

Vitamin D as a Treatment for Endometriosis

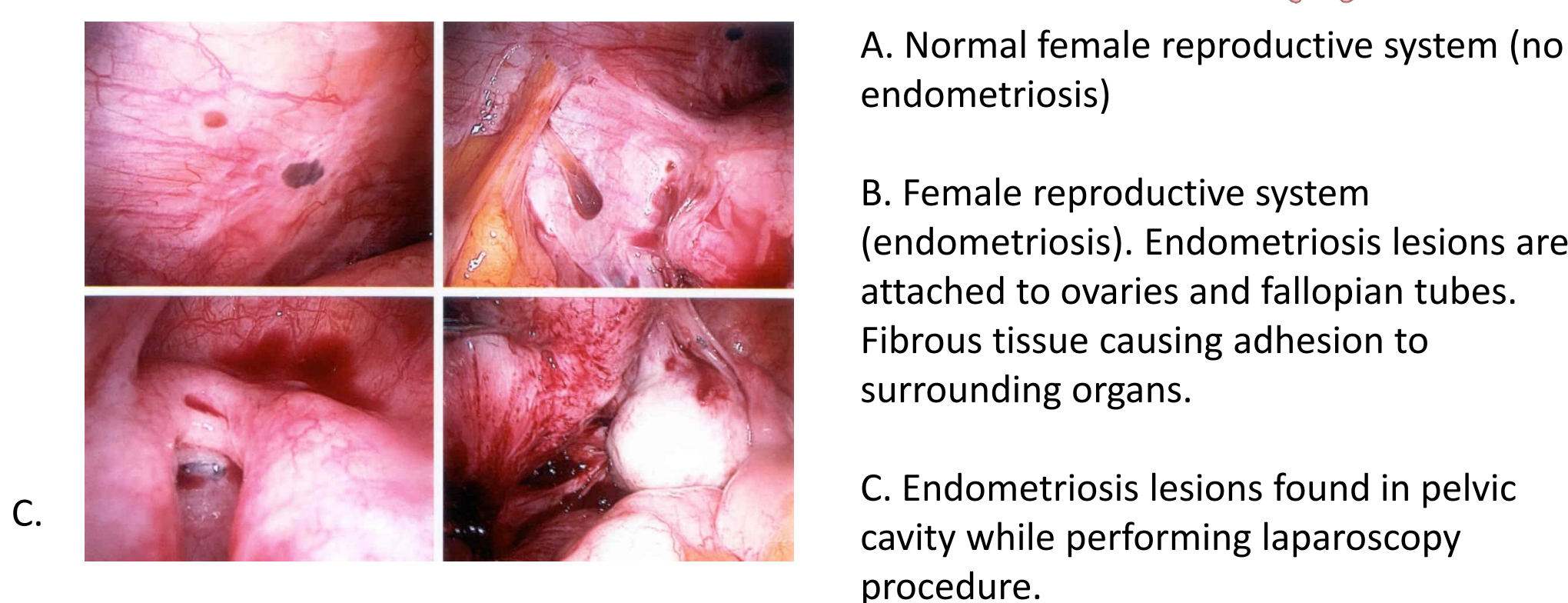
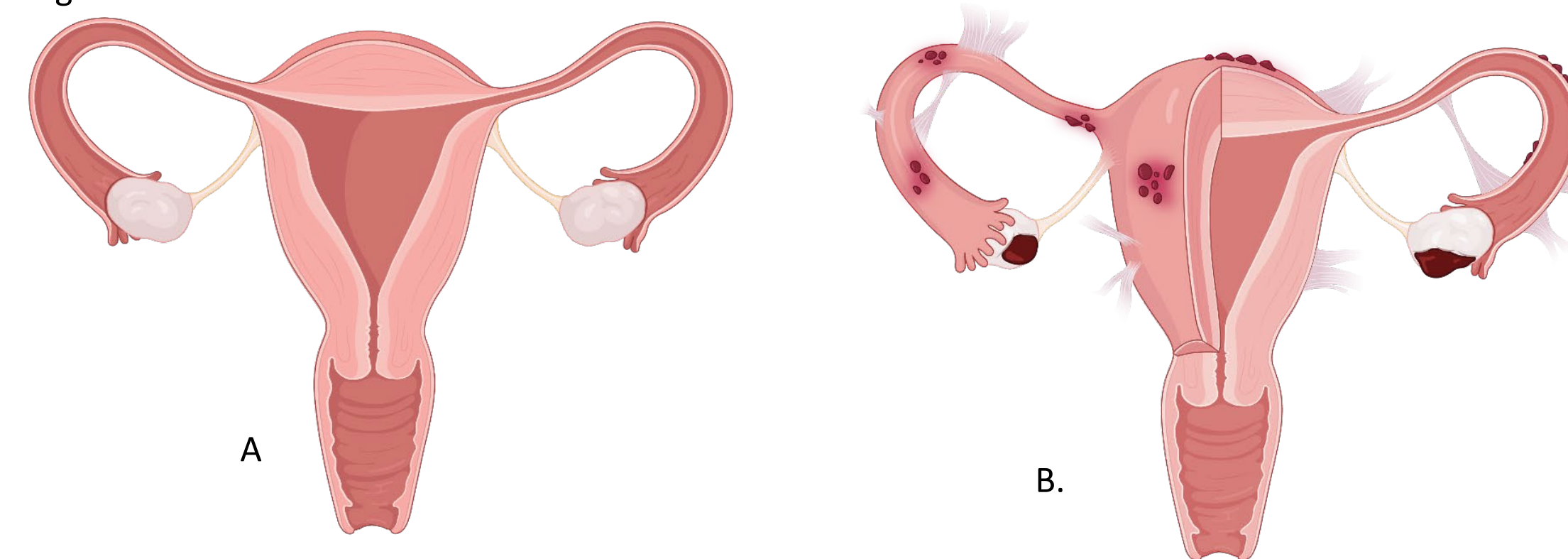
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Introduction:

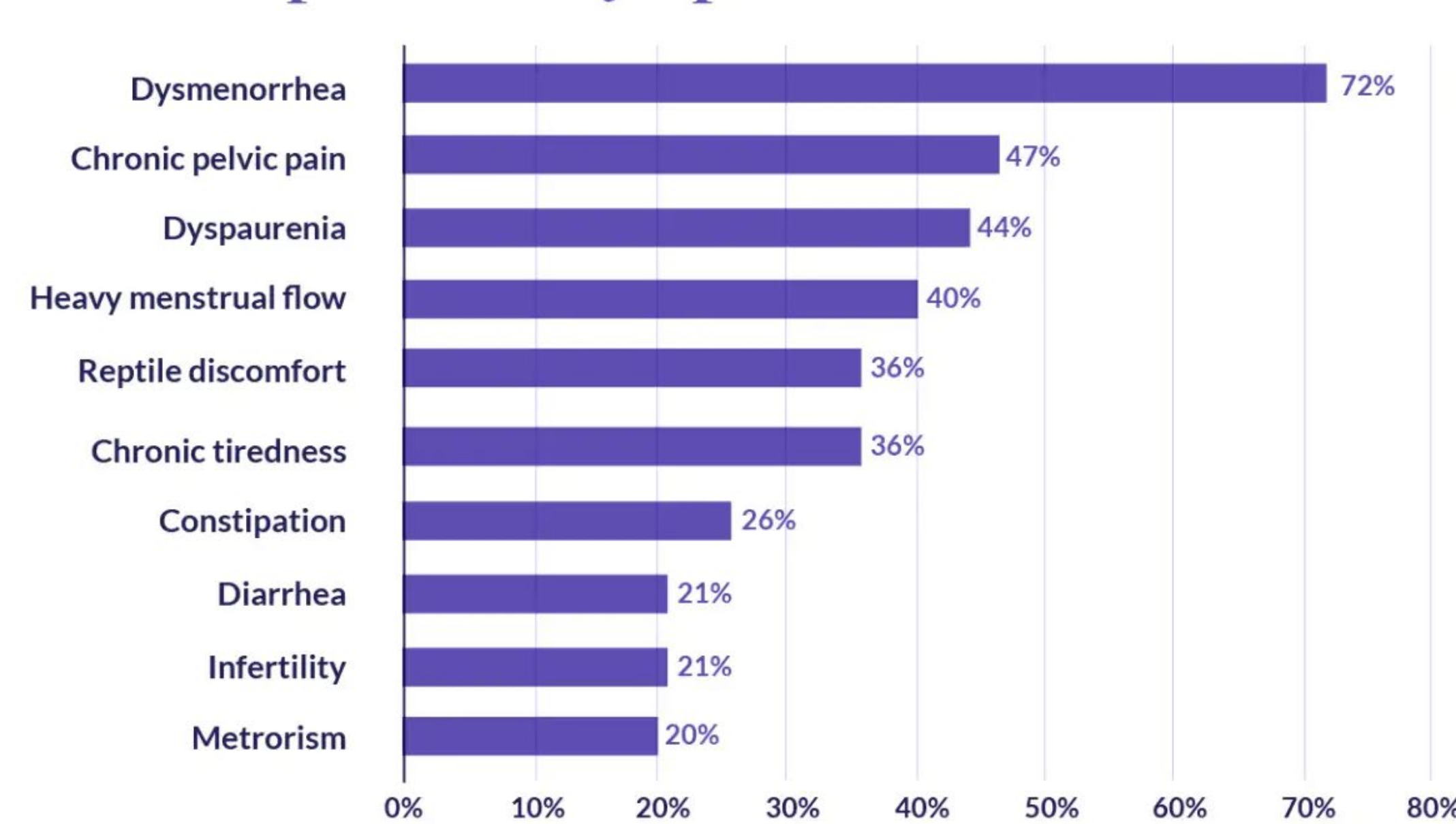
- Endometriosis is a gynecological disease that affects approximately 5-10% of women in child bearing years (Audebert et al, 2018).
- Endometriosis is characterized by endometrial tissue being present outside of the uterine cavity. The endometrial tissue attaches to surrounding structures and organs, and then the cells can cause deep infiltrating lesions and stomas in these structures. These lesions most commonly develop on the ovaries, fallopian tubes, and pelvic lining but in rare cases can even be found throughout the entire abdominal cavity (Balasubramanian et al, 2021).

Figure 1:



- Endometriosis causes many symptoms that affects women physically and mentally which negatively impacts the women's quality of life.

Figure 2: **Most prevalent symptoms of endometriosis**



Source: The Euro BioTech Journal, 2020

Figure 2: . Percent of women diagnosed with endometriosis that are effected by these various symptoms that occur with endometriosis

- Currently, there are no cures for endometriosis but there are a few options for treatment. These treatments are hormonal contraceptives, GnRH antagonists, and laparoscopy surgery. All of the current treatments may have adverse side effects and do not work for all women suffering from endometriosis (Koninckx et al, 2021).

Drug Category	Drugs	Mechanism of Action in Endometriosis	Dosing	Toxicity
NSAIDs	Ibuprofen, naproxen	Reversibly inhibits COX-1 and COX-2, resulting in decreased prostaglandin formation	May be prescribed at maximal doses. Ibuprofen: 400 mg po q4-6h prn. Naproxen: 500 mg po q12h prn	Epigastric pain/bleeding, edema, cross-sensitivity with aspirin-containing products, renal impairment
Combined estrogen-progestin contraceptives	Ethinyl estradiol combined with norethindrone, norgestrel, levonorgestrel, or desogestrel	Inhibits FSH and LH. Decreases cell proliferation and enhances endometrial apoptosis	Prescribed in monthly cycles for up to 3 mo or more	Thromboembolism, MI (age-dependent; highest in female smokers), increased risk of estrogen-dependent cancers
Progestin-only preparations	Norethindrone, medroxyprogesterone, levonorgestrel	Inhibits FSH and LH and stimulates atrophy or regression of endometrial lesions. Appropriate for patients with reported estrogen contraindications or those who are breastfeeding	Medroxyprogesterone acetate: initially 10 mg/day po; may increase up to 50 mg/day, depending on tolerance. Norethindrone acetate: initially 2.5 mg/day po; may increase to 30 mg/day	Weight gain, acne, breast tenderness, increase in LDL levels
Androgen	Danazol	Antiandrogen; inhibits enzymes involved in steroid formation. Decreases the release of gonadotropin	Mild disease: initially 200-400 mg/day in 2 divided doses; continue for 3-9 mo. Moderate-to-severe disease: initially 800 mg/day in 2 doses; continue for 3-9 mo	Teratogenic; hepatic injury, pseudotumor cerebri (rare; black box warning)
GnRH agonists	Leuprolide, goserelin	Chronic administration inhibits steroidogenesis due to reduced LH and FSH levels. The initial hormone flare is characteristic of GnRH agonists	Leuprolide: 3.75 mg IM q4w or 11.25 mg IM q12w. Goserelin: 3.6 mg SC every 28 days for 6 mo. Add-back therapy: norethindrone 5 mg/day	Hot flashes, vaginal atrophy, bone loss
Aromatase inhibitors	Letrozole, anastrozole	Blocks conversion of androgens to estrogen, which decreases endometrial proliferation	Letrozole: 2.5 mg/day. Anastrozole: 1 mg/day	Hot flashes, bone loss

Table 1: List of current treatments options used to treat endometriosis. Table comparing drug category, drug, mechanism of action, dosing, and toxicology between treatment types. Shows most common side effects of current endometriosis treatments.

- Endometriosis shares characteristics with autoimmune disorders by causing chronic inflammation and decreasing immune function (Abramiuk et al, 2022).

Methods:

- Research the causes and complications associated with endometriosis before conducting a literature review of primary articles and clinical trials that related to vitamin D's effects on endometriosis symptoms, inflammation, and the immune system.

Results:

- Vitamin D is able to reduce inflammation by increasing transforming growth factor (TGF) and interleukin-4 (IL-4) production in immune cells. TGF and IL-4 are anti-inflammatory cytokines and when TGF and IL-4 levels increased, inflammation is reduced (Sassi et al, 2018).
- Studies looking at the effect of vitamin D on arthritis showed that vitamin D is able to reduce inflammation in people with chronic inflammation conditions by decreasing IL-6 and IL-8. (Karonova et al, 2020).
- Vitamin D is able to decrease inflammation in women with premenstrual cycle by decreasing IL-12 and increasing total antioxidant capacity (Heidari, 2019).
- Research shows vitamin D increases function of immune cells and improve immune function as a whole (Charoenngam et al, 2020).
- The increased immune function is useful to women with endometriosis because of the associated increase of apoptosis rates in endometrial tissue (Moghadam et al, 2020).

- vitamin D is able to decrease CD44, which is a growth factor needed for the endometrial tissue, when decreased lesion progression is stopped (So et al, 2011).
- The only endometriosis symptom that vitamin D did not have an effect on was pelvic pain or painful menstruation. Studies showed that women taking vitamin D supplements saw no improvement in pain levels throughout their menstrual cycle (Lasco et al, 2012).

Figure 3:

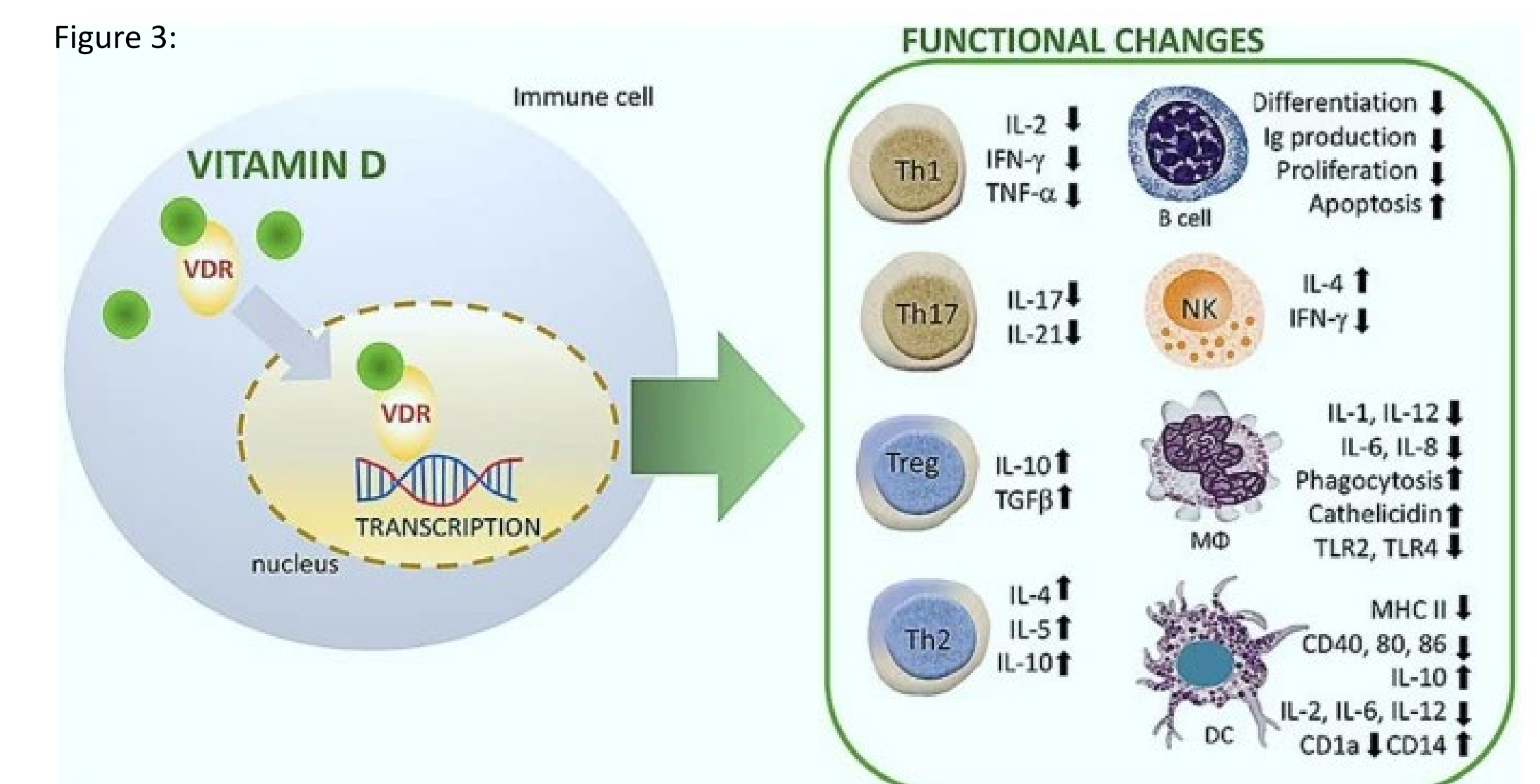


Figure 3: Chart showing the effects of vitamin D on multiple specific types of immune cells and the functional changes that occur caused by vitamin D

Conclusion:

- Vitamin D is able to lessen the inflammation and improve the immune system responses in endometriosis patients. It also stopped the progression of the lesions
- Vitamin D is not able to decrease the degree of chronic pelvic pain or painful menstruation so it will need to be used in conjunction with already available treatments to manage pain and improve quality of life.
- While vitamin D may not be the most effective treatment for endometriosis, it has led scientist to look at anti-inflammatory medications and pro-apoptosis medication as possible treatments (Dolmans et al, 2022, El-Zayadi et al, 2020).
- Fortunately, more research is being devoted to finding a better treatment for endometriosis and our focus on a disease that has been considered a "women's issue", shows a major improvement in gender equality within the medical system.

References:

