

Vocabulary

- *Progestin* describes synthetic and natural substances that mimic progesterone, categorized by generation
- *Generation* indicates when each drug was introduced to the market
- *Ovulation* is the period in the menstrual cycle when a woman is most fertile and likely to become pregnant. It is marked by the release of a mature egg from the ovaries.

Effects of Progestin/Role of Progesterone

Eight primary forms of progestin currently exist on the market and each have differing profiles “in terms of progestational, estrogenic, and androgenic” effects which are also dependent on the ratio of progestin to estrogen. As a result, each pill may affect women differently.

The effects of progestin are categorized into three types with the following functions:

Progestational Effects. How well the progestin binds to the progesterone receptor, thereby preventing ovulation and decreasing menstrual bleeding

Androgenic Effects. The degree to which the progestin produces undesirable, androgen-related side effects such as acne and excessive hair growth and how the progestin affects carb metabolism

Estrogenic Effects. How well the progestin combats androgenic effects in conjunction with ethinyl estradiol, a synthetic estrogen commonly found in oral contraceptives. This is mainly dependent on the concentration of estrogen in the pill, but is affected by the concentration of progestin as well because progestin has an antagonistic relationship with estrogen and may counter estrogenic effects

Classifying Progestins

Much like the iPods of the early 2000s, progestins are classified by generations which span from first to fourth based on when they were introduced to the market.

Additionally, those generations are grouped into two “families” based on molecular structure with the exception of drospirenone. The Estranes describe progestins that closely resemble testosterone and were the first progestins introduced the market (first generation). The Gonanes describe second and third generation progestins that have varying androgenic and estrogenic properties. Drospirenone, the newest progestin is not categorized as it differs significantly from the two families mentioned above. Generation classifications are as follows:

	1st Generation	2nd Generation	3rd Generation	4th Generation
Estrane	Norethindrone Norethindrone acetate Ethinodiol	-	-	-
Gonane	-	Levonorgestrel Norgestrel	Desogestrel Norgestimate	-
	-	-	-	Drospirenone

First Generation Progestins

Norethindrone. Low progestational effects and slight estrogenic effects. Less androgenic than second generation progestins, more androgenic than third and fourth generation progestins. **Advantages:** improves lipid profile (increases HDL, decreases LDL), many years of safety data, helpful for women who experience depression on other types of pills.

Disadvantages: intermediate effect on acne. **Brands:** Nortel, Brevicon, Modicon, Ortho-novum 1/35 and 7/7/7, Ovcon

Norethindrone Acetate. Low progestational and slight estrogenic effects. Less androgenic than second generation progestins, more androgenic than third and fourth generation progestins. **Advantages:** helpful for women who experience migraines or nausea on birth control pills. **Disadvantages:** intermediate effect on acne. **Brands:** Loestrin, Junel, Estrostep (tri-phasic).

Ethynodiol Diacetate. Medium progestational effects and minor estrogenic effects. Little androgenic activity. Easily converted into norethindrone in the body. **Advantages:** helpful for endometriosis **Disadvantages:** early, mid-cycle spotting (brands with high estrogen may combat this). **Brands:** Demulen, Kelnor, Zovia.

Second Generation Progestins

Levonorgestrel. High progestational and high androgenic effects. **Advantages:** lowest risk of blood clots of all combined oral contraceptives. Most widely prescribed world-wide. Approved for use as emergency contraception. **Disadvantages:** negatively affects serum level lipoproteins, increased incidence of androgenic effects like acne. **Brands:** Alesse, Aviane, Portio, Triphasil, Tri-Levelin, Nordette, Extended cycle: Seasonique, Seasonel, Lybrel.

Norgestrel. High progestational, strong antiestrogenic effects, and high androgenic effects. Mixture of an inactive isomer and levonorgestrel. **Advantages:** prevents endometriosis. **Disadvantages:** Acne, weight gain. **Brands:** Ovral, Lo/Ovral, Oggestrel, Lo-ogestrel, Cryselle, Ortho-novum 1/50

Third Generation Progestins

Desogestrel. High progestational effects, minimizing androgenic effects, and minimal estrogenic effects. **Advantages:** less weight gain, acne, less negative impact on metabolism, positive effects on lipoproteins. May help with migraines and painful cramps. **Disadvantages:** higher risk of blood clots, especially with 30/40mg dosage of estrogens. **Brands:** Mircette (low-dose, short placebo interval), Cyclessa (tri-phasic, low dosage), Ortho-Cept, Apri, Solia, Desogen, Cesia, Reclipsen, Velvivet, Casiant.

Norgestimate. High progestational effects, slight estrogenic effects, and low androgenic effects. **Advantages:** FDA approved to combat acne, minimal effect on lipoproteins and serum levels. **Disadvantages:** higher rate of headaches, reduced libido. **Brands:** Ortho-Tri-Cyclen-Lo (reduced nausea and vomiting than other pills containing this ingredient), Mylan, Sprintec, TriNessa, Previfem, Estarylla

Drospirinone. Low androgenic activity. Suppresses secretion of water and electrolyte regulating hormones. **Advantages:** reduces mild PMS symptoms and PMDD (appetite, negative mood, water retention). **Disadvantages:** higher serum potassium levels, higher risk of blood clots. **Brands:** Yaz, Beyaz, Yasmin, Zarah, Loryna, Syeda, Gianvi, Ocella, Vestura, Nikki

Common Side Effects that May be Reduced by Contraceptive Choice

- Acne
- Weight gain
- Breast Tenderness
- Migraines
- Spotting
- Menstrual Cramps
- Moodiness
- Depression

Question: how do these reduced effects interact with higher risks of blood clots for example.

Side Effect (Problem)	Progestin/Estrogen/Androgenic Effects	Try Using These Pill Brands to Minimize the Side Effect
Acne	higher estrogen, lower androgen potency	Demulen 1/50, Brevicon, Mircette, Modicon, Necon, Ortho-Cyclen, Ortho-TriCyclen, Yasmin
Breakthrough bleeding (spotting)	higher estrogen, higher progestin potency, lower androgen potency	Demulen 1/50, Desogen, Ortho-Cept, Ovcon 50, Yasmin, Zovia 1/50E, Estrostep FE**
Breast soreness	lower estrogen, lower progestin potency	Alesse, Levlite
Depression	lower progestin potency	Alesse, Brevicon, Levlite, Modicon, Necon 1/35, Ortho-Cyclen, Ortho-TriCyclen, Ovcon 35, Tri-Levlen, Triphasil, Trivora
Endometriosis or endometriosis prevention	lower estrogen, higher progestin potency, higher androgen potency	Demulen 1/35, Levlen, Levora, Loestrin 1.5/30, Loestrin 1/20 Fe, LoOvral, Nordette, Zovia 1/35E (used either continuously with no days of placebo pills or with only 4 days of placebo pills for prevention)
Headaches (not menstrual migraines)	lower estrogen, lower progestin potency	Alesse, Brevicon, Levlite, Modicon, Necon 1/35, Ortho-Cyclen, Ortho-TriCyclen, Ovcon 35, Tri-Levlen, Triphasil, Trivora
Moodiness or irritability	lower progestin potency	Alesse, Levlite, Loestrin 1/20 Fe, Yasmin, Yaz, Beyaz (or any pill with less estrogen than currently on)
Severe menstrual cramps	higher progestin potency	Demulen 1/35, Demulen 1/50, Desogen, Mircette, Loestrin 1.5/30, Ortho-Cept, Yasmin, Zovia 1/35E, Zovia 1/50E
Weight gain	lower estrogen, lower progestin potency	Alesse, Levlite, Loestrin 1/20 Fe, Yasmin, Yaz, Beyaz (or any pill with less estrogen than currently on)

Sources	https://www.verywellhealth.com/different-progestin-types-906936 https://www.verywellhealth.com/understanding-the-role-of-progestin-in-birth-control-906932 https://www.sciencedirect.com/science/article/pii/S0049384818302743?via%3Dihub
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