



Management of Fibroids with Leuprolide Acetate

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Outline

Definition

Epidemiology

Pathophysiology

Signs and Symptoms

Management Option

Uterine Fibroids

- **Monoclonal benign tumors that arise from the uterine smooth muscle tissue**
- Composed of disordered myofibroblasts buried in abundant quantities of extracellular matrix
- Increased Estrogen and progesterone receptors compared to surrounding myometrium
- Prevalence: 16.7% - 30% of reproductive-age
- By the age of 50 years 70-80% of women will have at least one fibroid
- **It is more common in African-descent**
- **20-50% are symptomatic**

SOGC 2015/ Eduard et al 2024



Etiology and Risk factors

- Exact aetiology not known
- Monoclonal origin (arising from a single cell)

Genetic basis definite-

- 40%-(translocation chromosome 12/14, rearrangement of short arm Ch6, rearrangement of long arm Ch10 , deletion at Ch3 , Ch. 7q, trisomy 12)
- Various growth factors like TGF β , EGF, IGF-1, IGF-2, and BFGF are recently implicated in the development of fibroids.

Hormonal dependence:

- estrogen may contribute to tumor enlargement by increasing the production of extracellular matrix. While Progesterone increases Mitotic activity

- Early menarche
- Null parity
- Age (Older women > younger age)
- African descent
- Family history of Fibroids
- Obesity

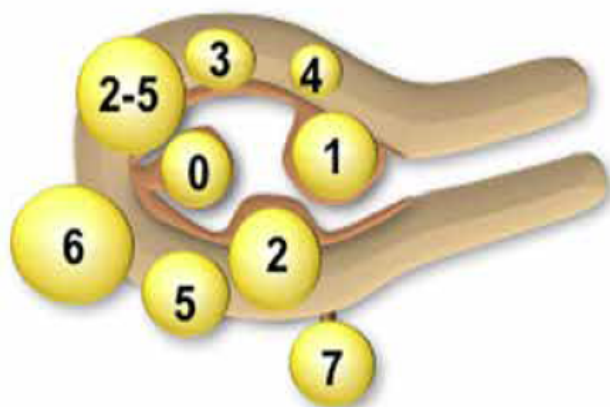
Factors that lower the risk for fibroids

- Pregnancy
- Low-term use of COC or injectable contraceptive

Stewart E.A et al BJOG 2017

FIGO SUBCLASSIFICATION

Leiomyoma Subclassification System



| | | |
|-----------------------|---|--|
| S – Submusosal | 0 | Pedunculated intracavitary |
| | 1 | < 50% intramural |
| | 2 | ≥ 50% intramural |
| O – Other | 3 | Contacts endometrium; 100% intramural |
| | 4 | Intramural |
| | 5 | Subserosal ≥ 50% intramural |
| | 6 | Subserosal < 50% intramural |
| | 7 | Subserosal pedunculated |
| | 8 | Other (specify e.g. cervical, parasitic) |

| | | |
|--|--|--|
| Hybrid leiomyomas (impact both endometrium and serosa) | Two numbers are listed separated by a hyphen. By convention, the first refers to the relationship with the endometrium while the second refers to the relationship to the serosa. One example is below | |
| | 2-5 | Submusocal and subserosal, each with less than half the diameter in the endometrial and peritoneal cavities, respectively. |

Pathology of Fibroids



Gross Appearance:

- Multiple, discrete, spherical, pinkish-white, firm capsulated masses protruding from the surrounding myometrium. Pseudo capsule is made up of compressed myometrium giving it a distinct outline

Microscopy-

- Non-striated muscle fibres are arranged in interlacing bundles of varying size & running in different directions (whorled appearance).
- Varying amounts of connective tissue is intermixed with smooth muscle fibres

Secondary changes- Hyaline, calcific, necrosis, red degeneration during pregnancy, fatty degeneration

Leiomyosarcoma- 0.49-0.79%, more common in the 5th decade, diagnosed with the presence of mitotic figures

Fibroids and symptoms

Fibroids growth is influenced by oestrogen and progesterone levels.

The biologically potent estrogen estradiol induces the production of PR by means of ER- α . PR is essential for the response of fibroid tissue to progesterone secreted by the ovaries

- Heavy or prolonged menstrual periods with associated anemia
- Abnormal uterine bleeding -.
- Pelvic pain
- Obstructive symptoms
- Torsion
- Infertility

Effects in pregnancy

- Abortions
- Pressure symptoms and Abdominal pain
- Malpresentation
- Preterm Labour
- Dystocia in Labour
- PPPH
- Poor sub involution
- Puerperal sepsis

Treatment

Individualized based on

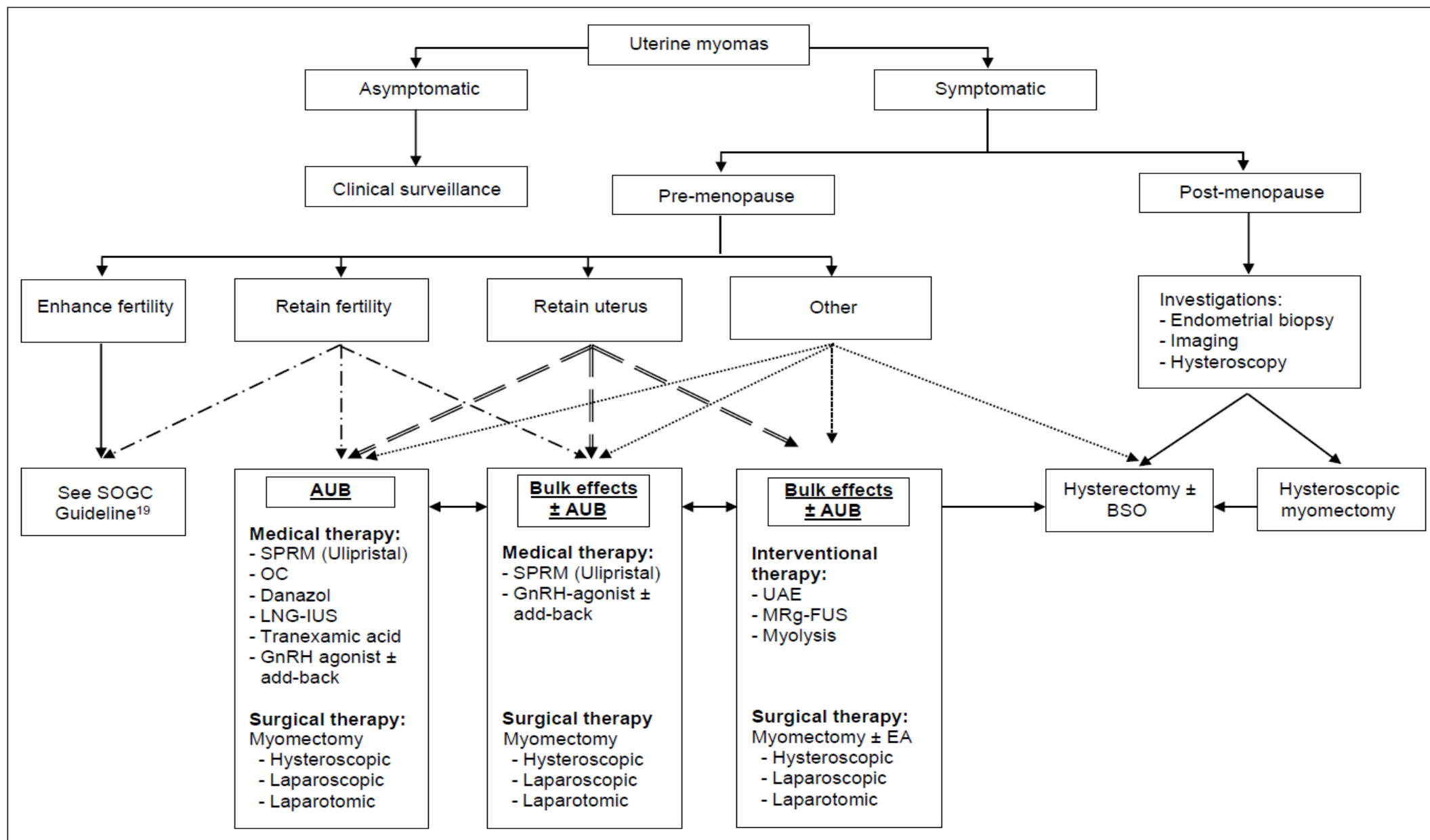
- Symptomatology,
- Size
- Location of fibroids
- Age
- Experience of the therapist.

Medical

- Non-steroidal anti-inflammatory drugs
- Levonorgestrel Intrauterine device
- **GnRH agonists**
- Ulipristal
- Danazole
- Oral contraceptives
- Uterine artery embolization
- Myolysis
- Magnetic Resonance focused scan

Surgical

- Myomectomy
- Hysterectomy

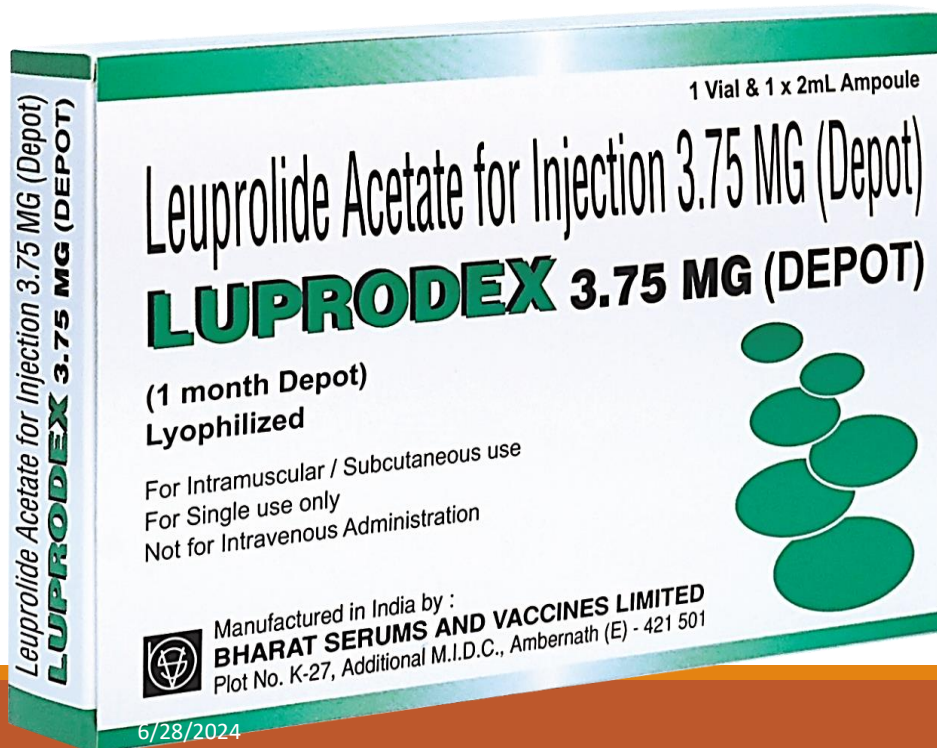


Rx **Luprodex**TM
Leuprolide Acetate Injection (DEPOT 3.75 mg)

Leuprolide acetate 3.75 mgs sc for 3 months

Effect

Produce profound hypoestrogenism



GnRH analogues

Gonadotrophin releasing hormone (GnRH) analogues are synthetic drugs(decapeptide) modeled like natural human hypothalamic Gonadotrophin releasing hormone.

GNRH agonists and Antagonists

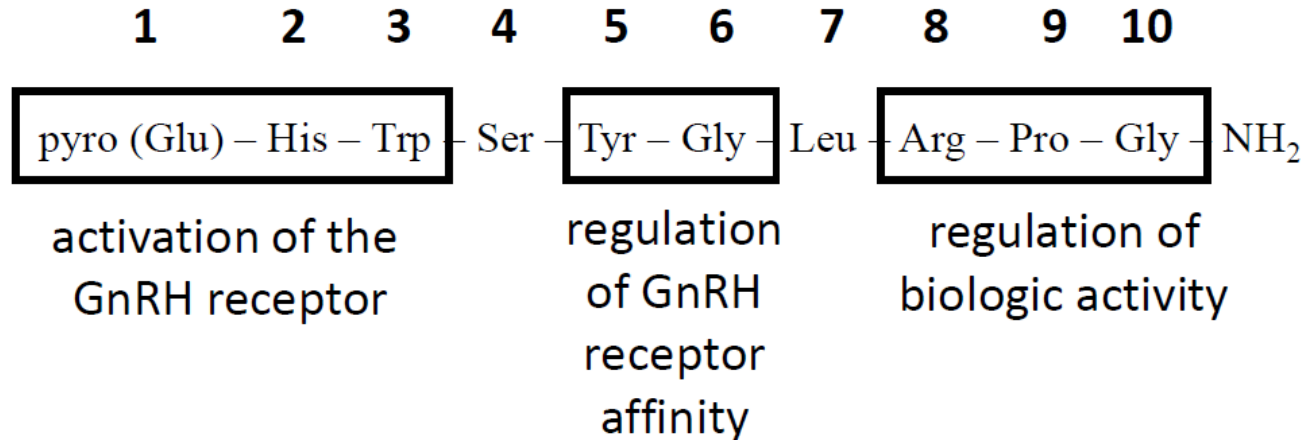
Substitution of an amino acid at the 6 or 10 position results in analogues with agonistic activity.

Modification at the 2 or 3 position results in analogues with antagonistic properties.

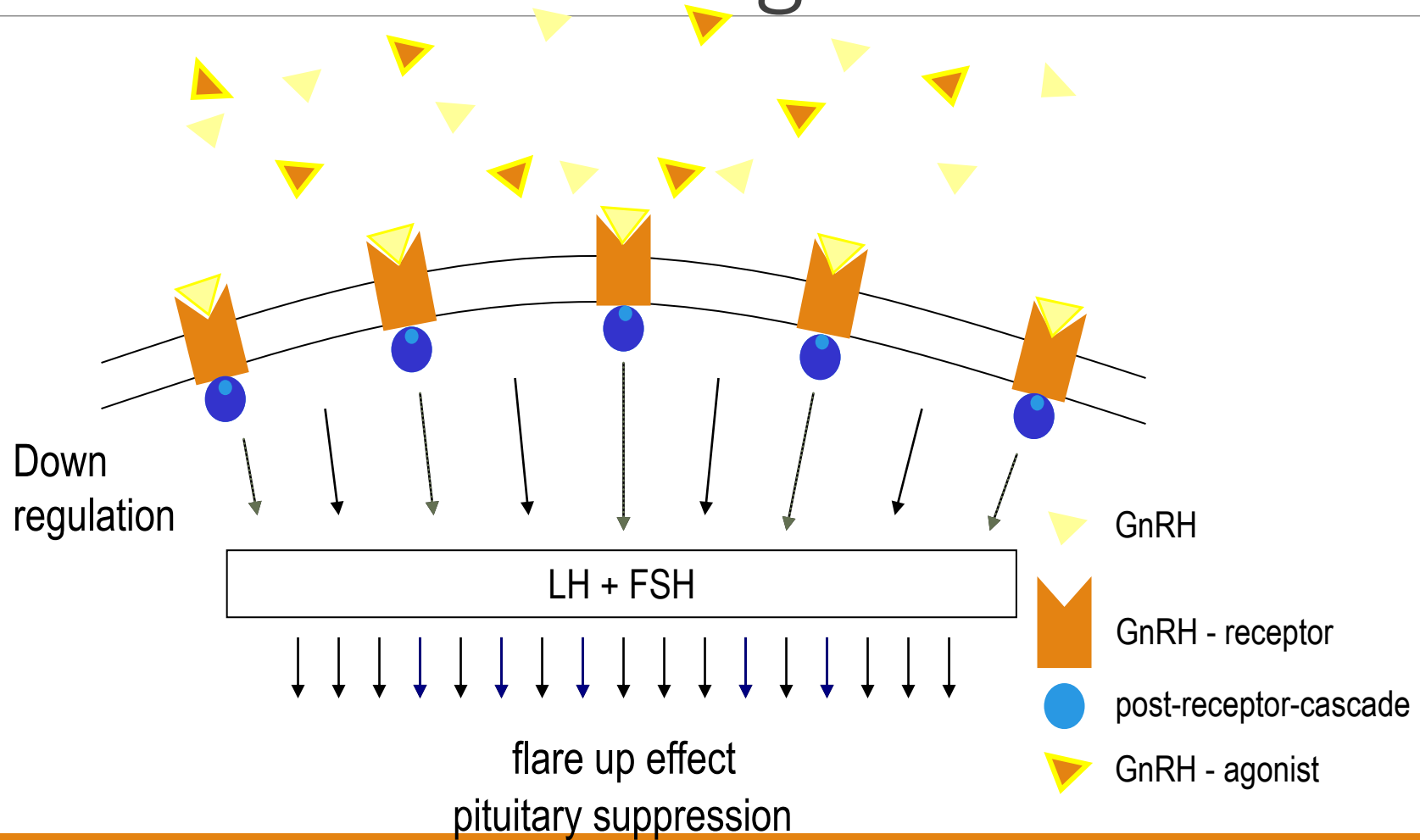
The deletion of an amino acid at the 10 position also increases the binding affinity of analogues

GnRH analogues

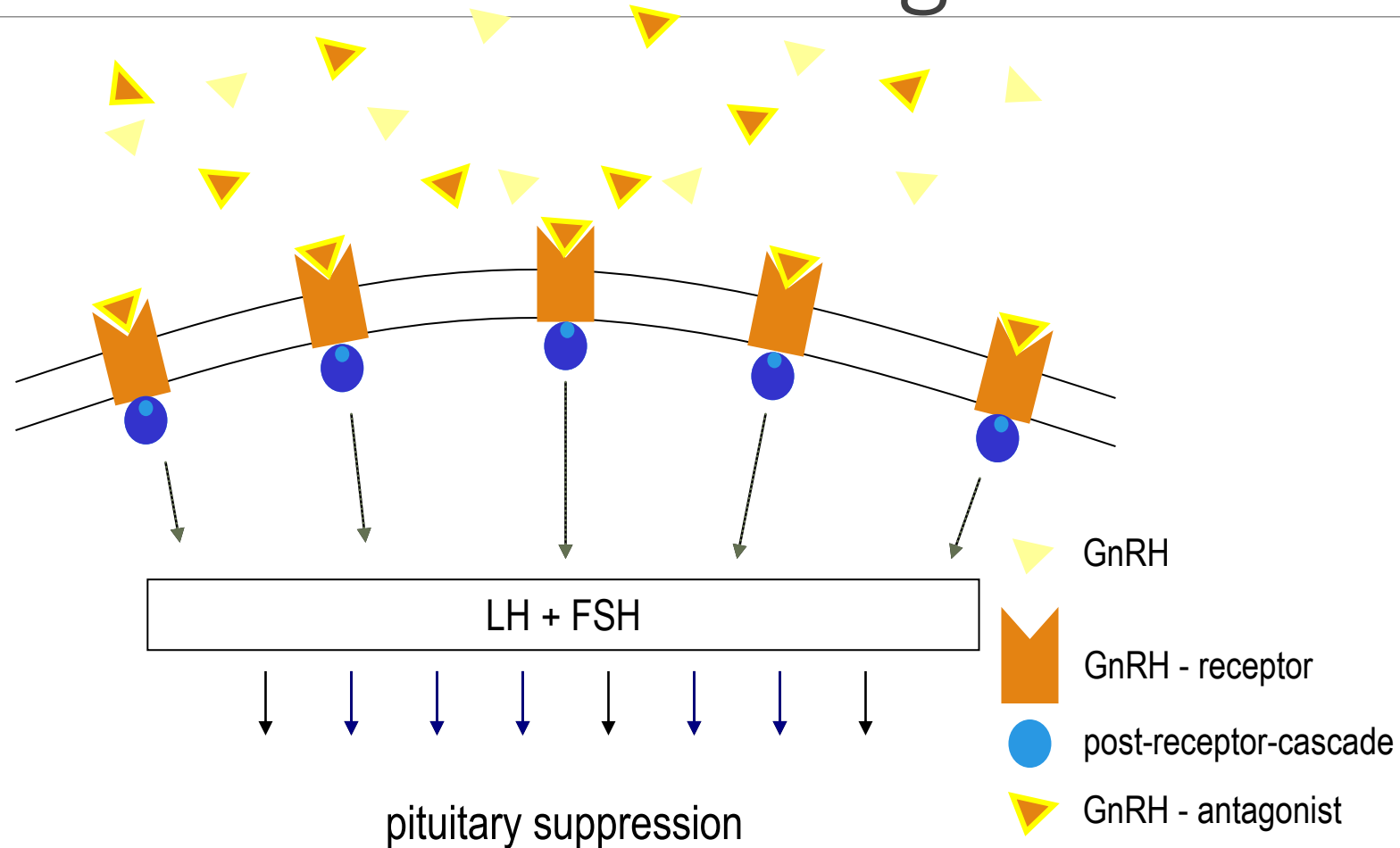
Structure of GnRH



Action of GnRH agonists



Action of GnRH antagonists



MOA of GNRH agonists & antagonists

GNRH AGONISTS

Repeated administration of an agonist in a continuous manner results in pituitary GnRH receptor downregulation, gonadotropin secretion of FSH, LH, and decreased steroidogenesis and gametogenesis.

GNRH ANTAGONISTS

Cause immediate, rapid gonadotropin suppression by **competitively** blocking GnRH receptors in the anterior pituitary gland, thereby preventing endogenous GnRH from inducing LH and follicle-stimulating hormone (FSH) release from the pituitary cells

Pre-Operative treatment with Leuprolid



Significant shrinkage of uterine fibroids-30%- 40%

Reduces vascularity

Drop in uterine volume-40% - 60%

Hemoglobin levels increased (Cessation of Menstruation)

Intra-operative blood loss significantly lower

Hence fewer blood transfusions

Surgical Management

■ Myomectomy



Abdominal
Vaginal
Hysteroscopy
Laparoscopic



Hysterectomy

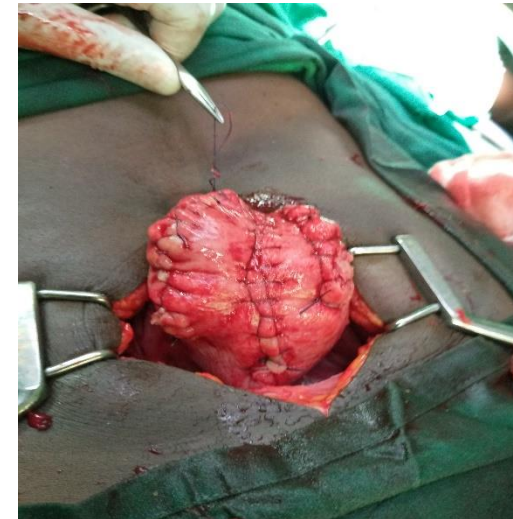
Abdominal
Vaginal
LAVH

GnRH agonists

Goal in treatment

- Decrease Size of Fibroids
- Decrease Bleeding during surgery

40-60 % decrease in mean uterine volume if given over a 3 months period



Other Medical pharmaceutical Drug options

➤ GnRH antagonists –Oral

Elagolix oral : 300mgs bid (with add back)

Relugolix /estradiol/Norethindrone combination – (40mgs /1mg/0.5mg) oral once daily

Linzagolix 100-200mgs daily

➤ Levonogestrol intrauterine Contraceptive device – Mirena

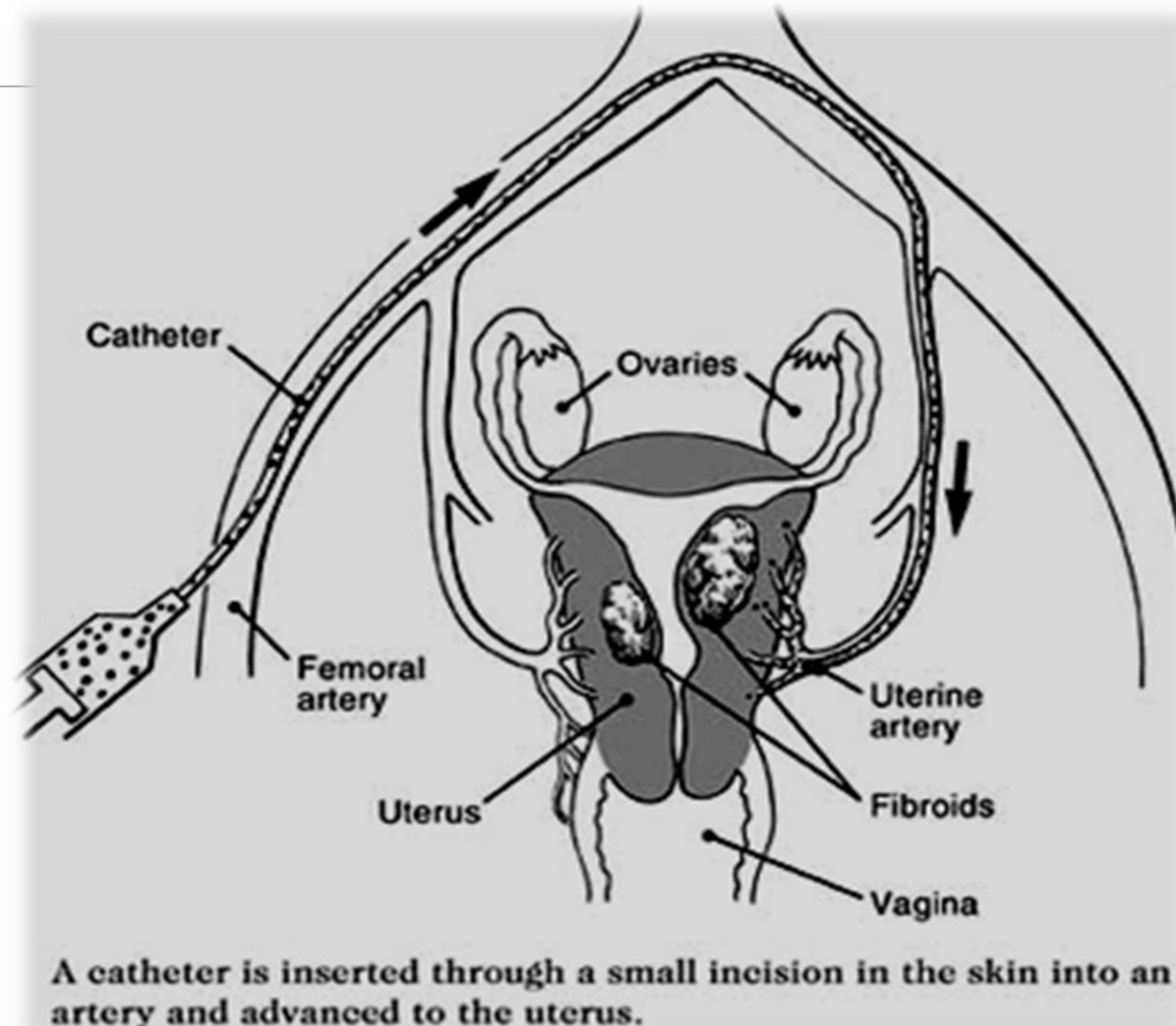
➤ Ulipristal Acetate 5mgs daily -

Uterine artery embolization



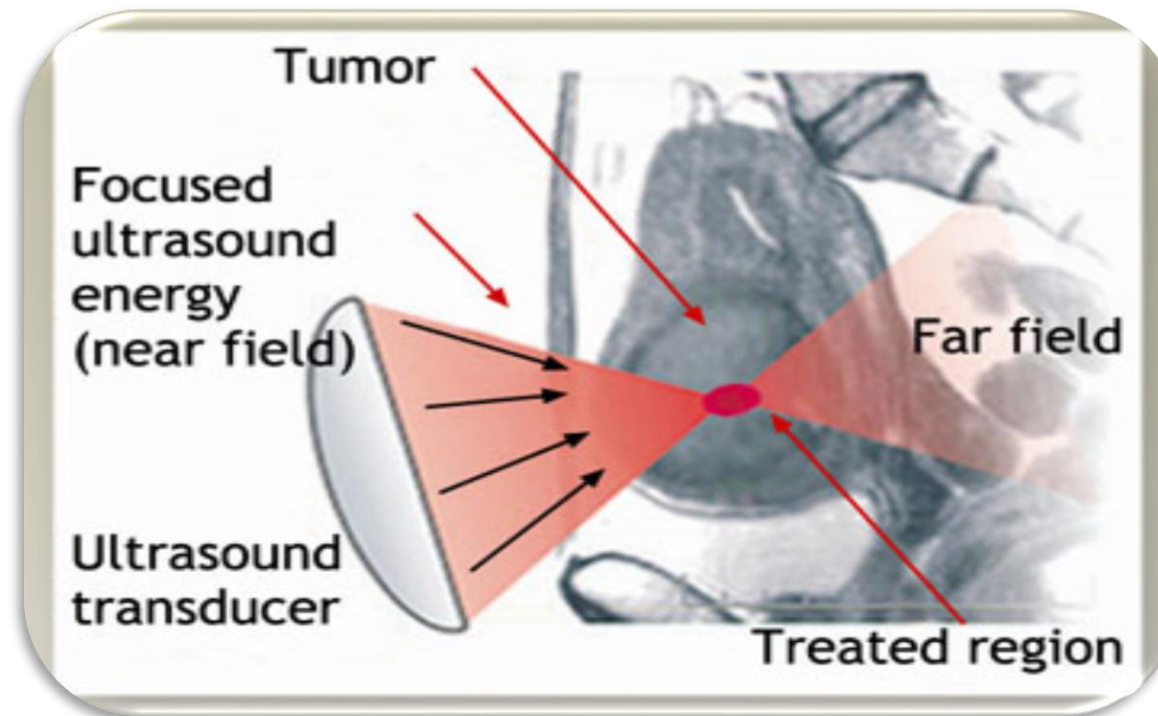
- By interventional radiologist
- Catheter is passed retrograde through Right femoral artery to bifurcation of aorta & then negotiated down to opposite uterine artery first.
- Polyvinyl alcohol (PVA) particles (500-700 um) or gelfoam are used for embolization.
- 60 – 65 % reduction in size of fibroid
- 80 – 90 % have improvements in menorrhagia & pressure symptoms

Uterine artery embolization



Newer Management- MRGFUS

- Permitted by FDA since 2004
- MRI guidance is used to direct ultrasound to tissues to elicit coagulative necrosis via thermal ablation.





THANK YOU AND QUESTIONS