasia (BPH), who are at increased risk of developing prostate cancer (PCa), has been suggested, although clinical data are lacking.

Therefore, this pilot study aimed to investigate the effects of lycopene supplementation in elderly men diagnosed with BPH.

A total of 40 patients with histologically proven BPH free of PCa were randomised to receive either lycopene at a dose of 15 mg/d or placebo for 6 mo.

The effects of the intervention on carotenoid status, clinical diagnostic markers of prostate proliferation, and symptoms of the disease were assessed.

Nutritional Therapy - Lycopene

- The primary endpoint of the study was the inhibition or reduction of increased serum prostate-specific antigen (PSA) levels.
  - The 6-mo lycopene supplementation decreased PSA levels in men (P < 0.05), whereas there was no change in the placebo group.
  - The plasma lycopene concentration increased in the group taking lycopene (P < 0.0001) but other plasma carotenoids were not affected. Whereas progression of prostate enlargement occurred in the placebo group as assessed by trans-rectal ultrasonography (P < 0.05) and digital rectal examination (P < 0.01), the prostate did not enlarge in the lycopene group.
  - Symptoms of the disease, as assessed via the International Prostate Symptom Score questionnaire, were improved in both groups with a significantly greater effect in men taking lycopene supplements. In conclusion, lycopene inhibited progression of BPH.

Herbal Therapy

• *Serenoa repens* (saw palmetto):
  – Mild inhibition of 5-alpha-reductase, anti-androgenic activity and an inhibition of androgen binding.
  – Anti-inflammatory and spasmolytic.

• *Urtica dioica* (stinging nettles):
  – Long tradition of use in Germany for the treatment of inflammations of the urinary tract, for the prevention of urinary lithiasis and for the treatment of BPH.

• *Pygeum africanum*:
  – Includes beta-sitosterol.
  – Reduces prostate enlargement and blocks DHT from binding to prostate cells.
Pre-Conception Care and Natural Fertility Management
Infertility

- The most commonly accepted definition of the term infertility is the lack of pregnancy (regardless of cause) after 1 year of unprotected intercourse. Infertility affects approximately 15% of couples of reproductive age.¹

- The level of childlessness among women born in 1967 (19%) is higher than for women born in 1940 (11%). ²

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Incidence of IVF Use in UK

- Since the first IVF baby was born in 1978, an estimated 5 million babies have been born worldwide after IVF treatment. In the UK 201,811 babies have been born after IVF treatment between 1991 and 2010.

- In 2011, 48,147 women had a total of 61,726 cycles of IVF or ICSI and 2,087 women had a total of 4,091 cycles of donor insemination.
Normal Reproduction Requires:

1. The release of a normal oocyte.

2. The production of adequate sperm.

3. The normal transport of the gametes to the fallopian tubes (where fertilisation occurs).

4. The transport of the cleaving embryo up to the endometrial cavity for its normal implantation and further development.
Causes of Infertility

Female:
• Cervical – mucous/sperm interactions.
• Uterine – endometriosis, congenital problems, surgery, fibroids.
• Ovarian- failure to ovulate, alterations to menstrual cycle.
• Tubal- congenital or acquired defects in fallopian tubes.
• Peritoneal – PID, congenital, infection, adhesions.

Male
• HPA axis – lesions, tumours, hormonal conditions.
• Testicular – congenital or acquired abnormalities such as varicocele, orchitis.
• Post-testicular- congenital or acquired abnormalities of the vas deferens, erectile dysfunction etc.

Male Infertility

• Causes of infertility in men can be explained by:
  – Deficiencies in sperm formation concentration e.g. oligospermia (too few sperm).
  – Azoospermia (no sperm in the ejaculate).
  – Transportation problems.

Accessed on the 27/1/10
Sperm Production

- Hypothalamic-pituitary-gonadal axis stimulatory and inhibitory signals.

- Gonadotropin-releasing hormone (GnRH) from the hypothalamus stimulates the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the pituitary.

- FSH stimulates the Sertoli cells to facilitate sperm production, while LH stimulates testosterone release from the Leydig cells. Feedback inhibition is from testosterone and inhibin.

Accessed on the 27/1/10
Male Infertility - Causes

- The hypothalamus also produces thyrotropin-releasing hormone (TRH) and vasoactive intestinal peptide (VIP), both of which stimulate prolactin release from the anterior pituitary, and dopamine, which inhibits prolactin release.

- Men with elevated prolactin levels present with gynecomastia, diminished libido, erectile dysfunction, and occasionally galactorrhea.

Male Infertility - Causes

• Idiopathic hypogonadotrophic hypogonadism:
  – E.g. Prader-Willi syndrome, Laurence-Moon-Biedl syndrome, CNS tumours, temporal lobe seizures, and many drugs (e.g., dopamine antagonists) may interrupt the hypothalamic-pituitary axis at the hypothalamus.

• Prolactinoma

• Isolated LH deficiency (fertile eunuch).

• Thalassemia- the excess iron from RBC break down can gather in the testes and become and oxidant.

Accessed on the 27/1/10
Male Infertility - Causes

- Cushing disease: Increased cortisol levels cause a negative feedback on the hypothalamus, decreasing GnRH release.

- The hypothalamus-pituitary axis may be interrupted by hormonally active peripheral tumours or other exogenous factors, due to cortical excess, cortical deficiency, or oestrogen excess.

- Chromosomal abnormalities.

Male Infertility - Causes

• Varicocele:
  – Varicocele is a dilation of the veins of the pampiniform plexus of the scrotum.
  – Although varicoceles are present in 15% of the male population, a varicocele is considered the most common correctable cause of infertility (30-35%) and the most common cause of secondary (acquired) infertility (75-85%). Varicoceles are observed more commonly on the left side than the right.
  – Varicoceles lead to an increased incidence of sperm immaturity, apoptosis, and necrosis with severe disturbances in meiotic segregation.
  – Generally all parameters will improve after repair.

Male Infertility - Causes

- Cryptorchidism
- Testicular trauma
- Chemotherapy or radiation therapy
- Orchitis
- Excessive use of alcohol, cigarettes, caffeine, and marijuana may lead to testicular failure.
- Idiopathic causes: Despite a thorough workup, nearly 25% of men have no discernible cause for their infertility.
- Antisperm, antibodies and autoantibodies.
- Oxidation and DNA fragmentation.

Accessed on the 27/1/10
Male Infertility - Therapy

- Medical conditions need to be managed.

- Patients should be encouraged to stop smoking cigarettes and marijuana and to limit environmental exposures to harmful substances and/or conditions. (We’ll talk more about that in a moment).

- Stress-relief therapy and consultation of other appropriate psychological and social professionals may be advised.

- Infections should be treated with appropriate antimicrobial therapy.
Male Infertility - Therapy

- A diet high in antioxidants such as vitamin C and vitamin E has been proposed to improve the quality of sperm by decreasing the number of free radicals that may cause membrane damage.

- Additionally, the use of zinc, fish oil, and selenium has been shown to be of benefit in some studies.

Male Infertility - Selenium

- Sixty-nine patients were recruited and received either placebo, selenium alone or selenium plus vitamins A, C and E daily for 3 months.

- This trial confirms the result of an earlier study, that selenium supplementation in subfertile men with low selenium status can improve sperm motility and the chance of successful conception.

- However, not all patients responded: 56% showed a positive response to treatment.

Male Infertility - Zinc And Heavy Metals

- Lead produces toxic effects on the germinal epithelium and altered the quality of semen which was improved by zinc in rats¹.

- The absence of zinc in semen has been linked with low sperm quality in humans².

- Zinc sulphate supplementation protected against vanadium free radical damage in rats³.

- Zinc supplementation also protected against cadmium poisoning⁴.

- It may be prudent to test for heavy metal toxicity in a male in idiopathic infertility.
Male Infertility - Carnitine

- L-Carnitine (LC) and acetyl-L-carnitine (ALC) are highly concentrated in the epididymis and play a crucial role in sperm metabolism and maturation. They are related to sperm motility and have antioxidant properties.

- The administration of L-C and/or LAC may be effective in improving pregnancy rate and sperm kinetic features in patients affected by male infertility. However, the exact efficacy of carnitines on male infertility needs to be confirmed by further investigations.¹

Male Infertility - Folic Acid

• Folic acid has been shown to reduce DNA damage in men that have had chemotherapy treatment¹.

• One trial with zinc sulphate and folic acid significantly increased sperm concentration in subfertile males².

Male Infertility

• The optimal timing to perform intercourse for conception is every 2 days at mid cycle.

• The use of spermatotoxic lubricants should be avoided.

• Limit testicular damage- minimise cycling, tight jeans or any conditions with excess heat to the testes

Causes of Infertility: Men & Women

- Environmental/occupational factors.
- Toxic effects related to tobacco, marijuana, or other drugs.
- Excessive exercise.
- Inadequate diet associated with extreme weight loss or gain.
- Advanced age.

• Please note, we will not review in this lecture disease processes that have been covered in the women’s health lecture, so please see your other notes to add the whole picture together!

Elizabeth E Puscheck, MD (2013) Infertility, Medscape Reference, last updated 10th June 2013
The main causes of infertility in the UK are:

- Unexplained infertility (no identified male or female cause) (25%)
- Ovulatory disorders (25%)
- Tubal damage (20%)
- Factors in the male causing infertility (30%)
- Uterine or peritoneal disorders (10%).

### Other Common Causes of Infertility

<table>
<thead>
<tr>
<th>Sterility</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>No eggs</td>
<td>Menopause, radiation damage, autoimmune disease.</td>
</tr>
<tr>
<td>No sperm</td>
<td>Arrested development, removed testicle, infectious causes, immature sperm.</td>
</tr>
<tr>
<td>Fallopian tube obstruction</td>
<td>Chlamydia, pelvic inflammatory disease, surgery, endometriosis, congenital.</td>
</tr>
<tr>
<td>No uterus or damage uterus</td>
<td>Hysterectomy, traumatic damage, ablation</td>
</tr>
</tbody>
</table>
### Other Common Causes of Infertility

<table>
<thead>
<tr>
<th>Male causes</th>
<th>Female causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low sperm count</td>
<td>Immunity issues- AB’s to sperm, AB’s towards phospholipid bilayer</td>
</tr>
<tr>
<td>Low motility of sperm</td>
<td>High vaginal pH</td>
</tr>
<tr>
<td>Low morphology of sperm</td>
<td>Irregular ovulation</td>
</tr>
<tr>
<td>High DNA fragmentation on the sperm</td>
<td>Unbalanced steroid hormone balance- oestriodiol, progesterone, thyroid or adrenal hormones</td>
</tr>
<tr>
<td>High oxidation of the sperm</td>
<td>Uterine environment problems- fibroids, endometriosis, infections</td>
</tr>
<tr>
<td></td>
<td>Genetic variations such as MTHF</td>
</tr>
</tbody>
</table>
Causes of Infertility - Advanced Age

• The prevalence of infertility rises dramatically as age increases.

• Studies report that among Mormons, fertility appears to be stable until age 36 years, declines slightly until age 40 years, and is followed by a sharp decline after age 42 years.

• In the North American Hutterite population where contraception is condemned, infertility rates are 11% after age 34, 33% after at age 40 and 87% at age 45.

Elizabeth E Puscheck, MD (2013) Infertility, Medscape Reference, last updated 10th June 2013
Causes of Infertility - Advanced Age

- Similar conclusions of the impact of age can be drawn from IVF programs using fresh eggs.

**Table 6: Pregnancy rate (per embryo transfer) for patients receiving IVF treatment using their own fresh eggs, 2010 and 2011.**

<table>
<thead>
<tr>
<th>Year of treatment:</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 – 34</td>
<td>41.1%</td>
<td>40.6%</td>
</tr>
<tr>
<td>35 – 37</td>
<td>35.9%</td>
<td>35.5%</td>
</tr>
<tr>
<td>38 – 39</td>
<td>29.0%</td>
<td>28.1%</td>
</tr>
<tr>
<td>40 – 42</td>
<td>21.2%</td>
<td>21.2%</td>
</tr>
<tr>
<td>43 – 44</td>
<td>10.3%</td>
<td>11.2%</td>
</tr>
<tr>
<td>45 +</td>
<td>4.2%</td>
<td>3.4%</td>
</tr>
<tr>
<td>All ages</td>
<td>34.1%</td>
<td>33.7%</td>
</tr>
</tbody>
</table>
The uterine cervix plays a pivotal role in the transport of the sperm after intercourse.

At the beginning of the menstrual cycle, cervical mucus is scanty, viscous, and very cellular. The mucus forms a netlike structure that does not allow the passage of sperm.

Mucus secretion increases during the mid follicular phase and reaches its maximum approximately 24-48 hours before ovulation. The water and salt concentration increases, changing the physical characteristics of the mucus.
Causes of Infertility – Cervical Mucous

- The mucus becomes thin, watery, alkaline, acellular, and elastic because of the increased concentration of sodium chloride, despite a fernlike pattern when the mucus is allowed to dry on a cover slide under the microscope.

Elizabeth E Puscheck, MD (2013) Infertility, Medscape Reference, last updated 10th June 2013
• Mucus secretion may be altered by hormonal changes and medications (such as the OCP and clomiphene citrate), surgical procedures, infections, hypoestrogenism, and radiation therapy.

• Cigarette smoking decreases the production of cervical mucous.
Causes of Infertility – Environmental, Occupational and Dietary Toxins

- Excessive **radiation** damages germinal cells.

- Exposure to **heavy metals** has also been associated with infertility.

- **Lead** may alter sperm quality in men, and cause irregular menstruation, induce preterm delivery, and cause miscarriage, stillbirth, and spontaneous abortion in women.

- **Mercury** can disrupt spermatogenesis and disrupt foetal development

Elizabeth E Puscheck, MD (2013) Infertility, Medscape Reference, last updated 10th June 2013
Sharma et al. Lifestyle factors and reproductive health: taking control of your fertility, Reproductive Biology and Endocrinology 2013, 11:66
Causes of Infertility – Environmental, Occupational and Dietary Toxins

- **Smoking** has been associated with infertility in both males and females. **Nicotine** and **polycyclic aromatic hydrocarbons** block spermatogenesis.

- **Marijuana** induces ovulatory disorders in women and decreases sperm count and the quality of the sperm in males.

- **Chronic alcoholism** may induce ovulatory dysfunction. Alcohol use by males interferes with the synthesis of testosterone and has an impact on sperm concentration. Alcoholism may inhibit sexual response and cause impotence.

Elizabeth E Puscheck, MD (2013) Infertility, Medscape Reference, last updated 10th June 2013
Causes of Infertility – Environmental, Occupational and Dietary Toxins

- **Caffeine** has been associated with an increase in the time to pregnancy if the amount is over 500 mg per day.

- The negative effects that are emphasized in recent research are miscarriage, spontaneous abortion, foetal death and still birth.

- Women who consumed **more than 100 mg** of caffeine a day were more likely to experience a miscarriage.

Causes of Infertility – Environmental, Occupational and Dietary Toxins

- High exposure to **air pollution** decrease sperm count in males.

- Exposure to **pesticides and endocrine disruptors** decreases fertility.

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Possible reproductive effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BPA</strong></td>
<td>Inhibits binding to androgen receptor, decreased semen quality, erectile dysfunction, chromosomal abnormalities in oocyte, recurrent miscarriage,</td>
</tr>
<tr>
<td>Disinfection by-products</td>
<td></td>
</tr>
<tr>
<td><strong>Organochemicals and Pesticides</strong></td>
<td>Change in hormone levels, irregular menstruation, decreased fertility, decreased semen quality, chromosomal abnormalities in sperm, altered histology of testes, decreased libido, fetal loss, miscarriage</td>
</tr>
<tr>
<td>e.g. DDT, DDE, Methoxychlor</td>
<td></td>
</tr>
<tr>
<td><strong>Dioxins</strong></td>
<td>Changes in hormone levels, altered puberty, altered start of menarche, endometriosis, decreased fertility, fetal loss</td>
</tr>
<tr>
<td><strong>Phthalates</strong></td>
<td>Decreased semen quality, oligozoospermia, earlier menarche, altered menstrual cycle, infertility</td>
</tr>
<tr>
<td><strong>Solvents</strong></td>
<td>Change in hormone levels, decreased semen quality, irregular menstruation, decreased fertility, miscarriage, fetal loss</td>
</tr>
</tbody>
</table>
Causes of Infertility – Environmental, Occupational and Dietary Toxins

• **Cell phone usage** has been linked with decreases in progressive motility of sperm, decreases in sperm viability, increases in ROS, increases in abnormal sperm morphology, and decreases in sperm counts.

• Many **prescription medications** have been shown to impact negatively on fertility.

Causes of Infertility –
Extreme Weight Loss or Gain

- **Obesity** has an impact on infertility only when the female patient's weight reaches extremes. Obese men are three times more likely to exhibit a reduction in semen quality than men of a normal weight.

- Obesity may be associated with anovulation and oligomenorrhea in women.

- Obese women have a higher rate of recurrent, early miscarriage.

Elizabeth E Puscheck, MD (2013) Infertility, Medscape Reference, last updated 10th June 2013
• Implantation rates are lower in obese women, these may by due to an increase in follicular fluid levels of insulin, lactate, triglycerides, and C-reactive protein; there may also be decreases in SHBG.

• Obesity also increases oxidative markers in both men and women.

• Weight loss associated with anorexia nervosa or bulimia induces hypothalamic amenorrhea.
Causes of Infertility - Exercise

• Exercise should be encouraged as it manages obesity and insulin resistance which will then increase the likelihood of conception.

• However, **compulsive exercise** is deleterious for fertility, especially for long-distance runners.

• Jogging stimulates the secretion of endorphins; excessive secretion of endorphins interferes with the normal production of FSH and LH, in turn inducing ovulatory disorders and luteal phase dysfunction, which accounts for lack of embryo implantation and first-trimester miscarriages. In males, exercise has been associated with oligospermia.

Elizabeth E Puscheck, MD (2013) Infertility, Medscape Reference, last updated 10th June 2013
Causes of Infertility - Stress

- Research has shown that males that rate a higher level of stress or stressful events have a lower sperm count than the standard classified by the WHO.

- Stress and depression are thought to reduce testosterone and luteinizing hormone (LH) pulsing, disrupt gonadal function and ultimately reduce sperm parameters.

- Women worked more than 32 hours a week experienced a longer time to conception compared to women who worked 16 to 32 hours a week.

Causes of Infertility - Stress

- Women who receive support and counselling may reduce their **anxiety** and **depression** levels increase their chances of becoming pregnant.

- Positive moods correlated with increased chances of delivering a live baby while higher levels of anxiety increased chances of stillbirth.

- Fertilization of oocytes decreases when stress increases.

Pre-Natal Stress and Effects on Infant

- **Exposure of the developing brain** to severe and/or prolonged stress may result in hyperactivity/hyperreactivity of the stress system, with resultant amygdala hyperfunction (fear reaction), decreased activity of the hippocampus (defective glucocorticoid-negative feedback, cognition), and the mesocorticolimbic dopaminergic system (dysthymia, novelty-seeking, addictive behaviours), hyperactivation of the HPA axis (hypercortisolism), suppression of reproductive, growth, thyroid and immune functions, and changes in pain perception.

Causes of Infertility – Methylation Problems

- Methylene tetrahydrofolate reductase (MTHFR) is a critical folate-metabolising enzyme which requires riboflavin as its co-factor.

- A common polymorphism (677C→T) in the MTHFR gene results in reduced MTHFR activity which leads to impaired folate metabolism and elevated homocysteine concentrations.

- Polymorphisms increase the risk of certain adverse pregnancy outcomes including neural tube defects, hypertensive disorders such as preeclampsia and gestational hypertension.

R. Reilly et. al. (2013) MTHFR 677TT genotype and disease risk: is there a modulating role for B-vitamins? Proceedings of the Nutrition Society, Page 1 of 10
Causes of Infertility – Excessive Oxidation

- In females – **excessive oxidation** has been linked to increase risk of miscarriage, early rupture of membranes and pre-eclampsia. The major sources may be **dietary**, environmental, caffeine, smoking, obesity and alcohol intake¹.

- In males – spermatozoa has a high content of the EFA **DHA**, so therefore is very susceptible to **lipid peroxidation**, which can impact on sperm count, morphology and mobility. ²

---


Causes of Infertility – Excessive Oxidation

• **Glutathione** is the primary anti-oxidant system utilised in spermatozoa.

• Supplementation with anti-oxidants in both males and females have seen mixed results, it is proposed that it is much better to decrease overall ROS load, and increase anti-oxidant load via dietary, lifestyle and environmental factors.


Investigations for Fertility

• Normally, fertility clients would have undergone a battery of diagnostic tests before they arrive with you, ruling out possible disease processes and structural abnormalities.

• Ask your clients to bring a copy of all tests to your clinic, so you don’t repeat anything that has already been done.

• If you choose to use testing, it will probably centre on some of the more nutritional, genomic and environmental factors, as they will have had plenty of hormonal tests at this stage.
## Nutritional Functional Investigations for Fertility

<table>
<thead>
<tr>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxic metals profile</td>
<td>Toxic metals profile</td>
</tr>
<tr>
<td>Homocystiene</td>
<td>Homocystiene</td>
</tr>
<tr>
<td>MTHFR and COMT genetic variations</td>
<td>MTHFR and COMT genetic variations</td>
</tr>
<tr>
<td>Immune profile- TH1/TH2 balance</td>
<td>DNA fragmentation index (oxidation)</td>
</tr>
<tr>
<td>Red blood cell minerals</td>
<td>Red blood cell minerals</td>
</tr>
<tr>
<td>Glutathione utilisation profiles</td>
<td>Glutathione utilisation profiles</td>
</tr>
<tr>
<td>Autoantibody investigations</td>
<td>Autoantibody investigations</td>
</tr>
<tr>
<td>AMH (normally already tested)</td>
<td>Serum or urine analysis of amino acids</td>
</tr>
<tr>
<td>Oxidative markers</td>
<td>Oxidative markers</td>
</tr>
</tbody>
</table>
AMH - A Marker of Ovarian Reserve?

• In women, AMH is produced by the granulosa cells (GC) of follicles.

• It is widely accepted that the reduction of AMH levels in serum is the first indication of a decline in the follicular reserve of the ovaries.

• AMH levels reflect with high accuracy the ovarian follicle reserve, and this has been demonstrated in numerous studies. Therefore, AMH evaluation has great clinical importance in predicting the success of IVF cycle.
The role of AMH in ovarian follicle development (red centre represents the oocyte, grey area the granulosa cell layer).
The Need for Pre-Conception Preparation

• Pre-conception care and acupuncture may be prudent to help increase the limited success rate of IVF- and also to hopefully save your clients the trauma and money if they fall pregnant naturally before hand.

• PCC is best done at least 3 months before planned conception but if a client is of an older age (past 38-40) do not hold off on any IVF cycles- as the older the age the chances of a life birth start to decrease rapidly.
Foresight PCC

• The following overview is taken from Foresight, the only UK charity whose primary role is to promote pre-conception care in the wider community.

• They promote a ten step program to be covered in PCC planning.

Website:

http://www.foresight-preconception.org.uk
The Foresight Overview

1. Optimise Nutrition.
2. Test for genitourinary infections.
3. Check mineral and heavy metal levels.
4. Eliminate voluntary social poisons.
5. Use natural family planning.
7. Identify allergens and intolerances.
8. Identify and rectify any dysbiosis issues.

• A Western dietary pattern high in **meat, pizza, and potatoes, and low in fruits**, was associated with a higher risk of a cleft palate.

• High intakes of **fish, garlic, nuts, vegetables, increased vitamin B12 and serum folate levels** decreases the risk of cleft lip or cleft palate risk compared with the Western diet.

• Iron and folic status are the most researched pre-natal nutritional deficiencies linked to poor birth outcomes.

• Before pregnancy, it is conducive to check ferritin levels and adjust the diet adequately to have an ample iron supply before conception, to maintain a healthy pregnancy.

• Folic acid should be supplemented at a minimum dose of **400mcg daily (800mcg in high risk and obese conditions)** as well as an increase in folate rich foods, to prevent the risk of neural tube defects.

• In any female with a MTHFR polymorphism, may have to take a methyl-folate instead.

• ‘The diet of well-nourished women in the preconception period and throughout most of pregnancy has a significant effect on birth weight, and proteins are the macronutrient that has the greatest influence’.

• Make sure protein intake is in between 0.8-1g per kg of body weight per day.

• Try to rely on vegetable proteins as much as possible, as well as fish, eggs, lean poultry and occasional lean red meat.
Optimise Nutrition - Omega-3 Fatty Acids

• Low DHA and PUFA levels have been associated with infertility both in males and females¹.

• A diet rich in un-oxidised PUFA’s such as fish, nuts and seeds and vegetables oils is of importance.

• Docosahexaenoic acid (DHA), accumulates in the brain during perinatal cortical expansion and maturation.²

• Low DHA levels have been linked with an increased risk of psychopathology in infants³.

Women with sufficient vitamin B6 had a higher adjusted hazard ratio of conception and a lower adjusted odds ratio of early pregnancy loss in conceptive than did women with vitamin B6 deficiency.

Poor vitamin B6 status appears to decrease the probability of conception and to contribute to the risk of early pregnancy loss.

Optimise Nutrition - Vitamin A

• Vitamin A is required for foetal tissue growth and maintenance as well as maternal metabolism; it plays an important role in cell differentiation therefore embryogenesis very early in pregnancy.

• Clinical and subclinical vitamin A deficiency is a public health concern in at least 75 countries worldwide, and contributes to impaired immune host response, maternal eye problems including xerophthalmia, night-blindness, as well as decreased haemoglobin levels and anaemia².

• On the other hand, **high amounts of supplemental Vitamin A are teratogenic** so food sources should be from the pro-vitamin A carotenoids

• A few studies are starting to show that pre-natal multi-vitamin supplementation is more beneficial than folic acid and iron alone for improving pre-natal and birth outcomes.

• This may be due to a reduction of serum oxidative markers.

• Prenatal and early postnatal zinc deficiency impairs learning and memory and these deficits persist into adulthood.

• Maternal zinc deficiency reduces NMDA receptor expression in neonatal rat brain, which persists into early adulthood.

• NMDA is the molecule that is responsible for creating plasticity changes in the brain, which in turn supports normal developmental learning.
Optimise Nutrition - Magnesium

• Magnesium plays a role in regulating body temperature, protein synthesis, and nerve and muscle function.

• In laboratory rats, magnesium deficiency was associated with higher systolic blood pressure and elevated plasma nitrite, suggesting that magnesium may play a role in controlling blood pressure.

• Magnesium supplementation during pregnancy has been associated with a reduced risk of foetal growth retardation, pre-eclampsia, and increased birth weight.

Low thyroid function during pregnancy can have devastating effects on infant development.

Various studies at regional centres have shown low thyroid function in women at the last trimester, due to low iodine intake.

Iodine levels should be evaluated before pregnancy (as well as thyroid hormones) to minimise risks.

Kung AW (2007) Iodine nutrition of pregnant and lactating women in Hong Kong, where intake is of borderline sufficiency, Public Health Nutr. 2007 Dec;10(12A):1600-1
• Selenium is an important co-factor for selenoproteins.

• Low sperm glutathione peroxidase activity is associated with reduced viability and motility in men. Mice lacking the selenoprotein Sel P gene exhibit male infertility.

• Developing mouse embryos that lack GPx4 die in mid gestation from developmental neurological defects.

Rising obesity rates around the world have had a profound impact on female reproductive health.

Women of reproductive age with high BMIs have a higher risk of ovulatory problems and tend to respond poorly to fertility treatment.

Obesity can aggravate symptoms of pelvic organ prolapse, stress urinary incontinence and increase the risk of endometrial polyps and symptomatic fibroids.

Weight reduction enhances reproductive outcomes.

Underweight and Fertility

• Obese and underweight women have an increased risk of miscarriage¹.

• Underweight woman are more likely to suffer from anovulatory cycles, reducing fertility.

• Avoid refined foods and carbohydrates (preferably a low GL or Mediterranean pattern of eating).
• Avoid additives, preservatives and chemicals.
• Increase fruit and vegetable intake (min 5 veg, 2 fruit).
• Avoiding social poisons such as caffeine, cigarette smoking, recreational drug intake and minimal pharmaceutical drug intake.
• Using organic where possible and affordable (reduce hormone disruptors).
• Increase intake of non-heme iron.
• Balancing nutritional needs and addressing underlying deficiencies (iron, zinc, Mg, folic acid, EFA and protein).
• Consider a pre-conception multi-vitamin, PUFA and folic acid supplementation.
Optimise Nutrition

You may also want to:

• Test for mineral needs or deficiencies to address specifically.
• Test for heavy metals and address if necessary.
• Test for polymorphisms of MTHFR.
• Test EFA serum levels and utilisation.
Women may wish to come off the OCP/coil (recommended) in a PCC workup. There are other methods of contraception available, which can also be used as ways of gathering information about the cycle. These include:

– Cervical mucous checking.
– Rhythm method (now made much easier with personal monitoring devices and ovulation monitors).
– Basal metabolic rate.
– Lunar cycles.

Cervical Mucous

• Observing cervical mucous can be a useful tool (when used in combination with other methods) for accessing fertility.

• As ovulation nears the mucous changes noticeably to be able to pre-empt ovulation.

• Low oestrogen results in sticky, tacky, opaque and scanty mucous with cellular matter in it.

• Higher oestrogen results in more profuse, wetter, clearer and thinner mucous.

• Just before ovulation the mucous becomes jelly like and resembles egg white and can be stretched between the fingers.

Cervical Mucous

• If the mucous does not change throughout the cycle—or if it has an offensive smell, burns, itches or causes irritation is probably an infection.

• This first must be treated before mucous charting can be used.

Basal Metabolic Rate

• Just before ovulation the BMR drops then rises 0.5 degree Celsius until menstruation due to the extra progesterone.

• Three over six rule- three days of a consecutively high temperature of a another 6 readings will give you the date of ovulation.

• First four days of cycle don’t count.

Rhythm Method

- Not very accurate, but depending on the length of a cycle, you can judge possible ovulation times.

- Personal machines with LH sticks have now made it much simpler to count!

- These personal machines measures the amount of LH in the urine- and can also store information on your previous cycles.

Rhythm Method

- In favourable circumstances, sperm can live for about 3 days. They can be found alive up to 6 days after sexual intercourse- but they are generally not viable at this time due to age and degeneration.

- An egg normally only survives up to 48 hours after ovulation.

- This means that avoiding intercourse 5 days prior to ovulation, and 3 days after reduces the chance of conception.
Other Lifestyle Factors

• Exercise:
  – Use of gentle exercise such as swimming, rebounding or yoga. It is best to pick something that can be taken in to pregnancy and does not cause excessive oxidation.
Other Lifestyle Factors

- Ascertain the presence, and rectify, any of the other possible mediators (covered in other lectures):
  - Sub clinical hypothryoidism
  - HPA axis dysfunction and stress
  - Dysbiosis and infections
  - Insulin resistance and metabolic syndrome
  - Inflammation and oxidation
  - Autoimmune conditions