

## ACT Meeting 4/7/2019 - Menopause

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### **A couple of updates on Infertility treatments:**

There is a trend now to move away from using Clomid to induce ovulation and instead to use Letrozole which is an Aromatase inhibitor (usually used for Breast cancer). Aromatase inhibitors inhibit the conversion of testosterone to progesterone which tricks the body to increase FSH. Letrozole doesn't thin the uterine lining so is preferable to Clomid.

There is some new evidence emerging which links increased DNA fragmentation in sperm to problems with the Microbiome.

The most frequent cause of high DNA fragmentation is infection. Chlamydia or NSU may be causative.

### **A thought about IVF**

During IVF more than one follicle is matured. In a normal woman's cycle only one follicle matures and thus there is self selection of the 'best' egg. IVF overrides this mechanism. There is thus a higher probability of the multiple eggs developed in IVF being abnormal or damaged – they wouldn't normally win the 'race'.

### **Menopause**

Definition: 1 year without a period (but this could also be a symptom of other problems)

Perimenopause: 7 years before Menopause

The woman's mother's age at Menopause is a good indicator of the daughter's age.

Gidon does not measure the woman's hormone levels because the symptoms say it all. FSH and AMH are not predictors for menopause and a low AMH does not indicate that a woman is likely to get premature menopause!

Symptoms are:

- psychological
- vasomotor related
- reduced libido
- urogenital atrophy

Mechanism: the ovaries release oestrogen, progesterone and testosterone. The release of these hormones drops dramatically at Menopause. Hot flushes are caused by the drop in oestrogen & not the level of the hormone.

It can be difficult differentiating menopause symptoms from depression symptoms as they present in similar ways. Gidon's approach is to treat the menopause symptoms first with HRT and if this doesn't help mood and energy then treat for depression.

## HRT (Hormone Replacement Therapy)

Has only one real medical indication which is to prevent Osteoporosis. It also helps women with risk factors for cardiac disease. It can help some women with other menopausal symptoms. Effectiveness is individual and cannot be predicted with hormone tests.

HRT is a combination of hormones. Oestrogen that isn't balanced with Progesterone causes endometrial hyperplasia (=build-up of endometrium) and risks uterine cancer because there is no monthly bleeding and shedding of uterine lining. However if the womb has been removed Progesterone is not needed.

The safest HRT is transdermal (patch or gel) because it gives the same oestrogens as we have during our reproductive years (Evorel®), this is available on the NHS. Oral HRT (Elleste®) or the pill (synthetic oestrogens) go through the liver, while dermal applications deliver metabolites which go straight to the organ receptors.

Patch – Gidon suggest to change this on Wednesday and Sunday. Patches can be cut in order to decrease the dose. The lowest dose possible should be used. He recommends the patch to be put below the tummy, but it can be put anywhere.

Conjugated equine oestrogens (like the old style Premarin) and 17-beta-oestradiol (like Evorel) have significant differences. 17-beta-oestradiol is identical to what the body produces and is much safer.

There are three main natural oestrogens:

- Oestrone (E1) – levels are higher after menopause
- Oestradiol (E2) – produced in reproductive years (Evorel and Elleste are oestradiol)
- Oestriol (E3) – produced by the placenta during pregnancy

Estestrol (E4) – is also produced in pregnancy by the baby's liver.

Blood tests need to be specific to the oestrogen you are looking for, otherwise you may get low or absent readings.

There are 3 types of prescribed oestrogens in HRT

- Estron (in Vagina)
- Conjugate Oestrogens (oral), e.g. Celeste® - synthetic and therefore can't be measured as oestrogen in test (also applies to the Oestrogen in the Pill). This is why Gidon does not measure oestrogens in patients, he prescribes it (and adjusts the dose by) observing whether the symptoms disappear.
- Oestradiol (oral or transdermal) – transdermal Oestrogen is very safe –oestrogen is very thrombosis inducing, but not if applied dermally (patch or gel)

Progestogens are not associated with cancer, however, artificial Progestogens are, e.g. norethisterone (however, not a problem in premenopausal women, or when used short term, as in IVF)

Femistan® is okay = neutral progesterone (if you want to use tablet)

There are 7 types of progestins (progesterone type molecules)

Artificial progesterones affect the water balance as well as the glucobalance (mineral imbalances, bloating, cholesterol imbalances = glucocortical effect)

Oestrogen protects from coronary artery disease through the prevention of plaques.

Patients can ask their GP for NHS referral to the Complex Menopause Clinic at the Whittington if they want HRT but the GP is unhappy or uncertain about prescribing it.

### **Side effects of HRT:**

- Increased risk of breast cancer, however this is difficult to estimate and depends on the type of HRT. The trial that showed a considerable risk for Breast cancer (12 in 1000) used old fashioned oestrogens. A woman's personal history is taken into consideration, not a family history of cancer.
- Heart attack (prothrombotic action), especially when starting late (5 years or more after menopause when atheroma may have already accumulated)
- Hair loss is NOT associated with HRT. Hair loss is due to genetic factors.

### **Indications for HRT**

- Sever menopausal symptoms
- Risk factors (osteoporosis and possibly heart disease) – Gidon does not like Fosamax for osteoporosis he prefers HRT for bone protection
- Possible protective effect for bowel cancer and Alzheimers

### **Contra-indications for HRT**

- Breast cancer
- Thrombosis risk
- Older women >60-65 (due to thrombosis risk and cancer risk)

### **When and how long to be on HRT?**

The benefits are in the 1<sup>st</sup> 5 years; after this period, the medical benefits decrease. Benefits are prevention of Osteoporosis (especially 1<sup>st</sup> 5 years) and heart disease (cardio-protective) - Oestrogen protects from heart attacks through the prevention of plaques. Women under the age of 50 have thus a lower incidence of heart disease. On its own oestrogen causes Hyperplasia of the womb because there is no bleeding. The normal window for HRT prescription is 50-55. The longer you're on HRT, the more the risk of breast cancer is increased, but the increase is slight. When HRT is started late there is a higher risk of Heart attack (through oestrogen's pro-thrombotic action).

Early Menopause: before the age of 40 may be due to early or faster decay/loss of eggs. This includes resistant ovary syndrome. The rate of decay is different in each woman. Despite an early Menopause there are still 5-10% spontaneous pregnancies.

She will develop osteoporosis – but there is NO increased risk of breast cancer, as that's only over 50.

Early Menopause can also be due to removal of the ovaries before the age of 45 and which leads to a crash of testosterone and the Women feel lousy.

IVF treatments don't contribute to early menopause. They only use the available antral follicles produced that month (which otherwise would give way to the lead follicle). There is the possibility of some ovarian damage from repeated egg retrievals though.

The treatment is to take HRT to prevent Osteoporosis. All these women should be on a low dose of transdermal HRT (which does not increase the incidence of breast cancer). An alternative is to take the combined pill (which is free), especially if the woman needs contraception. However, the latter has a higher risk of cancer and heart disease. The pill or HRT should be taken up until the age of 47 at which point Gidon talks about the risks and may recommend a Dexascan for bone density.

### **Other Hormonal replacement therapies:**

Oestrogen and Testosterone are very similar molecules – if you have your **ovaries removed** before 45 years of age your testosterone will crash. There is a test for this, but it is not licensed in the UK for the use in women.

Testosterone gel may increase hair growth in the local area it is applied to. Testosterone can lead to loss of libido or enjoyment, however only at higher doses.

Head hair loss is not associated with testosterone supplementation, it is due to genetic factors, iron deficiency, vitamin D deficiency or thyroid problems. Hair quality may improve with oestrogen supplementation.

Testosterone therapy is an additional option, however, GPs don't like to prescribe this.

For **perimenopausal women** who experience fluctuations in mood and periods which are driving them crazy Gidon recommends the pill up to the age of 50 as this is free on the NHS and helps.

The difference between the Pill and HRT is

- Type of oestrogen
- Dosage of oestrogen is much higher in the pill
- Artificial progesterone

### **Bio-identical hormones**

Seemed to be Gidon's pet hate! He thinks

- They're unnecessary as we have identical hormones available on NHS
- Practitioners make a huge amount of money from them
- He worries about the safety of using progesterone cream as not enough (or too much) may be absorbed to balance oestrogen being prescribed
- All hormones are made in factories so they are all 'synthetic'

Bioidentical hormones are known as cBHRT. They are custom compounded hormones from plant sources, oestrogens may include E1 and E3 as well as E2. Progesterone, testosterone and DHEA may also be included. They are marketed as natural supplements and are not regulated and not available on the NHS.

Gidon says that patients should be on micromized progesterone which provides a natural progesterone (but not cyclogest® or norethisterone). Although you can't get Bio-identical hormones on the NHS you can get transdermal hormones which are in effect bio-identical because they are not going through liver metabolism.

## Alternatives to HRT

### 1) For Osteoporosis :

- maximise Vitamin D (1000 IU/day) but not Calcium
- Good diet
- Weight bearing exercise (walking)
- not smoking or drinking (excessively)

HRT is however best for Osteoporosis prevention

### 2) for vasomotor symptoms (hot flushes)

- Venlafaxine (antidepressant)
- Clonidine (anti-hypertensive)
- Gabapentin (anti-epileptic, also used for nerve pain)

### 3) vaginal dryness

- Sylk or Replens (synthetic lubricants)
- Yes organic ([www.yesyesyes.org](http://www.yesyesyes.org))
  - o water based uses natural ingredients like aloe and flax
  - o oil based uses sunflower seed oil, shea butter and almond oil

### 4) palpitations

- beta-blockers
- avoid caffeine
- mindfulness

US/UK Doctors are wary of black cohosh in case of liver failure (comment from Pia, this goes back to feeding rats with high doses of black cohosh and observing liver failure)

If Gidon finds that menopause symptoms remain after using HRT, he will look at depression possibly causing the symptoms.

Gidon runs a complex menopause clinic. Patients include transgender people who eg.as men, find the experience of female menopause symptoms difficult; may need protection from osteoporosis but are reticent to take oestrogen

## Q&A

Tibolone – artificial – oestrogen, progesterone and androgenic (therefore good for libido) – very synthetic – steroid, therefore good for pain. Bi-product of treatment for breast cancer. It is an HRT – see above with regards to risks, complications and side effects.

Minutes by Eve Rogans, Julia Davis, Liz Jeannet, and Pia Huber