Maintaining Sexual Function in Later Life

Anti Ageing Conference London

September 10 -11th 2010

Dr Michael Perring
mikeperring@optimalhealth.org.uk

Maintaining Sexual Function in Later Life

There has been a revolution in our means to assist sexual function in the past 20 years.

Men have been particularly helped with regard to erectile function; women most notably with HRT.

In men and women many other factors assist continuing sexual activity eg Psychological/physical health and societal factors.

Maintaining Sexual Function in Later Life

What are the aids that enable men to maintain better sexual function?

PDE5 Inhibitors, I/c agents

Pharmaceutical Aids to Arousal

Sildenafil Citrate (Viagra).

- **Mode of Action**: A phosphodiesterase (PDE5) inhibitor. Its action releases nitric oxide (NO), relaxing endothelial smooth muscle in the corpora cavernosa to fill sinusoidal spaces and give an erection.
- Produces erection with direct stimulation to penis within 60 minutes: duration 12+ hours.

- **Dose**: 25 -100mg, (75% men respond to 50mg dose)
- **Reduced effectiveness**: anxiety, > libido/desire, and >absorption

Pharmaceutical Aids to Arousal

Sildenafil Citrate (Viagra).

Side-effects:

Vaso-congestion - mild and dose-related

Headaches (16%), GI tract (7%), nasal congestion (4%), and visual disturbances (3%).

Contra-indications:

Recent myocardial infarction, concurrent use of nitrates.

CV risk is negligible and sildenafil is compatible with drugs for hypertension.

Chetlin 1999

Pharmaceutical Aids to Arousal

Sildenafil Citrate (Viagra).

- Reported to have 80% efficacy in organic and psychological forms of ED

  Levine 1996

- In an older population with arteriosclerosis, hypogonadism, drug interactions, hypertension, and radical prostatectomy overall success rate about 50%

  Eidd 2000

Pharmaceutical Aids to Arousal

Tadalafil (Cialis)

Mode of action: PDE inhibitor.

- Compared to Sildenafil has slower onset (60+ mins).
- ½ life of about 18 hours, and is well-tolerated with similar side-effect profile.
- Efficacy: 80%?
- Dose: 10-20mg

Contra-indications: CVD (recent MI), unstable angina or angina on SI, arrhythmias and uncontrolled hypertension.

Pharmaceutical Aids to Arousal

Long term use of PDE5 Inhibitors:

- 60% of men using a PDE5 inhibitor were still using it 2 years later.
- 40% required an increased dose to maintain therapeutic efficacy

El-Galley 2001

Pharmaceutical Aids to Arousal

Alprostadyl (Prostaglandin E1) as injection: Caverject

- **Mode of action**: Relaxes penile vasculature, increasing blood flow into the corpora cavernosa to give an erection.
- Produces erection without direct stimulation to penis within 5 minutes lasting an hour.
- **Dose**: 5-20micrograms injected into the corpora cavernosa.
- **Side-effects**: Bruising; rarely priapism.

Non-Pharmaceutical Aids to Arousal

Penile ring:

The Ring converts grade 2 erection to grade 3-4 (with erections graded on a scale of 1-5)

Grade 4 erection is good enough for penetration

- Kegel's exercises: strengthen pelvic floor muscles to aid erection/penetration
- Breathing exercises: aids relaxation
- Sensate Focus training as a couple

Erectile Dysfunction (ED)

Definition:

- A persistent inability to attain and maintain an adequate erection to permit satisfactory sexual performance NIHCS 1992

Prevalence:

In a randomised sample of 1290 men:

- Total ED increased from 5-15% between the ages of 40 and 70.
- Some degree of impairment occurred in 52%
- In DM prevalence 15% at 30, < 55% aged 60

MMAS, Feldman 1994

Erectile Dysfunction (ED)

Pathogenesis:

- Physical factors primary cause in 75% of cases. (heart disease, hypertension, DM, and medication)
- Psychological factors predominate in 25% (anger, depression and control issues)
- A psychological reaction of anxiety and avoidant behaviour is a common reaction to established ED
- Life-style factors (stress, cigarette smoking) also correlate with ED

Feldman 1994

NB Most men over 60 will obtain better erections, quality of orgasm and enhanced sexual experience from the use of PDE5 inhibitors.

PDE5 Inhibitors plus Testosterone as the Optimal Aid for Arousal

In hypogonadal states where there is also erectile difficulty the best treatment is a combination of Testosterone with a PDE5 inhibitor (eg Sildenafil, Vardenafil, Tadalafil) or prostaglandin.

Is there still a place for traditional remedies: Yohimbine, Ginseng, Tribulis terrestris, Arginine, etc?

Androgens and Sexual Function in hypogonadal men

Androgens regulate sexual function with central and peripheral effects:

Centrally:

- < libido (interest and motivation)

Alexander 1999

Peripherally:

- Activates nitric oxide synthase which regulates activity in cavernosal smooth muscle to promote erection

Lugg 1996 Shabsigh 2004

Androgens: Other Actions

T has systemic actions other than on sexual function in older men:

- Maintain muscle strength and mass Melton 2000
- Reduce adipose tissue Wittert 2003
- Maintain Bone Density Tenover 1998
- Act on neurones and neuro-transmitters with effects on verbal fluency, memory and energy Alexander 1999

The above benefits to health and QOL, which are unrelated to sexual function directly, none the less benefit it indirectly.

Partial Androgen Depletion:

Andropause/male menopause

- S/S may be variable, gradual in onset, and subtle in clinical presentation. Gooren 1996
- ↓ Lean body mass, loss of muscle volume/strength
- ↑ Visceral fat
- ↓ Bone mineral density (osteopenia/osteoporosis)
- Fatigue, depression and irritability; ↓ mental fluency
- ↓ Libido and strength of erection (also ↓ spontaneous erections and sexual fantasies)
- ↓ Body hair and skin tone/thickness.

Morales 2000

General Health Evaluation:

Sexual activity is a function of health as a whole, including physical and emotional health.

Prior to assessing for HRT evaluate other pathology.

eg: CVD, DM and Cancer: Testosterone impinges on the progression of these conditions.

Actions of Androgens in Clinical Disease:

Ischaemic Heart Disease (IHD)

- T i/v increases coronary artery flow and decreases ischaemic pain
  Yue,1993;Webb,1999
- T reduces post-exercise ST segment depression in angina patients Jaffe, 1977
- T given for three months to men with chronic stable angina significantly improved tolerance and angina threshold English, 2000

Actions of Androgens in Clinical Disease:

Diabetes

- T levels are lower in patients with NIDDM compared to controls. Stellato 2000
- Low total and free T are associated with increased risk of type 2 diabetes. Stellato 2000
- Free T inversely related to glucose and insulin sensitivity. Haffner 1996
- Obesity associated with decreased T; T given to obese men increases insulin sensitivity

Endogenous testosterone and mortality:

In a prospective study of men aged 40-79 low testosterone levels were shown to be associated with a reduced life expectancy and an increased risk cardiovascular disease.

Khaw 2007

It is suggested routine testosterone levels be measured routinely from the age of 45 when men present at clinic.

Hormone Therapy: Assessment

Blood tests:

- Hormones: Total testosterone
- Sex Hormone Binding Globulin (SHBG)
- FTI
- Dehydrotestosterone (DHT)
- Dihydroepiandrosterone (DHEA)
- Oestradiol (E2)
- Luteinising Hormone (LH)
- Follicle stimulating Hormone (FSH)
- Prolactin.

Hormone Therapy:

Assessment

Other Blood Tests: Full Blood Count (FBC) and Liver Function Tests (LFTs)

- Bone Density: Dexascan
- Assess Prostate Function: ? Family History, current urinary symptoms, DRE, prostate specific antigen (PSA)
- If in doubt do rectal u/s.

HT Assessment:

Some Drugs can interfere with T metabolism:

- Alcohol: Promotes T conversion to E2; damages Leydig cells (sperm production)
- Aminoglutethamide, Ketoconazole: inhibit steroidogenesis and reduce T levels.
- Cimetidine,spironolactone, cyproterone acetate: androgen receptor antagonists
- Saw Palmetto, finasteride: 5-alpha-reductase inhibitors inhibit DHT production (decrease libido and produce ED).

HT Assessment:

Drugs that interfere with SHBG:

- Barbiturates, anticonvulsants: Hepatic enzyme induction increases SHBG reducing urinary clearance of T and FT, and producing symptoms of andropause.

- Danazol lowers hepatic synthesis of SHBG and displaces T from binding sites on SHBG. Produces increased FT levels and counters andropause symptoms.

Curruthers 2000

Treating with Testosterone

- Orally: Testosterone undecanoate (Restandol): 80mg twice daily; Natural testosterone 100mg/d
- Transdermal Patch: Testosterone (Andropatch) 5mg/d
- I/m testosterone as propionate 30mg, phenylpropionate 60mg, isocaproate 60mg, decanoate 100mg (Sustanon): 250mg every two/three weeks
- I/m testosterone undecanoate (Nebido)1000mg every 3 months
- Cream/gel: Testosterone (Androgel); DHT (Andractim)
- Implant: Testosterone 600mg every 3 months.

Testosterone Therapy:

Review of benefits from T therapy

Meta-analysis showed testosterone administration is associated with greater improvement in sexual function compared to placebo treatment in men with sexual dysfunction and low testosterone levels.

Jain 2000

Testosterone may also favorably affect partner interactions and intimacy due to an overall increase in sexual desire and sense of well-being, independent of the change in erectile function.

Bhasin 2001

The Oestrogen Family

derived as a hormonal cascade from cholesterol to pregnenolone, DHEA, progesterone, E2 and testosterone.

Estradiol E2 (7%) Derived ovarian oestrogen, the first route of admin increases estrone and 16-alpha-hydroxysterone production

Estrone E1 (3%) After menopause is derived from adrenal and fat tissue, metabolites are 2-hydroxyestrone, 4-hydroxyestrone

and 16-alpha-hydroxyestrone

Low 2:16 ratio relates to Br cancer risk. Phytoestrogens convert 16 to 2-hydroxy estrone

Estriol E3 (90%) weakest action, occupying E-receptor sites has moderating action,

effective for vaginal dryness

Oestrogen Depletion

Begins at the perimenopause (35+) and declines rapidly at the menopause (50 years)

Symptoms:

Hot flashes, night sweats, disturbed sleep, fatigue, flatness of affect and anxiety.

Signs:

Physical changes: urinary and vaginal tract atrophy with loss of lubrication and soreness on SI

Cognitive changes: memory, concentration, learning capacity

Metabolic effects: altered lipid metabolism

Non systemic HRT management of menopause in women

Symptoms:

- Vaginal and introital dryness, irritation and dysparunia
- Urinary incontinence

Signs

- Atrophy, inflammation
- Poor pelvic muscle tone

Treatment:

- E2 or Estriol as cream, pessary or tablet
- Kegel's exercises
- Treatment of thrush if necessary

Hormone Therapy (HRT) for Women
Risks re-evaluated

After 5 years of combined HRT (Oestrogen and progestogen) for every 1000 women their will be:

- Deep Vein Thrombosis: 4 extra cases in women over 50
- Ovarian cancer: 1 extra case for every 2500 women
- Strokes: 1 extra case aged 50-59 years
  4 extra cases for women 60+ years
- Breast cancer: 2-6 extra cases

Wisdom; Women's Health Initiative; The Million Women Study, Oxford Uni

Hormone Therapy for Women In Summary

- We think HT safer than we did – the number of women taking HT remains lower than before the WHI report
- It's better to start HT early – at the beginning of the menopause for protection against CVD or osteoporosis, as well as for treatment of acute menopausal symptoms such as hot flushes and night sweats
- Some women want to continue HT to age 60+ because of benefits to well-being, libido and sexual function
- They have a choice of replacement therapy with conventional or bio-identical hormones systemically, or topical treatment.

Hormone Therapy for Women

Androgens

Rationale for Treatment

- Pre-menopausal women produce 300 µg/day of testosterone
  - 50% from the ovaries
  - 50% from the adrenal gland
- Post-menopausal women produce about 150 µg/day from the adrenal gland.

Despite treatment with E2 many postmenopausal women continue to have libido, frequency of SI and sexual satisfaction.

Hormone Therapy for Women
Androgens

- 150-300 µg/day of transdermal testosterone was given to a group of 65 oophorectomised women aged 31-56 years with impaired sexual function.

- The women reported a dose-related increase in sexual thoughts, desires and activities. At the higher dose there was also improvement in mood and well-being

Shifren 2000

Hormone Therapy for Women
Dehydroepiandrosterone (DHEA)

Hormone replacement?

- Normal Range 0.95 -11.6 mmol/L (women)
  2.20 -15.2mmol/L (men)

- Levels are reduced 50% between age 25 and 55

HRT Treatment
Dehydroepiandrosterone (DHEA)

Replacement doses with DHEA 50mg orally in a double-blind cross-over study of a population aged 40-70 years (study in men and women)

Showed improvement in:

- Energy
- Well-being
- Quality of sleep
- The ability to handle stress.

Morales 1994

HRT Treatment
Dehydroepiandrosterone (DHEA)

DHEA 50mg given for one year to 280 healthy men and women aged 70+ showed (in women only): □ libido, sexual fantasies, activity and satisfaction.

Baulieu1999

Hormone Therapy

Dehydroepiandrosterone (DHEA)

Treatment:

Dose: Oral 50-100mg (men)

10-25mg (women)

S/L 25mg (men)

5-15mg (women)

Side-effects: Changed patterns of hair growth.

NB. Increased levels of testosterone and IGF-1

Social Factors

The most common reason for older people to stop having sex is because they have lost or have no partner

Studies of Sexual Lifestyles

NatSal Survey 1994

Frequency of sexual activity:

- Related to availability of a partner
- Inversely related to age
- Inversely related to duration of relationship

ie Sixty year old in new relationship may be more sexually active than 40 year old in 15 year relationship

The US Consumer's Report

Becker 1976

Surveyed population over age 50

Termed them 'The Silent Generation'

Reported increasing range of sexuality with age

Poor correlation of satisfaction/dysfunction

Sexual activity declined with interest

Importance of intimacy despite absence of SI

The National Council on Aging Report

1988

Report on 1300 Americans over 60:
Sexually Active: 61% of men, 37% of women

- Satisfied with level of sexual activity 39%
- An active sex life important men 79% women 66%
- Sex more emotionally satisfying than aged 40 in 66%
- Qualities sought in a partner: 90% cited high moral character, pleasant personality, humour and intelligence. Men>women cited sex; women>men cited financial security

AARP/Modern Maturity Sexuality Survey 1999

- Quality of interpersonal relationships rated more highly than good sexual relationships
- A generation gap was reported in attitudes to sexuality: the new old will be less accepting of abstinence and dissatisfaction.

Maintaining the Relationship

The frequency of sexual intercourse relates to sexual satisfaction as well as other factors:

Women in later life may participate in sex primarily to maintain their relationship.

Sexual Satisfaction/Disatisfaction in women

Frequency of sexual interest, thoughts and SI correlated with satisfaction in preM and PM women

In sexually dissatisfied women frequency of SI did not correlate with being preM or PM

It is suggested women have SI to maintain their relationship

Manderson 2005

Psychological Factors

Loss of sexual desire in long term relationships: ‘Brothers and sisters’, separation of interests, unresolved emotional issues (eg ‘betrayal’)

General health

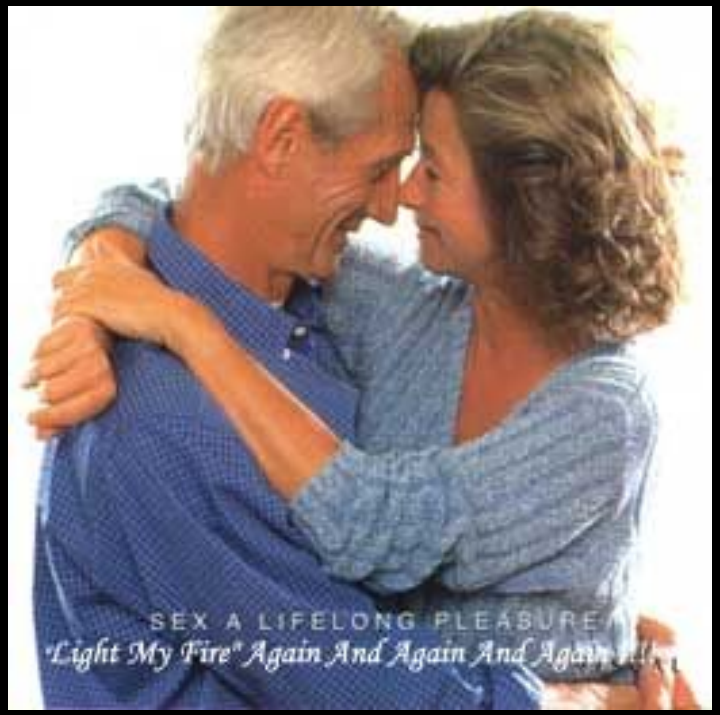
In an older population a review of general health is important in maintaining good sexual function

Hormones and chemical aids to arousal are only part of a complex social/biological system

We should consider:

- Life style factors: nutrition, exercise, ‘stress’
- The relationship: communication skills, intimacy and co-dependency/autonomy.
- Cultural and socio-economic factors

Demographics
Life expectancy

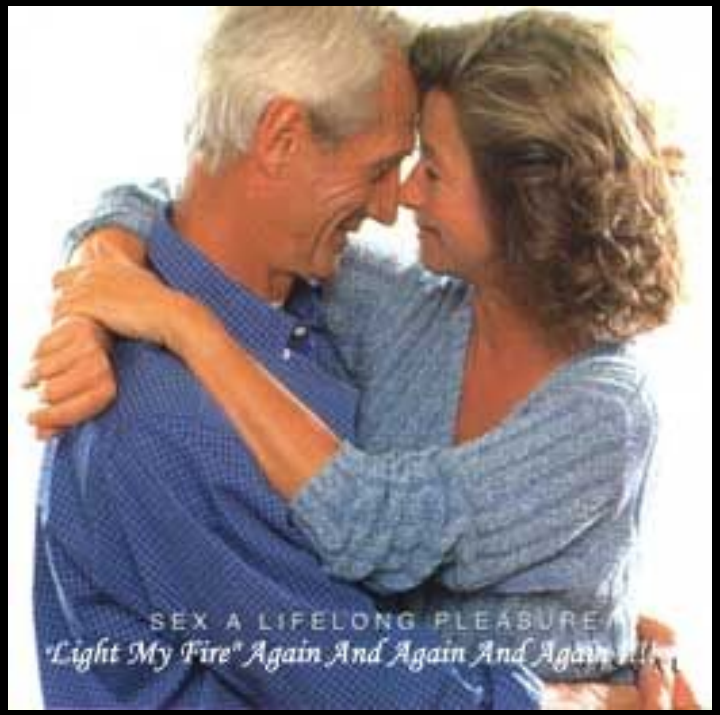


For every 24 hours of adult life a further 5 hours of additional life may be added to life expectancy.

It will be common place for our children to live into their late 90's.

No ceiling to the increase in life expectancy has been demonstrated.

Demographics
Life expectancy at 65

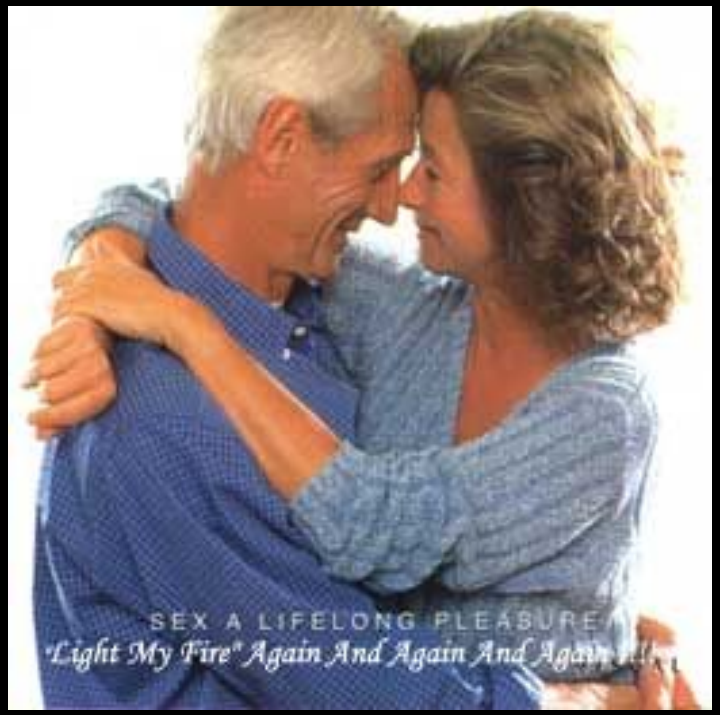


On average, once we reach 65, men can expect to live an additional 16.6 years and women an additional 19.4 years.

A child born in 2006 can expect to live 31 years longer than one born in 1900.

Source: United Kingdom National Statistics 2006.

Demographics
Life expectancy at 65



QuickStats: Life Expectancy at Age 65 Years, by Sex and Race --- United States, 1999-2004

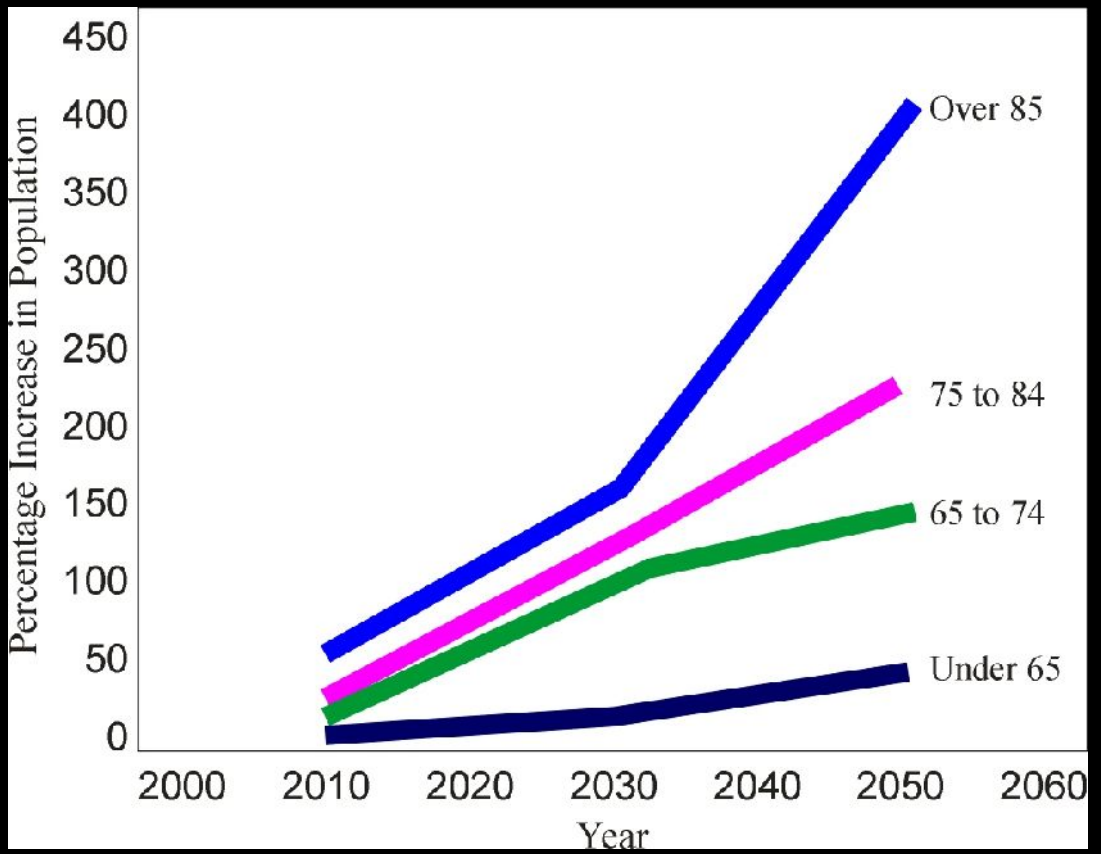
During 1999--2004, life expectancy at age 65 years increased by 1.0 year for the overall U.S. population, 1.1 years for white men, 0.8 years for white women, 0.9 years for black men, and 1.3 years for black women.

SOURCES: CDC. United States life tables. Available at http://www.cdc.gov/nchs/datawh/statab/unpubd/mort
.

Demographics
Aging trends in the western world

By 2030 people over 65 will increase by 200% and account for 20% of the population.

Reproduction rate is 1.8 per couple. Net gain in population will be due to immigration (less population emmigrating)

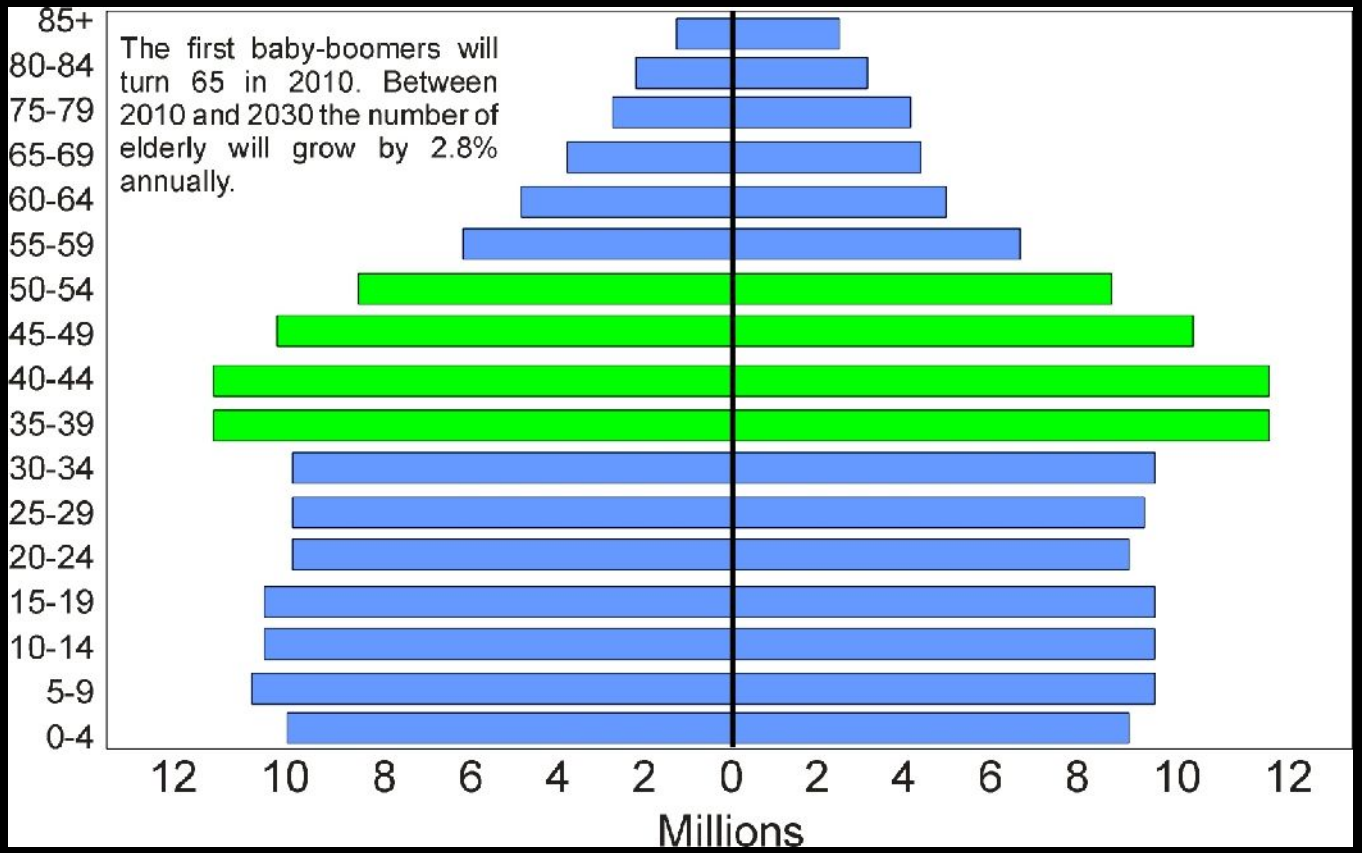


Stats produced by the Administration on Aging, www.aoa.dhhs.gov/aoa/stats/aging21

World Health Organisation Ageing & Health, www.who.int/ageing/scope.html

Population growth of 65 year olds

65+ Age Groups will Experience a Surge of Growth Starting in 2010



Data Base News in Aging: Sponsored by National Institute on Aging.

Introduction

The Context

The Demographics of Ageing

Surveys of Sexual Lifestyles

Hormonal Influences on Sexual Ageing

Clinical Presentation

Male:

- Partial Androgen Depletion
- Sexual Dysfunctions
- Hormone Therapy and PDE Inhibitors

Female:

- HRT: E2, Progesterone, Testosterone and DHEA
- Female Sexual Disorders (FSD)

The Kinsey Report

Kinsey A, Pomeroy W, Martin C. Sexual Behaviour in the Human Male. Saunders, 1948
Kinsey A, Pomeroy W, Martin C, Gebhard P. Sexual Behaviour in the Human Female, Saunders, 1953

Pros:

Ground-breaking
Fresh insights
Showed variety of sexual behaviours

Cons:

Unrepresentative
Few old, old people

(Cochran et al, 1953)

Global Study of Sexual Attitudes and Behaviour

Cross-national study of sexual well-being in older men and women Laumann 2006

Sample of 27,000 aged 40-80 (49% response rate) showed gender and cultural differences:

- Men > women reported sexual well-being;
- Men>women effected by smoking, lack of exercise and biological ageing
- Depression was inversely related to sexual satisfaction
- West Europe, US and Australia higher emotional satisfaction and better sexual relationship cf Mediterranean, Asia and Brazil
- Highest rated importance of sex in Med, Korea, Malaysia, Philippines and Brazil
- Other Asian countries with 'male-centred' regimes rated reproduction > sexual satisfaction

NB The importance of socio-economic factors on life expectancy, well being and reduced morbidity AND the continuation of sexual activity

Continuing sexual activity as a barometer of well-being in a couple's relationship

Introduction

The Context

Demographics of Ageing

Surveys of Sexual Lifestyles

Hormonal Influences on Sexual Ageing

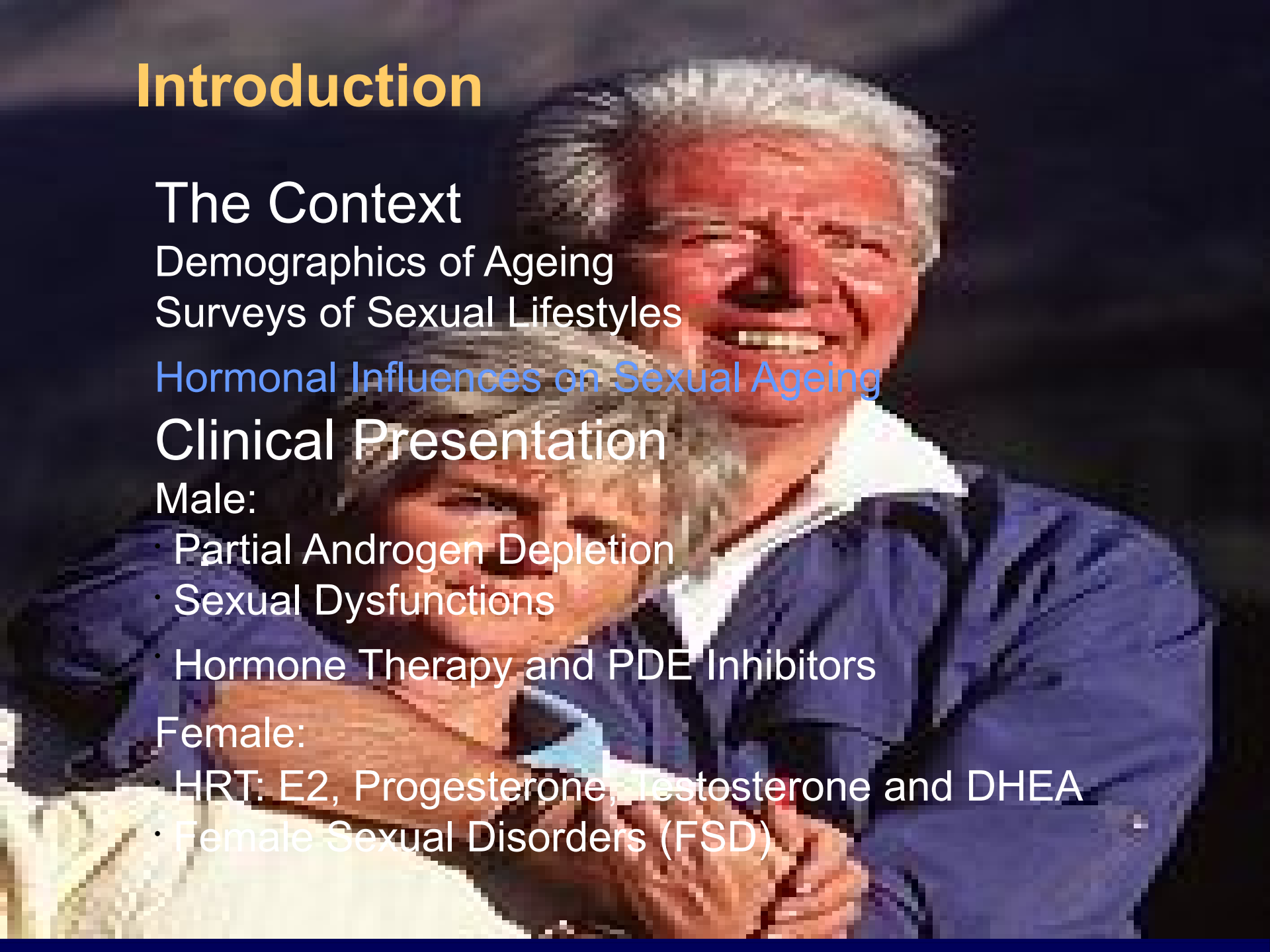
Clinical Presentation

Male:

- Partial Androgen Depletion
- Sexual Dysfunctions
- Hormone Therapy and PDE Inhibitors

Female:

- HRT: E2, Progesterone, Testosterone and DHEA
- Female Sexual Disorders (FSD)



Hormonal Influences on Ageing

Hypopysial-pituitary axis

Hypothalamus (Arcuate nucleus):

▼ Gonadotrophic Releasing Hormone (GRH)

Ant. Pituitary:

▼ LH, FSH, Prolactin

Testes: Testosterone (T), E2, DHEA

Spermatogenesis (Sertoli cells)

Ovary: E2, Estriole, Estrone, DHEA, T

The Androgenic Family

- DHEA, DHEA(S)
- Testosterone
- Dehydrotestosterone (DHT)
- Androstenedione
- Androstenediol

The Androgenic Family Testosterone

Production:

- Leydig cells produce 5-7mg/ 24 hours,
- ½ life 12 hours
- Dependent on LH
- Release is pulsatile, max between 7-9am, reduced 60% at 5-6.00pm

The Androgenic Family Testosterone

Transport:

- T not stored in testis
- Bound to SHBG (60-70%), albumen (30%), FT (2-3%)

Clearance:

- Aromatisation at target sites (brain, fat, liver, hair follicles)
- Metabolised by 5 alpha-reductase to DHT (prostate, genitals)
- Conjugation to androsterone, which is water soluble, for excretion.

Prolactin

Increased prolactin levels:

- < 500pmol/L associated with stress, may depress T production.
- > 1000pmol/L look for prolactinoma (0.4% of andropause patients)
- Drugs: phenothiazines, imipramine (dopamine antagonists); alpha-methyl dopa (interferes with dopamine synthesis); reserpine (interferes with dopamine stores); H2 blockers and E2 (increase prolactin synthesis).
- Diseases: hypothyroidism, chr renal failure.

Androgens and Sexual Function in (young) hypogonadal men

T replacement increases

- Sexual activity
- Sexual daydreams, thoughts and desires
- Spontaneous and nocturnal erections

Alexander 1999

- Penile rigidity

Lugg 1996

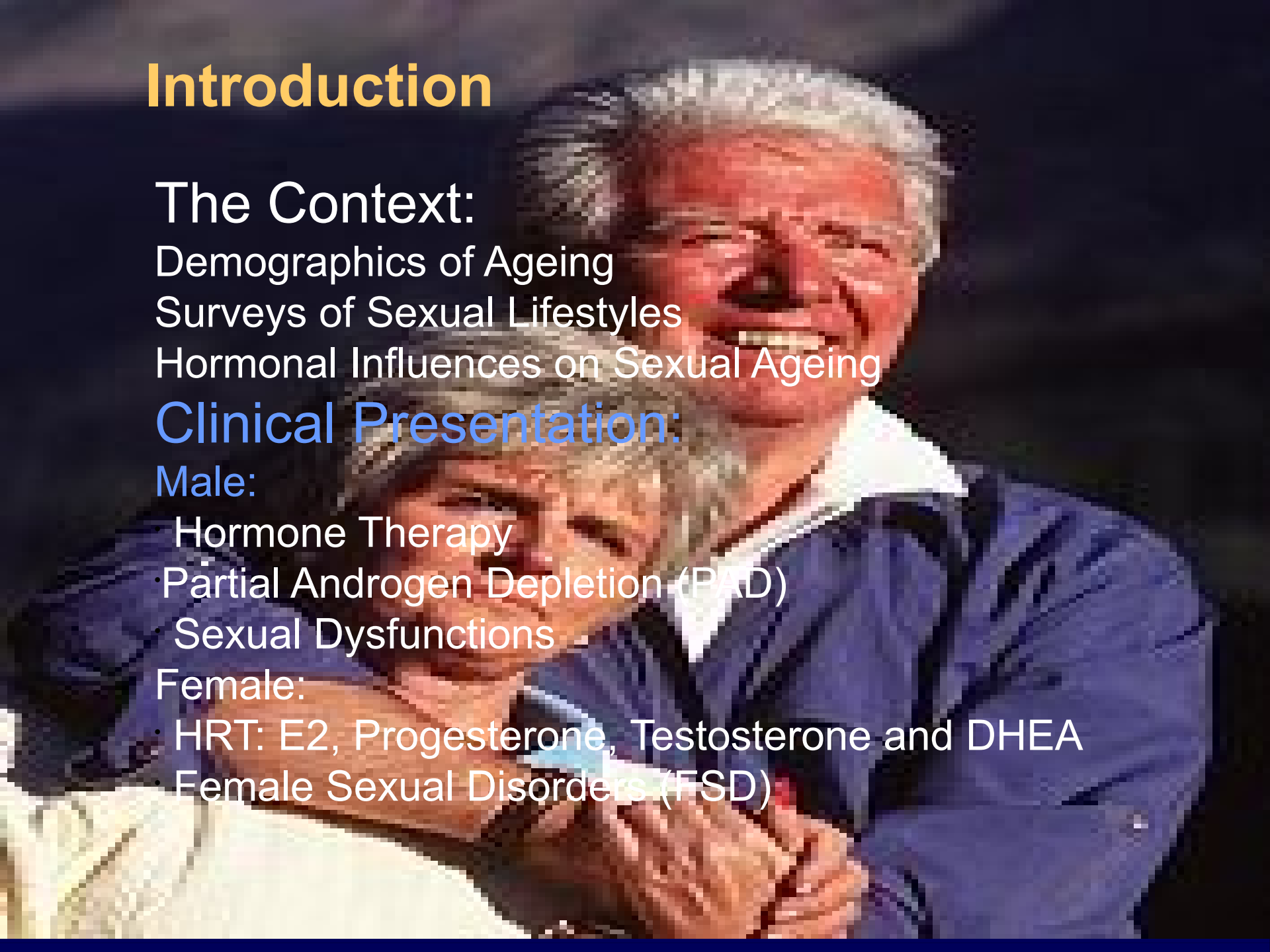
- Penile sensitivity

Orgasm and ejaculation are androgen dependent

Oestrogen Excess or Dominance

Symptoms:

- Uterine bleeding
- Tender swollen breasts
- Water retention
- Increased body fat
- Headaches
- Hypertension
- Irritability



Introduction

The Context:

Demographics of Ageing
Surveys of Sexual Lifestyles
Hormonal Influences on Sexual Ageing

Clinical Presentation:

Male:

- Hormone Therapy
- Partial Androgen Depletion (PAD)
- Sexual Dysfunctions

Female:

- HRT: E2, Progesterone, Testosterone and DHEA
- Female Sexual Disorders (FSD)

Follow-up of patients receiving Testosterone

- PSA, DRE and evaluate BPH at 3, 6, and 12 months and then annually.
- Hb and hematocrit at 3, 6, and 12 months and then annually.
- Enquire about sleep apnoea.
- Consider general health including life-style factors.

Andropause Consensus Statement, 2000

Follow-up of patients receiving Testosterone

‘The decision to institute testosterone replacement in older men with low testosterone levels must be individualised and accompanied by a detailed discussion of the potential risks and benefits.’

Bhasin 2001

Hormone Therapy

HCG (Human Chorionic Gonadotrophin)

Rationale for use:

Promoting the bodies' production of testosterone with HCG is physiological whereas replacement of testosterone exogenously suppresses endogenous production.

Hormone Therapy

HCG (Human Chorionic Gonadotrophin)

- Indication: In ‘the young old’ with partial androgen deficiency and a low FSH.
- Derived human placenta has FSH-like action.
- Stimulates Sertoli cells and sperm production
- Increases Testosterone and FTI
- Increases morning erections
- Improves skin texture
- Dose: 1250-2500iu s/c twice weekly

Hormone Replacement Therapy

HCG (Human Chorionic Gonadotrophin)

625 men with ADAM, aged 40-87, in a 2.5 year study showed increased T with hCG administration.

Patients showed increase in T by <250%, with improvement to physical and mental health, improved memory, libido and potency. Lipid profiles improved and bone turnover showed increased osteoblastic activity and decreased urinary Ca excretion

Gomula, Kalintchenko 2002

Introduction

The Context:

Demographics of Ageing

Surveys of Sexual Lifestyles

Hormonal Influences on Sexual Ageing

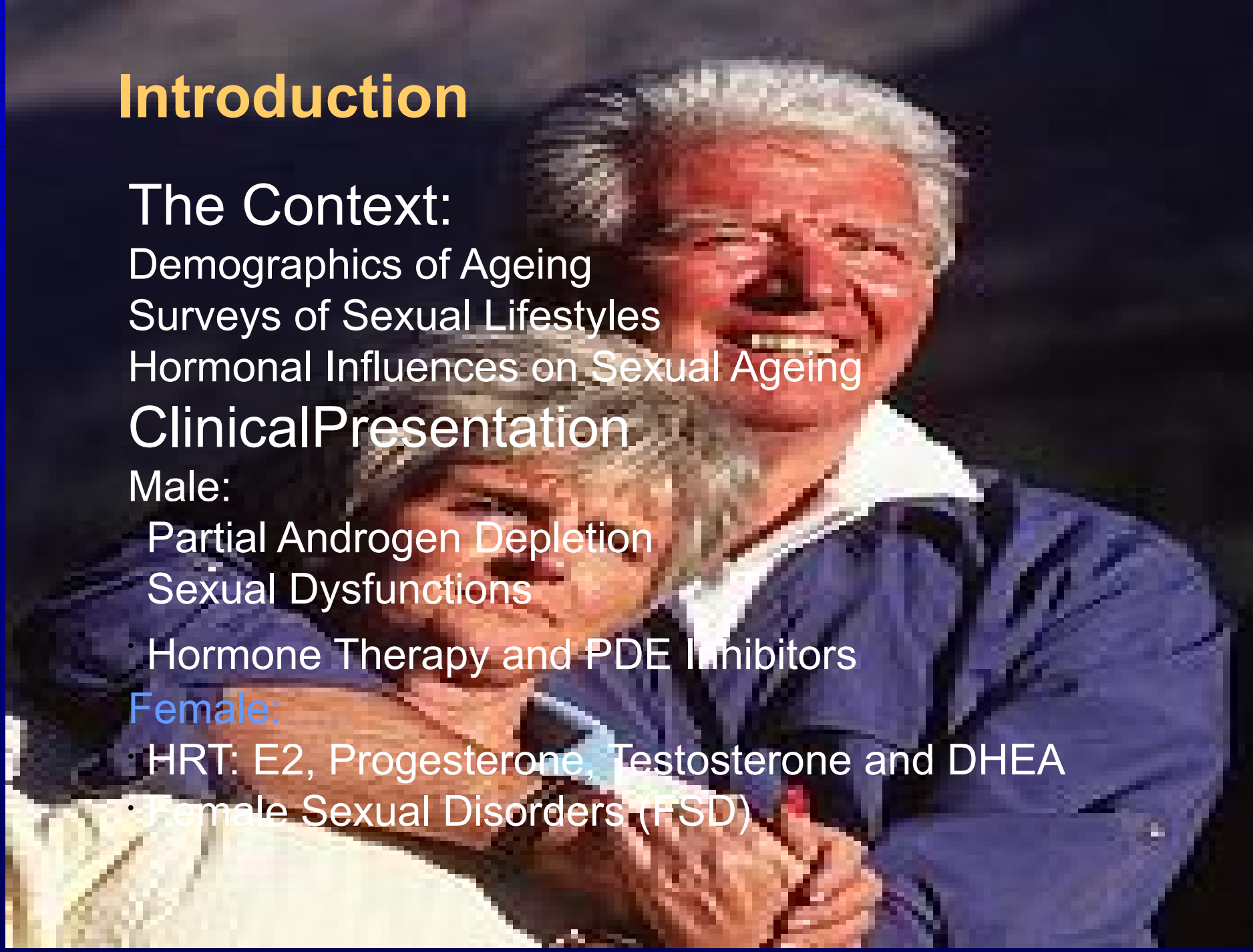
ClinicalPresentation

Male:

- Partial Androgen Depletion
- Sexual Dysfunctions
- Hormone Therapy and PDE Inhibitors

Female:

- HRT: E2, Progesterone, Testosterone and DHEA
- Female Sexual Disorders (FSD)



Hormone Therapy (HT) for Women: Oestrogens

- Numerous observational studies showed oestrogens associated with life expectancy and QOL Cauley 1997

- E2 is treatment of choice for:

  - Menopausal symptoms: hot flushes, sleep disturbance, mood swings, libido.

  - Atrophic changes: skin, vagina (urinary tract infections and incontinence)

  - maintaining bone density and prevention of fractures

Hormone Therapy (HT) for Women: E2: observational and intervention studies

- Numerous observational studies show oestrogens are associated with CVD; early menopause associated CVD
- First Prospective Randomised Controlled (HERS) study showed coronary events in year one. With established CVD risk of thrombosis. Study stopped after 4.1 years
- WHI study showed CEE 0.625 and MPA 2.5mg associated Br Ca (8 extra /1,000), CT (7 extra/1,000), stroke (8/1,000) and PE (8/1,000). Study stopped after 5.2 years

NB Findings should not be extrapolated to younger women, different routes of admin, lower dose, or different forms of HT

Hormone Therapy (HT) for Women
Risks re-evaluated: HERS study

- Mean age 67 years
- High dose HT
- Showed women with established vascular disease on high dose HT will be at high risk of thrombotic event in the first year .
- Post menopausal women should not be put on HT to reduce CV risk.
- Previous thrombo-embolic disease contraindicates HT

Hormone Therapy (HT) for Women
Risks re-evaluated

WHI non-HRT randomised arm:

Treatment with Calcium, Vitamin D and a low fat diet did not reduce the incidence of:

Osteoporosis,
Ca breast, colon/rectum,
CVD

Hormone Therapy in Women (HT)

Predictors of HT use:

- Socio-economic status: Higher status associated greater use.
- Age: Early menopause
- Type: Surgery (hysterectomy) associated with use of HT 3 times more often

Hormone Therapy (HT) for Women: Oestrogens

Investigations:

E2

LH, FSH,

TT, SHBG, FTI

DHEA(S)

TSH + thyroid profile?

Lipids, LFT's

Hormone Therapy (HT) for Women: Oestrogens

Minimum dose to maintain bone density:

- Conjugated equine oestrogens 0.625 mg (Premarin)
- Oestrogen sulphate 1.5mg (Harmogen)
- Oestradiol 17ß as:
    - Oral (Progynova, Climaval) 1-2mg
    - Transdermal (Progynova TS) 0.05mg
    - Implant 6 monthly 50mg

Hormone Therapy (HT) for Women: Oestrogens

Side-effects:

- Mastalgia (painful breasts)
- Bloating
- Bleeding
- ‘Premenstrual Tension’
- Depression

Hormone Therapy (HT) for Women: Oestrogens

Endometrial Cancer:

'Unopposed' oestrogens increase the risk; progesterone protects against it:

- Sequential combined (Cyclical) therapy: Progesterone is given for 12 days per month and is followed by withdrawal bleeding
- Continuous combined therapy: Progesterone is given continuously; there may be spotting/unpredictable bleeds (resolves in < 9 months); usually only commenced 1yr after menopause

Hormone Therapy (HT) for Women: Oestrogens

Weigh up risks and Benefits

Breast Cancer Risk (Prevalence per 10,000 women):

- No oestrogens/oestrogens for less than 2 years is 45
- E2 for 5 years is 47
- E2 for 10 years is 52
- E2 for 15 years is 57

The risk of breast cancer continues into the 7th decade and later. ? Mammogram

Increased risk if FH of breast cancer.

Hormone Therapy (HT) for Women: Progestogens

Minimum dose for endometrial protection:

For 12 days per month:

- Norgestrel (Neogest) 0.15mg
- Norethisterone (Micronor) 1mg
- Medroxyprogesterone (Provera)# 10mg
- Dydrogesterone (Duphaston 10mg
- Micronised progesterone 200mg

For continuous therapy dose of Medroxyprogesterone is 2.5mg

Introduction

Demographics of Ageing

Surveys of Sexual Lifestyles

Hormonal Influences on Sexual Ageing

Clinical Presentation:

Male:

- Partial Androgen Depletion
- Sexual Dysfunctions
- Hormone Therapy and PDE Inhibitors

Female:

- HRT: E2, Progesterone, Testosterone and DHEA
- Female Sexual Disorders (FSD)

Hypoactive Sexual Desire Disorder (HSSD)

Definition

Impairment of sexual interest, thoughts and fantasies, and a lack of responsive desire;

Motivation to becoming sexually aroused is reduced;

Lack of interest (in sex) is greater than that accounted for by ageing alone or the lengthening of a relationship.

Basson 2004

Hypoactive Sexual Desire Disorder

- The symptom of low sexual desire is only a disorder when an individual feels it to be distressful.
- The consequent effects on a relationship may also motivate requests for treatment.

Dennerstein, 2006

Hypoactive Sexual Desire Disorder

Prevalence:

Age 20-49: 16% [7%*]; 29% [16%*] with surgical menopause.

Age 50-70: 42% [9%*]; 46% [12%*] with surgical menopause.

* Indicates distress

Dennerstein, 2006

ie □ E2 due surgery before leads to □ desire and distress in

Hypoactive Sexual Desire Disorder Aetiology

Biological factors:

- **Central (limbic system and rhinencephalon); Mediated by neurochemicals: dopamine (arousal) and endorphins (satisfaction); E2 and androgen dependent.**

- **Peripheral (cavernosal bodies, introitus) Androgen and E2 dependent. Androgens quantitatively predominate**

Dennerstein, 2005

Hypoactive Sexual Desire Disorder Aetiology

Psychological factors

Motivational:

Recreation, reproduction, intimacy, 'Instrumental' sex ie other benefits.

Cognitive:

Relational factors (the nature of the relationship), beliefs, contextual factors.

Dennerstein, 2005

Testosterone therapy in hypoactive desire disorder:

- Endogenous testosterone and sexual function may not correlate.
- Testosterone therapy (<24 weeks) with traditional HT improves sexual function in postmenopausal women (particularly surgically menopausal women).
- Adverse effects on lipids (>HDL) are associated with oral methyltestosterone

Hormone Therapy (HT):

Androgens for Women

Study: 6 women with impaired sexual function (oophorectomised).

- Age: 31-56
- T/d testosterone (Intrinsa): 300 µg – as patch 2- 3 times weekly.

Result:

- Low dose: increase in sexual thoughts, desires and activities.
- High dose: also improvement in mood and well-being

Shifren

Hormone Therapy (HT):
Clinical use of other hormones in women?

Oxytocin

- ‘I find it deeply interesting to know that when I fall in love with someone my initial lustful feelings are enhanced by dopamine, a neurohormone produced by the hypothalamus that triggers the release of testosterone and drives my sexual desire, and that my deeper feelings of attachment are reinforced by oxytocin, a hormone synthesized in the hypothalamus and secreted into the blood by the pituitary. Anon, comment on internet

- Syntocinon 10micrograms s/c give < frequency of orgasms and desire for physical contact

Sexual Aversion Disorders (SAD)

Definition

Severe anxiety/disgust at the thought of sexual activity

- Autonomic (neurovegetative), involuntary phobic symptoms

[cf Avoidant: voluntary with predominantly psychological factors]

- Complex causality: incest, rape, may lead to panic attacks, PTSD, assd anxiety disorders
- Older women may have SAD consequent to cultural expectations, body image, and physical health concerns about self or partner
- Stress causes secondary androgens, estrogen
- Co-morbid HSSD

Whipple, A Graziottin 2006

Female Sexual Arousal Disorders (FSAD)

Definition

A reduced or absent experience of sexual arousal (subjective and/or genital sensation) from any type of sexual stimulation. Hence Subjective, Genital and Combined Arousal Disorder

- Subjective arousal correlates poorly with genital congestion

Basson 2004

- Prevalence increases with age over 50. Dunn 1998
- Aetiology: Arousal requires intact vascular and nerve supply and hormonal milieu: associated conditions include ↓ E2, DXR, urinary tract infection, pain, psychosocial factors

Whipple, A Graziottin 2006

NB Persistent sexual arousal disorder (PSAD) is a separate diagnostic category

References

Surveys

National Council on Aging (NCOA) with Pfizer, 1998 ‘Sex after 60’.

Heath H, 1999 Sexuality in old age. NT Books, London

Grigg E, 1999 Sexuality and older people. Elderly care, 11 (7): 12-15

Borissova AM, Kovatcheva R, Shinkov A 2000 Changes in sexual behaviour

Kinsey A, Pomeroy W, Martin C. Sexual Behaviour in the Human Male. Saunders, 1948

Gorer G. Sex and Marriage in England Today. Thomas Nelson and Seons, 1971

Johnson A, Wadsworth J, Wellings K, Field J. The National Survey of Sexual Attitudes and Lifestyles (NATSAL), Blackwell Scientific Press, 1990

Partial Androgen Deficiency

8 Andropause Consensus Statement. Endocrine Society, 2000.

9 Zmuda J et al: Longitudinal relation between endogenous testosterone and cardiovascular risk factors in middle-aged men. A 13 year follow up of former multiple risk factor intervention trial participants. 1997 Am J of Epidemiol, 146: 609

Webb CM et al, 1999 Circulation;100:1690-6

11 Alexandersen P et al, The relationship of natural androgens to coronary heart disease in males: a review. 1996 Atherosclerosis, 125: 1

12 Uyanik B et al, Beneficial effects of testosterone undecanoate on the lipotrotein profiles in healthy elderly men. A placebo controlled study. 1997 Jpn Heart J, 38:73

13 Shippen E, Fryer W, 1998 The Testosterone Syndrome, Evans and Co, Inc. NY

Tremblay R, Morales A: Canadian practice guidelines for screening, monitoring and treating men affected by andropause or partial androgen deficiency. 1998 Aging Male, 1:213

Gomula A, Kalintchenko S, 200 Personal communication,

E-mail:Kalinchenko@rambler.ru

Bhasin S, Buckwalter J: Testosterone Supplementaion in older men: A Rational Idea Whose Time Has Not Yet Come, J of Androl, 2001, 22; 5, 718-729.

28 Ayta I et al, The likely worldwide increase in erectile dysfunction 1995 and 2025 and some possible policy consequences. BJU Int, 1999; 84: 50-6

29 Gooren L The age-related decline of androgen levels in men: clinically significant. Br J of Urology, 1996; 78: 763-8.

30 Morales A, Yen S, Effects of Replacement Dose of DHEA in Men and Women of Advancing Age, 1994 J. Clin Endocrinol Metab, 78, 1360-1367

31 Baulieu E et al, DHEA, DHEA sulfate, and aging: contribution of the DHEAge Study to a sociobiomedical issue. PNAS, 97 (8) 4279-84

32 Morales A et al, Oral androgens in the treatment of hypogonadal impotent men. 1994 J Urol, 152: 1115

33 Yue P et al Testosterone Relaxes Rabbit coronary arteries and aorta 1994, Circulation; 91: 4, 1154-1160

34 Jaffe M, Effect of testosterone on postexercise ST segment depression 1977 British Heart Journal; 39: 1217-1222

35 Thomas J et al, Effects of oestrogens on the prostate. 1994 J of Androl, 15: 9

36 Tenover J, Androgen deficiency in aging men. 1998 The Aging Male, suppl.,1: 16

37 Zmuda J et al: Longitudinal relation between endogenous testosterone and cardiovascular risk factors in middle-aged men. A 13 year follow up of former multiple risk factor intervention trial participants. 1197 Am J of Epidemiol, 146: 609

38 English K et al, Low dose t/d testosterone therapy improves angina threshold in men with with chronic stable angina. Circulation 2000;102:1906-11.

Erectile Dysfunction

39 Levine S Intrapsychic and interpersonal aspects of impotence: psychogenic erectile dysfunction. 1996 In Rosen R et al Erectile Disorders. New York: Guildford Press, 198-225

40 Eid J Sildenafil citrate: current clinical experience.2000 Int J Impotence Res; 12: S 62-S6

41 Aversa A et al New Oral Agents for erectile dysfunction: what is changing in our practice? 2001 Asian J Androl; 3: 175-9

42 Chetlin M et al Consensus Document. Use of Sildenafil in patients with cardiovascular disease 1999 J Am Coll Cardiol ; 33 : 273-83

43 Wessels H et al Melanocortin receptor agonists, penile erection, and sexual motivation: human studies with melanotan 11. 2000 Int J Impotence Res;12:S74-9

44 Read S et al J Public Health Med, 1997, 19:387-91

45 Lauman E et al 1999 JAMA; 281:537-44

46 NIHCS. National Institute of Health Consensus Statement 10. 1 December 1992

47 Feldman A et al Impotence and its medical and psycho-social correlates: results of the Massachusetts Male Aging Study. J Urol 1994:151:54-61

OPTIMAL HEALTH
OF
HARLEY STREET

Dr Michael Perring MA MB B.Chir FCP (SA) DPM UKCP Registered Psychotherapist
www.OptimalHealth.org.uk