

Hormones and Breast Cancer: Still More Questions than Answers

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Old Paradigm

Estrogen is to the breast as
gasoline is to the fire!!

Why doesn't HRT cause more
breast cancer?

For every 1000 women who begin to take postmenopausal hormones at age 50 and who take them for

- ten years there are 6 excess cases of breast cancer
- fifteen years there are 12 excess cases of breast cancer

Study of Osteoporotic Fractures

97 women with breast cancer/244 controls

Postmenopausal/white/not on hormones

- Estradiol levels 30% higher in cases than controls
- Testosterone levels 28% higher in cases than controls

Serum estrogen levels

- Postmenopausal : 5-20 picograms
- HRT : 40 picograms

Paradoxes

- Tamoxifen
 - Hyperestrogenic in premenopausal women and yet prevent second tumors as well as recurrence
 - Stimulation after five years
 - benefit persists for at least 15 years after stopping
- Proliferative disease
 - HRT does not increase cancer in women with proliferative disease
 - Tamoxifen reduces risk with ADH 86%
- BRCA 1
 - pregnancy increases risk
 - Tamoxifen does not decrease risk
 - Oophorectomy decreases risk
 - most cancers are ER negative

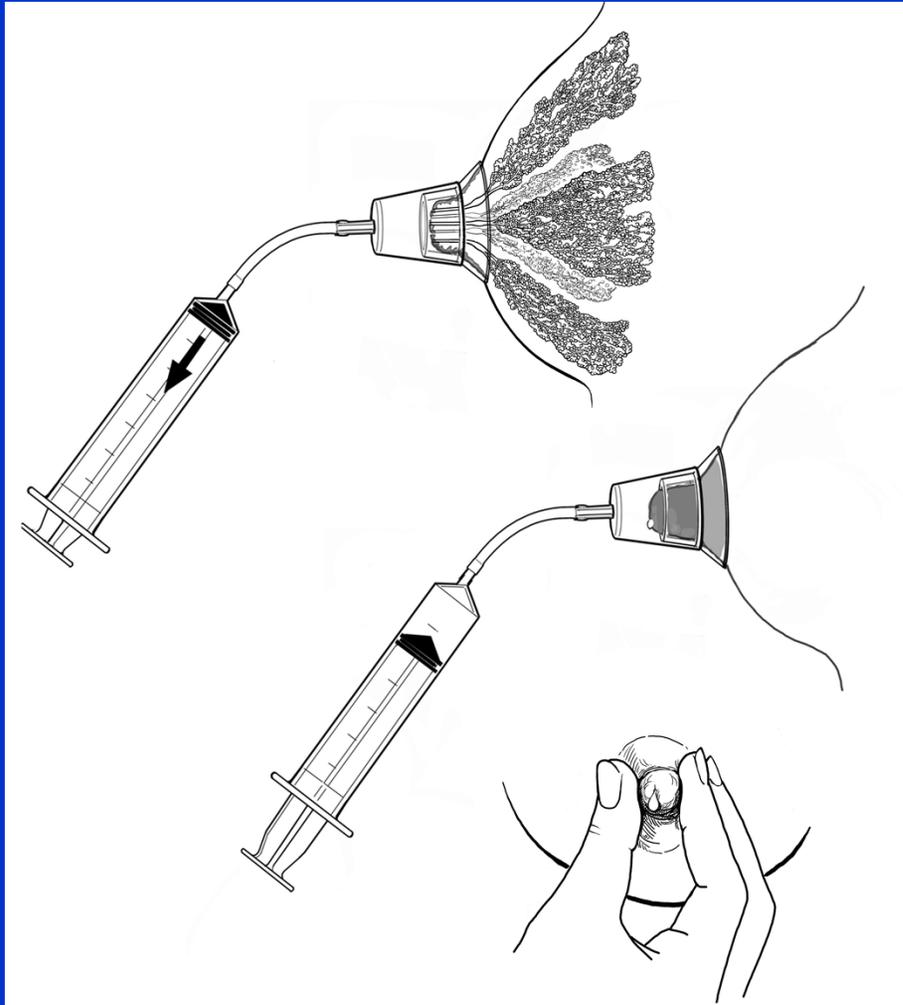
Some thoughts

- There is a threshold level of estrogen and progestin necessary to promote breast cancer
 - HRT has more risk in thin women(Schairer 2000)
 - Raloxifene decreases cancer in women with higher levels of estradiol (Cummings 2000)
 - Breast cancer patients already are there (aromatase?) so more doesn't matter
- Tamoxifen is NOT an antiestrogen
- Could it be local levels are more important?

Intraductal Hormone Levels Independent of Serum Levels

- Premenopausal levels do not fluctuate with the menstrual cycle and are higher than serum
- Pregnancy and breast feeding cause levels to decrease and they gradually climb over 4 years
- Postmenopausal women continue to have higher levels which can be as much as 40 times the level in blood

Nipple Aspirate Fluid



- Gentle suction applied to the nipple
- Massage of the breast
- A drop or two of fluid can be obtained in 80% of women

Breast Duct fluid contents

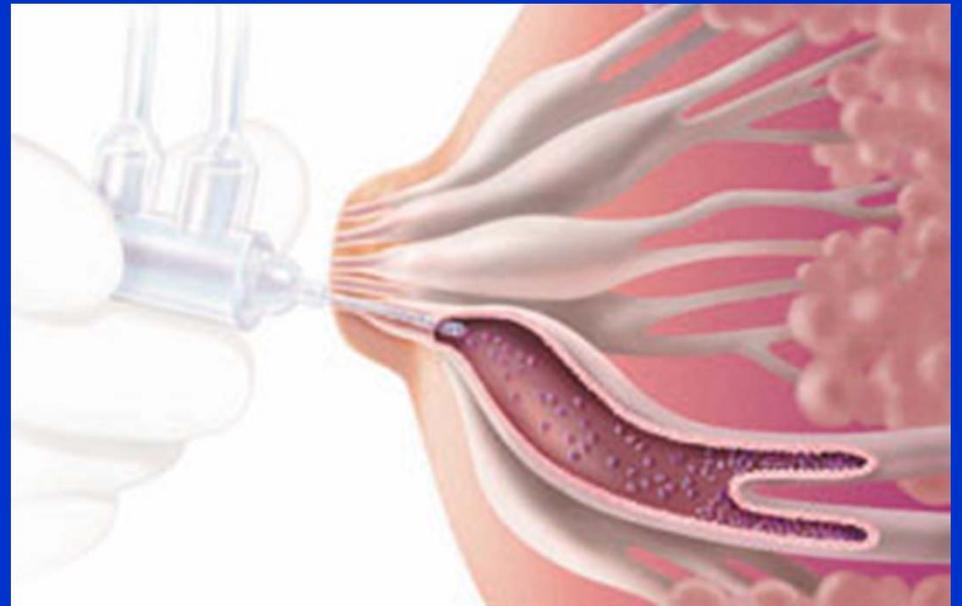
- Immunoglobulins
- Proteins
- Carbohydrates
- Cholesterol and metabolites
- Estrogen
- Testosterone
- Prolactin
- Progesterone
- Dehydroepiandrosterone sulfate
- PSA
- CEA
- LDH
- P53
- Her 2neu
- Nicotine
- Pesticides

Are the ducts different?



Intraductal Access

- Study local environment of the breast ductal cells
- Study metabolism of the non lactating breast



We need some new paradigms!

What do I tell women?

- Short term use of HRT is probably safe if you are not at high risk of heart disease or thrombosis
- After four to five years you should get off
 - Cold turkey
 - Taper over months
- Life style changes are still the best prevention: exercise, diet, not smoking!

Critiques of WHI

- Only studied Prempro
 - Have to assume that everything is dangerous until it is proven to be safe
- Must be the progestin
 - Estrogen alone also increases breast cancer but at a slower rate
- Natural progesterone is okay
 - Increased mammographic density as much as progestin

Women are confused?

We should be excited that we finally have
data

Medicine is a work in progress and this is
progress