



BIO-IDENTICAL
H O R M O N E
REPLACEMENT

Bio-Identical Hormones Introduction & Concepts

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Presenter/Speaker Personal Disclosure

- Presenter's Name: Igor Shaskin
- I have no current or past relationships with commercial entities
- I have received a speaker's fee from the Pharmacy Technician Society of Alberta for this learning activity.

Learning Objectives

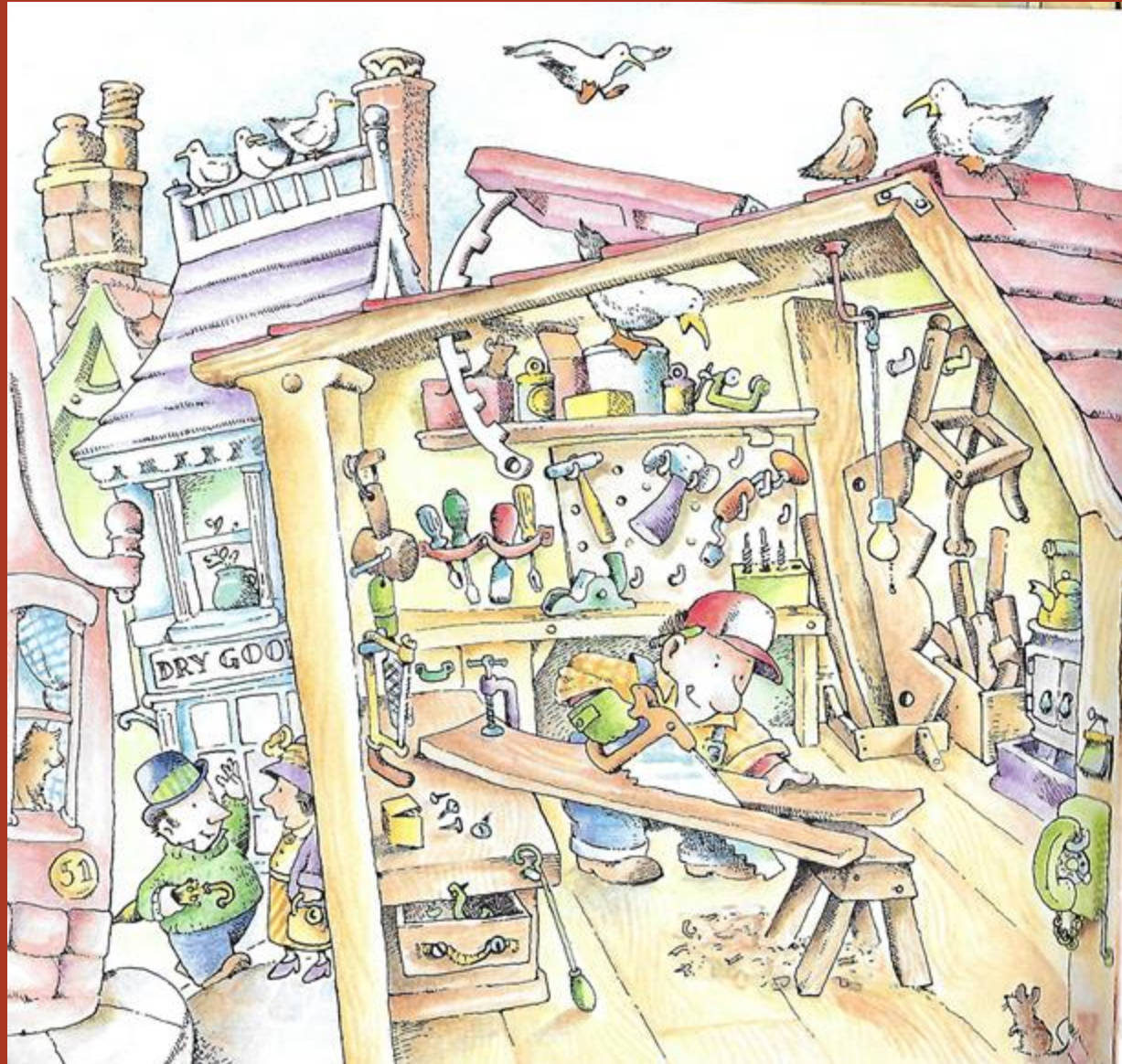
By the end of this presentation, attendees will be able to:

- Determine what bio-identical hormones are
- Determine how they differ from commercially available hormone products
- Understand what makes bio-identical hormones different
- Determine how to discuss route of administration considerations
- Understand how customized hormone therapy works as part of individualized patient care

Why Talk About Bio-Identical Hormone Therapy?

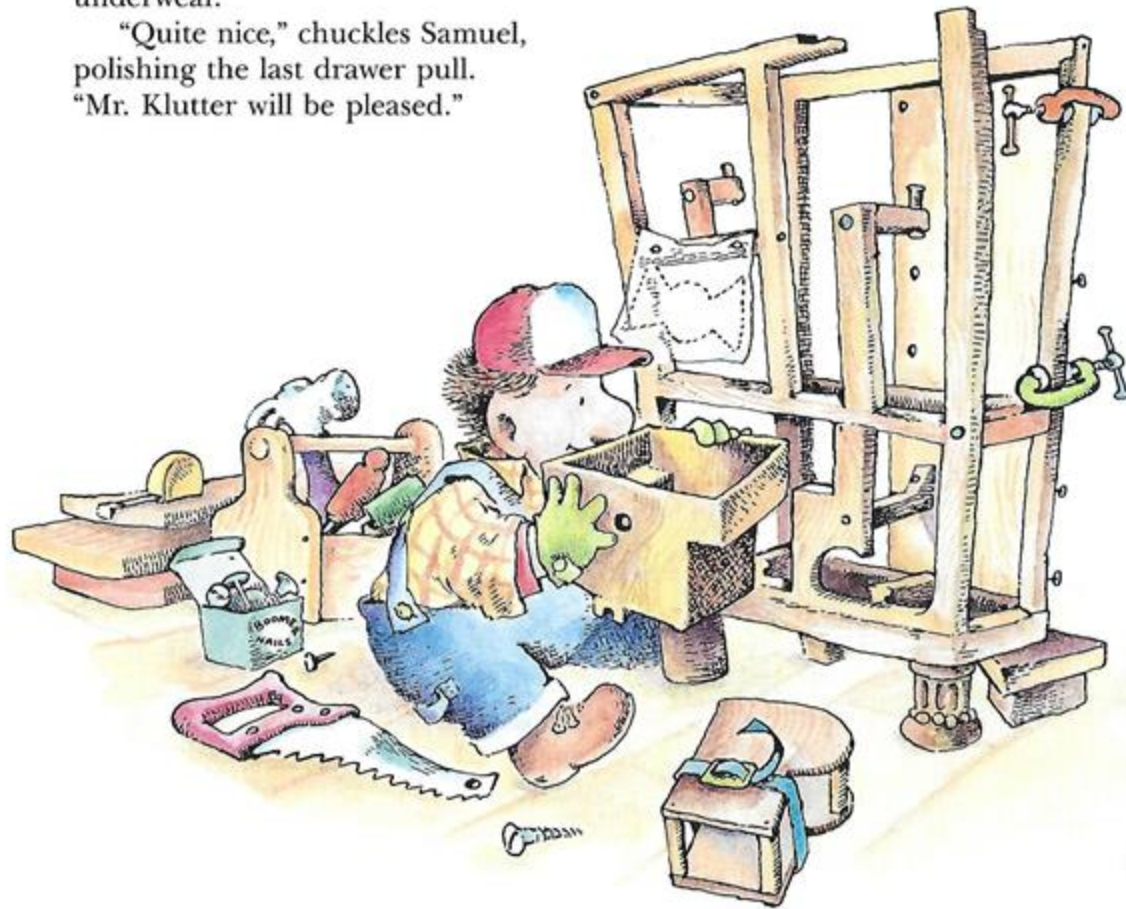
- Began with demand from patients to address symptoms of hormone imbalance
- Patient demand for improved quality of life
- Women's Health Initiative Study (WHI) misguided prescribing of hormones
- Recent re-interpretation of WHI Study
- Years of experience with Bio-identical hormone therapy with positive health outcomes

The Clever Carpenter



He makes a drawer for socks that looks like a sock. He makes a drawer for shirts that looks like a shirt. He makes drawers for ties and pants and underwear that look like a tie and pants and underwear.

"Quite nice," chuckles Samuel, polishing the last drawer pull. "Mr. Klutter will be pleased."



But the next day Mr. Klutter is not pleased.
“These drawers are all wrong. They have funny shapes,”
he complains. “This is not a proper same-drawer-above-as-
below chest at all!”



Mr. Klutter goes away and leaves the chest of drawers.

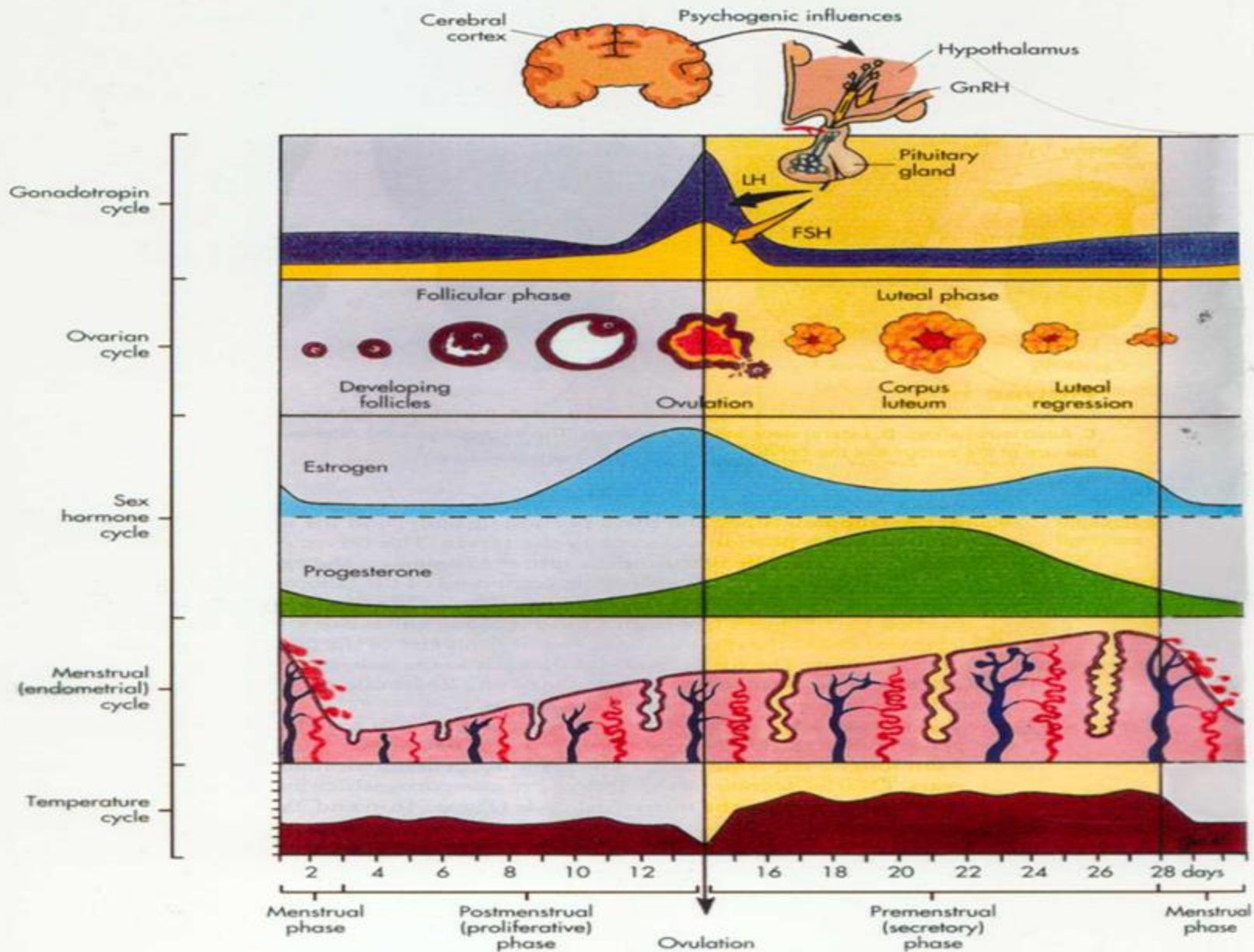


FIGURE 16-6

Female menstrual cycle. Diagram shows the interrelationship of the cerebral, hypothalamic, pituitary, and uterine functions throughout a standard 28-day menstrual cycle. The variations in basal body temperature are also shown.

From Thibodeau and Patton, 1996.

Hormone Balance Disruption

- Surgical menopause
- Premature Menopause – Primary Ovarian Insufficiency
- Perimenopause
- Menopause
- Post Menopause
- Exposure to hormone disruptors

Symptoms

- Irregular periods
- Hot flashes (vasomotor symptoms)
- Night sweats
- Vaginal dryness
- Insomnia
- Dry skin, dry eyes or dry mouth
- Emotional changes
- Worsening premenstrual syndrome
- Breast tenderness

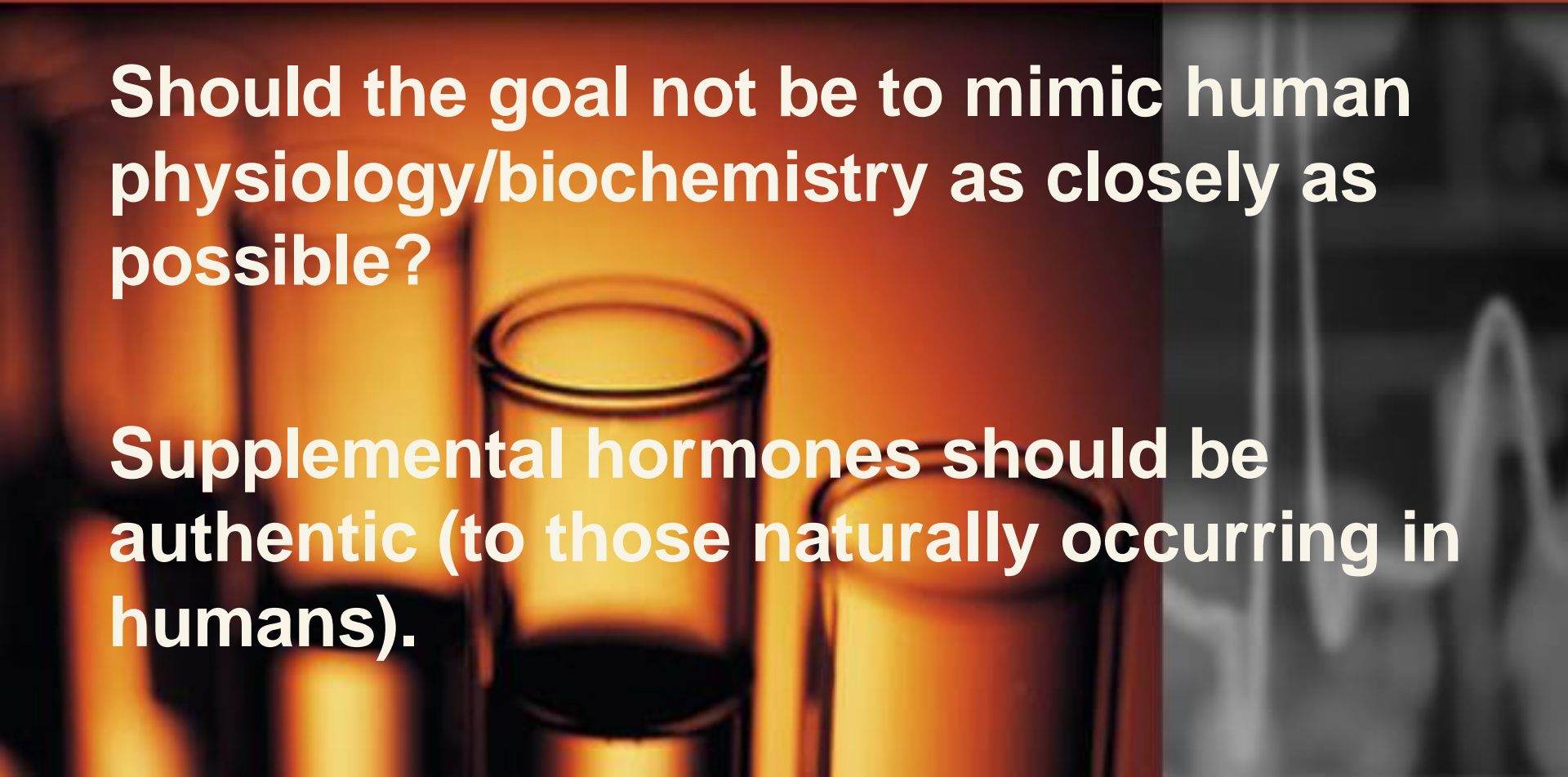
Treatment

- Many require little or no treatment measures
- When symptoms affect quality of life or lead to secondary health issues
- Hormone replacement is warranted
- What hormones should be supplemented and how?

If physiologic hormone replacement is needed...

Should the goal not be to mimic human physiology/biochemistry as closely as possible?

Supplemental hormones should be authentic (to those naturally occurring in humans).



Hormone Replenishment



A logical treatment strategy is to supplement the hormone or hormones that are deficient, bringing physiology back into balance.

Menopause is a natural period of transition. A reasonable treatment approach involves supplementing with adequate hormone – Progesterone and/or Estrogens to maintain the balance, and allowing for the natural overall decrease in hormone levels.

What is a Bio-Identical Hormone?

- The term “bio-identical” indicates that the chemical (molecular) structure of the replacement hormone is identical to that of the hormone that exists intrinsically in the human body.
- This identical structure is important for that hormone to replicate all the functions within the human body. A small structural change can result in a completely different effect and may result in physiologic hormone action being blocked.
- Bio-identical hormones are derived from sources such as soy or wild yam and are **converted in a lab to be bio-identical**.
- Bio-identical characteristic is defined by its structure and function, **NOT** by where it was sourced

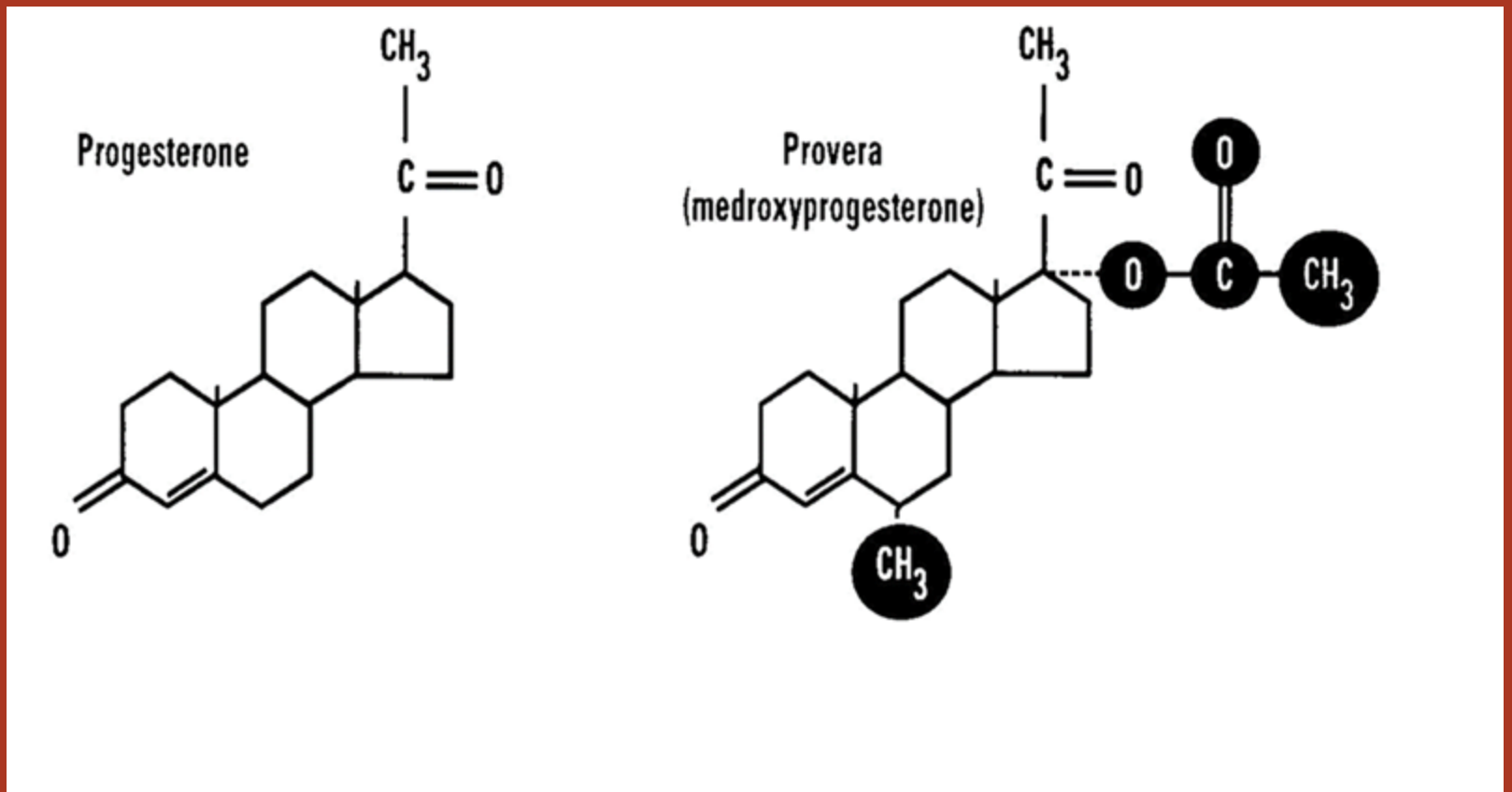
Examples of Hormone Therapeutics

- Diabetes (Type 1): Human insulin
- Human growth deficiencies (GHD): human growth hormone
- Hypothyroidism: thyroid supplementation (T3 and/or T4)

Synthetic Analogs

- Chemical substitution with pharmaceutical drug, not always a true hormone, that mimics some hormonal functions
- Side chains are added to the natural substance to create a synthetic product which is patentable by a manufacturer but creates a drug which may lack full effects of the hormone.

Progesterone vs medroxyprogesterone



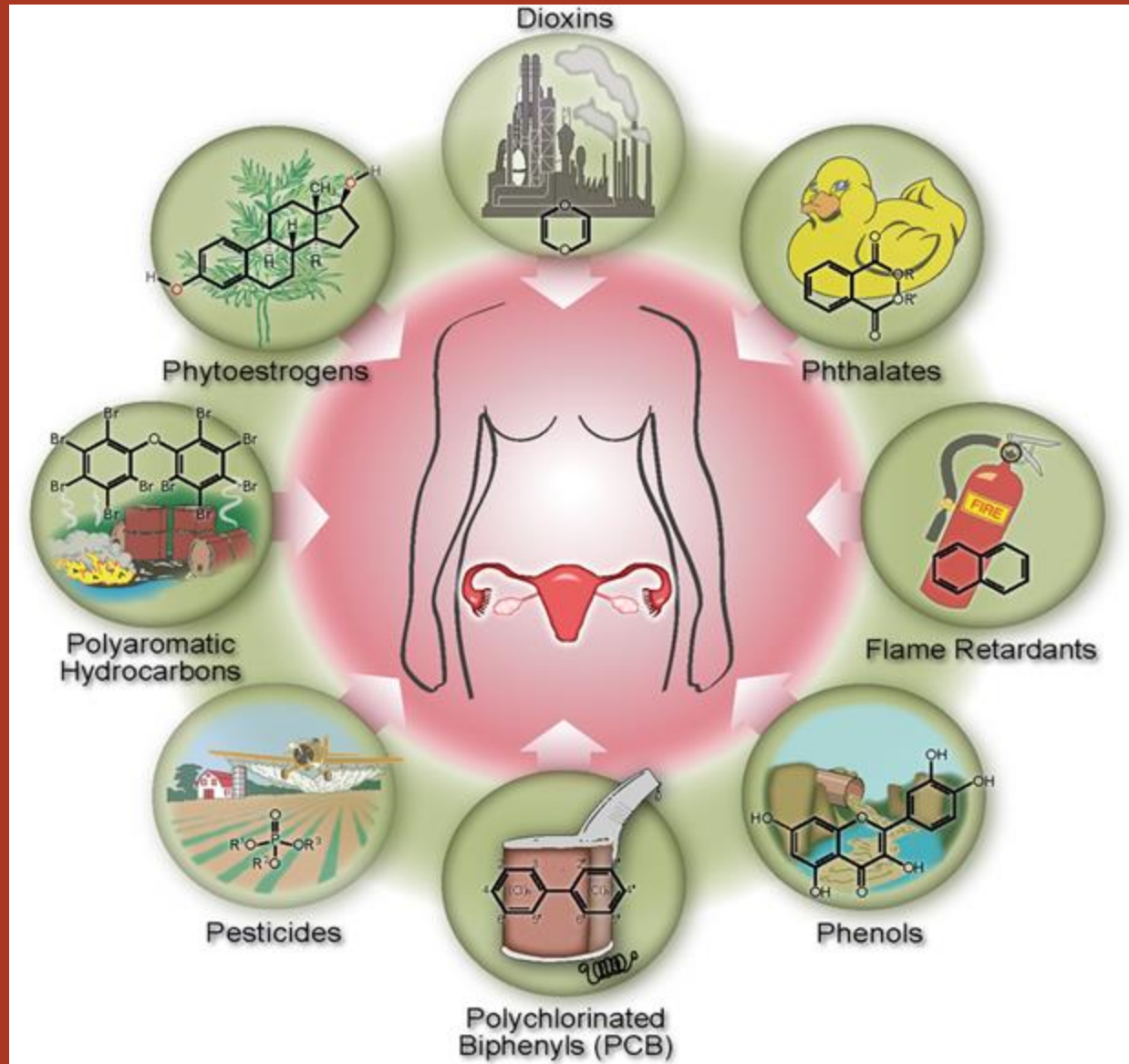
Bio-identical hormones are natural...but natural does not mean bio-identical.



Phytoestrogens

- Not natural estrogens but “**estrogen-like**” compounds.
- Very weak estrogenic activity
- May take long time to get any beneficial effect
- May not provide all the benefits of bio-identical estrogen replacement
- May be a **hormone disruptor**
- Another example of a natural product which is not bio-identical

Hormone Disruptors



Bio-identical hormones of interest

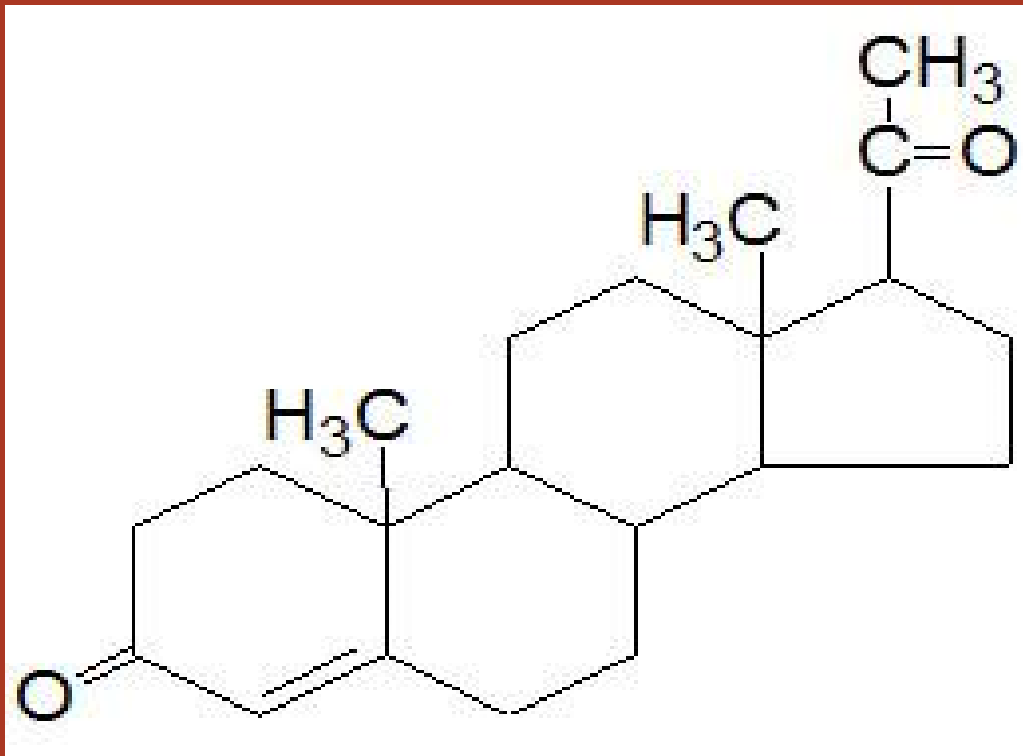
“sex steroid hormones”

- **Progesterone (P4)**
- **Estrogens:**
 - **Estriol (E3),**
 - **Estradiol (E2),**
 - **Estrone (E1)**
- **Testosterone**
- **Pregnenolone**
- **DHEA**

Physiology-Based Hormone Replacement

- Use molecules **identical** to those in the body
- Deliver to tissues in **doses comparable** to or less than normal daily hormone production
- Use a **natural rate** of administration
- Don't feed hormones directly to the liver
- Aim for the same pattern of metabolites as for endogenous hormones
- **Progesterone** as first line

Progesterone



Progesterone

- Oldest known sex hormone
- Present in every human regardless of age
- Secreted by the corpus luteum
- **Has receptors in almost every cell in the body**
- Acts on uterus, breasts, brain, smooth muscle, kidneys, bones, and cellular membranes.
- Metabolized to other active hormones

Progesterone

- Natural anti-depressant and anti-anxiety properties
- Improves sleep quality
- Helps normalize thyroid
- Mobilizes fat for energy
- Has a positive effect on cholesterol
- Works in harmony with Estrogens to prevent bone loss and promote bone growth

Progesterone

- High levels in pregnancy (we all swam in it)
- Causes cells to stop growing and triggers differentiation
- Balances estrogens
- Progesterone level starts to fall in mid to late 30's and with few exceptions shows a rapid drop at menopause
- At menopause, many women see a drop in progesterone before a decrease in estrogen

Oral vs. Transdermal Delivery

- **Oral progesterone** supplementation heavily favours metabolite production (10:1), so 200 mg of oral Pg = 180 mg of metabolites.
- With transdermal delivery, most of the progesterone dose stays as progesterone allowing doses of 30 mg instead of 100 mg.

Progestins

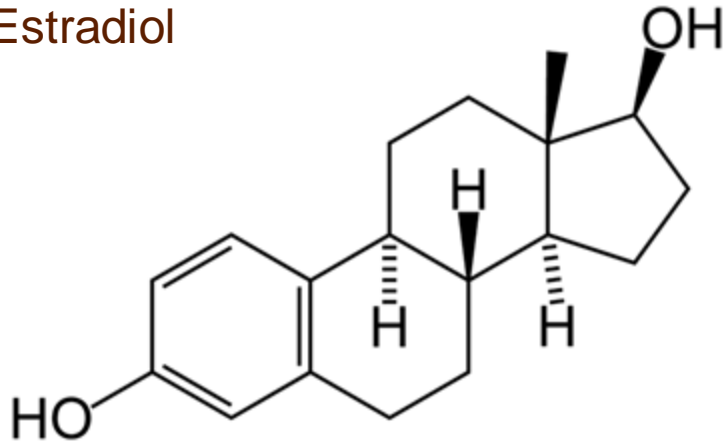
- Progestins (or progestogens) are synthetic, man-made molecules developed to mimic the actions of natural progesterone
- Progestins do not have the full range of activity of natural progesterone

Progesterone Metabolites

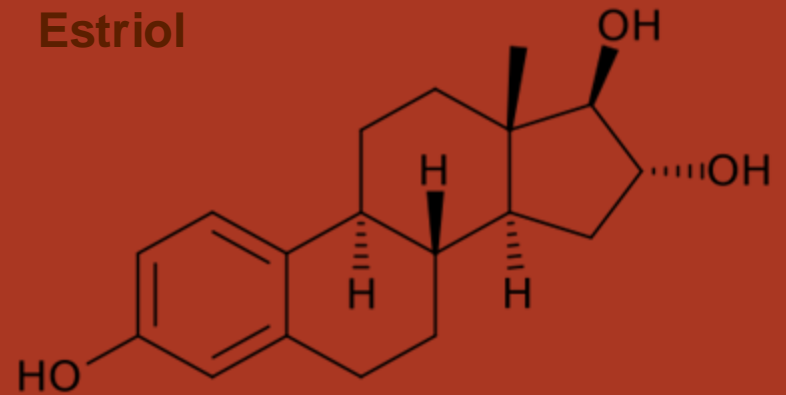
- Sedating metabolites of progesterone are widely recognized:
 - Pregnanolone
 - Allopregnanolone
 - Hydroxypregnanone
- Calm, mellow feeling much like in late pregnancy
- **Oral dosing used** to help with sleeplessness, anxiety, insomnia

Estrogens

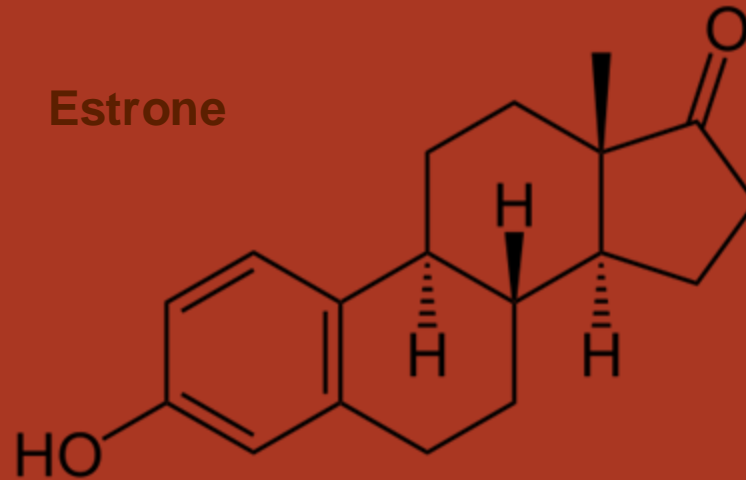
Estradiol



Estriol



Estrone



Endogenous Estrogens

- **Estrone (E1):** the primary estrogenic hormone in the post-menopausal woman. Produced by oxidation of estradiol, also produced in peripheral tissues (adipose cells, liver, and skin) from androstenedione. 50-70% less activity than estradiol
- **Estradiol (E2):** the primary estrogen of ovarian origin and the major estrogenic hormone in the pre-menopausal woman. It is formed by the aromatization of testosterone and a conversion from estrone.
- **Estriol (E3):** a biologically weak estrogen created from the conversion of estrone. Can not be converted to estradiol or estrone. It is at its highest level during pregnancy.

Functions of Estrogens

- Responsible for normal growth and development of female sex organs
- Responsible for maintenance of secondary sex characteristics
- Protect against bone loss, heart disease and other aging dilemmas
- Produce progesterone receptors and control the amount of estrogen receptors
- Promote proliferation and growth of specific cells in the body

Benefits of Bio-Identical Estrogen Replacement Therapy

- Relief of symptoms of menopause
- Reduced risk of heart disease and cardiovascular events
- Improved lipid profile
- Prevention of osteoporosis
- Prevention of memory disorders
- Maintenance of nervous system
- Maintenance of skin health
- Maintenance of oral health
- Maintenance of eye health
- Prevention of urogenital and vaginal atrophy

What have we been doing wrong with Hormone Replacement Therapy (HRT)?

Treated human female patients with:

- Oral Equine estrogen,
- Oral, physiologically similar estrogen,
- Physiologically similar estrogen delivered transdermally,
- Oral Medroxyprogesterone acetate

Similar does not mean **the same or identical**.

This distinction is important.

Bio-Identical Estrogen Replacement

- Estradiol patches (17β estradiol)
- Estradiol gel (17β estradiol)
- Transdermal Estriol-based estrogen combinations (compounded creams) such as:
 - Tri-mix, Bi-mix combinations (compounded) representing estriol/estradiol/estrone or estriol/estradiol.
- Estriol vaginal creams/suppositories
- **And always with Progesterone as part of the regimen!**

Transdermal Estradiol

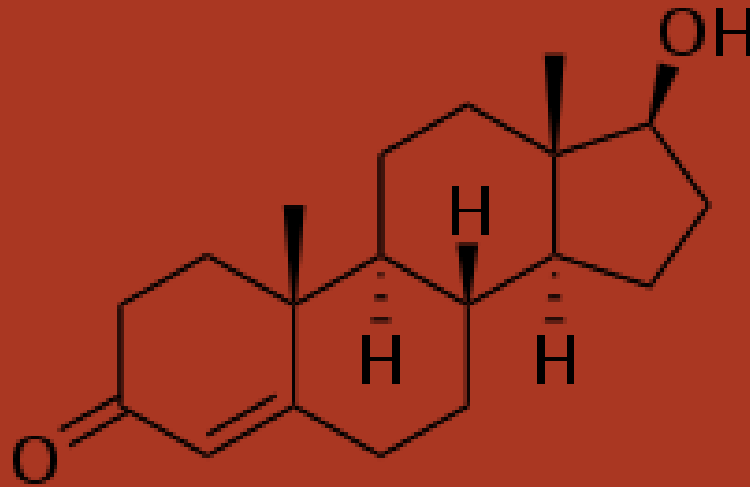
- Efficient delivery – bypassing first pass liver metabolism.
- Allowing a dose that is 20 to 40 times lower than oral dosage forms
- Transdermal Estradiol establishes a normal ratio of Estradiol/Estrone
- Transdermal Estradiol does not affect blood clotting
- Transdermal estradiol does not elevate C-Reactive Protein (CRP)

Oral Estrogen

- Very inefficient way to give estrogen
- We are giving milligram doses
 - 10-50x overdose
- We thought most of it wasn't absorbed
- Much of it goes to estrone and estrone metabolites

NOT the preferred dosing route!

Testosterone



Testosterone in Female Physiology

- Classed as an androgen commonly referred to as the 'male' hormone
- Testosterone production in females
 - 5-25% directly from ovaries
 - Production by the ovary varies with the menstrual cycle, peaking at ovulation due to the LH surge
 - 5-25% directly from adrenals
 - Women produce about 0.3 mg of testosterone daily pre-menopausal
- As women age, ovarian production of testosterone decreases

Benefits of Testosterone

- Maintains normal libido and response
- Increases bone mineral density and preventing further decline into osteoporosis
- Maintains lean body mass
- Increases muscle tone and strength
- Improves memory and structural integrity of the brain itself
- Increases sense of wellbeing ,mood, self esteem

Custom Compounding

- Customized formulations, dosing, and dosage forms to the patient
- Individualize the therapy
- Dosage forms that include oral, sublingual, topical (transdermal), and vaginal
- Infinite dosing options.
- “One size does not fit all”

Progesterone Formulations

- Topical
 - creams/gels
 - 30mg/gm to 200mg/gm
- Oral
 - delayed release capsules
 - 100mg, 200mg
- Vaginal suppositories
 - 100mg, 200mg, 300mg

Estrogen Formulations

- Topical Creams/gels
 - Estriol, Estradiol, Estrone (Tri-Est) 80%/10%/10%
 - Estriol, Estradiol (Bi-Est) 80%/20%
- Estrogen topical dosing: 1ml, 0.5ml, 0.2ml
 - Estriol only
 - 1mg/gm to 20mg/gm
- Vaginal Creams/gels
 - Estriol only
 - 1mg/gm to 20mg/gm
- Some Estriol creams are used both topically and vaginally

Testosterone

- Topical creams
 - 0.25mg/gm to 5mg/gm
- Transitioning to smaller topical volumes
 - Instead of 0.5ml or 1ml, can dispense in 0.2ml metered pumps.
- Larger concentrations only prescribed for males
 - Up to 200mg/gm

Summary – Take Home Notes

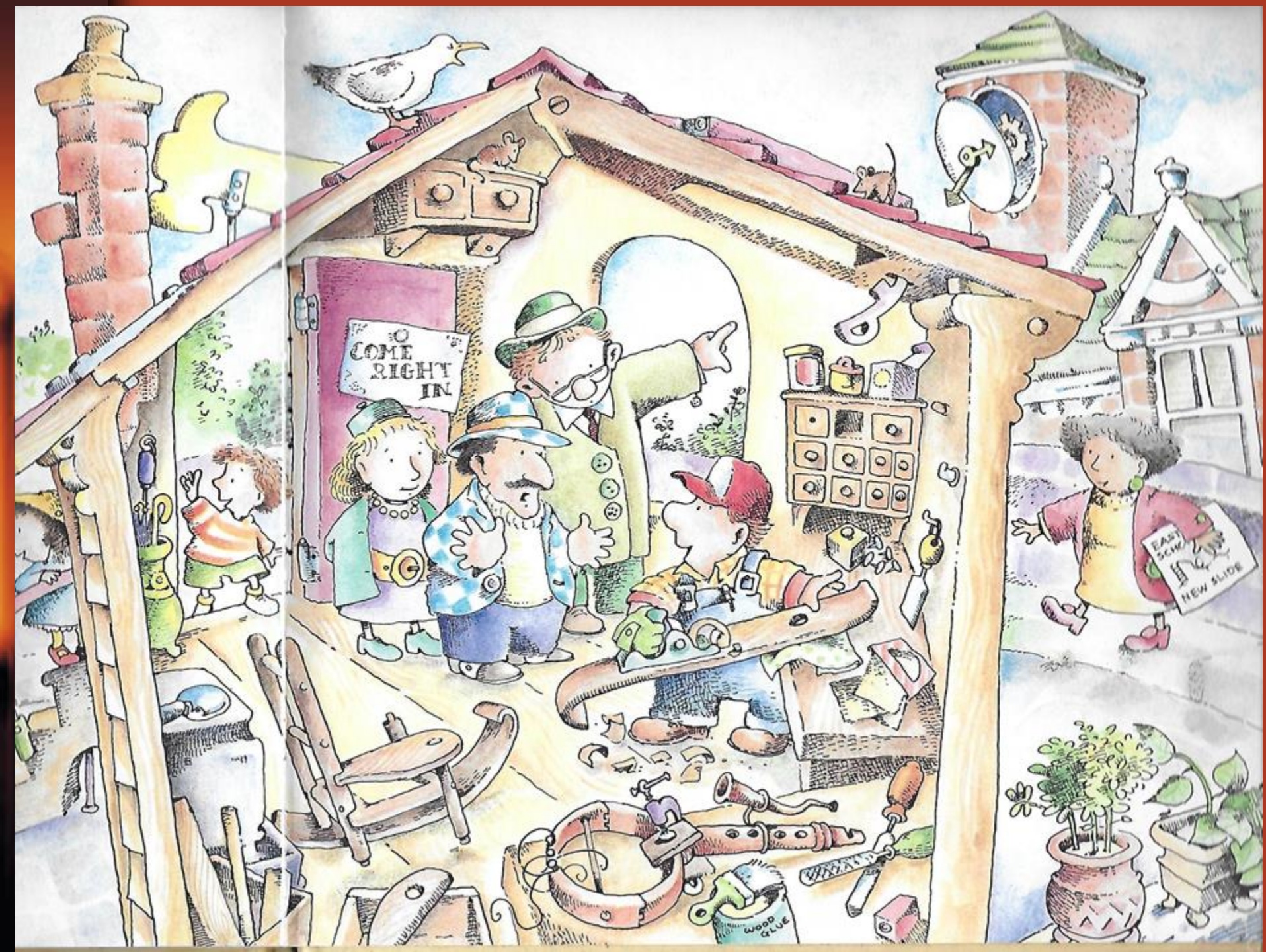
- Bio-identical hormones represent a strategy already in use. Eg., human insulin, human growth hormone, T3/T4 or as whole thyroid.
- Bio-Identical hormones used are identical to those hormones in human physiology
- Human female and male physiology already know what to do with these molecules.
- Absorption, physiologic activity, metabolism and elimination already established.

Summary – Take Home Notes

- Not enough to focus on one hormone
- Recognize the complex inter-relationships between all hormones.
- Must also consider nutrition, lifestyle, stress, existing drug therapy.
- **Customized bio-identical hormones offers flexibility and patient specific therapy.**

Whatever happened to Samuel the Clever Carpenter?





COME
RIGHT
IN

EASY
SCREW
NEW SLIDE

WOOD
GLUE



BIO-IDENTICAL
H O R M O N E
REPLACEMENT

Questions?

