

# Understanding the Role of Progestins in the Management of Oral Contraceptives

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## Financial Disclosures

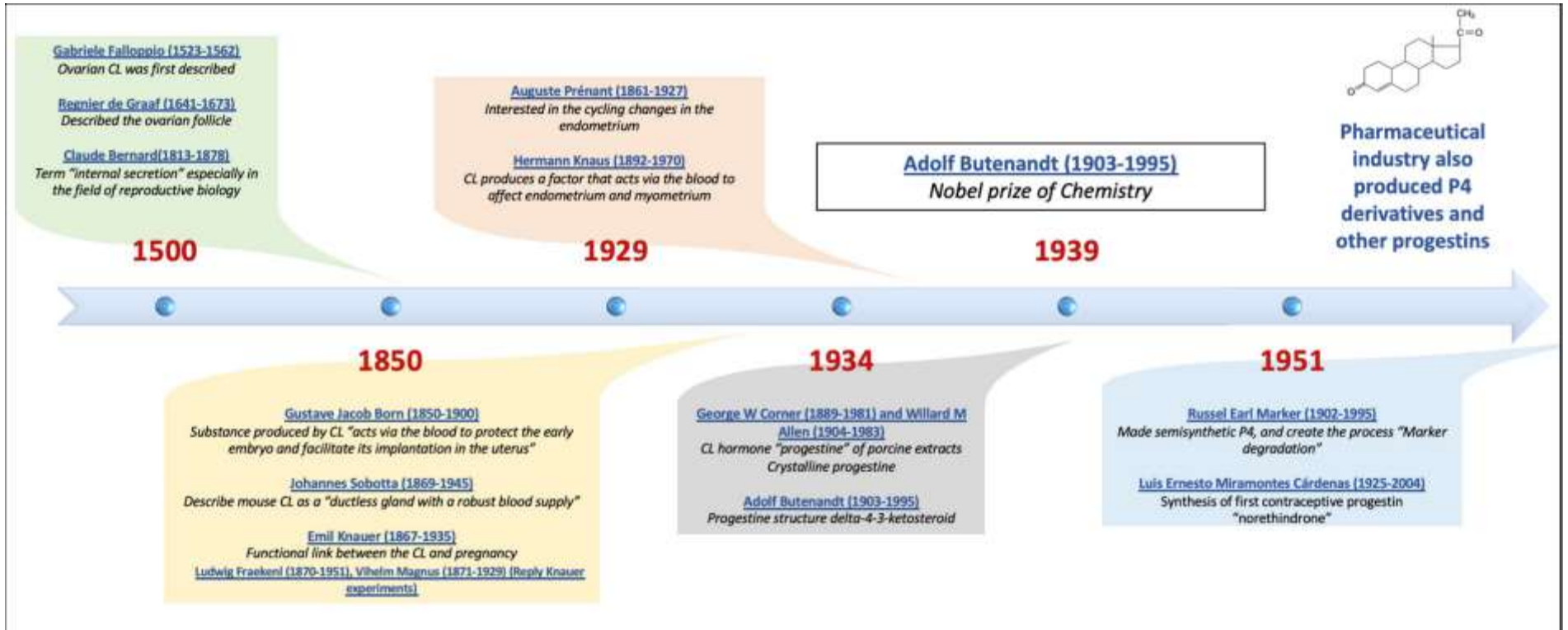
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# Objectives

- Explain the three specific progestin actions: progestational, anti-estrogenic, and antiandrogenic activity.
- Differentiate the biological activity of the different progestins using interactive case studies to identify key considerations in pill management.
- Compare and contrast COCs to determine appropriate initial pill selection and adjustment.

# History of Progestins



(García-Sáenz et al., 2023)

# Progesterone Overview

OCPs contain 2 synthetic steroid hormones

- Estrogen- most common → ethinyl estradiol
- Progestin (synthetic progestational agents)
- Progesterone (P4)
  - Steroid hormone
  - 21 carbons
  - Synthesized by (ovaries, adrenals, testicles)
  - Coordinates ovulation, endometrium transformation, and pregnancy maintenance
- Prodrug
  - Review
- Classifications
  - Generations are only based on timing on introduction to market
  - Structural classifications

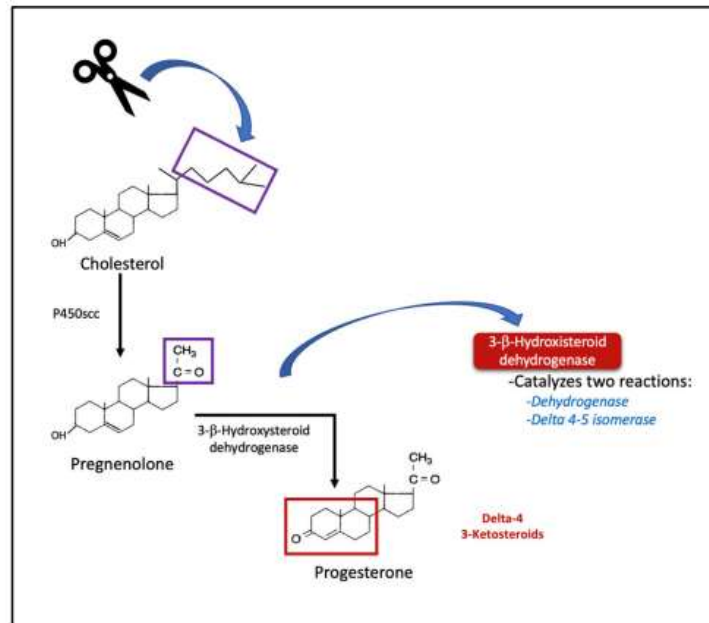
## Progestin use examples

- Contraception
- Hormonal replacement therapy (HRT)
- Treatment for endometriosis
- Treatment for PCOS

# Definitions

- Progestogen: all compounds that promote changes to maintain pregnancy
- P4 (Progesterone): synthesized by (ovaries, adrenals, testicles)
- Progestin: synthetic drug- evaluated based on endometrial effects
- PR: P4 receptors, nuclear transcription factor
  - Acts through P4 response within target genes to regulate transcription
  - Two isoforms (A and B)

# Chemical structure



**Figure 1.** Synthesis of progesterone from cholesterol. Initial steps of steroidogenesis and delta-4 products. p450scc = cholesterol side chain cleavage enzyme.

Garcia-Saenz et al., (2023)



# Review of receptors

- Estrogen receptor (ER)
- Androgen receptor (AR)
- Glucocorticoid receptor (GR)
- Mineralocorticoid receptor (MR)

# Actions of Progestins

- Progestational
- Anti-estrogenic
- Anti-androgenic
- Effect on endometrium

# Properties

- Pharmacokinetics
  - Absorption
  - Bioavailability
  - Distribution
  - Metabolism
  - Excretion

# Classification

## Classification Based on Structural Properties

Structural Properties	Examples	Action
Pregnanes	<i>(medroxyprogesterone acetate, norgestrel acetate)</i>	
Estranes	<i>(Norethindrone, norethindrone acetate, ethynodiol diacetate, norethynodrel)</i>	
Gonanes	<i>(levonorgestrel, desogestrel, norgestimate, gestodene)</i>	
Spirolactone derivative	drosperinone	

<b>Biological activities</b>  (adapted from Schindler et al., 2008)	Progestational	Endometrial	Androgenic	Estrogenic
Norethindrone	1.0	1.0	1.0	1.0
Norethindrone acetate	1.2	0.4	1.6	1.5
Levonorgestrel	<b>5.3</b>	5.1	<b>8.3 (H)</b>	0
Desogestrel	<b>9.0</b>	8.7	3.4	0
Norgestimate	1.3	1.2	1.9	0
Spironolactone derivatives (droseprinone)	0.5	0	<b>NA (L)</b>	0
Ethinyl estradiol	0	0	0	100

# Targeted treatment

Issue	Selection
Endometriosis	
Flow of menses	
Dysmenorrhea	
Irregular menstruation	
Menstrual migraines	
PMS/PMDD	

# Targeted treatment

Issue	Selection
Elevated lipids	
Hirsutism	
Acne	
PCOS	
Weight	
Estrogen sensitivity	
Progesterone sensitivity	

## Case 1- Which one would you select?

- 17-year-old
  - Regular to light menses
  - 2-4 days of flow
  - Mild to no cramps
  - Non-smoker
  - Normal weight
- A. Norethindrone acetate 1.5/30
- B. Levonorgestrel 0.1/20
- C. Norethindrone 35
- D. Norethindrone 0.05, 1.0, 0.5/35



## Case 2- Which one would you select?

- 23-year-old
  - Regular menses, moderate flow
  - 4-6 days
  - Moderate cramping
  - Non-smoker
  - Normal weight
- A. Norethindrone acetate 1.0/20FE 24 day
- B. Desogestrel 0.15/20,10
- C. Norethindrone 0.5/25
- D. Levonorgestrel 0.15/20 84 days, 0/10 7 days

## Case 3- Which one would you select??

- 32-year-old
  - Heavy, but regular menses
  - 6 + days
  - Bad cramps
  - Non-smoker
- A. Norgestrel 0.3/30
- B. Norethindrone acetate 1.5/30
- C. Levonorgestrel 0.1/20
- D. Norethindrone acetate 1.0/20

## Case 4- Which one would you select?

- 25-year-old
    - Irregular periods
    - Infrequent
    - Heavy
    - Acne
    - Oily skin
    - Hirsutism
    - Concerns about weight gain the last 2 years
- A. Levonorgestrel 0.1/20
  - B. Norethindrone 0.35
  - C. Drospirenone 3/30
  - D. Norethindrone acetate 1.5/30

## Case 5- Which one would you **NOT** select?

- 19-year-old
    - Regular periods
    - Light to moderate flow
    - Approx 4 days of bleeding
    - Can have some cramping, but not bad
    - Weight 102 pounds
- A. Norethindrone 0.8/25Fe
  - B. Desogestrel 0.15/30
  - C. Levonorgestrel 0.1/20
  - D. Norethindrone acetate 1.0/10 Fe

## Case 6- Which one would you select?

- 37-year-old
  - Moderate bleeding
  - 5-6 days
  - Weight 200 lbs
  - Non-smoker
  - Cramping is “reasonable”
- A. Norgestimate 0.18, 0.215, 0.15/25
- B. Norethindrone acetate 1.5/30
- C. Levonorgestrel 0.1/20
- D. Levonorgestrel 0.05, 0.075, 0.125/30

# References