Clinical Endocrinology: Safety & Efficacy of BHRT in a Clinical Setting

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Abstract

Dr. Henri Knafo is presently the Medical Director of ERFA Canada the only licensed provider of natural desiccated thyroid in Canada. He has given numerous conferences around the globe on anti-ageing. Dr Knafo was trained first as a Biologist in Montreal (Quebec) where he obtained his Master’s in Biomedical Research. He then got his MD at Semmelweis Medical School in Budapest, (Hungary) just before returning to Canada where he trained as a Neurosurgical resident for 5 years. His lecture will focus on clinical endocrinology with an emphasis on bio-identical hormones, safety, efficacy and using them in a clinical setting.
Disclaimer

- The information and reference materials contained herein are intended solely to provide background information.
- They were written for an audience of physicians (MD and NP) as participants of this conference.
- The speaker is in no way paid additional money by any pharmaceutical companies mentioned in this presentation.
- The speaker is working as a medical director for ERFA Canada 2012 Inc. but does not receive additional money or additional compensation for this presentation.
Introduction

Brief endocrinology review

Thyroid hormones
  Levothyroxine
  Desiccated Thyroid

Female hormones
  Estrogens
  Progesterone

Male hormone
  Testosterone

Adrenal hormones
  DHEA

Conclusion
Introduction

What will you learn in this presentation?

- Identify patients that need BHRT.
- Define a proper treatment protocol for these patients.
- Inform the patient about possible side effects of the medication.
- Know what to do if a side effect occurs.
Replacing hormones that are identical, on a molecular level, with endogenous hormones in our body.

Hormones come from plants, animals or are chemically synthesized.

Bioidentical hormones are medications

Like any medication they can have short term and long term side effects
Historical perspective

AD 1025  Chinese extracted sex hormones from human urine (ch'iu shih)

1930 James Collip developed a method to extract an orally-active estrogen from the urine of pregnant women (Emmenin)

1941 Premarin easily-manufactured conjugated equine estrogens – Not Bioidentical

1998 the FDA approved Prometrium an oral bioidentical progesterone

J.B Collip in his office at McGill University Ca. 1930
PHARMACOVIGILANCE

• Product monograph – Read it!
• Side effect reporting mechanism in the world
• Health Canada/Europeen adverse reaction database
• Pubmed
Brief Endocrinology review

- Consists of discrete individual glands that produce and secrete chemical messengers known as hormones.
- Hormones travel from endocrine organs to their targets via the blood.
- Target cells are cells that have receptors for specific hormones on them.
Brief Endocrinology review
The Six Major Anterior pituitary hormones are:

1. Thyroid Stimulating Hormone (TSH or thyrotropin)
2. Follicle Stimulating Hormone (FSH, a gonadotropin)
3. Luteinizing Hormone (LH, a gonadotropin)
4. Adrenocorticotropic Hormone (ACTH, or corticotropin)
5. Growth Hormone (GH)
6. Prolactin (PRL)
Thyroid gland
Greek "thyreoeides", meaning "shield-shaped"
Front of neck
A butterfly
Measuring approximately 4 cm
It is normally not, or barely palpable

Secretes hormones
bone growth, mental development,
stimulation of oxygen consumption of tissues,
transformations of fats and sugars

Secretes T3 and T4
Thyroid

**Primary hypothyroidism** - It comes from the gland
chronic iodine deficiency;
autoimmune thyroiditis (Hashimoto's thyroiditis)
infiltrative disease (sarcoidosis, amyloidosis, hemochromatosis ...)
enzymatic disorder of the thyroid (genetics)
Congenital thyroid dysgenesis

**Secondary hypothyroidism** comes from the brain
hypopituitarism
Hypothalamic lesion
TRH deficiency
HypoThyroid

- Frequency 3.6% of the population
  More common in women thin
- More common in the elderly -
  5.9% of women > 60 years
  2.4% of men > 60 years
- The most common cause worldwide - iodine deficiency
- Mortality unusual
Symptoms of Hypothyroidism

- Fatigue
- Weakness
- Weight gain or increased difficulty losing weight
- Coarse, dry hair
- Dry, rough pale skin
- Hair loss
- Cold intolerance (you can't tolerate cold temperatures)
- Muscle cramps and frequent muscle aches
- Constipation
- Depression
- Irritability
- Memory loss
- Abnormal menstrual cycles
- Decreased libido
HypoThyroidism

Indication of Hormone replacement

Hypothyroidism

Contraindication

Adrenocortical insufficiency
Thyrotoxicosis
Hypersensitivity
Heart disease (uncontrolled)
Protocole

Patients with thyrotoxicosis usually have a TSH value of <0.1 mU/L.
** Excess replacement does increase the risk of osteoporosis and arrhythmias, especially in elderly subjects.
† Immunoassays for thyroid function tests are subject to analytical interference due to heterophile antibodies, TSH isoforms, or preanalytic factors.
Hypothyroidism

Standard Treatment

Levothyroxine
ELTROXIN
EUTHYROX
SYNTHROID

T3
CYTOMEL TAB

Desiccated Thyroid
THYROID

Narrow therapeutic window
Desiccated Thyroid

Porcine thyroid glands, dried and powdered for therapeutic use

Developed in the late 19th century

Contains a mix of T4 (thyroxine), T3 (triiodothyronine) in the proportions usually present in pig thyroids (approximately 80% T4 and 20% T3).

Use to have inconsistent dosages. There is no more than 10% variation from batch to batch nowadays.

Did you feel a positive difference when switching from Leothyroxine to Thyroid?

Available in 30mg, 60mg, 125mg
Safety

Health Canada adverse reaction report

Very few side effects since 20 years

Well tolerated by most patients

No recalls since 30 years

Data confirms it’s a safe medication
Thyroid

What is the best treatment?

Compare the effect of combination therapy with thyroxine (T4) and T3 versus T4 monotherapy
Double-blind, randomised cross-over.
Tests for quality of life (QOL) and depression
59 patients (55 women); median age 46 years.

49% percent preferred the combination and 15% monotherapy

treatment groups, T4/T3 combination therapy T3 (20 µg) given once daily seemed superior to T4 monotherapy

Desiccated thyroid contains T3 and T4!
Hypothyroidism

2009 study suggests that it's possible that a subgroup of patients with a polymorphism in the type 2 deiodinase might benefit from combined therapy.

15% of patients do not respond to levothyroxine

Only randomized studies comparing desiccated to levothyroxine
female hormones

Estrogens

Ovaries

• **Secrete** the female steroid sex hormones estrogen and progesterone and the peptide hormone **inhibin**.

• Estrogen is important for **egg development** inside the ovarian follicles.

• **Progesterone is important after ovulation** for maintaining the integrity of the uterine lining and during pregnancy.

• **Inhibin regulates the secretion of FSH** from the anterior pituitary in a negative feedback mechanism.
estrogens

3 types of estrogens:

E1: Estrone  
E2: Estradiol  
E3: Estriol

Produced during menopause  
Predominant in nonpregnant women  
Primary estrogen of pregnancy

- From menarche to menopause the primary estrogen is 17β-estradiol.
- In postmenopausal women more Estrone is present than Estradiol.
- Estrone is weaker than estradiol.
estrogens

• Structural
• promote formation of female secondary sex characteristics
• accelerate metabolism
• reduce muscle mass
• increase fat stores
• stimulate endometrial growth
• increase uterine growth
• increase vaginal lubrication
• thicken the vaginal wall
• maintenance of vessel and skin
• reduce bone resorption, increase bone formation
• morphic change (endomorphic -> mesomorphic -> ectomorphic)
• protein synthesis
• increase hepatic production of binding proteins
• coagulation
• increase circulating level of factors 2, 7, 9, 10, plasminogen
• decrease antithrombin III
• increase platelet adhesiveness

• Lipid
• increase HDL, triglyceride
• decrease LDL, fat deposition
• Fluid balance
• salt (sodium) and water retention
• increase cortisol, SHBG
• Gastrointestinal tract
• reduce bowel motility
• increase cholesterol in bile
• Melanin
• increase pheomelanin, reduce eumelanin
• Cancer
• support hormone-sensitive breast cancers
• Lung function
• promotes lung function by supporting alveoli (in rodents but probably in humans)
Menopause

Symptoms

Vascular instability

• Hot flashes or hot flushes, including night sweats and in a few people cold flashes, Atherosclerosis, Migraine, Rapid heart beat

Urogenital atrophy

• Thinning of the membranes of the vulva, the vagina, the cervix, Itching, Dryness, Bleeding, Watery discharge, Urinary frequency, Urinary incontinence, Urinary urgency, Increased susceptibility to inflammation and infection for example vaginal candidiasis, and urinary tract infections
MENOPAUSE
Symptoms

Skeletal
Back pain, Joint pain, Muscle pain, Osteopenia and the risk of osteoporosis gradually developing over time

Skin, soft tissue
Breast atrophy, breast tenderness +/- swelling, Decreased elasticity of the skin, Formication (itching, tingling, burning, pins and needles, or sensation of ants crawling on or under the skin), Skin thinning and becoming drier

Psychological
Depression and/or anxiety, Fatigue, Irritability, Memory loss, and problems with concentration, Mood disturbance, Sleep disturbances, poor quality sleep, light sleep, insomnia

Sexual
Dyspareunia or painful intercourse, Decreased libido, Problems reaching orgasm, Vaginal dryness and vaginal atrophy
Estradiol replacement therapy

Levels of Estradiol with age

20-29
30-39
40-49
After 50

pg/ml

0
75
150
225
300
Frequency of symptoms

Table-1: Clinical presentation of menopause.

Vasomotor symptoms 85% of peri- and 66% of postmenopausal women
Uro-Genital symptoms (atrophic vaginitis) 50-70% of postmenopausal women
Psychological disturbance 10%
Osteoporosis 30%
Gynaecological malignancy 10%
Post-menopausal bleeding 3.3%
Back pain 1%
BHRT Treatment

**Indication:**

Symptoms of menopause

**Contraindication:**

- Allergy to the drug
- Endometrial cancer (estrogen dependent) or hyperplasia
- Breast Cancer or history of breast cancer
- Liver disease and cancer
- Abnormal genital bleeding (undiagnosed)
- History of arterial thromboembolic disease
- DVT
- Loss of vision (if due to vascular disease)
Treatment

Availability of Estradiol:

Oral: Estrace (Canada), Zumenon (UK). Be careful of oestradiol valerate (not bioidentical)

Transdermal: Climara (25 to 100 microg/day)
- ESTRADERM (UK)
- ESTRADOT
- ESTROGEL
- SANDOZ ESTRADIOL DERM 50, 75 and 100

Vaginal ring: Estring (UK, Canada)
Tablet: Vagifem (UK, Canada)

Oral is currently the most commonly utilized route of administration in the United States.

Transdermal drug delivery may mitigate some of these effects by avoiding gut and hepatic first-pass metabolism.
Treatment
Treatment

The ring should be pressed into an oval and inserted into the upper third of the vaginal vault.
Oral vs transdermal:
**Pharmacokinetic differences**

- Oral estrogens must be administered in relatively high doses
- Pass the gut and hepatic first pass
- Variations in the metabolism of oral estrogens
- Elevated TGs or hypertension

<table>
<thead>
<tr>
<th>ORAL</th>
<th>TRANSDERMAL PATCH</th>
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</thead>
<tbody>
<tr>
<td>Higher risk of DVT</td>
<td>Lower risk of DVT</td>
</tr>
<tr>
<td>Increase the TG levels</td>
<td>No increase in TG</td>
</tr>
<tr>
<td></td>
<td>Better for libido</td>
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<td></td>
<td>Fewer systemic adverse effects (vaginal bleeding, breast tenderness)</td>
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Orally administered estradiol is rapidly metabolized by the liver to estrone and its conjugates.

Transdermal administration produces therapeutic plasma levels of estradiol with lower circulating levels of estrone.
Efficacy

**Vasomotor symptoms**

**Study in Sweden**

459 early postmenopausal non-hysterectomized women

primary endpoint was change in frequency and severity of moderate to severe hot flushes at 12 weeks

estradiol valerate (E2V) and medroxyprogesterone acetate (MPA)

The frequency of hot flushes was reduced by \( \geq 70\% \) after one month

**Study in UK**

577 postmenopausal women were enrolled

0.5 mg 17beta-estradiol + 0.1 mg NETA

Low-dose transdermal estradiol gel 0.1%

**Significant decrease in the frequency and severity of hot flushes was achieved by week 3**

Similar results with gel

2 mg estriol in 168 postmenopausal patients was markedly effective in 22.6% of cases, effective in 45.2%, fairly effective in 14.3%, and ineffective in 17.9% of cases

Estriol not accepted by Health Canada but estradiol has a similar effectiveness profile
**Atrophic vaginitis**

**Efficacy**

Systemic (oral) vs local (cream, tablet, ring)

Local seams to have similar efficacy then systemic

230 patients were randomized to receive either placebo, 17β-estradiol 10 µg or Vagifem® (25 µg estradiol)

Patients inserted one tablet intravaginally each day for 14 days, then one tablet twice weekly for the remaining 10 weeks.

Less dryness, soreness and irritation then placebo

Cream, tablets, ring have similar efficacy in randomized studies
Efficacy

Psychological disturbance

Schizophrenia

BHRT Works on younger menopausal women
Efficacy

Psychological disturbance

Schizophrenia

BHRT Works on younger menopausal women
Efficacy

Psychological disturbance

SCHIZOPHRENIA

DEPRESSION

PERIMENOPAUSAL

AFFECTIVE DISORDERS

ALZHEIMERS
Efficacy

Psychological disturbance

ovarian hormones modulate serotonin and noradrenaline neurotransmission

2 double-blind, placebo-controlled trials with similar results

- 34 perimenopausal women with depression
  - After 3 weeks of estradiol, depression rating scale scores were significantly decreased

1 randomized study did not get those results

- Younger perimenopausal, but not older postmenopausal, depressed women respond to short-term estradiol therapy

87 patients all randomized => NO DIFFERENCE WITH PLACEBO. They took women 5-10 years post natural menopause

BHRT Works on younger menopausal women

effects of low-dose 17beta-estradiol and norethisterone (hormone therapy [HT]) versus placebo in women with Alzheimer Disease (AD)

HT may reduce depressive mood and give less cognitive decline.
The North American Menopause Society position is to treat young menopausal women.

**BHRT works for osteoporosis**

*Women’s Health Initiative showed that postmenopausal hormone replacement therapy (HRT) prevents fractures*

25% to 29% lower risk of osteoporotic fracture (P < 0.0001) in 1 year

Women who had stopped HRT more than 5 years had similar fracture then non users
Efficacy

Osteoporosis

HIP
ARM
VERTEBRAL
FRACTURE
WERE
LOWER
WITH HRT
Estrogen is an effective treatment for Menopause

- Start treatment early for better results
- Good for vasomotor symptoms
- Good for treating atrophic vaginitis
- Good to prevent osteoporosis

- Hormone replacement therapy reduced total mortality in trials with mean age of participants under 60 years.
- No change in mortality was seen in trials with mean age over 60 years.
Breast cancer

WHI study (2002):
Continuous combined HRT was associated with an increased breast cancer risk if used for four years or more.
However this increased risk dissipates quickly once use is discontinued.

Increased risk of breast cancer that was 1.29 times those who never used estrogen.
Synthetic progestin was used in combination with estrogen 1.69 times.

They did not use Bioidentical hormones in WHI
conjugated equine estrogens vs Bioidentical estradiol (premarin)
SAFETY

Bioidentical estradiol (premarin) vs Conjugated equine estrogens

Estradiol

Estrone sulfate

Mr Good Guy

Mr Bad Guy
Safety

Breast cancer

Institut National de la Santé et de la Recherche Médicale
Compared the association between different HRTs and breast cancer risk

Results from the E3N cohort study

2,354 cases of invasive breast cancer occurred among 80,377 postmenopausal women
Relative risk was

1.00 (0.83–1.22) for estrogen–progesterone
1.16 (0.94–1.43) for estrogen–dydrogesterone
1.69 (1.50–1.91) for estrogen combined with other progestagens.

No risk of breast cancer when Bioidentical progesterone was used.
Safety

Breast cancer

Finnish study
Cohort included 110,984 postmenopausal women aged over 50 (from national cancer registry) who had used estrogen alone for more than six months.

Women who took estradiol orally or transdermally (with no progesterone) for less than five years were no more likely to get breast cancer than women of a similar age in the general Finnish population.

Longer use of systemic therapy was associated with a significant rise in breast cancer incidence (ratio 1.44 (1.29 to 1.59)).

Link between breast cancer and long term treatment with oral or transdermal estradiol in postmenopausal Finnish women

Use of estrogen alone for less then 5 years to lower risk of breast cancer
Safety

Coronary artery disease, Stroke, DVT

1990’s it was though that estrogen alone can lower the risk of cardiovascular diseases.

Incidence of myocardial infarction (MI) is much more common in men than in women before age 50.

WHI enrolled 161,809 postmenopausal women between 1993 and 1998 for this series of trials. Increased risk of CHD (acute MI), silent MI, or CHD death, with a hazard ratio (HR) of 1.29 (CI, 1.02-1.63).

When the data from this study were analyzed by age group, the HR for CHD with estrogen use in women aged 50 to 59 years was 0.63 (CI, 0.36-1.08)
women aged 60 to 69 years, 0.94 (CI, 0.71-1.24)
women aged 70 to 79 years, 1.11 (CI, 0.82-1.52)

Age 50 to 59 years reduces their risk of CHD by about 40%
SAFETY

Transdermal estradiol

In contrast to oral estrogen, which causes a 3- to 4-fold increased risk of venous thromboembolism (VTE), transdermal estrogen does not appear to increase the risk of VTE.
Progesterone is produced in the ovaries (corpus luteum), the adrenals and placenta.

- Stored in adipose (fat) tissue.
- Placenta produces about 250 mg progesterone per day.
- Progesterone in milk.
- Synthesized from Cholesterol.
Progesterone

Reproductive system

• "Hormone of pregnancy"
• Many roles relating to the development of the fetus
• Converts the endometrium to secretory stage to prepare the uterus for implantation
• Affects the vaginal epithelium and cervical mucus
• If pregnancy does not occur, progesterone levels will decrease, leading to menstruation
• Normal menstrual bleeding is progesterone withdrawal bleeding.
• Progesterone decreases contractility of the uterine smooth muscle.
• Inhibits lactation during pregnancy.
• The fall in progesterone levels following delivery is one of the triggers for milk production.
• Increases core temperature during ovulation.
• Reduces spasm and relaxes smooth muscle.
• Acts as an antiinflammatory agent and regulates the immune response.
• Reduces gall-bladder activity
progesterone

Indication:

In vitro fertilization
Hormone replacement therapy
progesterone

Contraindicated:

- Undiagnosed vaginal bleeding,
- Liver dysfunction or disease,
- Known or suspected malignancy of the breast or genital organs,
- Known or suspected progesterone-dependent neoplasia,
- Known sensitivity to progesterone
- Missed abortion,
- Thrombophlebitis, thromboembolic disorders, cerebral apoplexy or patients with a history of these conditions,
- Acute porphyria
progesterone

Route of administration

Oral: PROMETRIUM (micronized progesterone)
Gel: Crinone (8% gel)
Intra-muscular: PROGESTERONE INJ 50MG/ML

Micronized: decreased destruction in the gastrointestinal tract, a longer half-life, and enhanced bioavailability

200 mg daily for the last 14 days of estrogen treatment per cycle
(i.e. from day 8 to day 21 for a 28-day cycle, and from day 12 to day 25 for a 30-day cycle)

1.125 g CRINONE 8% Vaginal Gel
From the day of embryo transfer
Efficacy of progesterone

In HRT for menopause: used to oppose the effects of estrogen
Endometrial protection: preventing uterine hyperplasia and malignancy in response to estrogens
Neuroprotective and neurotrophic effects
Efficacy of progesterone

Blood vessels

Low dose: No vascular toxicity
MPA: Vascular toxicity

Mammary glands

Low dose: No mitotic effect
High dose: Stimulate the proliferation of breast epithelial cells

Bones

Promote bone formation

Reduce the risk of endometrial hyperplasia
Efficacy of progesterone

PEPI Trial: no significant bone-protective effect (both with bioidentical and MPA)

Postmenopausal Estrogen/Progestin Interventions (PEPI) trial

875 healthy postmenopausal women aged 45 to 64 years at seven clinical centers in the U.S.

(1). Placebo

(2). 0.625 mg of estrogen per day

(3) 0.625 mg of estrogen per day plus 10 mg of a synthetic progestin taken daily for 12 days,

(4) 0.625 mg of estrogen daily plus 2.5 mg of synthetic progestin taken daily

(5) 0.625 mg of estrogen daily plus 200 mg of a natural (micronized) progesterone (MP) taken daily for 12 days per month.
Efficacy of progesterone

Results

70 and 90 percent of the increase in BMD occurred during the first year of the study.

No difference between the groups with or without progesterone (bioidentical or not).

Does adding progesterone really helps decrease fracture?

Data shows that estrogen is more important.
Safety progesterone

The Heart and Estrogen/Progestin Replacement Study (HERS) Trial

compared the effects of conjugated equine estrogens (CEE) plus medroxyprogesterone acetate (MPA) treatment with placebo increase in coronary heart disease during the first year of hormone treatment and no overall cardiovascular benefit with longer follow-up.

MPA = Experimental carcinogen, neoplastigen, tumorigen, teratogen.

Progesterone = Limited evidence that this may be a possible carcinogen.
Safety Progesterone

French cohort (E3N cohort)
54,548 postmenopausal women

No risk of having Breast cancer 8 years after treatment when Bioidentical progesterone was used instead of MPA

Progesterone has a safe pharmaceutical profile
Progestosterone is safe - Pregnant women can prove it!
Testosterone

Testosterone is a hormone produced primarily in the testes. It helps maintain:
• Bone density
• Fat distribution
• Muscle strength and mass
• Red blood cell production
• Sex drive
• Sperm production

Testosterone level gradually declines with age after age 30.
testosterone

Symptoms of testosterone deficiency

Changes in sexual function.
- reduced sexual desire
- fewer spontaneous erections
- infertility.

Changes in sleep patterns.
- insomnia
- other sleep disturbances.

Emotional changes.
- decrease in motivation or self-confidence
- feel sad or depressed
- trouble concentrating

Physical changes.
- increased body fat
- reduced muscle bulk and strength
- decreased bone density.
- Gynecomastia
- hair loss are possible
- hot flashes
- less energy
Testosterone replacement therapy

Age-related Decline In Testosterone Levels

- Free Test (nmol/l)
  - 0.775
  - 0.5
  - 0.375
  - 0.25

- SHBG ($10^{-8}$ nmol/l)
  - 8
  - 7
  - 6

- Total Test (nmol/l)
  - 25
  - 20
  - 15
  - 10

Years: 18-29, 30-49, 50-59, 60-69, 70-79, 80-89, 90-100, >100
testosterone

Indication:

• Testosterone replacement therapy

Contraindication:

• Hypersensitivity
• Carcinoma of the prostate or breast
• Women
• Diabetic taking insulin
• Patient on corticosteroid
• Anticoagulant
• Patient on cyclosporine

Available forms

Injectable: testosterone cypionate or testosterone enanthate in oil = NOT BIOIDENTICAL

ORAL: ANDRIOL (TESTOSTERONE UNDECANOATE) = NOT BIOIDENTICAL

Transdermal Patch: ANDRODERM
applied nightly (10:00 PM.) and worn for 24 hours, providing a total dose of 5 mg of testosterone/day.

Gel: ANDROGEL
TESTIM 1%
Efficacy testosterone

TIMES2 Study

220 hypogonadal men with type 2 diabetes
Randomized, double-blind, placebo-controlled study.
Followed them for 1 year
glycemic control was significantly better in the TRT group
Improvements in total and LDL cholesterol, sexual health

Other studies

Beneficial effect of testosterone replacement therapy on Bone Mass Density with improvements over several years.

No convincing evidence of an adverse effect of testosterone replacement therapy on coronary heart disease

Testosterone has a well known efficacy - Just look at body builders
Safety

Adverse events associated with testosterone administration.

209 men (mean age, 74 years)
high prevalence of hypertension, diabetes, hyperlipidemia, and obesity among the participants
testosterone group had higher rates of cardiac, respiratory, and dermatologic events than did the placebo group
testosterone gel was associated with an increased risk of cardiovascular adverse events (23 vs 5)
improvements in leg-press and chest-press strength and in stair climbing while carrying a load

Clinical review: Adverse effects of testosterone therapy in adult men: a systematic review and meta-analysis.
51 included studies

There was no significant effect on mortality, prostate, or cardiovascular outcomes

Health Canada reported 1 case of Prostate Cancer since 2001
DHEA

Major secretory steroidal product of the adrenal glands
Produced by gonads and brain
most abundant circulating steroid in humans

Measurement:
Diagnosis of adrenal cancer/hyperplasia and polycystic ovary syndrome
DHEA

Used for:

- Depression
  - Anti-depressant effect
  - Diminish cortisol level
- Alzheimer disease
  - Not effective
- Improve memory
  - pre-hippocampal memory processing
  - prefrontal dependent cognitive abilities during stress
- Physical performance
  - muscle-building
  - no effect on lean body mass, strength, or testosterone levels
- Cardiovascular disease and risk of death

2006 study found no correlation between DHEA levels and risk of cardiovascular disease or death in men.
DHEA

Cancer
- anti-proliferative effect
- increased risk of developing breast cancer

Diabetes and carotid atherosclerosis
- inverse relationship between serum DHEA and carotid atherosclerosis

Erectile dysfunction
- Some studies demonstrate that it could be useful

Men over 65
- increase in testosterone
- decrease LDL

Longevity
- 940 men and women ranging from age 21 to 88
- following them from 1978 until 2005
- higher DHEA-s levels are a "strong predictor" of longevity in men NOT in women

Improving the function of the immune system
- Can help patient with Lupus

SOLD as supplement in the USA
Canada: Not available although listed as a New Drug
DHEA Safety

- cardiovascular effects such as heart palpitations
- may worsen or increase the risk of cancer (breast)
- estrogen-like properties (can worsen endometriosis, uterine fibroids)
- testosterone-like properties (worsen PCOS)
- It can decrease HDL
- Liver problem
- Report of mania in a few patients with depression or bipolar disorder
Drug interaction - DHEA

Hormone therapy for breast cancer, such as:

- Anastrozole (Arimidex®)
- Exemestane (Aromasin®)
- Fulvestrant (Faslodex®)
- Letrozole (Femara®)
- Tamoxifen (Nolvadex®)

Various other medications, including (but not limited to):

- Alprazolam (Xanax®)
- Amitriptyline (Elavil®)
- Amiodarone (Pacerone®, Cordarone®)
- Buspirone (BuSpar®)
- Citalopram (Celexa®)
- Felodipine (Plendil®)
- Fexofenadine (Allegra®)
- Itraconazole (Sporanox®)
- Ketoconazole (Nizoral®)
- Lansoprazole (Prevacid®)
- Losartan (Cozaar®)
- Lovastatin (Mevacor®)
- Midazolam (Versed®)
- Ondansetron (Zofran®, Zuplenz™)
- Prednisone (Deltasone®)
- Sertraline (Zoloft®)
- Sibutramine (Meridia®)
- Sildenafil (Viagra®, Revatio®)
- Simvastatin (Zocor®)
- Triazolam (Halcion®)

Verapamil (Calan®, Calan SR®, Covera-HS®, Isoptin SR®, Verelan®, Verelan PM®).
Thank YOU