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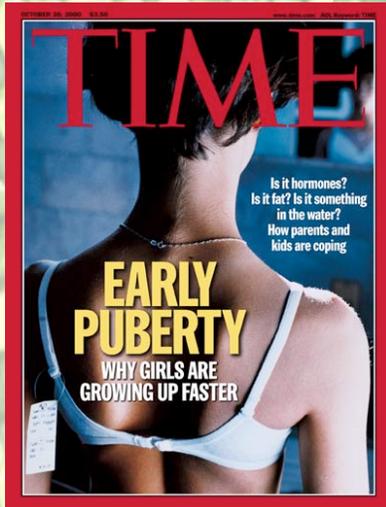


# **Dietary Genistein Decreases the Age and Body Weight of Puberty Onset in Female Syrian Hamsters**

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# Female Puberty



➤ Occurs at a species-specific age

Ovulatory Cycles Begin:

Girls: 12.5 years

Rats: 35 days

Hamsters: 30 days

➤ Puberty is accelerated by environmental factors

Higher plane of nutrition (calories)

Estrogen treatment

Treatment with leptin

Constant light

# **Genistein: an isoflavone found in soy beans and other plants**

## **➤ Isoflavones are a type of phytoestrogen**

- ❖ **Plant-derived, nonsteroidal compounds that are weakly estrogenic or antiestrogenic.**
- ❖ **Bind to the estrogen receptor.**
- ❖ **Found in many soy products such as infant formula, tofu, etc.**

## **➤ Isoflavone Effects**

- ❖ **depend upon the species, the sex, the tissue and the hormonal environment of the individual**
- ❖ **Estrogenic effects: some isoflavones mimic estrogen**
- ❖ **Anti-estrogenic effects: some block estrogen**

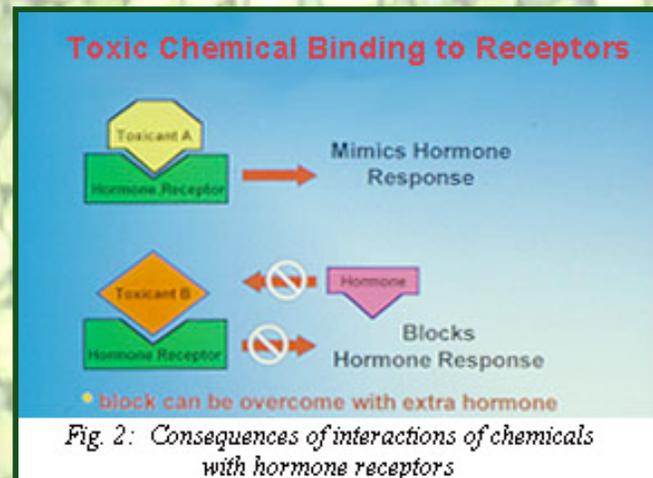
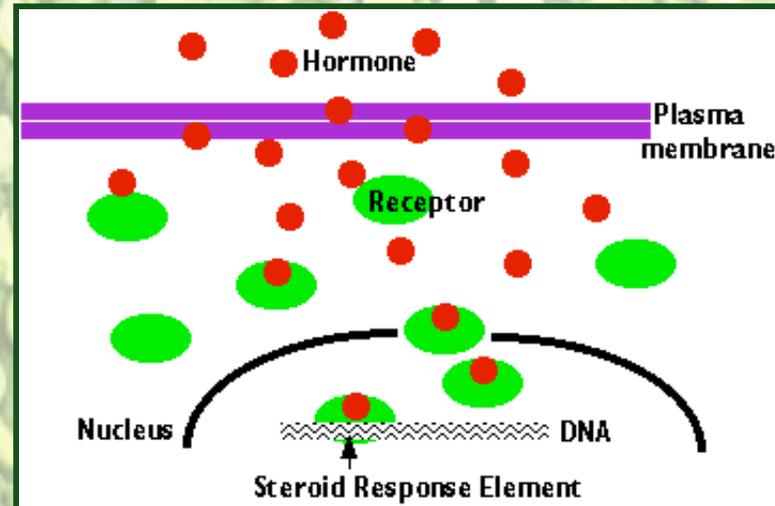
# Isoflavones Bind to Estrogen Receptors

Estrogen binds to estrogen receptors (ER- $\alpha$ , ER- $\beta$ . .) in brain, ovary, uterus and many other body tissues.

Functions of E: puberty, sexual differentiation, bone growth, breast development, brain function, memory, promotes some types of cancer

Other molecules, including soy isoflavones, also bind to ER.

Sometimes they mimic and sometimes they block estrogen action on ER



# Hypotheses

**Genistein, being an estrogen-binding molecule, has the ability to influence the onset of puberty and might also interact with energy availability and storage. Thus. . .**

**❖If genistein mimics estrogen's influence on puberty, we predict puberty will occur earlier in hamsters treated with genistein relative to those fed an isoflavone-free diet and treated with vehicle.**

**❖If genistein blocks estrogen's influence on puberty, we predict puberty will be delayed by genistein treatment.**

**❖If genistein mimics estrogen's influence on energy balance but not on puberty, genistein will decrease food intake and possibly delay puberty.**

# **Syrian Hamsters: A Model System for Female Puberty**

**Signs of sexual maturity:**

**An invariant 4-day estrous cycle**

**Day of ovulation (day 4) determined by  
visual inspection of the vaginal  
discharge**

**Stereotypical sex behavior (lordosis)**



# Diets and Treatments

**At the time of weaning (18 days of age), each litter of hamster pups was divided into 4 groups fed these diets until full sexual maturation:**

**Fat-fed**

**Chow-fed**

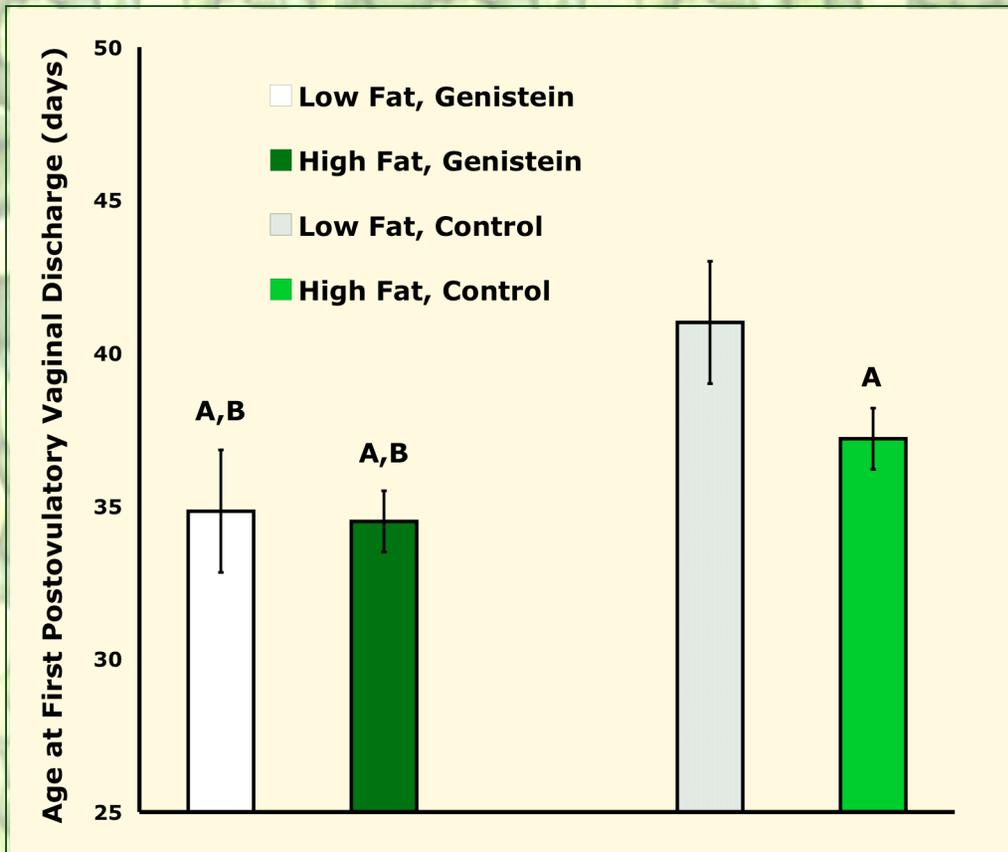
**Fat-fed + genistein**

**Chow-fed + genistein**

**Chow: powdered Harlan Teklad Isoflavone-free Global Diet. The fat-fed groups received this diet mixed with vegetable shortening (2:1)**

**0.1% genistein (Sigma Chemical Co.) was added directly to the food**

## Genistein Treatment Accelerated the Onset of Puberty



**A = significantly different from low fat control**

**B = significantly different from genistein groups**

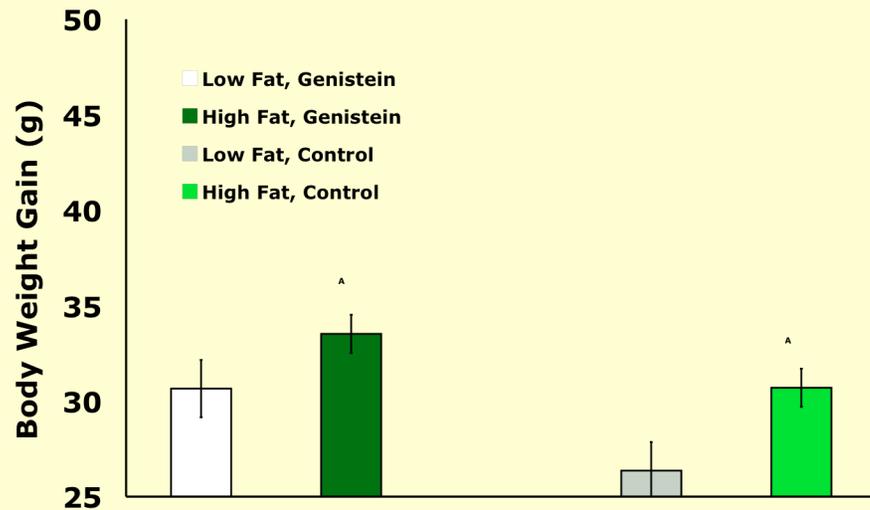
**Two-way ANOVA:**  
significant main effect of genistein, diet and diet X genistein interaction ( $p < 0.05$ ).

**Genestein advanced the age of puberty.**

**High fat diet accelerated puberty in the absence of genistein.**

**High fat diet did not exaggerate the effect of genistein**

## High-fat Diet and Genistein Increased Body Weight Gain

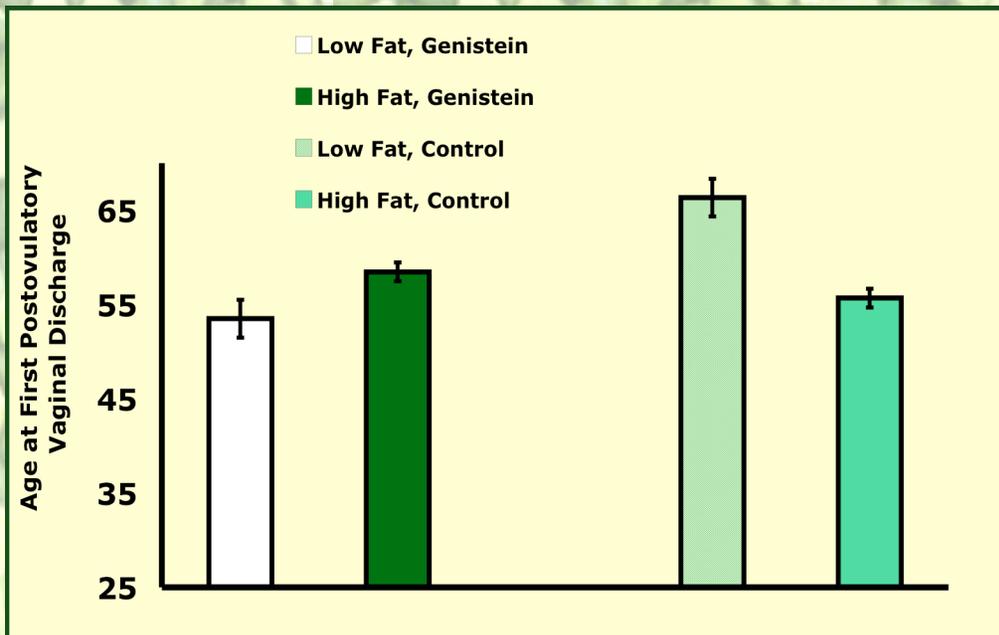


**Two-way ANOVA:**  
significant main effect of high fat diet and genistein ( $p < 0.05$ ), no diet X genistein interaction.

Effects of genistein and diet are additive with respect to body weight gain.

**A = significantly different from low fat control**

## Genistein and High-fat Diet Decrease the Body Weight At Puberty



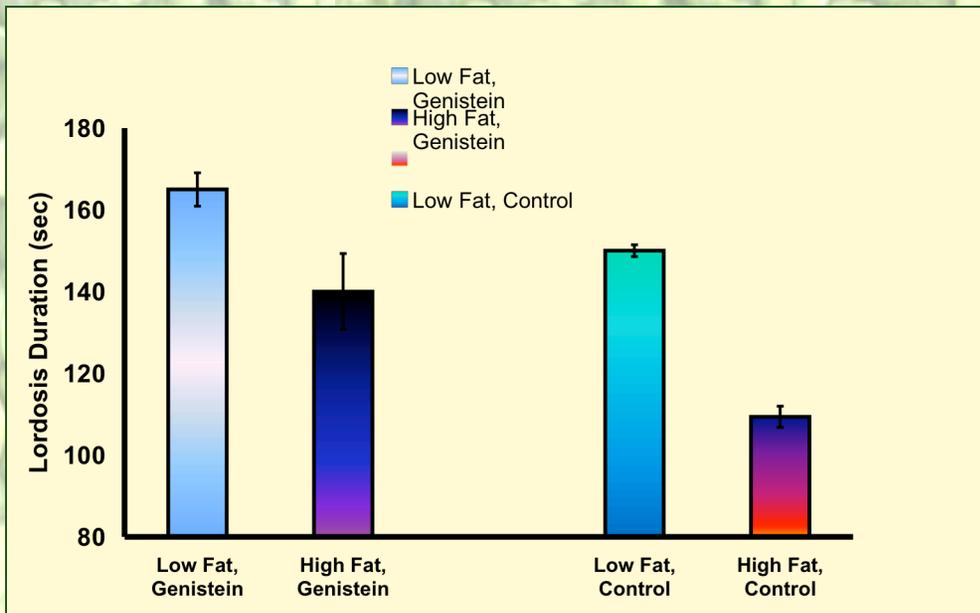
A = significantly different from low fat control

Note that the body weight at puberty differs among the groups:

Two-way ANOVA:  
significant diet X genistein interaction ( $p < 0.01$ ).

Genistein and high-fat diet decreased the body weight at puberty, and the high-fat diet was more effective in decreasing body weight at puberty without genistein.

## Genistein Increased Aspects of Female Sex Behavior in Young Adults



**A = significantly different from low fat control**

**It is interesting that these effects on behavior occurred 12 or more days after the end of genistein treatment**

**Genistein treatment decreased the latency to show adult-typical levels of sex behavior in response to a sexually experienced male.**

**Genistein increased duration of the the sexually-receptive posture (lordosis).**

**High-fat diet decreased lordosis duration and increased latency to lordosis, and counteracted effects of genistein.**

**Genistein delayed the onset of puberty and sex behavior in males (data not shown).**

# Summary

## **Treatment with genistein significantly**

- **decreased the age of onset of estrous cycles**
- **decreased the body weight at which puberty occurred**
- **increased sexual behavior (long after the end of treatment)**
- **caused significant increases in body weight gain, but these gains were not as large as those produced by a high-fat diet.**

## **A high-fat diet**

- **increased caloric intake and body weight gain**
- **decreased the age of onset of estrous cycles**
- **decreased the body weight at puberty**

**A high-fat diet did not accentuate the puberty-advancing effects of genistein, but enhanced the effect of genistein on weight gain, and attenuated the effects of genistein on sex behavior.**

**Puberty did not occur at the same body weight in all groups, demonstrating that puberty does not depend on reaching a “critical body mass.”**

# Discussion

The puberty advancing effects of genistein in hamsters were similar to the known puberty advancing effects of E treatment in rats (Fig. 1 and Piavec, 1975).

It is unlikely that genistein caused early puberty by enhancing growth because early puberty occurred at a lower body weight, and the effects of genistein were not enhanced or attenuated by a growth-inducing high-fat diet (Figs. 2 & 3).

It is most likely that genistein advanced puberty via its ability to act as an agonist to the estrogen receptor (ER), not indirectly via effects on energy balance.

The high-fat diet also caused earlier puberty and faster weight gain, but the advanced puberty was probably not caused by the increasing body weight, because early puberty in the high-fat group occurred at a lower body weight than chow-fed controls. Furthermore, the high fat diet did not enhance the puberty-advancing effects of genistein.

It is possible that the high fat diet enhanced E levels or sensitivity to E, perhaps because fat cells produce aromatase (the enzyme that converts testosterone to E) and leptin (which is known to increase E synthesis/secretion).

In other words, genistein and the diet might have been doing the same thing to puberty via the brain E receptors.

# Caveats

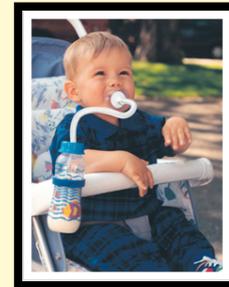
**This study is only a beginning and other investigators have conducted far more sophisticated and thorough investigations of the effects of isoflavones (see references).**

**This study was done in hamsters, and there is no guarantee that the effects of genistein in this study can be generalized to human beings.**

**This study used only one isoflavone and cannot necessarily be used to generalize to other isoflavones (such as daidzein) and cannot be used to generalize to soy infant formula or other soy products, which contains a variety of isoflavones.**

**TAKE HOME MESSAGE (TATOO FACT): Compounds in soy products have effects on the reproductive system in mammals, including long lasting effects on behavior, usually by binding to the estrogen receptor.**

**IT IS WORTH INVESTIGATING THESE EFFECTS BEFORE FEEDING THEM TO PEOPLE, ESPECIALLY BABIES.**



## References (Updated Regularly)

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