

FERRARA, 22 MAGGIO 2015

RIDOTTO TEATRO COMUNALE
Cso Martiri della Libertà

LE INFEZIONI DEL BASSO
TRATTO UROGENITALE
FEMMINILE



Contracezione ormonale ecosistema vaginale ed esposizione alle infezioni del basso tratto uro-genitale femminile

Filippo Murina

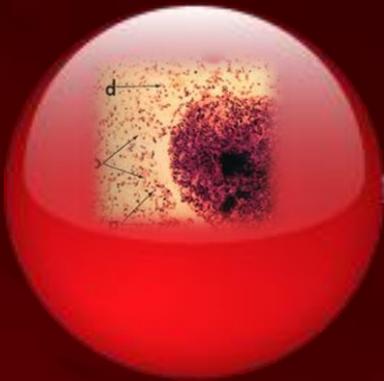
Servizio di Patologia Vulvare

Osp. V. Buzzi-ICP-Università di Milano

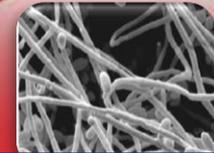
Direttore Scientifico Associazione Italiana Vulvodinia

E-P – Ecosistema Vaginale – Infezioni

Vaginosi Batterica



Candidosi



- Lactobacillus Crispatus
- Lactobacillus Jensenii
- Lactobacillus Gasseri
- Lactobacillus Vaginalis

Flora

Lattobacillare



Hormonal contraception and risk of bacterial vaginosis diagnosis in an observational study of women attending STD clinics in Baltimore, MD

Samara B. Rifkin^a, Marsha R. Smith^{b,c}, Rebecca M. Brotman^{a,d},
Renee M. Gindi^a, Emily J. Erbelding^{a,b,c,*}

-Prevalenza 30 % c

Table 2
Association between hormonal contraception and BV diagnosis

Homonal contraception	Patient visits, <i>n</i>	BV diagnosis
Combined hormones	847	1
Progestin alone	247	1
None	357	1

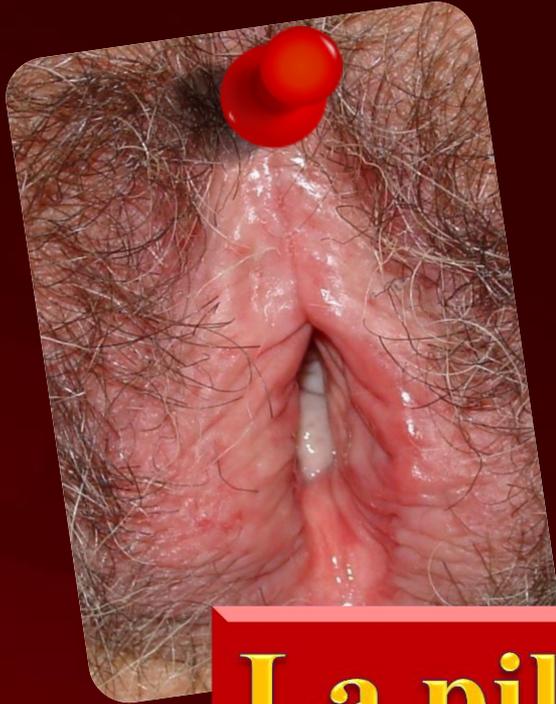
E-P e Vaginosi=

- Adeguati livelli di estrogeni
- fonte di carboidrati
- Controllo mestruazione

Table 1. Frequency of microorganisms isolated from the endometrium of women with clinically diagnosed pelvic inflammatory disease.

Microorganism	Percentage of women
<i>Chlamydia trachomatis</i>	9.9
<i>Neisseria gonorrhoeae</i>	13.4
<i>Mycoplasma hominis</i>	6.8
<i>Ureaplasma urealyticum</i>	6.8
H ₂ O ₂ -producing <i>Lactobacillus</i> species	7.6
Non-H ₂ O ₂ -producing <i>Lactobacillus</i> H ₂ O ₂ species	8.6
Diphtheroids	11.2
<i>Gardnerella vaginalis</i>	30.9
Group B <i>S treptococcus</i> species	8.3
<i>Enterococcus</i> species	3.6
Viridans streptococci	12.9
Coagulase-negative <i>Staphylococcus</i> species	6.8
<i>Escherichia coli</i>	2.5
Any anaerobic gram-negative rod ^a	21.9
Black-pigmented gram-negative rod	10.8
Nonpigmented gram-negative rod	15.1
<i>Bacteroides fragilis</i> ^b	0.7
<i>Fusobacterium</i> species ^c	0.7
Any anaerobic gram-positive cocci ^d	15.8
Anaerobic <i>S treptococcus</i> species	4.7
Bacterial vaginosis ^e	53.5

Candidosi vulvovaginale ed E-P quale relazione?



-90% ca delle donne ha almeno
1 episodio di candidosi
-10 % ca ha una forma ricorrente

**La pillola contraccettiva
è causa di Candidosi?**

Candidosi Vulvo-Vaginale

Commensalismo

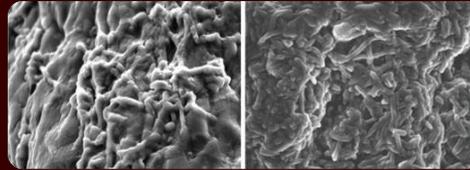
Malattia



Dr. Yeast

Mr. Hypha

I biofilm permettono la sopravvivenza di microrganismi in un ambiente ostile



**Biofilm “buoni”
che difendono**

**Biofilm “cattivi”
la vagina**

I Lattobacilli sono in grado di produrre un biofilm protettivo che riveste la mucosa vaginale

Candidosi Vulvo-Vaginale

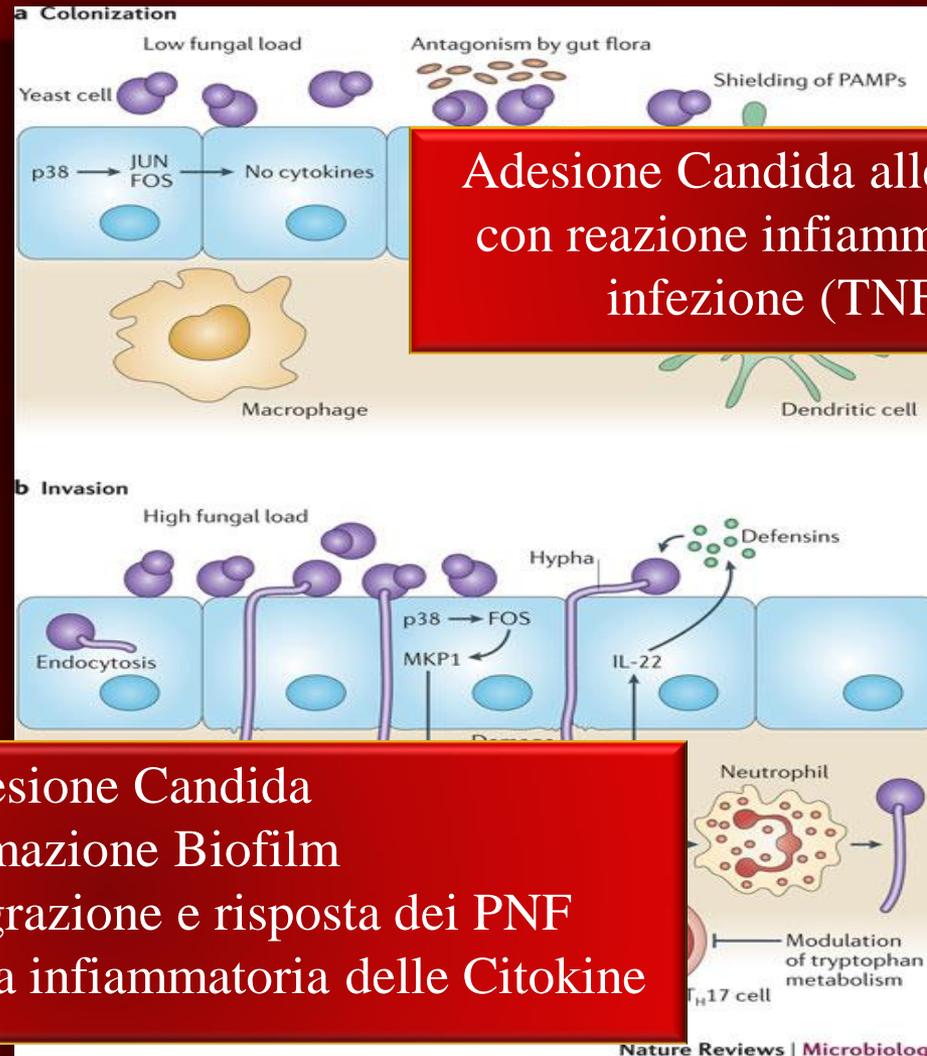
Vagina

- Cellule epiteliali
- Biofilm vaginale



Immunita'

- Importante attività infiammatoria



Adesione Candida alle cellule epiteliali con reazione infiammatoria che limita infezione (TNF-Citokine)

- Adesione Candida
- Formazione Biofilm
- Aggressiva migrazione e risposta dei PNF
- Accentuata risposta infiammatoria delle Citokine

Vulvovaginal Candidiasis

Symptoms severity and signs of inflammation appear to be unrelated to the severity of infection

A positive culture does not always confirm the diagnosis

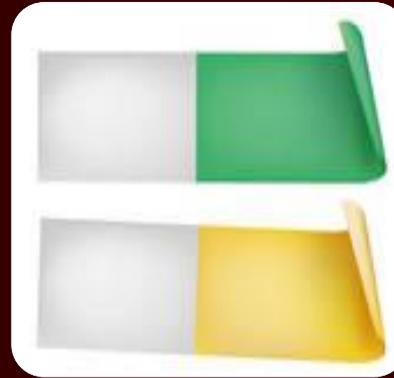
- 20/25 % of asymptomatic women have a positive culture
- 30% of symptomatic women were culture negative on presentation



Microscopy

on of vaginal
aration should be
presence hyphae
itivity

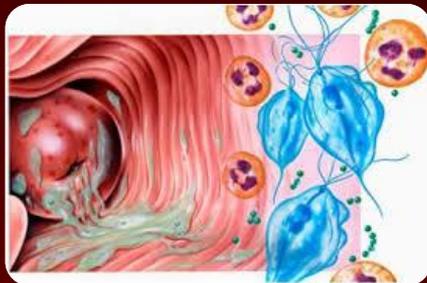
Infezioni Vaginali: Diagnosi



**Ph Vaginale normale
3.5-4.5**

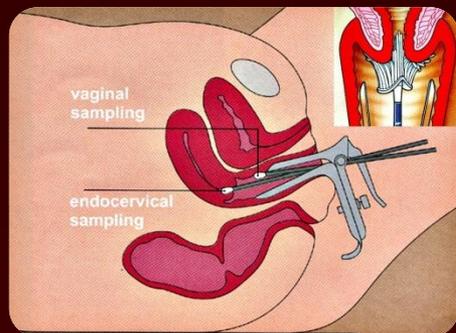


**Es. microscopico a fresco
delle secrezioni vaginali**



**Valutazione della
Sintomatologia**

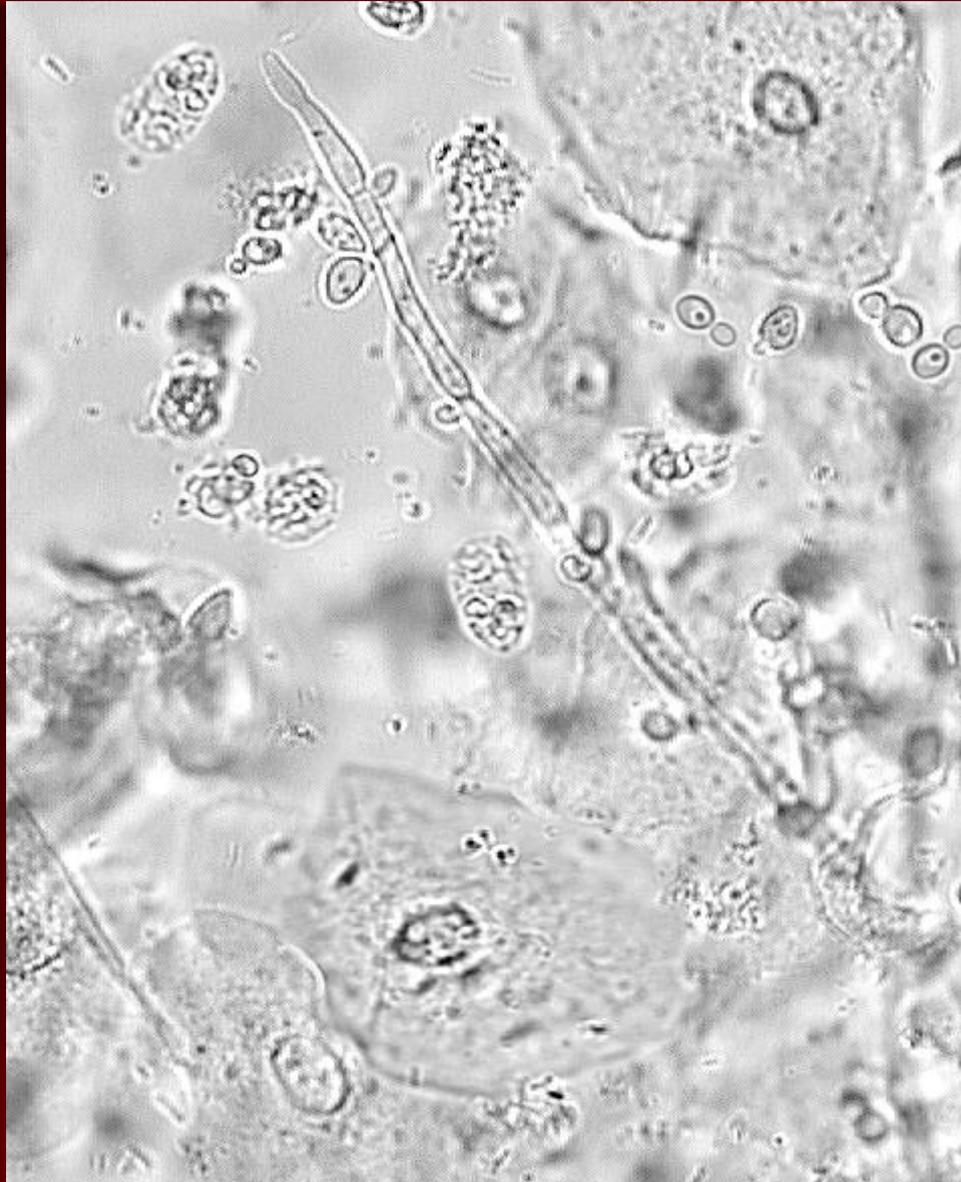
Esame microscopico a fresco



Esame microscopico a fresco



Esame microscopico a fresco



E-P ed ambiente vaginale

Table 2
Characteristics of vaginal discharge and microbial flora at baseline and after 2 months of oral contraceptive use

	Baseline visit (n = 30)	2-month visit on OC (n = 30)	p-value
Any <i>Lactobacillus</i>	26	23	.5
Any H ₂ O ₂ positive	17	15	.7
≥10 ⁵ H ₂ O ₂ positive ^a	16	9	.04
Only H ₂ O ₂ negative	8	7	.9
≥10 ⁵ H ₂ O ₂ negative	4	2	.7
Other <i>Lactobacillus</i>	1	1	.9
<i>Candida albicans</i> /yeast	3	3	.9
≥10 ⁵ Non- <i>Lactobacillus</i> isolates	16	11	.3
Any Group B streptococci	2	4	.6
Any <i>Gardnerella vaginalis</i>	12	8	.3
Any <i>Escherichia coli</i>	4	5	.9
≥10 ⁵ <i>Prevotella</i> sp.	3 (12) ^b	1 (10) ^b	.5
≥10 ⁵ Anaerobic gram positive cocci	2 (9)	2 (11)	.9
≥10 ⁵ Anaerobic gram negative rods	3 (12)	1 (12)	.5
<i>U. urealyticum</i>	15/28	10/29	0.04

No modificazioni nella flora batterica vaginale
-Lattobacillare
- Commensale

<i>Candida albicans</i> /yeast	3	3	.9
≥10 ⁵ Non- <i>Lactobacillus</i> isolates	16	11	.3
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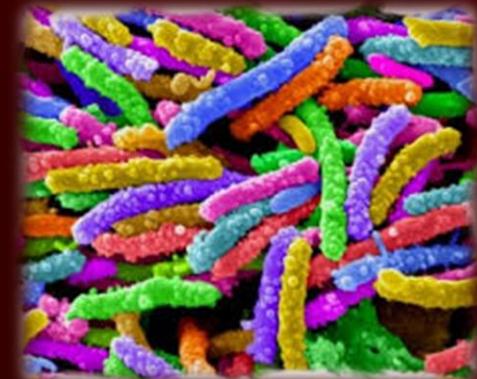
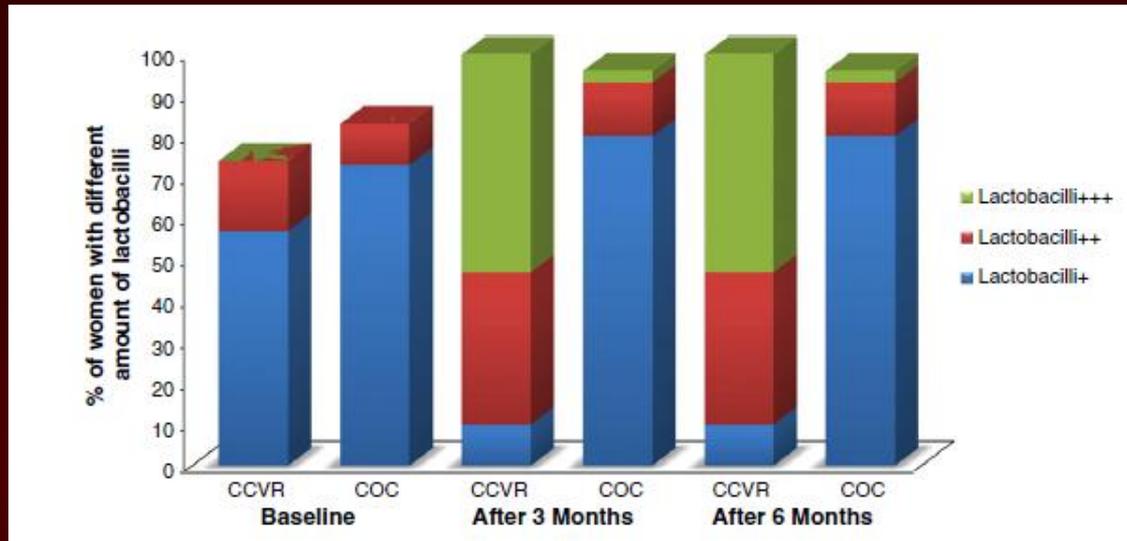
Baseline visit
(n = 30)

2-month visit
on OC
(n = 30)

p-value

26	23	.5
17	15	.7
16	9	.04
8	7	.9
4	2	.7

Contracezione ormonale ed ambiente vaginale



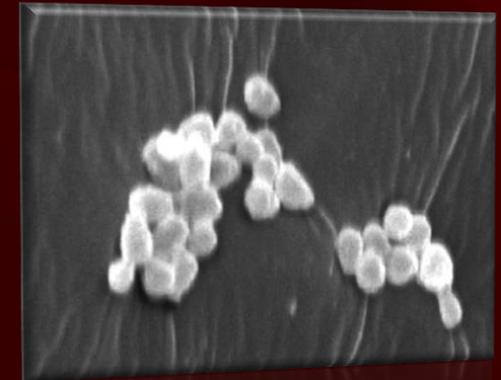
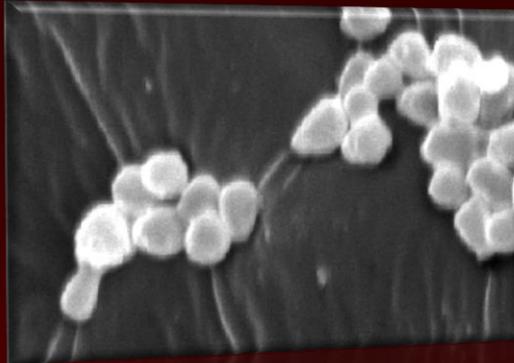
**No variazione significativa
della popolazione lattobacillare**



Original research article

Vaginal yeast adherence to the combined contraceptive vaginal ring (CCVR)[☆]

Daiane Pereira Camacho^a, Márcia E.L. Consolaro^b, Eliana Valéria Patussi^a, Lucélia Donatti^c, André Gasparetto^d, Terezinha I.E. Svidzinski^{a,*}



**-Adesività della Candida alla superficie del device
- Effetto potenziale facilitante allo sviluppo di
Candidosi ricorrente in soggetti predisposti**

E-P – Ecosistema Vaginale – Infezioni

ESTROGENI



PROGESTINICI

Tipo di Estrogeno (Sintetico/ Naturale)

Tipo di Progestinico

Regime di somministrazione

Effects of estroprogestins containing natural estrogen on vaginal flora

Francesco De Seta¹, Stefano Restaino¹, Rubina Banco¹, Ester Conversano¹, Rossella De Leo¹, Maddalena Tonon¹, Gianpaolo Maso¹, Giulia Barbati², and Stefano Lello³

GYNECOLOGICAL
ENDOCRINOLOGY

2014

E-P – Ecosistema Vaginale – Infezioni

Table 1. Comparison of vaginal milieu at baseline and at three and six months.

	Baseline				Three months				Six months			
	E2V+DNG	E2V+DNG	E2+NOMAC	E2+NOMAC	E2V+DNG	E2V+DNG	E2+NOMAC	E2+NOMAC	E2V+DNG	E2V+DNG	E2+NOMAC	E2+NOMAC
	Baseline				Three months				Six months			
	E2V+DNG	E2V+DNG	E2+NOMAC	E2+NOMAC	E2V+DNG	E2V+DNG	E2+NOMAC	E2+NOMAC	E2V+DNG	E2V+DNG	E2+NOMAC	E2+NOMAC
	N=28	N=28	N=30	N=30	N=28	N=28	N=30	N=30	N=28	N=28	N=30	N=30
	N	%	N	%	N	%	N	%	N	%	N	%
Lacto +	11	39	12	40	9	32	12	40	5	18	13	43
Lacto ++	2	7	4	13	7	25	11	37	9	32	11	37
Lacto +++/++++	13	46	13	43	12	43	7	23	14	50	6	20
GBS	2	7	0	0	5	18	0	0	2	7	0	0
Lacto ++	2	7	4	13	7	25	11	37	9	32	11	37
Lacto +++/++++	13	46	13	43	12	43	7	23	14	50	6	20
GBS	2	7	0	0	5	18	0	0	2	7	0	0

-NO incremento di Vaginiti/Vaginosi
 -Incremento flora lattobacillare
 - Riduzione Ph e Leucociti vaginali

E-P ed ambiente vaginale

Table 3

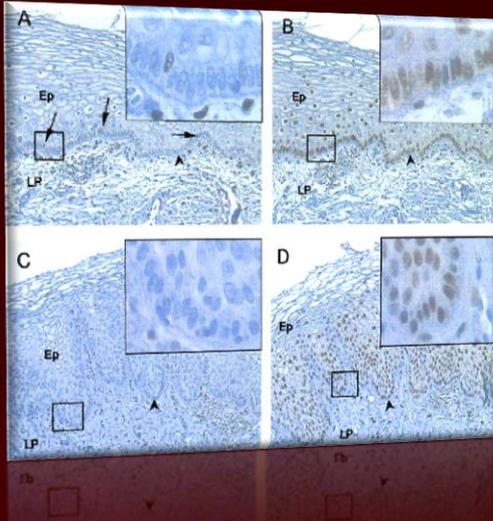
Characteristics of vaginal epithelium at baseline and after 2 months of oral contraceptive use

	Baseline visit (n = 30)	2-month visit on OC (n = 30)	p-value
Vaginal epithelium			
Mean number of cell layers ± S.E.	30.2 ± 1.0	29.6 ± 0.9	0.5
Vaginal epithelial thickness			
Total thickness ± S.E. (mm)	1.0 ± 0.1 (n = 14)	1.1 ± 0.1 (n = 14)	0.4
Vaginal epithelium cell population			
Mean # neutrophils in five fields	8.2 ± 0.8	7.2 ± 0.6	0.3
≥5 Neutrophils in 5 nonadjacent fields	15	13	0.8
Mitotic divisions	6	3	0.4
Plasma cells	1	4	0.4

**No variazione
significativa
nelle caratteristiche
dell'epitelio vaginale**



Contraccezione ormonale ed ambiente vaginale



- **Contraccettivi E-P**
- **LNG impianto**
- **MAP iniettivo**

- Riduzione recettori vaginali del progesterone e degli estrogeni con MAP
- No variazioni significative recettoriali con E-P e LNG



ELSEVIER

Contraception 72 (2005) 383–392

Original research article

Steroid receptor expression in vaginal epithelium of healthy fertile women and influences of hormonal contraceptive usage

Anna Ildgruben^{a,b,*}, Inga Sjöberg^a, Marie-Louise Hammarström^b, Torbjörn Bäckström^a

Contraception

Vulvovaginal Candidiasis in Postmenopausal Women: The Role of Hormone Replacement Therapy

Journal of Lower Genital Tract Disease, 2011

Gayle Fischer, MBBS, FACD¹ and Jennifer Bradford, MBBS, FRANZCOG²

Table 2. Characteristics of Postmenopausal Patients With VVC (n = 34)

Age at presentation, mean (range), y	61.3 (47–78)
Age at menopause, mean (range), y	5.9 (40–58)
Duration of HRT, mean (range), y	6.2 (0.1–26)
Duration of symptoms, mean (range), y	2.8 (0.1–17)
Time from onset of HRT to onset of symptoms, mean (range), y	3.4 (0.1–9)
Organism at low vaginal swab, n (%)	
<i>C. albicans</i>	32 (94)
<i>C. glabrata</i>	2 (6)
HRT, n (%)	
Systemic	17 (50)
Topical	27 (50)
Topical + systemic	8 (24)
History of recurrent or chronic candidiasis before menopause, n (%)	23 (67%)
History of previous failure of antifungal treatment	22/34 (100%)
History of recurrent or chronic candidiasis before menopause, n (%)	23 (67%)
Signs, n (%)	
Itch	26/34 (76)
Sore	26/38 (76)
Dyspareunia	18/24 (75)
Burning	3 (8)
Swelling	2 (7)
Splitting	2 (7)
Discharge	2 (7)
Dysuria	3 (8)
Signs, n (%)	
Erythema of labia minora and vagina	34 (100)
Edema of labia minora	5 (15)

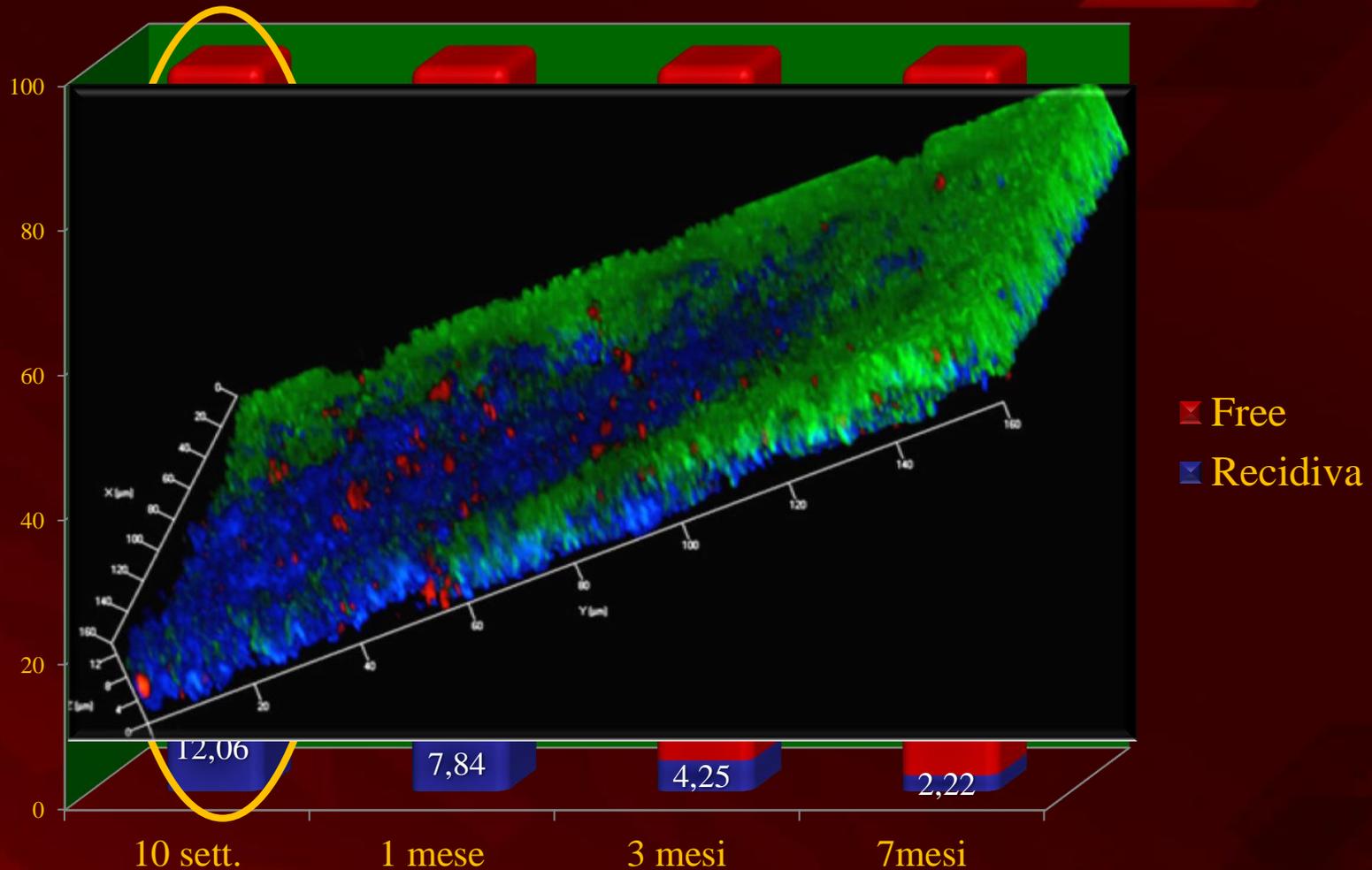
- Maggiore incidenza di candidosi nelle donne in TOS
- 70% dei casi candidosi ricorrente prima della MP

Estrogenizzazione



Predisposizione

Can *Lactobacillus fermentum* LF10 and *Lactobacillus acidophilus* LA02 in a slow release vaginal product be useful for prevention of recurrent vulvovaginal candidiasis? A clinical study.



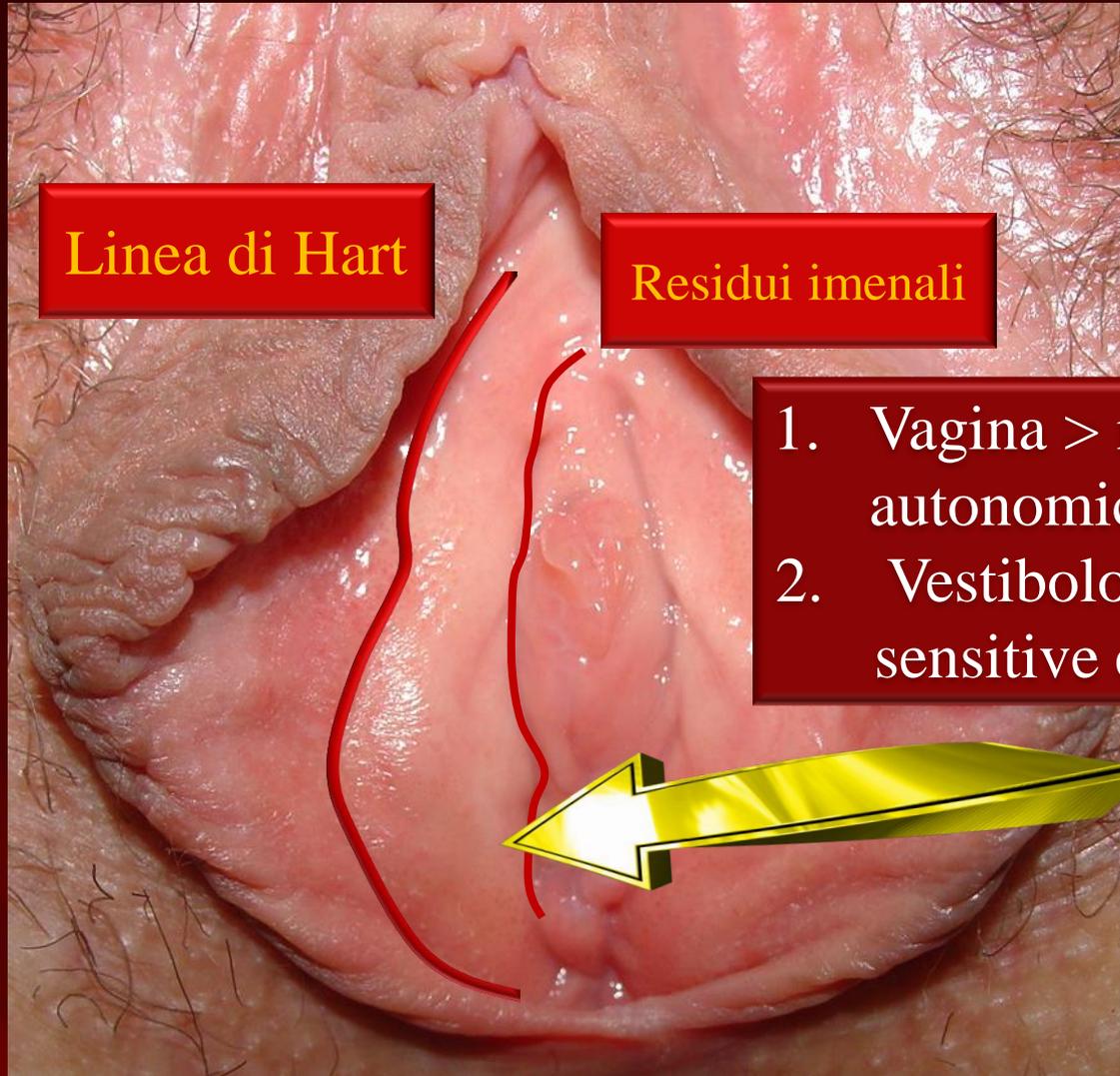
Candidosi vulvovaginale ed E-P quale relazione?



**La pillola contraccettiva
NON è causa di Candidosi
MA**

- Soggetti predisposti**
- Biofilm protettivi**

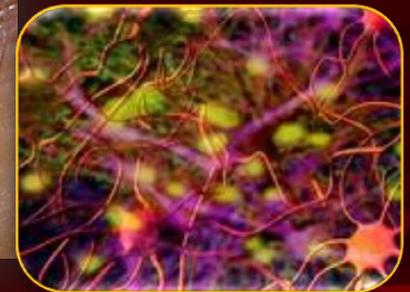
Vestibolo Vaginale



Linea di Hart

Residui imenali

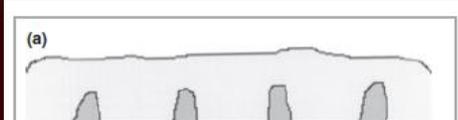
1. Vagina > n° terminazioni autonome
2. Vestibolo > n° terminazioni sensitive e > n° recettori EE



The vulval vestibular mucosa—morphological effects of oral contraceptives and menstrual cycle

U. Johannesson, B. Blomgren,* M. Hilliges,† E. Rylander and N. Bohm-Starke

British Journal of Dermatology 2007

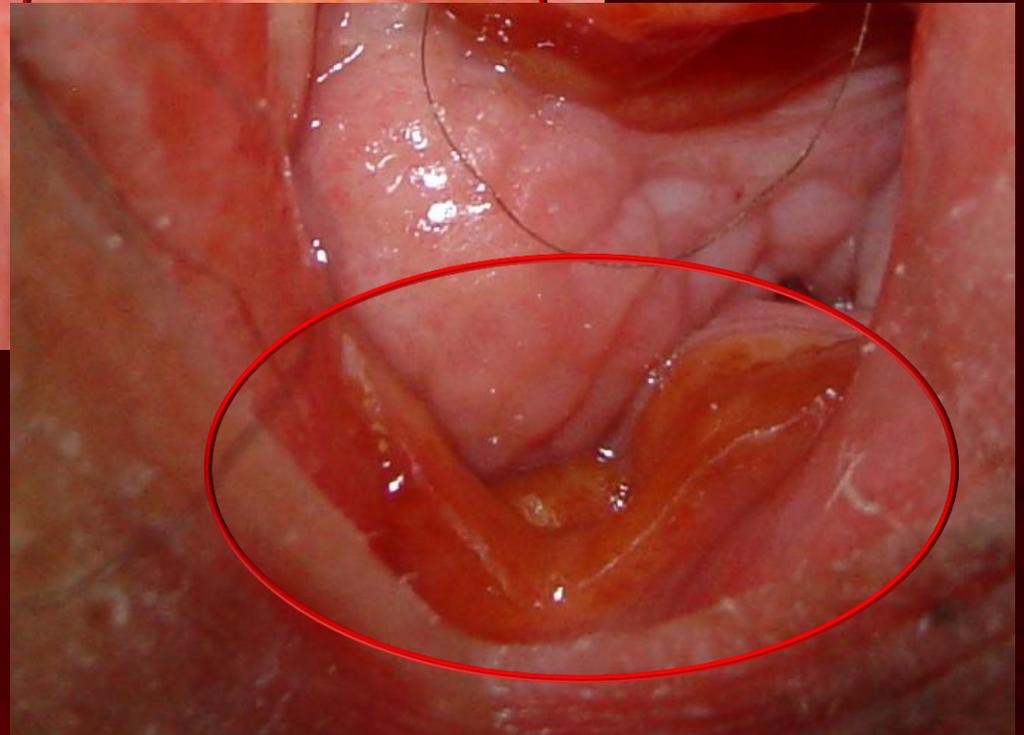
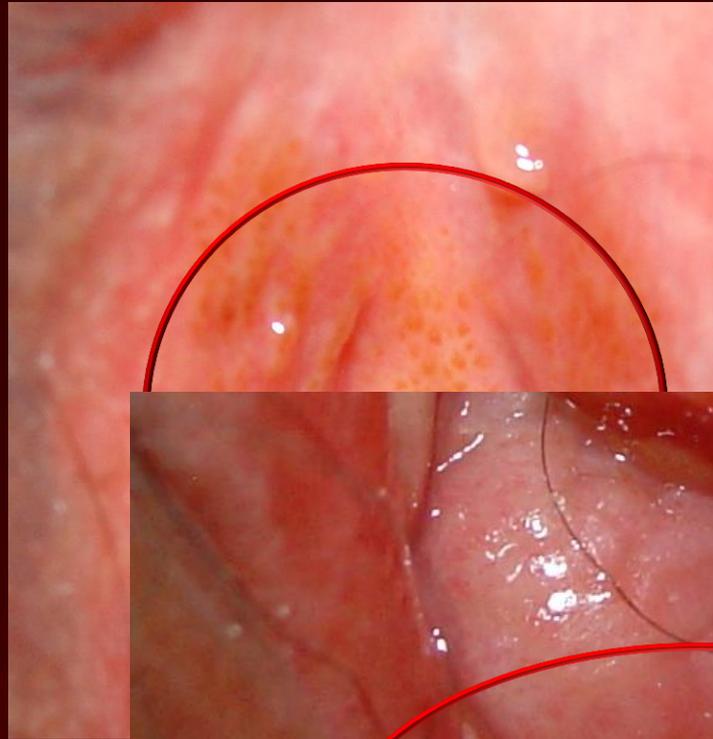


Attività biologiche dei progestinici

Progestinici	Antiestrogenico	Estrogenico	Androgenico	Antiandrogenico	Glucocorticoide	Antimineralcorticoide
Clormadinone	+	-	-	+	+	-
Ciproterone acetato	+	-	-	++	+	-
Dienogest	+/-	+/-	-	+	-	-
Drospirenone	+	-	-	+	-	+
Deso/Etonogestrel	+	-	+	-	-	-
Gestodene	+	-	+	-	+	+
Levonorgestrel	+	-	+	-	-	-
Medrossiprogesterone acetato	+	-	+/-	-	+	-
Nomegestrolo acetato	+	-	-	+/-	-	-
Noretisterone	+	+	+	-	-	-
Norelgestromin	+	-	+	-	-	-
Progesterone	+	-	-	+/-	+	+

Aspetto simile nelle donne in fase luteale che non usano E-P

Modificazioni Vestibolari



Take home messages

Corretta
Diagnosi

Fisiopatologia
e concetto di
Biofilm

Contracezione
personalizzata



E-P – Ecosistema Vaginale – Infezioni

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