





### Impact of menopause on future health?

- Obesity, Metabolic Syndrome and Diabetes
- Cardiovascular Disease
- Osteoporosis and Chronic Arthritis
- Dementia, Cognitive Decline and Depression
- Cancer

### **British Menopause Society**

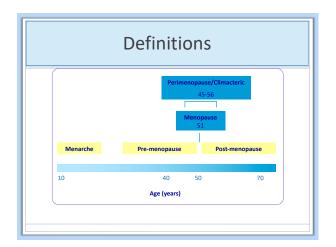
- Modernizing the NHS: observations and recommendations from the British Menopause Society 2011
- Every woman should be offered a health check at 50 for a health and lifestyle consultation

### Information and advice NICE 2015

- an explanation of the stages of menopause
- common symptoms and diagnosis
- lifestyle changes and interventions that could help general health and wellbeing
- the benefits and risks of treatments for menopausal symptoms.
- Explain to women that as well as a change in their menstrual cycle they may experience a variety of symptoms associated with menopause, including: (list of symptoms..)
- Offer treatment....

### **Quality Standards**

- February 2017
  - Diagnosis over 45
  - Diagnosis under 40
  - Three month follow up of HRT
  - Young women treat with HRT or OCP
  - Women about to be rendered menopausal- advice

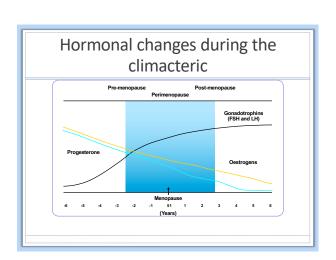


### Defining the menopause Last menstrual period (LMP) – 12 months Can only be established retrospectively Hormonal assays might help but not definitive

### Types of menopause • Spontaneous • Surgical • latrogenic

AGE	Numbers of oocytes
20 weeks	2 million
Birth	1 million
Puberty	500,000
Age 40	84,000
Menopause	<1000

# Pathophysiology of Menopause • Fewer and fewer follicles are available until no follicles develop at all • FSH and LH levels become persistently elevated • Estrodiol levels stabilize at low level



### Diagnosis

- Menstrual history
- Symptoms
- Age
- Hormone assay NICE 2015
- NICE 2015 Care Algorithm

### Diagnosis NICE 2015

Diagnose menopause on history and symptoms

- •>45yrs with menopausal symptoms No FSH (or other hormones) Quality Standard
- •< 40yrs when menopause suspected 2x FSH min Quality standard
- •age 40-45, with meno symptoms Consider FSH
- NB OCP or high dose prog do not use FSH

### Hormone Assays NICE 2015

- No assay >45yrs with menopausal symptoms
- > 45yrs do not use AMH, Oestradiol, Inhibin A,B, Antral follicle count,
- OCP or high dose prog do not use FSH
- Consider FSH age 40-45, with meno symptoms < 40 when menopause suspected

### Premature Ovarian Insufficiency

Diagnosis NICE 2015

Menopause symptoms +/- no or irreg periods

2 x raised FSH 4-6 weeks apart

No – routine AMH

Take into account clinical history

"If diagnosis is in doubt – refer to specialist"

### Physical symptoms

- Hot Flushes
- · Night sweats
- 80% of women modsevere
- Average 5 years
- 30% for over 10yrs
- 3% none
- Penn Ovarian Ageing Study 2014



### Other causes of flushes

Thyroid conditions

**Epilepsy** 

Infection

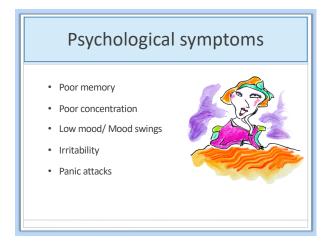
Some cancers

Medications

Autoimmune disorders

### **Physical symptoms**

- Headaches
- Fatigue
- Joint pains
- Palpitations
- Formication



### Sexual symptoms

- · Reduced sex drive
- Dyspareunia
- · Vaginal irritation
- · ?body image change

# Influence on symptoms Diet and lifestyle Stressors Culture and attitude Support

## Physical symptoms Bladder Frequency Urgency Leakage Recurrent UTI "I've reached that age where I've given up on Mind Over Matter and am concentrating on Mind Over Bladder."

### •Clinically apparent 4 years+ post meno •Affects 40% of women •Few actively seek help •Easy to treat

### How do you assess symptoms?

Greene Climacteric Score Menopause Rating Scale Symptoms assessment Score (NPH)

"How much is it affecting your life at home and at work?"

### **Assessment**

- Describe symptoms
- Discuss menses pattern
  - Is it menopause?
- Is there anything else it may be?
  - What does she want to do?

### Investigations?

- Hormone assay
- FBC
- TFT
- Lipids
- Thrombophilia
- Pelvic exam/TVU
- Auto-antibodies
- Chromosomes
- AMH

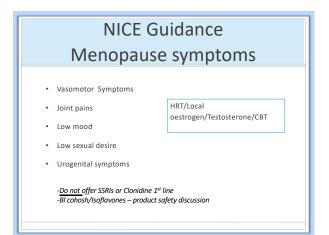
### What women want...

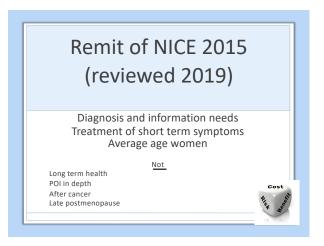
- Explanations
- Information
- Choices
- 'Signposting'

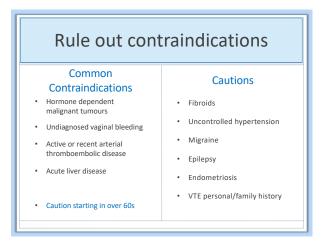
### Signposting

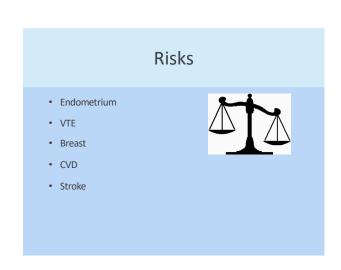
- Weightwatchers/Slimming Club/Gym
- www.menopausematters.co.uk
- www.womens-health-concern.org.uk
- www.daisynetwork.org
- Specialist Clinic/Gynaecologist

### Time for a break









### CVD and NICE 2015 CV risk factors are not a contraindication for HRT as long as they are optimally managed" eg Smoking Obesity BP Migraine

### NICE Guidance 1.4.21 Consider referring women to a HCP with expertise in menopause if they have menopausal symptoms and contraindications to HRT NG 23 Diagnosis and management of menopause 2015

### NICE 2015 - Breast

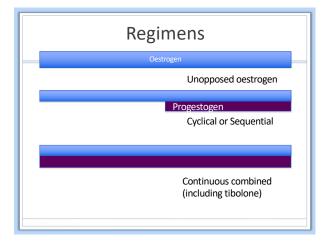
- HRT with oestrogen alone is associated with little or no change in the risk of breast cancer
- HRT with oestrogen and progestogen can be associated with an increase in the risk of breast cancer
- any increase in the risk of breast cancer is related to treatment duration and reduces after stopping HRT.
- (NICE 1000/7.5 yrs 5 extra cases with E+P
- Baseline 22.5)

AMH

### **HRT Choices**

- Which regimen
- Which route
- · Which progestogen
- Which dose
- · How long for

### Investigations? - Hormone assay - FBC - TFT - Lipids - Thrombophilia - Pelvic exam/TVU - Auto-antibodies - Chromosomes



### Route - Oral

Convenient, calendar packs
Choice of doses
E, P and E+P
Cyclical and continuous

### Who should Have Transdermal?

- Gastric upset eg Crohns
- Need for steady absorption eg migraine/epilepsy
- Perceived increase risk of VTE, including BMI >30 (NICE)
- ?Patient choice

### Routes

### **IUS**

- Progestogen
- Licensed for HRT use 4yr FSRH – 5 years
- Alongside any oestrogen route

### **Implant**

- · Not widely available
- · High doses
- Intermittent absorption
- Tachyphylaxis if unmonitored

### Vaginal Oestrogen

- · Long term treatment, regular use
- No need for progestogen or review ultrasoun.
- · Can increase dose (specialist advice suggested)
- · Caution with Aromatase inhibitors
- · Lancet 2019 no increase br ca risk
- 2 new ones 2019 Imvaggis and Blissel



### Progestogen/progesterone

- Only given for endometrial protection
  - But will influence
  - Thromhosis risk
  - Lipids
  - Metabolic profile
  - Side effects
  - bleeding

Schumacher M et al (2007). Novel perspectives for progesterone in hormone replacement therapy, with special reference to the nervous system. Endocr Rev 28:387–439!

### **Testosterone**

- No licensed products for women
- NICE 15 use publication where indicated
   GP President where indicated
- Eg Testogel 50mg divided doses over 7-8 days, Tostran 10mg every other day
- Measure? FAI T/SHBG x 100 no guidelines
- Safety short term good, long term, limited data

### **HRT Monitoring**

Annual review once settled Effective?
Bleeding/Side effects
Any changes in health?
Dose/Type still appropriate?
Is it time to stop?

### How long?

- · MHRA 2007 and 2019
- "...lowest effective dose,...shortest possible time..." "annual review required"
- "No single recommendation on duration of treatment or safe upper-age limit..... Will be specific to every woman's circumstances"
- No arbitrary limits BMS Guidelines 2020

### Ospemifene (Senshio)

- A Selective Estrogen Receptor Modulator (SERM)
- · 60 mg tablet daily
- Improves pain on intercourse and vaginal dryness
- Same low thrombosis risk as oestrogen and tamoxifen
- May occasionally aggravate flushes and sweats initially
- ? With breast cancer

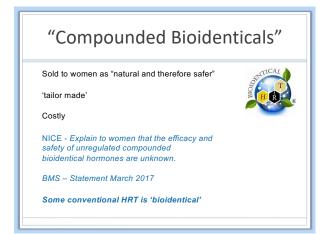
### Prasterone 6.5mg (Intrarosa)

- DHEA vaginally
- "treatment of vulvar and vaginal atrophy in postmenopausal women having moderate to severe symptoms"
- · Daily dose

A statistically significant decrease in percentage of parabasal cells. increase in percentage of superficial cells, decrease in vaginal pH.

A statistically significant improvement of moderate to severe dyspareunia and most bothersome VVA symptom to her at screening and at baseline

## Ris OKto prescribeup to 12 months of HRT providing you are happy with the HRT check This is based on ANE2 guideline (Nozelly Published dote: (Noze



### Questions?

### Options 1. Lifestyle 2. Prescribed medication other than HRT 3. Dietary & herbal. 4. Complementary therapies





### Increased vasomotor, and menopausal symptoms in general Increased risk CVD, independent of other factors Increased risk VTE Increased risk cancer No magic cure May need to control symptoms before changes can be made EMAS position statement: Managing obese postmenopausal women Lambrinoudaki et al. Maturitas 66 (2010) 323-326

### Increased menopausal symptoms (vasomotor, insomnia, psychological) Increased CVD risk Increased osteoporosis risk Mechanisms—toxicity to ovarian follicles, reduced estrogen, earlier age of menopause

Clonidine

# Non HRT choices Clonidine SSRI/SNRI- low does anti depressants for hot flushes Vaginal oestrogen Vaginal moisturisers and lubricants CBT Phytoestrogens and herbal remedies

### Mixed evidence 25-50mcg bd Stop gradually Side effects NICE 2015 — in the absence of data, discuss with those who don't want pharmacological treatments

### SSRIs / SNRIs

- Venlafaxine 37.5-150mg
- · Paroxetine 10mg \*
- Fluoxetine/Citalopram
- 50-70% flush improvement

### Side effects

\*Caution with Tamoxifen – inhibits enzyme for metabolism

### SSRIs/SNRIs

• NICE 2015

Do not routinely offer first line

No clear evidence for use for mood/anxiety in absence of depression

Discontinuation rates high

### Gabapentin

- Anti-epileptic
- Short term trials show benefit (60%)
- Dose titration up to 900mg over three days or more
- Side effects drowsiness, nausea
- ?Extended release USA
- NICE 2015 Evidence sparse specialist use in women with breast cancer

### Vaginal radiofrequency and laser- thermal or non thermal treatment

- "Remodel collagen, restore tissue"
- Private sector Er-Yag/CO2/RF
- Usually three treatments over 12 weeks
- Duration of effect/comparison/safety/cost effective?
- NICE 2021 for research
- Aug 2018 FDA Alert



### Women with breast cancer

- •Lifestyle changes
- •Therapy approach
- Venlafaxine/Paroxetine
- Gabapentin
- Vaginal oestrogens with care
- Vaginal moisturisers
- Support and information
- Practical clinical guidelines for assessing and managing menopausal symptoms after breast cancer M. Hickey Annals of Oncology June 2008

### NICE – breast cancer and menopausal symptoms

- HRT in exceptional cases
- SSRis
- SNRI:
- Clonidine, Gabapentin
- Tibolone, progestogens, isoflavones, vitamin E and magnets not advised - NICE CG 80

### **NICE 2015**

- Isoflavones
- Black Cohosh
- 'may have evidence for relief of vasomotor symptoms….discuss quality of product" NICE 2015

### Isoflavones

- Naturally occur soybeans, chickpeas flaxseeds, cereals/brans
- Supplements quality variable
- Usual OTC dose 40-80mg
- Trial doses to 200mg
- (40mg=700ml soy milk,10 cups chickpeas,2 cups split peas)

### Isoflavones

- RCTs marginally beneficial effect
- Syst Review No sig benefit Cochrane Database Syst Rev. 2013
- Reduction in frequency Chen 2015 Syt rev
- Vasomotor symptoms Lipovac 2011- Gynae Endo 2011 1-5 ,
- Mood and anxiety improvement Lipovac 2010 Maturitas
- Vaginal dryness improved (90mg)
- Menopause. 2014 Nov 24.

### **Black Cohosh**

Cochrane Review - September 2012

Insufficient evidence to support the use of black cohosh for menopausal symptoms

- >poor quality studies
- >further work justified

### After Cancer?

- Does not appear to effect breast density
- Safety and effectiveness in women with breast cancer , not clear
- "is black cohosh oestrogenic"?
- Mixed evidence

### Other OTC remedies

Ginseng(mood)	Cochrane 2014
Oil of evening primrose (-)	Chenoy 1994
Vitamin E (marginal benefit) (+)	Barton 1998
Multivitamin and minerals	No studies
Sage (-/+)	Bommer 2011
Pollen extract (+)	Hellstrom 2012
Natural progesterone gel (-)	Benster 2009
Magnets	nil

### Beware of interactions

- BLACK COHOSH Caution with salicylate sensitivity
- ?caution with chemo/Tamoxifen
- DONG QUAI Caution with warfarin.
- GINKGO BILOBA Has anti-coagulation effect.
- ST JOHNS WORT DIGOXIN, THEOPHYLLINE, WARFARIN, ANTIEPILEPTICS, IMMUNOSUPRESSANTS, CYCLOSPORIN and HIV DRUGS. Be cautious with antihypertensive therapy. Photosensitivity has been reported.

### Traditional Herbal Registration • Registered with MHRA (not food supps) • Meets standards in terms of quality and safety • 'Traditionally used for', not evidence based

### Therapy approach

- Reflexology
- Massage
- Acupuncture
- Music therapy
- CBT
- Mindfulness
- QOL or symptoms?

### Looking ahead

- Neurokinin 3 receptor antagonist –
- For vasomotor symptoms
- Non oestrogen treatment
- Pre-licensing stage

### Summary

- Women want to make informed choice about natural options as well as medications
- Non-drug options should be viewed as a different approach not as a substitute for HRT
- Select a small number of well-researched natural products
- Be specific in your recommendation knowing you are safe

