LUPRON: DOES LUPRON PUT YOU INTO MENOPAUSE?

Amenorrhea (loss of your menstruation) can be due to four different causes:
1. disorders of the pituitary gland;
2. disorders of the hypothalamus and central nervous system;
3. disorders of the ovaries;
4. disorders of the uterus. (9, 12)

I. HYPOPHYSECTOMY
A Hypophysectomy is the destruction or excision [removal] of the pituitary gland.

1. In 1988, Bischof and Herrmann stated their "results as well as clinical evidence indicate that sustained treatment with GnRH agonists most likely abolishes pituitary function." (6)

2. In 1988, Henig, Rawlins, Weinrib and Dmowski stated that a "medical [drug] hypophysectomy [is] induced with gonadotropin-releasing hormone agonists (GnRHa)." (4)

3. In 1989, Florence Comite, a lead investigator of GnRH-a at the NIH (National Institute of Health) stated that "GnRH analogs decrease ovarian steroidogenesis through selective hypophysectomy." (5)

DOWN-REGULATION or DESTRUCTION of PITUITARY RECEPTORS:

Downregulation of Receptors - "the unusually rapid loss of receptor activity called 'downregulation' has been confused with receptor blockade [blocking the receptor] and is now understood to be due to a disappearance of the receptor." (13)

1. "Continuous therapy with leuprolide [Lupron] apparently produces a decrease in the number of pituitary GnRH receptors." (14)
2. Friedman et al stated that "down-regulation of pituitary GnRH receptors is usually achieved" "between treatment weeks 2 through 7." (15)

H. The Hormone Profile of a Woman on Lupron DOES NOT MATCH The Hormone Profile of a Woman in Menopause.

A. FSH & LH (Gonadotropins) Levels

B. Estrogen (Estradiol) Levels

A. FSH & LH Levels In Menopause vs. Lupron:
(HYPERgonadotrophic Hypogonadism vs. HYPOgonadotrophic Hypogonadism)
**Hypogonadotrophic** - decreased FSH and LH [occurs with Lupron]
**Hypergonadotrophic** - increased FSH and LH [occurs in menopause]
**Hypogonadism** - low estrogen / testosterone levels.

FSH - Follicle stimulating hormone LH
- Luteinizing hormone

Chart I. COMPARISON OF FSH, LH & ESTROGEN LEVELS* (* approximate values)
1. Lupron causes "hypogonadotropic [decreased FSH & LH] hypogonadism" and both surgical ovariecotomy [removal of ovaries] and menopause cause "hypergonadotrophic [increased FSH & LH] hypogonadism." (7)
2. Kurabayashi et al stated that hypogonadism due to the administration of GnRHa is different from that caused by surgical ovariecotomy [removal of ovaries] or menopause." (7)
3. In gonadal failure associated with low estradiol [estrogen] levels in women, gonadotropin [FSH, LH] measurements help separate primary from central hypogonadism:
   a. high gonadotropin [increased FSH, LH] concentrations are indicative of primary gonadal failure [See Chart I #1 above];
   b. low or normal gonadotropin [decreased FSH, LH] concentrations suggest hypothalamic or pituitary disease [See Chart I #2 above]." (8)

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Normal Menstruating Woman</th>
<th>Menopause (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol (E2) (pg/ml):</td>
<td>23-56</td>
<td>23-500 lower than 20 *</td>
</tr>
<tr>
<td>Follicle Stimulating Hormone (FSH) [(mIU/ml):</td>
<td>5-28</td>
<td>5-41 30-170</td>
</tr>
<tr>
<td>Luteinizing Hormone (LH) (mIU/ml):</td>
<td>5-26</td>
<td>2-187 30-150</td>
</tr>
<tr>
<td>Progesterone (ng/ml):</td>
<td>0.2-0.6</td>
<td>0.2-32 lower than 0.2</td>
</tr>
</tbody>
</table>

Table II. FSH & LH LEVELS IN MENOPAUSE vs. LUPRON

<table>
<thead>
<tr>
<th>MENOPAUSE</th>
<th>Follicle Stimulating Hormone (FSH)</th>
<th>Luteinizing Hormone (LH)</th>
<th>Estrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypergonadotropic Hypogonadism</td>
<td>Increases</td>
<td>Increases</td>
<td>Decreases</td>
</tr>
<tr>
<td>LUPRON</td>
<td>HYPOgonadotropic Hypogonadism</td>
<td>Decreases</td>
<td>Decreases</td>
</tr>
</tbody>
</table>
B. Estrogen Levels In Menopause vs. Lupron

1. ESTROGEN LEVELS IN MENOPAUSE:
   a. Barbieri stated that a "severely hypoestrogenic state is an estradiol [E2] concentration of 10 pg/ml." (2)
   b. A menopausal level of estradiol (E2) is equal to or less than 20 pg/ml. (See Table 1 above)

2. ESTROGEN LEVELS WITH LUPRON:
   a. According to FDA documents that examined the suppression of estradiol levels (E2) in women taking Lupron for endometriosis, when "monthly E2 levels were drawn, it appears that at month 2 and 4, mean E2 levels were higher than the upper limits of normal for postmenopausal E2 levels." (3) (See Table III below and compare to Table I)
   b. The drug company (TAP/Abbott) stated that "complete E2 suppression is NOT required for treatment of symptoms of endometriosis. In fact, lack of ovulation, probably plays a major role. They provided some papers to substantiate their claim." (3)

   Table III Estradiol Levels of Lupron Patients Reported to the FDA (3)

<table>
<thead>
<tr>
<th>MONTH</th>
<th>Mean (Average) E2 levels (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>38 NOT A MENOPAUSAL LEVEL (Menopause =&lt;20 pg/ml)</td>
</tr>
<tr>
<td>3</td>
<td>19 NOT A MENOPAUSAL LEVEL (Menopause =&lt;20 pg/ml)</td>
</tr>
<tr>
<td>4</td>
<td>39 NOT A MENOPAUSAL LEVEL (Menopause =&lt;20 pg/ml)</td>
</tr>
<tr>
<td>5</td>
<td>21 BORDERLINE (Menopause =&lt;20 pg/ml)</td>
</tr>
<tr>
<td>6</td>
<td>14</td>
</tr>
</tbody>
</table>

   c. In this study [SEE Table III above] "E2 [estrogen] levels were done every month, thus there is a great deal of information." (3)
   In the next study done for endometriosis, and studies for their fibroid application, "E2 [estrogen] levels were only done at 3 and 6 months, providing incomplete information." (3)
   d. "Most of the patients with high E2 [estrogen] levels had either menstrual bleeding or 'breakthrough' bleeding." (3)
      - "Instances of spotting were reported on at least one occasion after suppression* of menses in 17 of the 27 [63%] LA [Lupron] patients." (3) *"Suppression was defined as no menstrual-like bleeding for more than 60 days."
      - "68% of lupron patients noted irregular bleeding." (3)

REFERENCES:

(3) US Food and Drug Administration, NDA # 120-011; Lupron Depot for the treatment of endometriosis.