

J. M. Foidart

Yasmin®—Added Value in Oral Contraception

Added value in oral contraception: the unique properties of Yasmin®



Family planning: a matter of public health

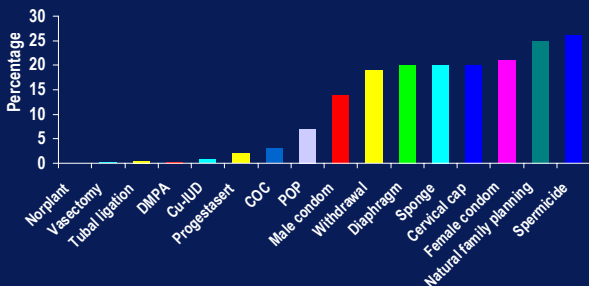
- 185 million pregnancies/year
- 75 million unwanted pregnancies/year
- 45 million abortions/year
- 20 million unsafe abortions/year
- 585,000 maternal deaths/year
- 200,000 avoidable maternal deaths

UNESCO-UNICEF

The ideal contraceptive



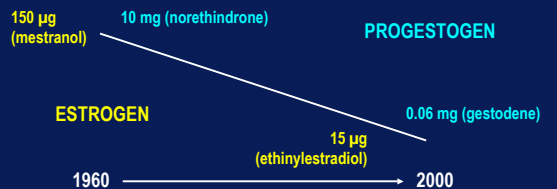
Pregnancy prevention First-year typical user failure rate



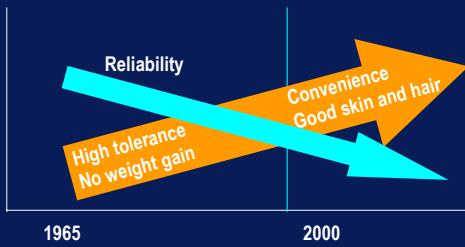
Trussell, 2000

An overview of oral contraceptives

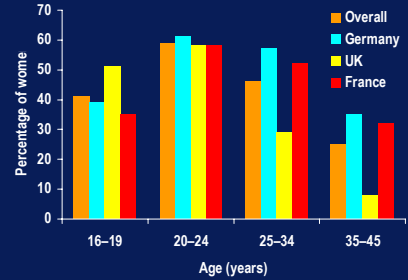
- Use: > 60 million women worldwide
- Efficacy: '99%' method effectiveness



Women's concerns about oral contraception

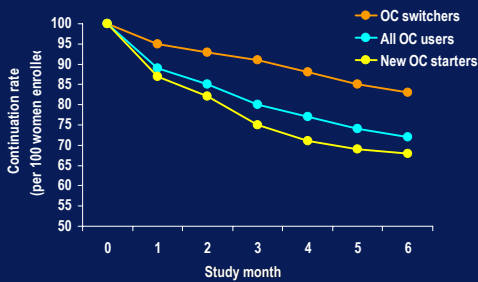


Incidence of current oral contraceptive usage



Fuchs et al., 1996

Oral contraceptive continuation rates



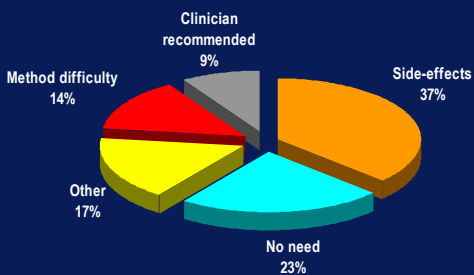
Adapted from Rosenberg MJ et al. *Am J Obstet Gynecol* 1998;179:577-82

Oral contraceptive discontinuation

- Many patients discontinue oral contraceptive use prematurely
 - one-third to one-half stop within 1 year
 - most stop within 6 months (most within first 2 months)
 - 50% of adolescents stop within 3 months
 - new starters discontinue more frequently

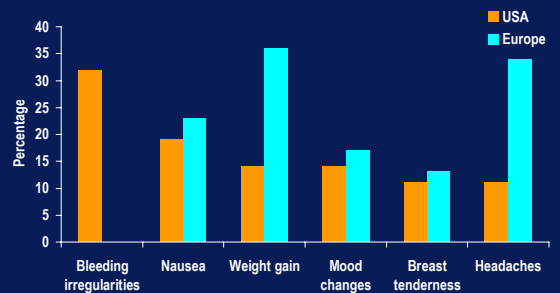
Rosenberg et al., 1998

Reasons for oral contraceptive discontinuation



Rosenberg MJ et al. *Am J Obstet Gynecol* 1998;179:577-82

Discontinuation/side-effects



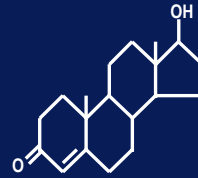
Fuchs et al., 1996; Rosenberg et al., 1998

What happens when women discontinue use of oral contraceptives

- 42% discontinue without consulting their health-care provider
- 19% discontinue without selecting another contraceptive method
- 70% choose a less effective contraceptive method
- Not all oral contraceptives are the same – they differ in dosage or progestogen

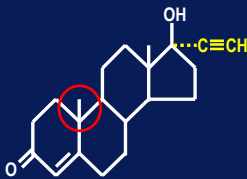
Rosenberg *et al.*, 1998

Progestins derived from testosterone



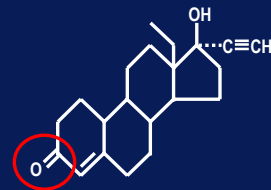
Testosterone

Progestins derived from testosterone



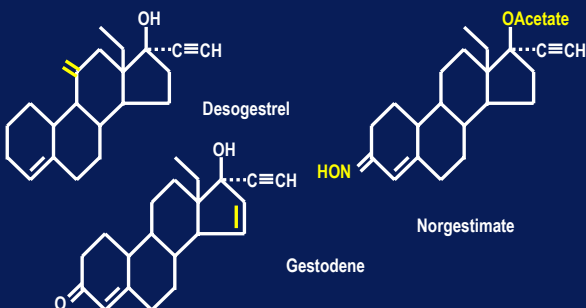
Ethisterone

Progestins derived from testosterone third generation

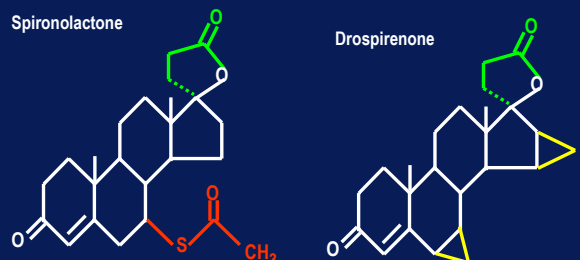


Levonorgestrel

Third-generation progestins



Drospirenone and spironolactone

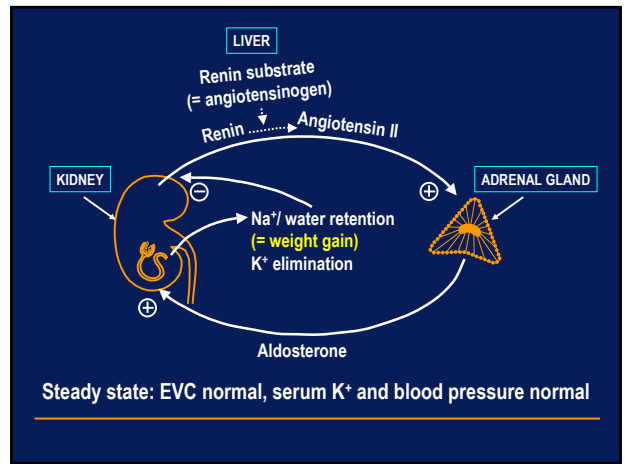


Pharmacological profile of drospirenone and other progestogens

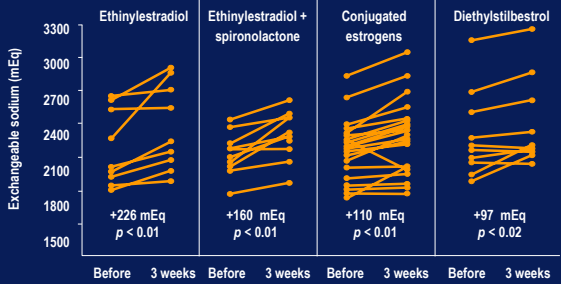
	Progestogenic activity	Glucocorticoid activity	Androgenic activity	Antiandrogenic activity	Antimineralocorticoid activity
Progesterone	+	-	-	(+)	+
Drospirenone	+	-	-	+	+
Cyproterone acetate	+	(+)	-	+	-
Desogestrel*	+	-	(+)	-	-
Dienogest	+	-	-	+	-
Gestodene	+	-	(+)	-	(+)
Levonorgestrel	+	-	(+)	-	-
Norgestimate**	+	-	(+)	-	-

*, active metabolite 3-ketodesogestrel; **, main metabolite
 +, effect; (+), negligible at therapeutic dosages; -, no effect

Foidart et al., 2000

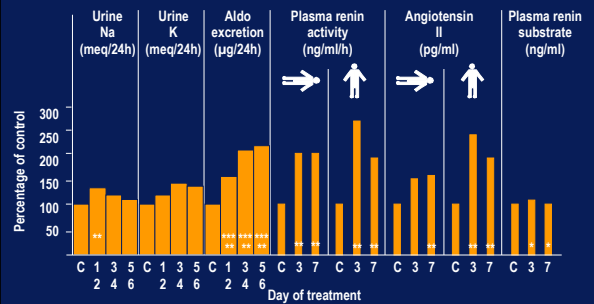


Effects of different estrogens on exchangeable body sodium



Crane and Harris, 1974

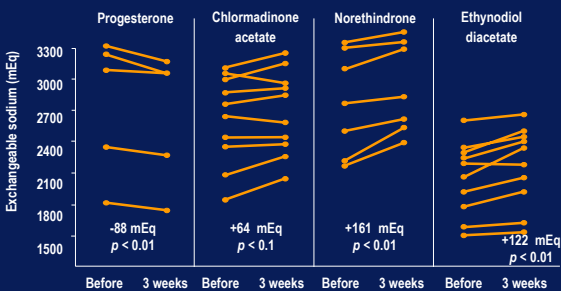
Effects of progesterone on the RAAS



*p < 0.05; **p < 0.01; ***p < 0.001 vs control

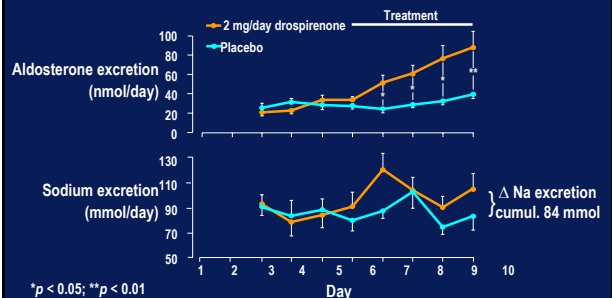
Oelkers et al., 1974

Effects of progestogens on exchangeable body sodium



Crane and Harris, 1974

Effects of drospirenone on sodium and aldosterone excretion



*p < 0.05; **p < 0.01

Oelkers et al., 1991

Ovulation inhibition

- **Complete ovulation inhibition** **100%**
- **Follicle development** **15%**
- **Contraceptive efficacy**
 - 29,735 cycles in 2236 women were evaluable
 - 13 pregnancies during Yasmin exposure occurred, 11 of which were clear user failures (omitted tablets, diarrhea, vomiting, etc.)
- **Pearl index = 0.57**
Corrected Pearl index = 0.09
- **Reference preparation, 150 µg desogestrel/ 30 µg ethinylestradiol, Pearl index = 0.43**
Corrected Pearl index = 0.09

Drospirenone

- Has a pharmacological profile close to that of natural progesterone
- Displays progestogenic, antiandrogenic and antimineralocorticoid properties
- At 3 mg/day effectively inhibits ovulation, and increases the viscosity of cervical mucus
- The antimineralocorticoid activity counteracts the ethinylestradiol-induced stimulation of the RAAS and reduces fluid retention
- Has positive antiandrogenic effects on skin

Yasmin®

Antimineralocorticoid activity

+

Antiandrogenic activity

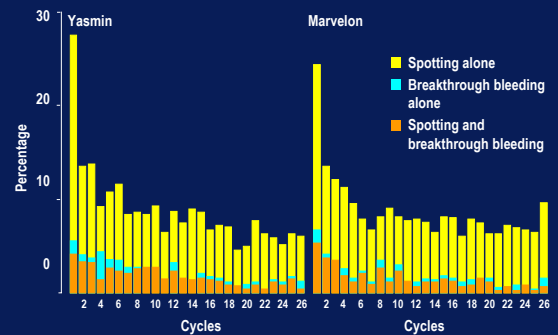
- Progesterone-like effects on sodium and water retention
 - breast tension
 - edema
 - body weight
 - some premenstrual symptoms



- Blockage of androgen receptor
 - acne
 - seborrhea



Intermenstrual bleeding



Foidart *et al.*, 2000

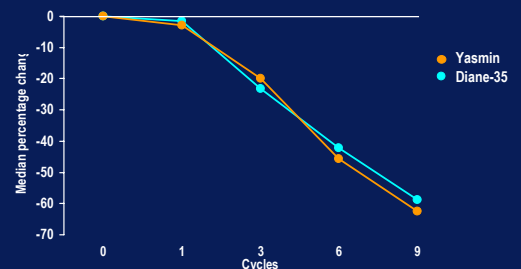


Before



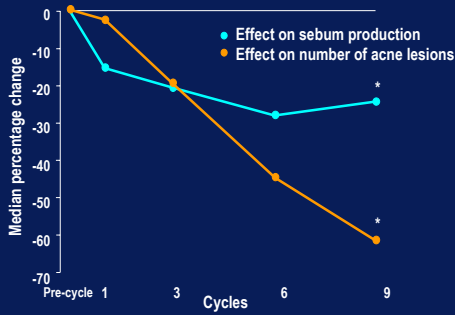
After

Effect of Yasmin on acne lesions



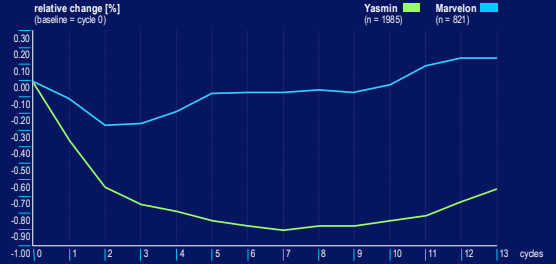
Explorative comparison to baseline, $p < 0.05$ from cycle 3 onwards

Effect of Yasmin on acne and seborrhea



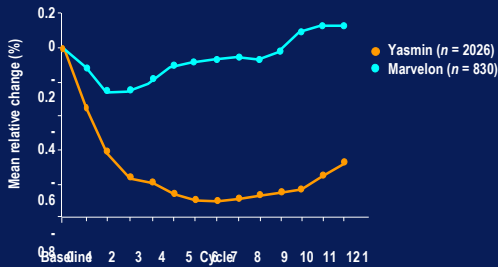
Boschitsch *et al.*, 2000

Body weight change in percent



Foidart *et al.*, Eur J Contracept Reprod Health Care, 5, 2:124-34, 2000
Huber *et al.*, Eur J Contracept Reprod Health Care, 5, 1:25-33, 2000

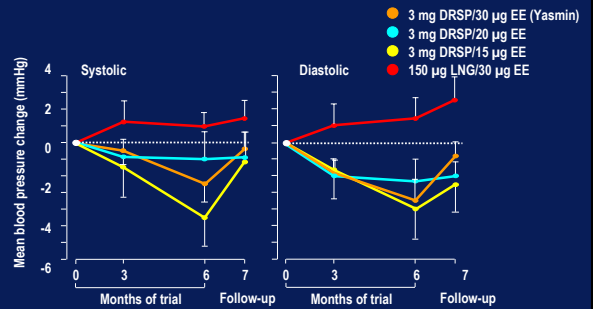
Relative changes in body weight: combined data



Explorative comparison of treatment, $p < 0.05$ from cycle 1 onwards

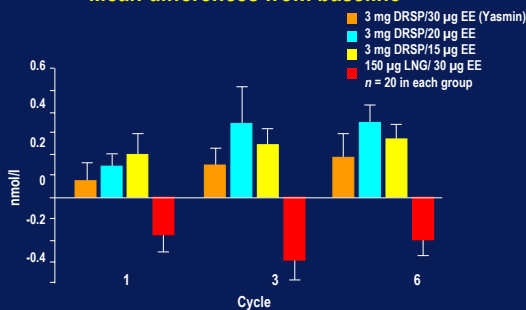
Huber *et al.*, 2000; Foidart *et al.*, 2000

Effects of drospirenone/ethinylestradiol on blood pressure



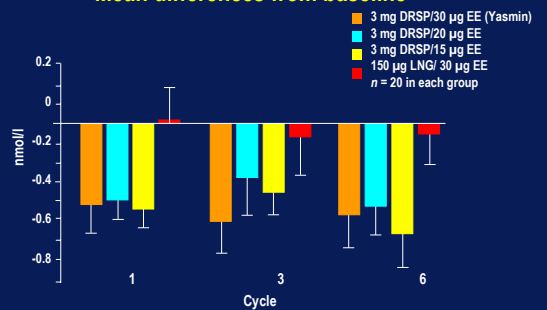
Oelkers *et al.*, 1995

Changes in HDL cholesterol Mean differences from baseline



Oelkers *et al.*, 1995

Changes in LDL cholesterol Mean differences from baseline



Oelkers *et al.*, 1995

Yasmin®: adverse events

	Frequency (% cycles) (n = 2827 / 34,720 cycles)
Menstrual disorder	3.1
Headache	3.7
Breast tenderness	2.1
Depression	0.5
Nausea	1.3
Vomiting	0.3
Dizziness	0.3
Intermenstrual bleedings	0.1
Nervousness	0.3

Conclusion

- Drospirenone-containing oral contraceptives (Yasmin®) offer the same traditional non-contraceptive benefits; however, due to its unique antimineralocorticoid and anti-androgenic properties, new and unique benefits have been observed
 - acne is well controlled as would be expected from its inhibition of ovulation, antiandrogenic activity and no attenuation of the estrogen-mediated increase in SHBG
 - its antimineralocorticoid activity gives rise to reduced bloating and improved mood

Conclusion

Day-to-day compliance and the duration of intake of an oral contraceptive are dependent on the woman's satisfaction with the pill she is taking

Yasmin meets these expectations and offers a real new choice to women

Conclusions

The combination of a positive effect on PMDD, body weight and skin condition, adding up to a general feeling of well-being, meets women's expectations

Conclusions

Yasmin® opens up a completely new category of oral contraceptives. It provides not only contraceptive benefits but also additional user-related non-contraceptive benefits that are unique in their completeness and beneficial influences