

FERRARA 07.10. 2016

OSTETRICIA e GINECOLOGIA 2016

*Centro Salute Donna
Azienda USL Ferrara*



**SALA IMBARCADERO
CASTELLO ESTENSE**

11.20 Contraccezione e via vaginale - *F. De Seta*



PERSONALIZZAZIONE

Tollerabilità, sicurezza,
compliance ed efficacia
contraccettiva

- Molecole
- Formulazioni
- Vie di somministrazione

	Available		Not available		Withdrawn (in most countries)		
June 2014	Progestin type						
Estrogen dose (µg)	Norethi-sterone	Levonor-gestrel	Norges-timate	Desogestrel or etonogestrel	Gestodene	Drospirenone	Cypro-terone acetate
Combined hormonal contraception							
50 µg EE							
30 – 40 µg EE							
20 µg EE							
E2	E2V DNG			E2 NOMAC			
Non-oral			Patch	Vaginal ring			
Progestin only contraception							
Oral				Desogestrel		Drospirenone	
Non-oral	Depot	LNG-IUS		Implant			





PRATICA in CERCA di TEORIA



VAGINAL RING:THEORY

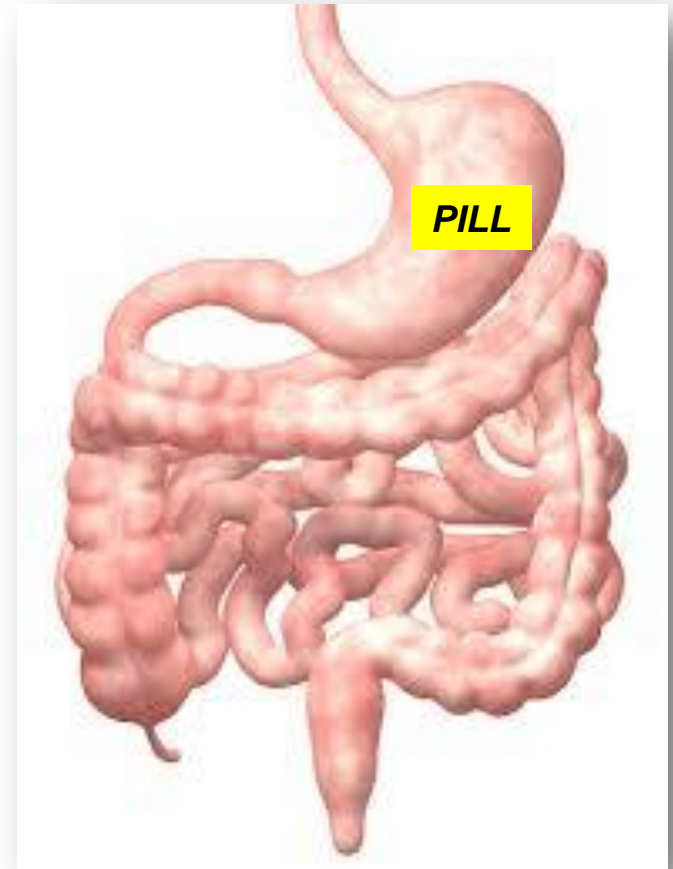
15 µg EE / 120 µg etonogestrel



- ⑩ Long acting contraceptive "user controlled"
- ⑩ Capability of vaginal epithelium to absorb steroids
- ⑩ Avoiding **gastrointestinal absorption** and hepatic first pass metabolism
- ⑩ **Slow diffusion at constant rate**
- ⑩ **Greater bioavailability and lower dose**

Individual variation in pill-users

- Absorption
- Metabolism (gut and liver)
- Degree of binding to transport proteins (SHBG)
- Re-absorption by the large-bowel flora
- Target organ sensitivity



the pill-free week

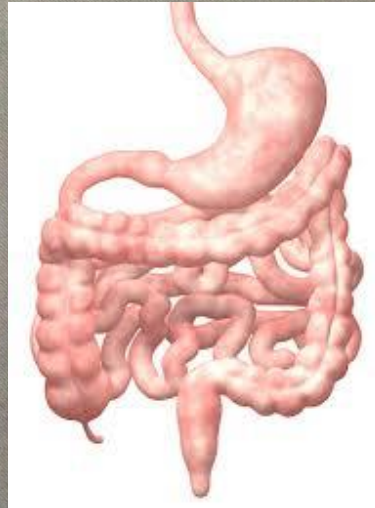
10 Diffusion (at constant rate)

Artificial
E+P

Days of pill cycle
Tablet taking

15 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5 6 7 → 21
○ ● ● ● ● ○ ○ ○ ○ ○ ○ — — \bar{x} \bar{x} \bar{x} \bar{x} — ○ ○ ○ ○ ○ ○ ○ ● ● ● ● ○

WTB



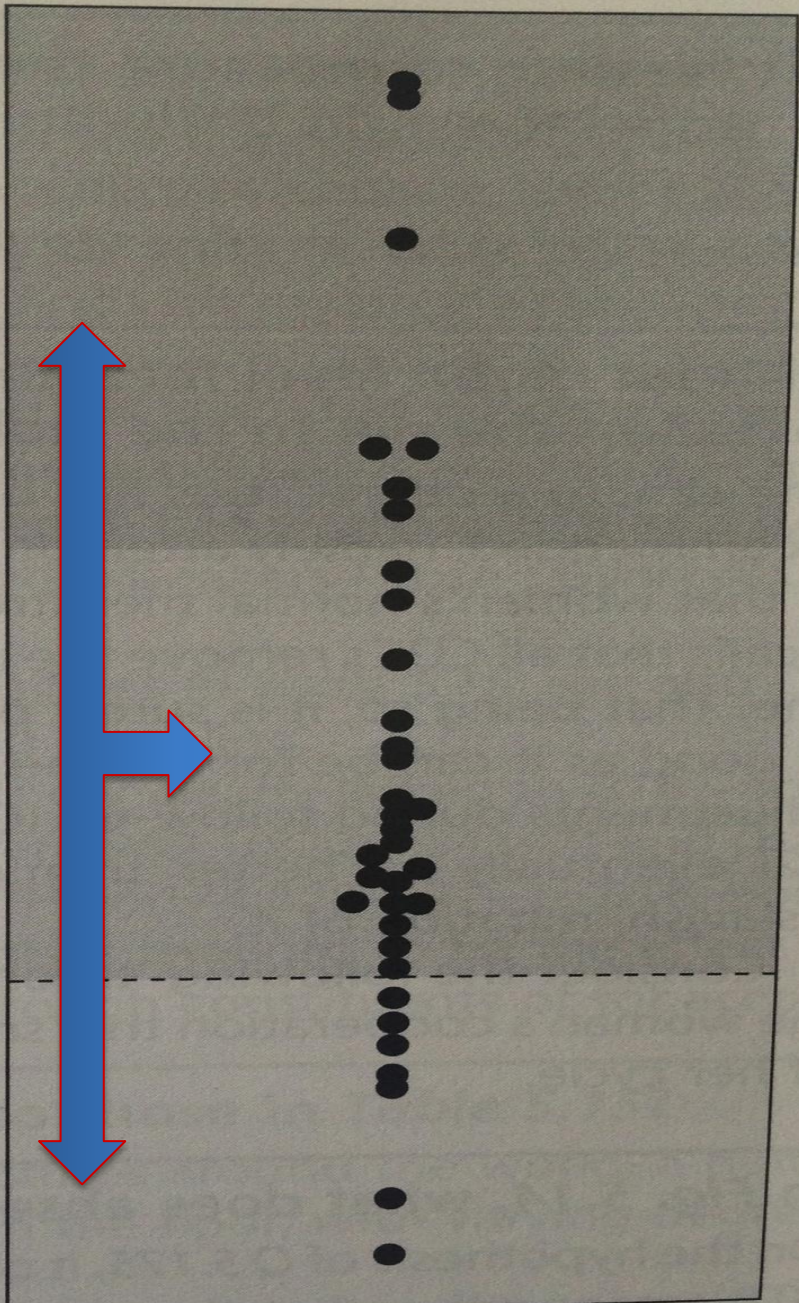
Titration of COC dose

Zone of high blood levels
(& metabolic impact?)

'Ideal' zone

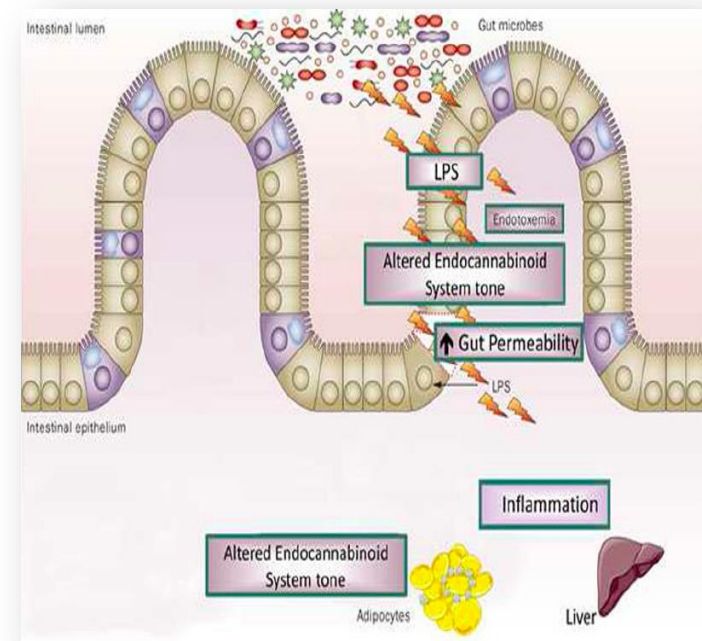
Bleeding threshold

Zone of BTB

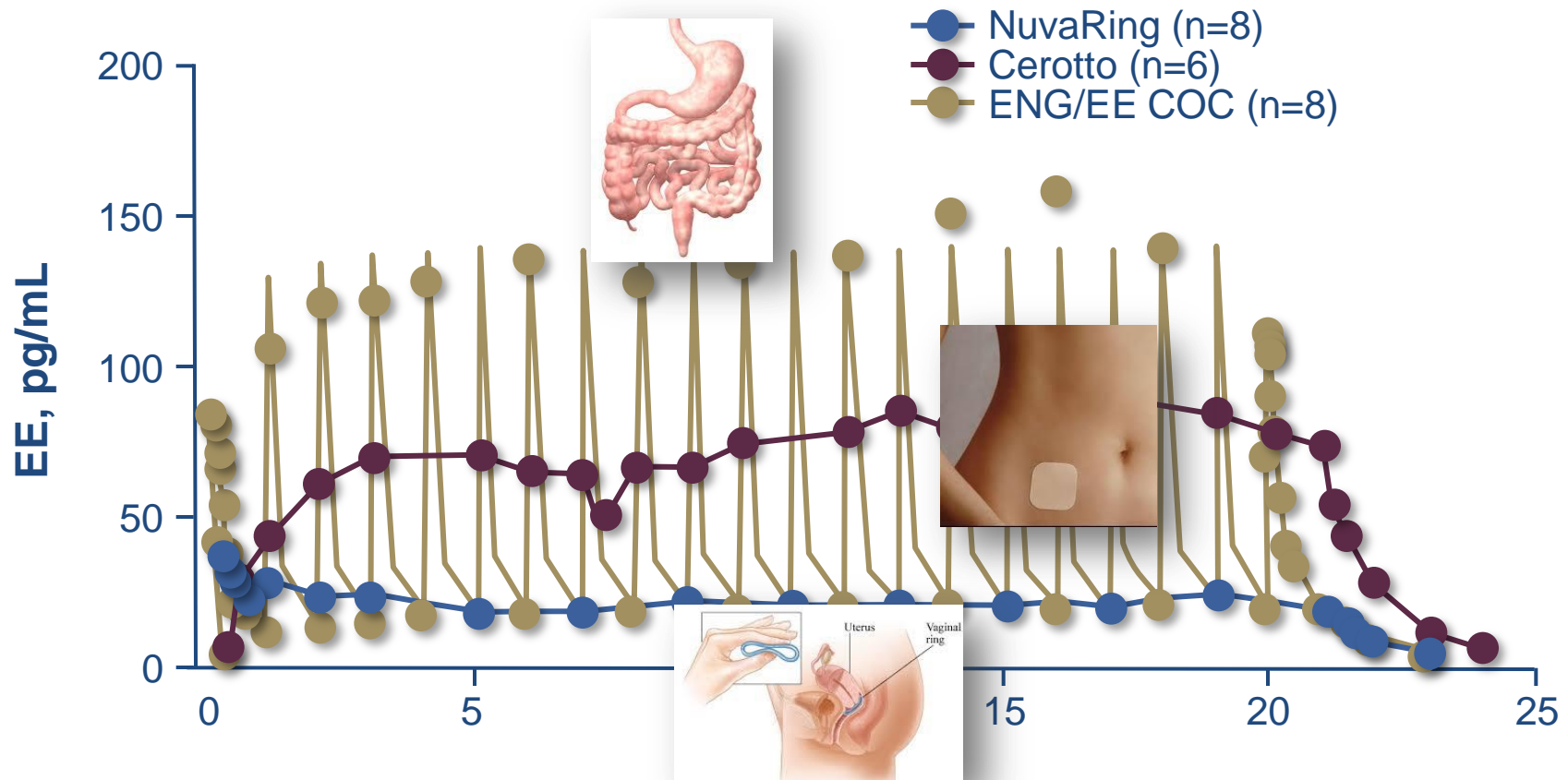


GI Tract and hormones

- **Estrobolome and diet**
 - Breast are bigger than in the past
 - Increase of Breast cancer
 - Increase of infertility
- **Estrogens and gut**
 - **Microbes are the “switchers” that determine whether the estrogen goes out of the body or is reabsorbed**



Advantages of slow release system of administration



⑩ Greater bioavailability and lower dose

La via vaginale: dalla teoria alla pratica

COMPLIANCE ?

COMPLIANCE



Improving compliance to
medicine has a greater
impact than any
improvement in
medical treatment

(World Health Organisation 2003)



AUTHORS' CONCLUSIONS

Skin patch and vaginal ring versus combined oral contraceptives for contraception (Review)

Lopez LM, Grimes DA, Gallo MF, Schulz KF

Implications for practice

Patch users had increased risk for breast discomfort, painful periods, nausea, and vomiting. In contrast, ring users had less nausea,

Patch users had increased risk for breast discomfort, painful periods, nausea, and vomiting. In contrast, ring users had less nausea, irritability and depression than COC users in single trials. Ring users often had fewer bleeding problems but more vaginal irritation and discharge.

THE COCHRANE
COLLABORATION®

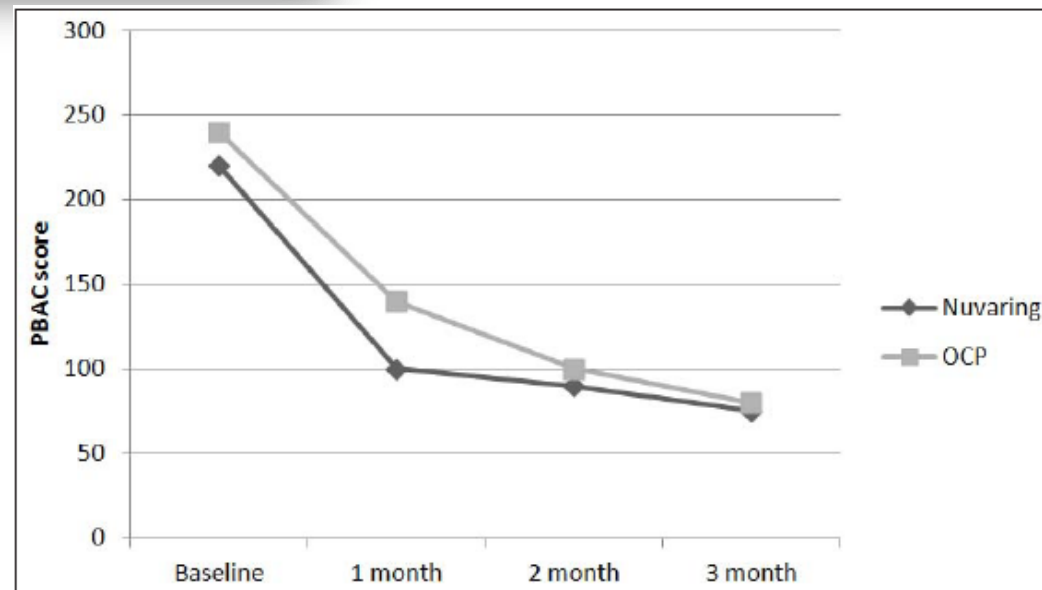
ials. Ring
inal irrita-

nal ring
should be reported in a manner consistent with CONSORT
guidelines. More detailed reporting on data collection instruments
and their analysis would aid interpretation of compliance and sat-
isfaction results. The validity of results could be compromised by
high losses to follow up and losses that differed between the study
groups.

A Randomised Controlled Trial
Comparing the Efficacy and Side-Effects
of Intravaginal Ring (Nuvaring®) With
Combined Oral Hormonal Preparation in
Dysfunctional Uterine Bleeding

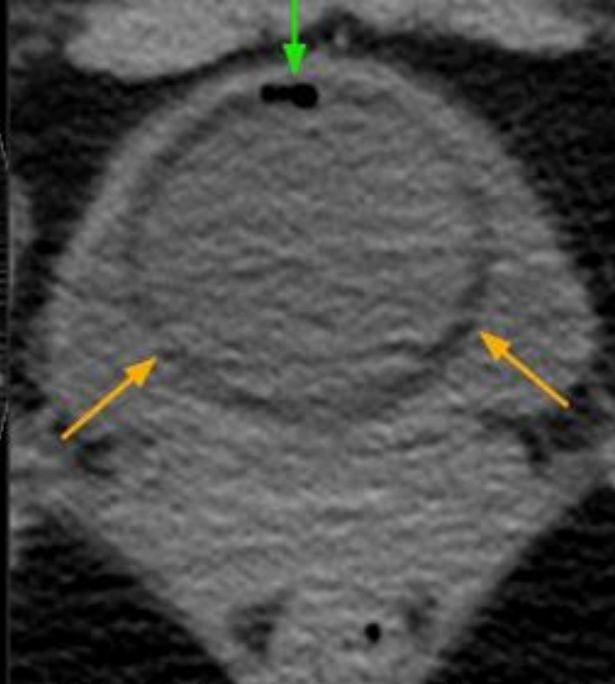
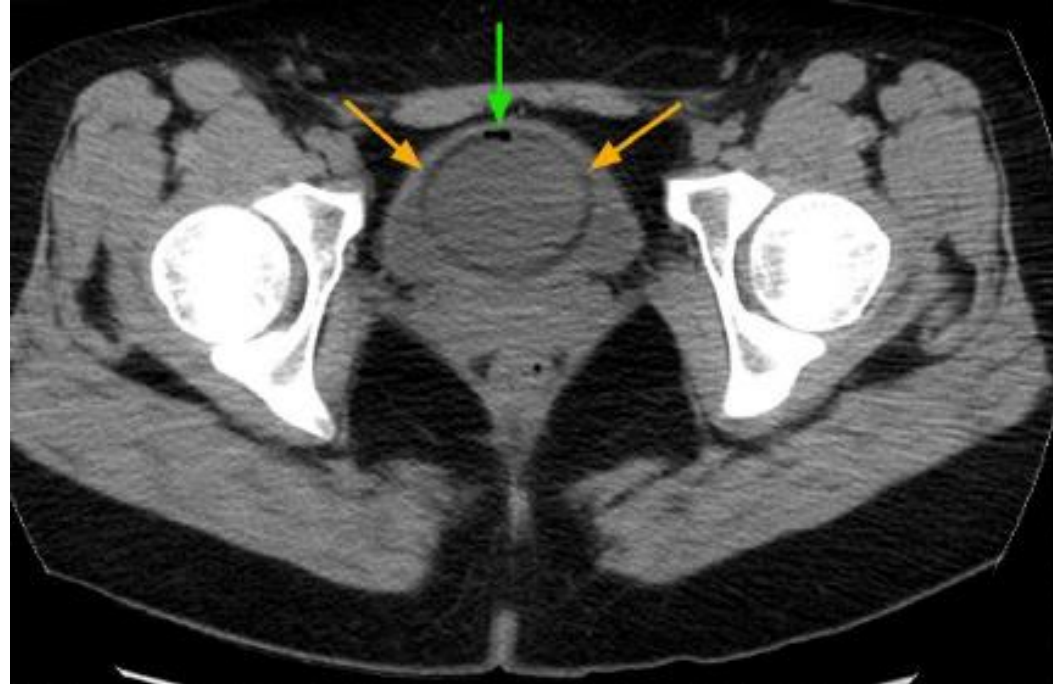
Parameters	Nuvaring (N=30)	OCP (N=28)	p-value
Satisfaction	29 (96.7%)	23 (82%)	0.854
Recommendation	27 (90%)	20 (71%)	0.704
Continuation	27 (90%)	20 (71%)	0.488
Discontinuation	03(10%)	08 (28.5%)	0.783

A Randomised Controlled Trial
Comparing the Efficacy and Side-Effects
of Intravaginal Ring (Nuvaring®) With
Combined Oral Hormonal Preparation in
Dysfunctional Uterine Bleeding



Conclusion: Present study shows Nuvaring® to be as effective as COC in controlling heavy menstrual bleed, better cycle control, with minor acceptable systemic side effects.

A 31 year old Caucasian female presented to our emergency department after being unable to retrieve a NuvaRing® for its scheduled removal 3 weeks after its initial self-placement. The patient had not experienced expulsion of the device and therefore feared that she had placed the NuvaRing® transurethrally. The patient was G2P2, 2 months postpartum, and had just started NuvaRing® contraception for the first time after the birth of her second child. She acknowledged urinary frequency and mild dysuria over the past few weeks. When questioned, the patient described some discomfort during initial placement of the NuvaRing®, but was unaware that the discomfort was abnormal since it was her first time placing the device. Surgical history was remarkable



Inadvertent intravesicular placement of a
vaginal contraceptive ring:
a case report and review of literature

Etiology	Incorrect placement of NuvaRing® device	
Incidence	Rare, only 3 other case reports acc	
Gender ratio	Essentially can only occur in	
Age predilection	Can occur in any age would seek contr related iss	nts
Risk factors	No	
Treatment		
Prognosis		
Findings on		the ability to determine

TEACHING POINT

The flexible construction of the NuvaRing® can allow for potentially asymptomatic transurethral passage of the device, and thus radiologists should be familiar with the radiologic appearance of intravesicular NuvaRing® positioning since clinicians may have incorrectly assumed interim expulsion

...ense to surround urine. An air locule
...lled bladder should be possible, but

... a circular/ovoid structure with hypointensity on T1 and T2
... placed within the bladder, the ring will be better visualized on fluid
... improved contrast from the surrounding hyperintense urine.

... bladder should be adequately distended for the examination. NuvaRing® will then be
... a hyperechoic structure within a bladder filled with anechoic urine. Since the ring will
... ally be imaged in cross-section, 2 hypoechoic foci will typically be seen.

- Scintigraphy- Due to the small thickness of the NuvaRing®, it will likely not be amenable to visualization on scintigraphy.

Vaginal route: PMS ?



Sindrome premestruale e disturbo disforico premestruale

L'uso di qualsiasi contraccettivo ormonale e' associato ad una significativamente piu' bassa prevalenza di sintomi premestruali



Preferibili associazioni con....



Progestinico a azione anti-mineralcorticoide

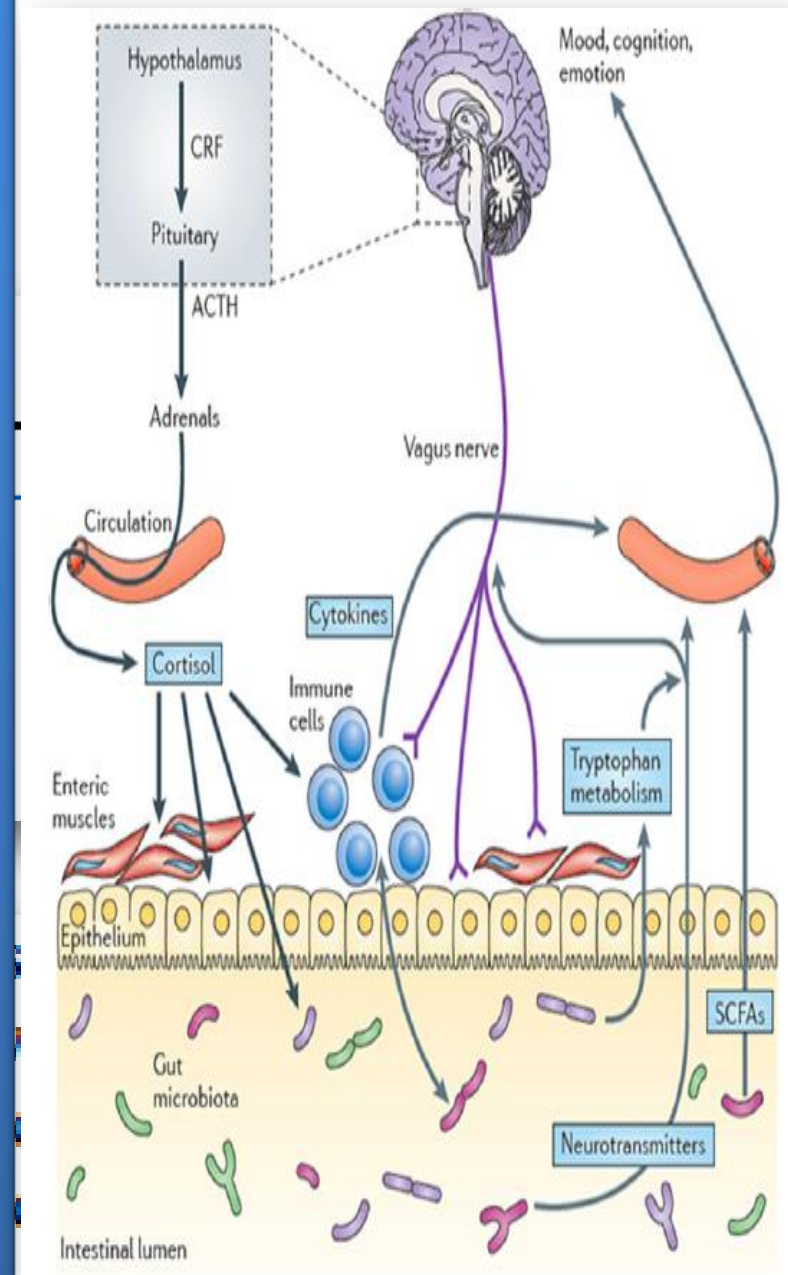
azione anti-androgenica

azione positiva a livello centrale

- Bassa dose della componente **estrogenica**
- Persistente inibizione delle **fluttuazioni** degli
steroidi ovarici (regime di somministrazione)

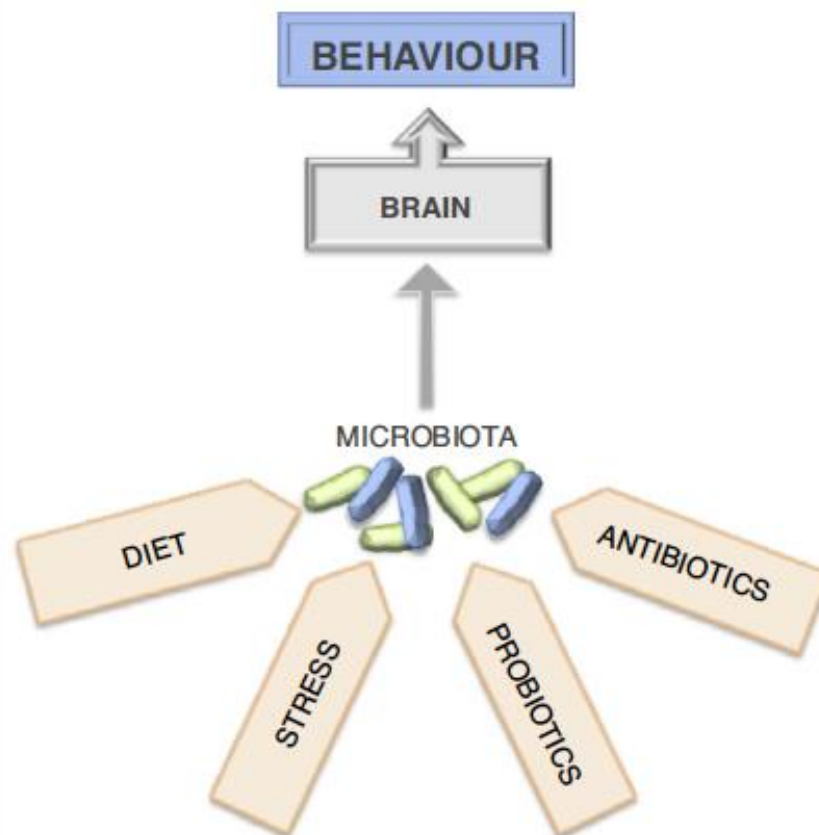


- Gut microbes are involved in early brain development (**brain-gut interaction**)
- Gut neurotransmitter serotonin involved in learning, mood and sleep
- Neuroendocrine cells in gut produce 80% of serotonin and gangliosides
- Bacteria are talking to these neuroendocrine cells



Gut brain axis: diet microbiota interactions and implications for modulation of anxiety and depression

Ruth Ann Luna^{1,2} and Jane A Foster^{3,4}



Vaginal route: STI or VAGINITIS ?




Hormonal contraception and HPV



- COC as promoter for HPV-induced carcinogenesis
- The use of COCs for >6 years is associated with an increased risk of infection with any HPV [RR 1.88] and any HR-HPV [PR: 2.68] as compared to never users
- Women with persistent HPV, who used oral contraceptives for more than 5 (WHO) or 8 (RCOG) years, had an increased risk of squamous-cell cervical cancer, compared to women with HPV who had never used OCs

Hormonal contraception and HPV

	COC	P	R	CIC	
CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN) 	2	2	2	2	Evidence: Among women with persistent Human papilloma virus (HPV) infection, long-term COC use (≥ 5 years) may increase the risk of carcinoma in situ and invasive carcinoma.(30;297) Limited evidence on women with low-grade squamous intraepithelial lesions found use of the vaginal ring did not worsen the condition.(30)
CERVICAL CANCER* (awaiting treatment)	2	2	2	2	

carcinoma.(30;297) Limited evidence on women with low-grade squamous intraepithelial lesions found use of the vaginal ring did not worsen the condition.(30)



Local adverse events and Nuvaring

Adverse event	Treatment-related
Vaginal discharge	5.3%
Vaginitis	5.0%
Device-related events	3.8%
Vaginal discomfort	2.2%



Roumen et al, Hum Reprod, 2001;16:469–75

A Comparison Between the Vaginal Ring and Oral Contraceptives

Sharry Veres, MD, Leslie Miller, MD, and Bart Burington, MS

CONCLUSION: Some women may notice an increase in vaginal wetness during contraceptive ring use yet the method is well tolerated and appears to improve the vaginal flora. (Obstet Gynecol 2004;104:555- 63. © 2004 by The American College of Obstetricians and Gynecologists.)

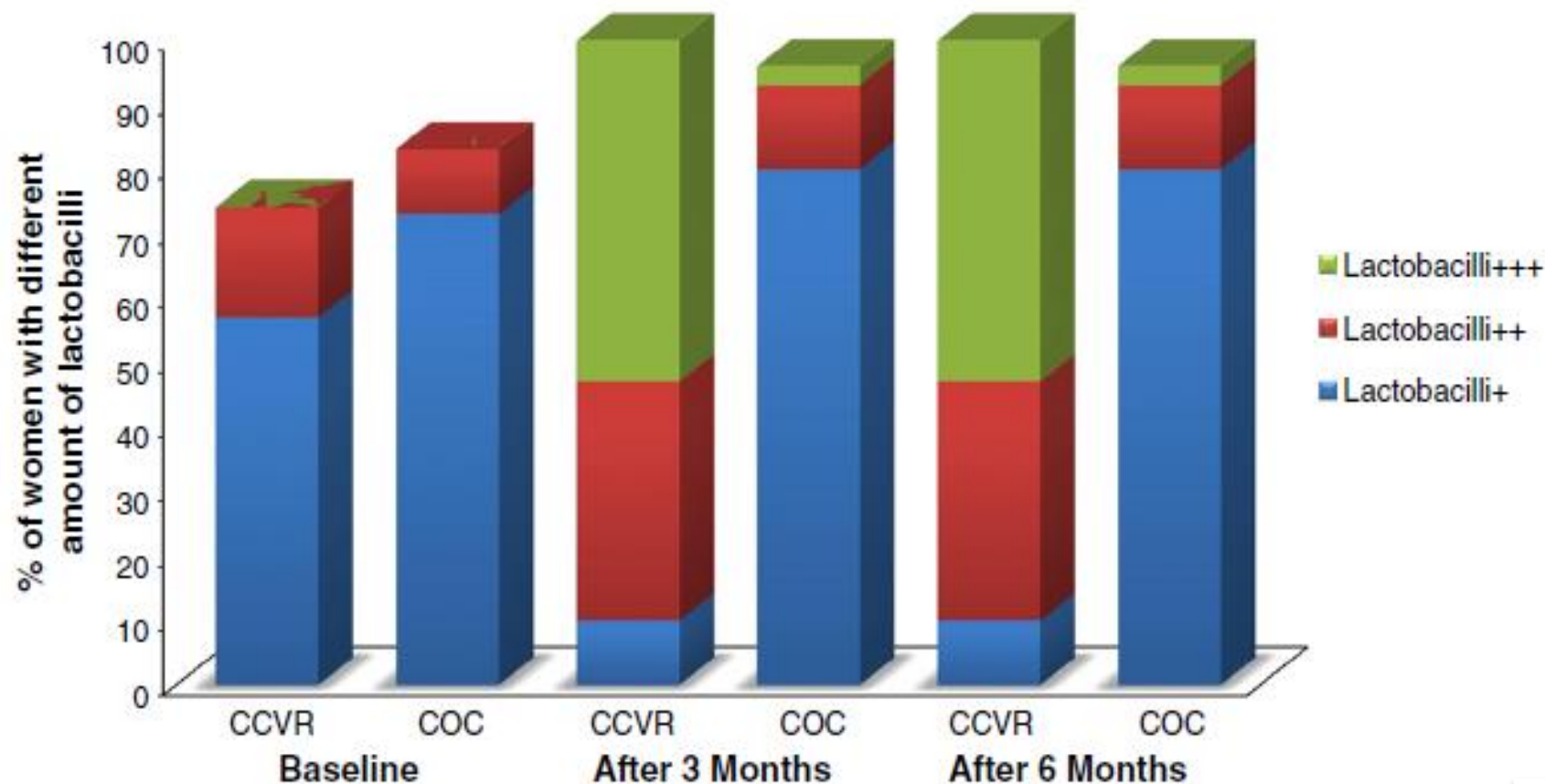
LEVEL OF EVIDENCE: I



Effects of hormonal contraception on vaginal flora.

De Seta F, Restaino S, De Santo D, Stabile G, Banco R, Busetti M, Barbati G, Guaschino S.

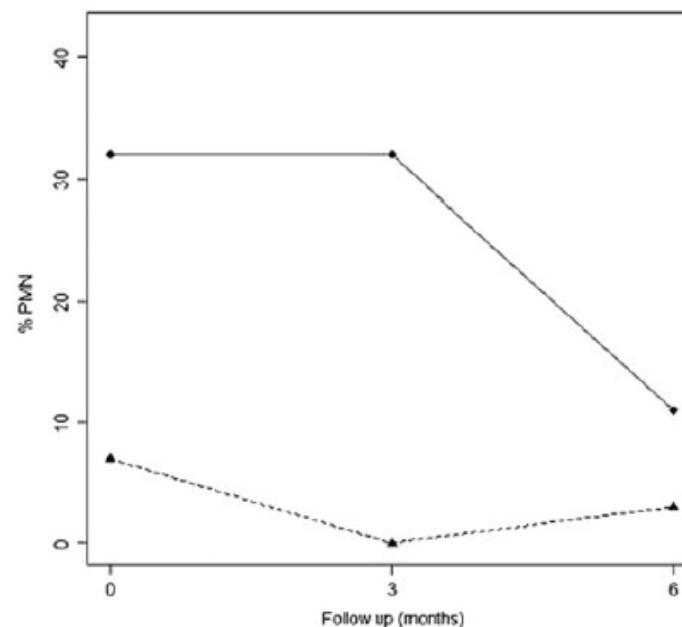
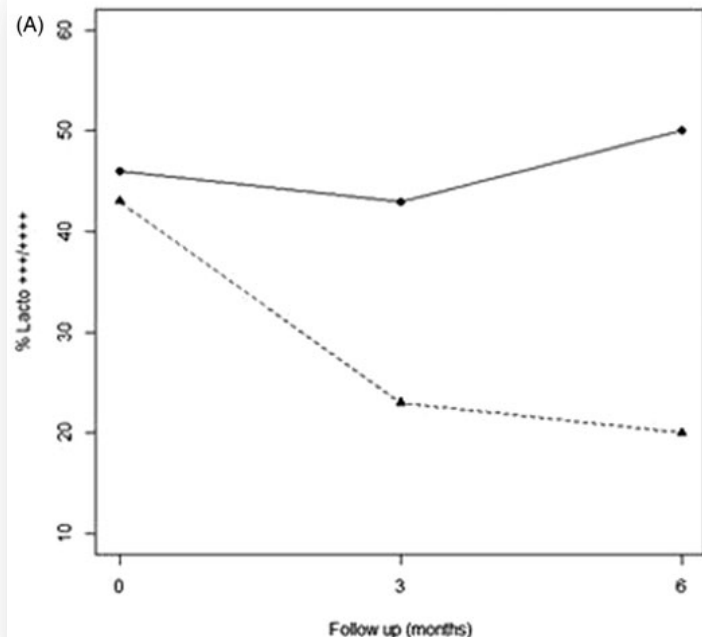
disegno di studio	materiali & metodi	risultati	discussione	conclusioni
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ORIGINAL ARTICLE

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 Barbatì², and Stefano Lello³



E2V/DNG rather than EV/NomAc showed a modification of vaginal milieu in terms of increase of lactobacillar flora, reduction of vaginal pH and less recovery of vaginal leukocytes,

Vaginal Route: PCOS ?



Acne / iperandrogenismi

Sindrome metabolica

**Iperandrogenismo
in paziente con sindrome
metabolica**

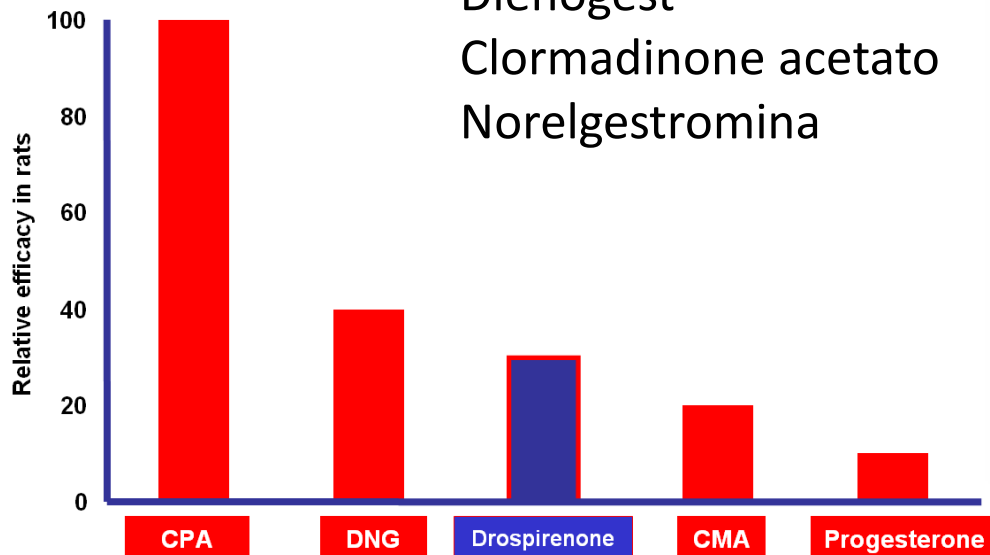


Tutte le associazioni OC sono capaci di

- ❑ Ridurre/sopprimere Iperandrogenismo biochimico
- ❑ **Aumentare SHBG**

Alcune associazioni OC contengono Progestinici ad azione antiandrogena specifica

Ciproterone acetato
Drospirenone
Dienogest
Clormadinone acetato
Norelgestromina



Contraception and diabetes

- Diabetogenic effect of hormonal contraception
 - EE responsible for insulin resistance
 - Progestins are associated with changes in the insulin half-life and increased insulin response to glucose
- The most androgenic progestins may be associated with impaired glucose tolerance and increased insulin resistance
- Thrombotic risk



Carbohydrate metabolism

- Progestin-only formulations or COC with desogestrel or low-dose norethisterone were associated with the most favorable profiles (Godsland,1992)
- No changes with transdermal therapy (Godsland,1993) and NOMAc (less impact than second-generation COC)
- **Vaginal contraception has favorable effect on carbohydrate metabolism than the oral route (Cagnacci,2009)**



PIU RISCHIOSA ?



Rischio patologia arteriosa nelle COC users

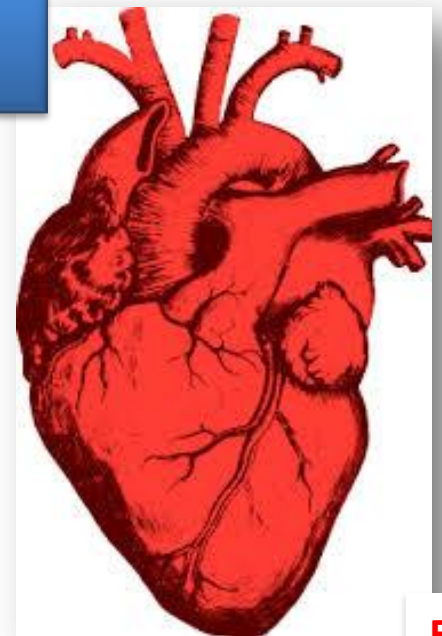
Possibile minor rischio per i progestinici a minor impatto androgenico

Dati su associazioni con progestinico di 2° e 3° generazione

Dosaggio estrogenico < 30 mcg

POP / IUD LNG e no rischio arterioso

Eta`, fumo, ipertensione, emicrania, profilo lipidico, diabete



The relative risk of thrombotic stroke in current users of different types of hormonal contraception according to estrogen dose, progestin type and route of administration.



High-risk products (RR \geq 4.5)



Low-risk products (RR 1.5 – 4.4)



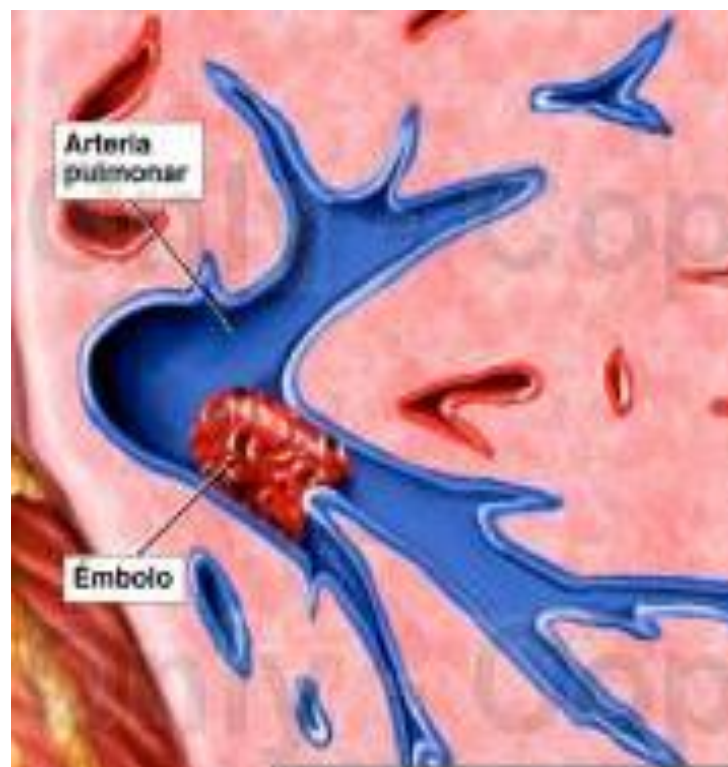
No risk products (RR < 1.5)



No data available

Estrogen dose (μg)	Norethis-terone	Levonor-gestrel	Norges-timate	Desogestrel or etonogestrel	Gestodene	Drospirenone	Cyproterone acetate
Combined hormonal contraception							
50	3*						
30 – 40	2.2*	1.7*	1.5*	2.2*	1.8*	1.6*	1.4
20				1.5*	1.7*	0.9	
E2	E2V DNG		E2 NOMAC				
Non-oral			Patch 3.2	Vaginal ring 2.5*			
Progestin only contraception							
Oral	1.4			Desogestrel 1.4		Drospirenone	
Non-oral	Depot 1	LNG-IUS 1		Implant 1			

Rischio tromboembolico venoso nelle COC users



Possibile minor rischio per i progestinici a maggior impatto androgenico (LNG)

Non ancora disponibili dati per associazioni con E2V ed E2

The relative risk of venous thromboembolism in current users of different types of hormonal contraception according to estrogen dose, progestin type and route of administration



High-risk products (RR \geq 4.5)



Low-risk products (RR 1.5 – 4.4)



No risk products (RR < 1.5)



Limited data



No data available

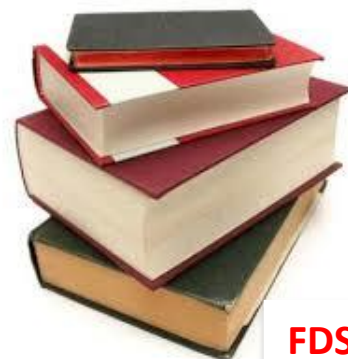
Estrogen dose (μ g)	Norethisterone	Levonorgestrel	Norgestimate	Desogestrel or etonogestrel	Gestodene	Drospirenone	Cyproterone acetate
<i>Combined hormonal contraception</i>							
50	6						
30 – 40	3	3	3	6	6	6	6
20				5	6		
E2	E2V DNG 4.5			E2 NOMAC			
Non-oral			Patch 7	Vaginal ring 6			
<i>Progestin only contraception</i>							
Oral	1			Desogestrel 1		Drospirenone	
Non-oral	Depot 2	LNG-IUS 1		Implant 1.4			

Nuvaring un passo indietro?

**"NuvaRing Update: October 2011
FDA Study Finds Increased Risk Of
Pulmonary Embolism (PE) And
Deep Vein Thrombosis (DVT)"**

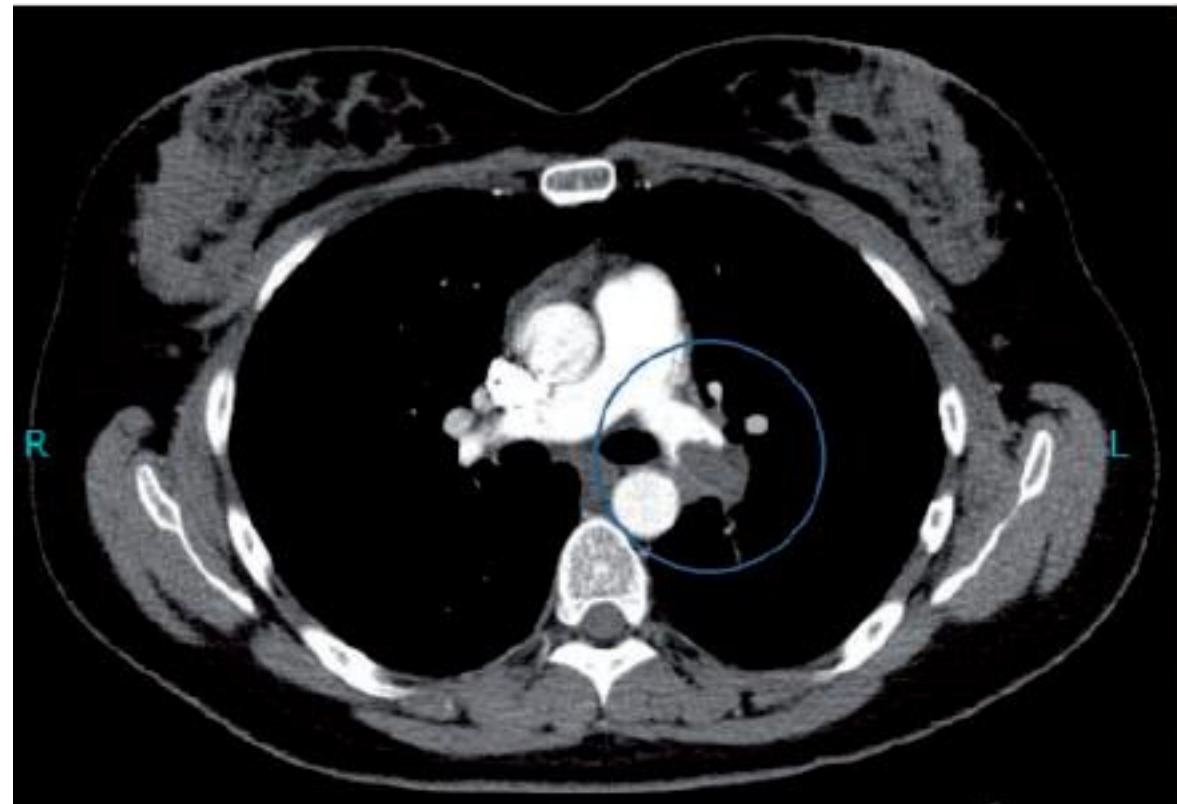


- **Studio Danese**: studio su database retrospettivo (2001-2010) con solo la all-user analisi. COC comparatori contenenti Levonorgestrel. Nessuna informazione su BMI, fumo, storia familiare.
- **StudioTASC**: studio prospettico osservazionale di coorte: tutte le 33.000 donne incluse nello studio sono “new users”(starters e re-starters and recurrent users). Diversi COC comparatori. Informazioni su tutti i rilevanti fattori di rischio TEV.
- **Studio FDA**: studio su database retrospettivo con new-user analisi (solo le starters, n=573,680) tra gennaio 2001 e dicembre 2007 . COC a base di DRSP, Cerotto transdermico, Nuvaring comparati con diversi COC di II generazione: Nessuna informazione su BMI, fumo, storia familiare.



Pulmonary embolism due to a contraceptive vaginal ring (NuvaRing®)

I Krivokuca¹ and J-WJ Lammers²





A 29-year-old female, user of a VCR NuvaRing, presented to our emergency department with an eight-day history of dyspnea and chest pain. Usually she runs almost every day but since eight days she finds it difficult even to walk slowly due to dyspnea.



Her father was known with an antiphospholipid syndrome with pulmonary embolism but *she was healthy and has* no antiphospholipid syndrome or other clotting abnormalities.

Contraceptive Vaginal Rings: Do They Pose an Increased Risk of Venous Thromboembolism in Aesthetic Surgery?

Aesthetic Surgery Journal
2015, Vol 35(6) 721–727
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DOI: 10.1093/asj/sju166
www.aestheticsurgeryjournal.com

OXFORD
UNIVERSITY PRESS

Robert J. Paresi Jr., MD, MPH; Robert S. Myers, MD;
and Alan Matarasso, MD

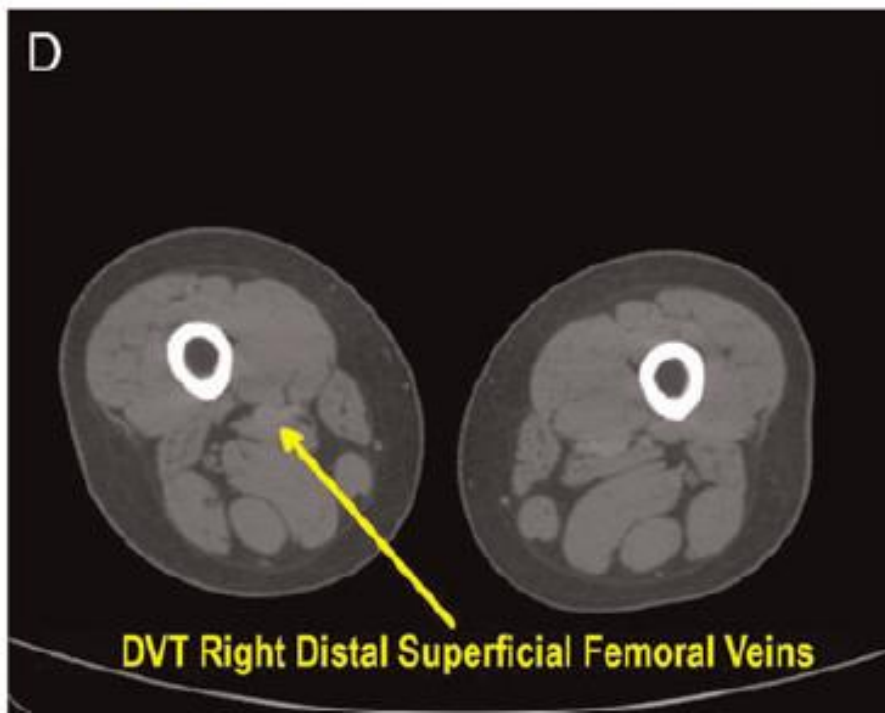
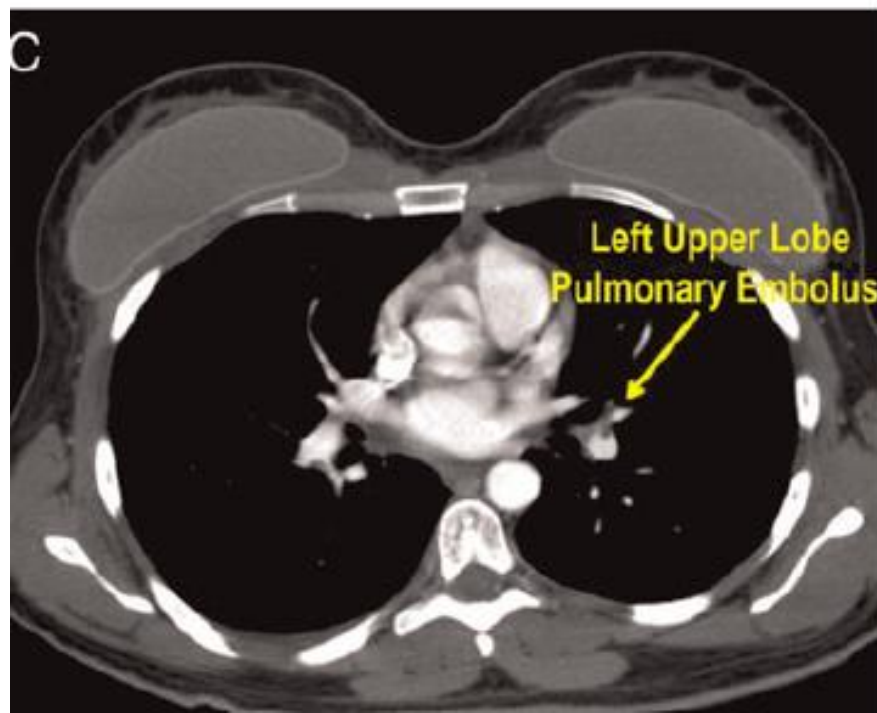
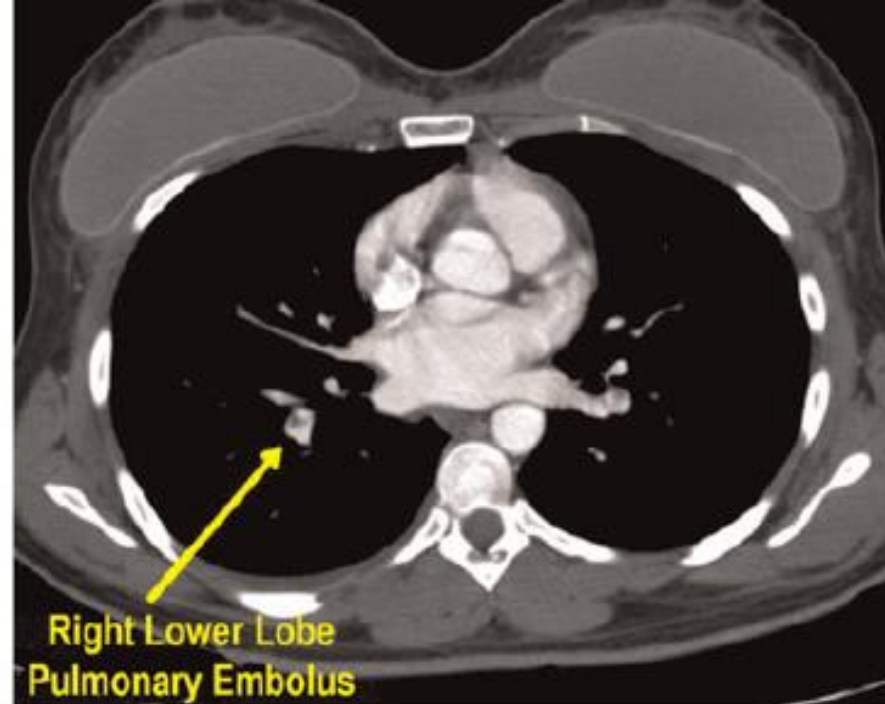
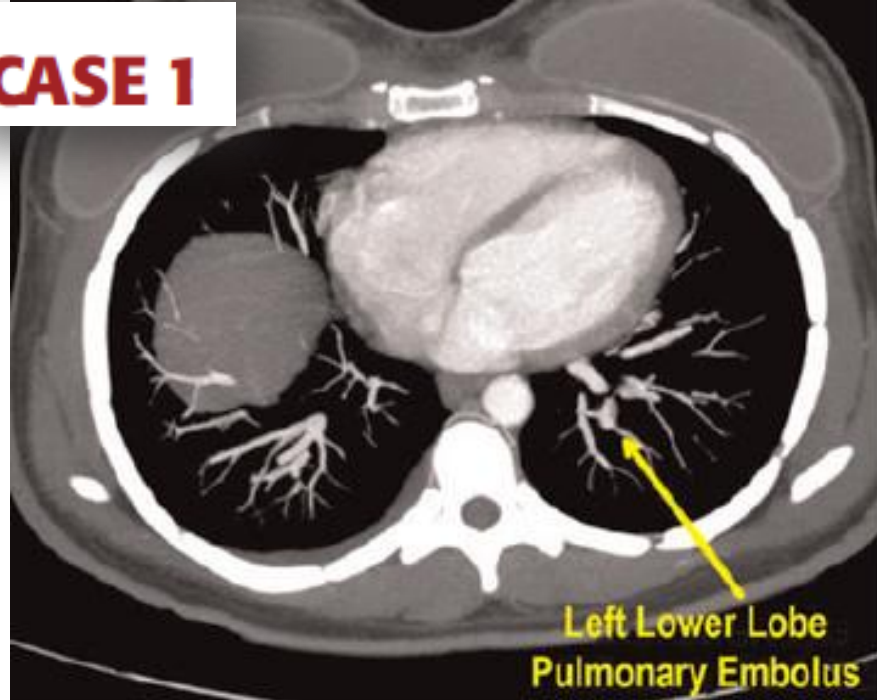
CASE 1

A healthy 26-year-old African-American female presented to the first surgeon's clinic in May 2011 for breast augmentation. Her medical and surgical history was only

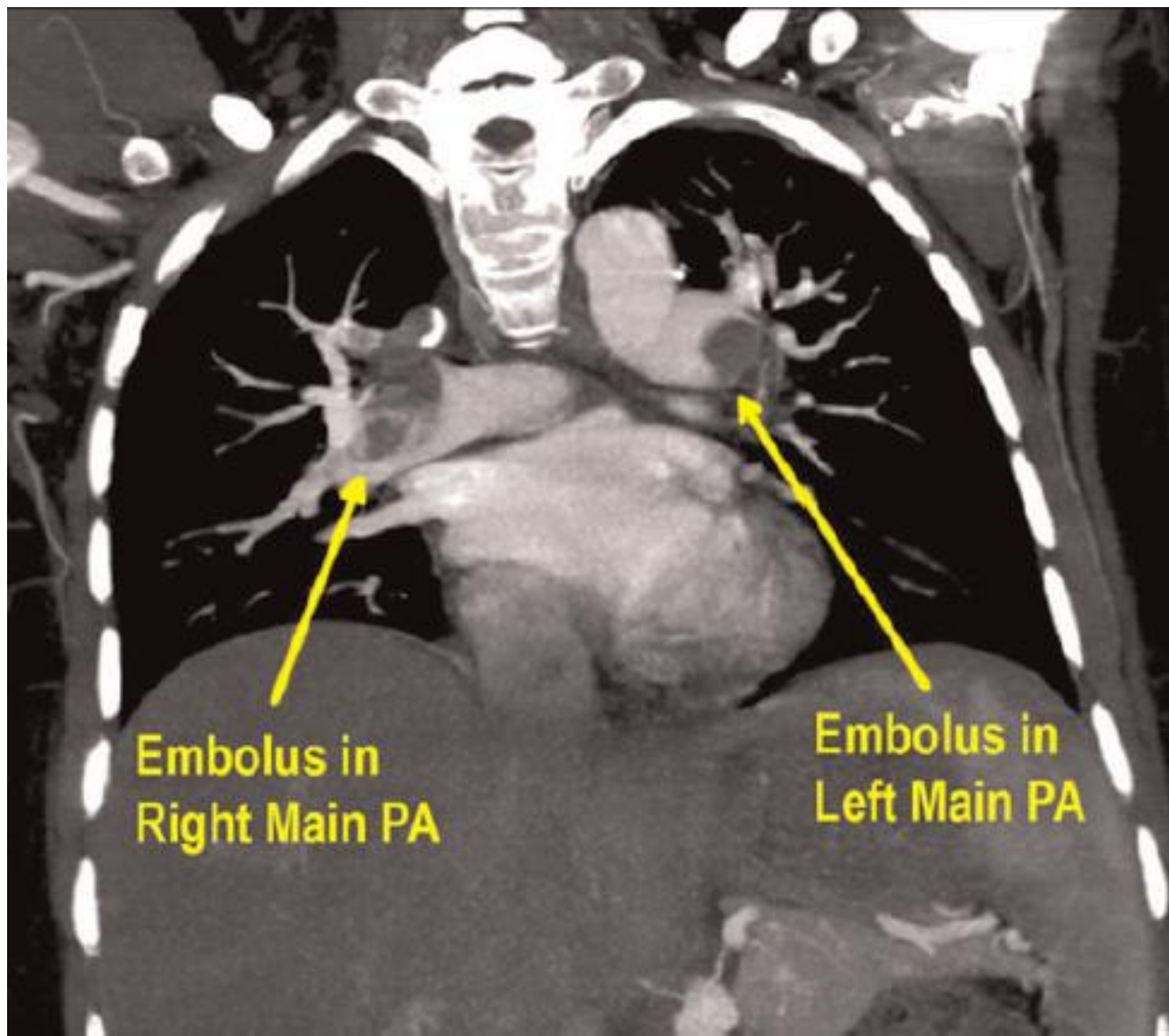
CASE 2

A healthy 29-year-old non-smoking Caucasian female presented to the second surgeon's office in June 2011 for an abdominoplasty. The patient's past medical history was sig-

CASE 1



CASE 2





Add up all your points to get your
total Caprini DVT Risk Score

**What does your Caprini
DVT Risk Score mean?**

- Risk scores may indicate your odds of developing a DVT during major surgery or while being hospitalized for a serious illness.
- Studies have shown if you have 0-2 risk factors, your DVT risk is small. This risk increases with the presence of more risk factors.

risk for VTE using the Caprini risk score.

patients. A British Medical Journal study points out a 10 time increased risk of VTE in female middle-aged women having day surgery than those not having surgery. This risk increases to 70 times more likely in patients having inpatient surgery and persists for up to 12 weeks after surgery.⁴

dence of VTE: a low risk score of 0-1 corresponded to a VTE incidence of 0%; moderate risk score of 2 to a VTE incidence of 0.7%; a high risk score of 3-4 with a VTE incidence of 0.97%; and the highest risk score of 5-9+ with a VTE incidence of 1.33-6.51%. As expected, the incidence of VTE

CASE 1

Directions:

Check all statements that apply to you.

Enter the number of points for each of your checked statements in the space at right.

3. Add up all points to reach your total DVT Risk Score.

Then, share your completed form with your doctor.

Add 1 point for each of the following statements that apply **now or within the past month**:

- ☐ Age 41–60 years _____
- ☐ Minor surgery (less than 45 minutes) is planned _____
- ☐ Past major surgery (more than 45 minutes) within the last month _____

☐ Visit _____

☐ A h _____

(for _____)

☐ Sw _____

☐ Ov _____

☐ He _____

☐ Co _____

☐ Se _____

☐ Lu _____

- ☐ On bed rest or restricted mobility, including a removable leg brace for less than 72 hours _____

- ☐ Other risk factors (1 point each)*** _____

***Additional risk factors not tested in the validation studies but shown in the literature to be associated with thrombosis include BMI above 40, smoking, diabetes requiring insulin, chemotherapy, blood transfusions, and length of surgery over 2 hours.

For women only: Add 1 point for each of the following statements that apply:

- ☐ Current use of birth control or Hormone Replacement Therapy (HRT) **X** _____
- ☐ Pregnant or had a baby within the last month _____
- ☐ History of unexplained stillborn infant, recurrent spontaneous abortion (more than 3), premature birth with toxemia or growth restricted infant. _____

Add 2 points for each of the following statements that apply:

- ☐ Age 61–74 years _____
- ☐ Current or past malignancies (excluding skin cancer, but not melanoma) _____
- ☐ Planned major surgery lasting longer than 45 minutes (including laparoscopic and arthroscopic) **X** _____
- ☐ Non-removable plaster cast or mold that has kept you from moving your leg within the last month _____
- ☐ Tube in blood vessel in neck or chest that delivers blood or medicine directly to heart within the last month (also called central venous access, PICC line, or port) _____
- ☐ Confined to a bed for 72 hours or more _____

the need for chemoprophylaxis in those patients.²⁷ Using the Caprini scoring system, the patient in case 1 would have been classified as high risk based on her pretreatment risk score of three: one point for the use of contraceptives and two points for the 1 hour major surgery. With the non-

that apply **now or within the past month**:

- ☐ Elective hip or knee joint replacement surgery _____
- ☐ Broken hip, pelvis or leg _____
- ☐ Serious trauma (for example, multiple broken bones due to a fall or car accident) _____
- ☐ Spinal cord injury resulting in paralysis _____
- ☐ Experienced a stroke _____



Add up all your points to get your total Caprini DVT Risk Score

What does your Caprini DVT Risk Score mean?

- Risk scores may indicate your odds of developing a DVT during major surgery or while being hospitalized for a serious illness.

- Studies have shown if you have 0–2 risk factors, your DVT risk is small. This risk increases with the presence of more risk factors.

For more information call ISMS at 1-800-782-4767, ext. 1678

www.isms.org

CASE 2

Directions:

Check all statements that apply to you.

Enter the number of points for each of your checked statements in the space at right.

3. Add up all points to reach your total DVT Risk Score.

Then, share your completed form with your doctor.

Add 1 point for each of the following statements that apply **now or within the past month**:

☐ Age 41–60 years _____

☐ Minor

☐ Past the last

☐ Visible

☐ A his (for a

☐ Swol

☐ Over

☐ Hear

☐ Cong

☐ Serio

☐ Lung

☐ On b remo

☐ Other

***Addition to be associated with insulin, ch

abdominoplasty. The patient's past medical history was significant for non-Hodgkin's lymphoma of the chest, diagnosed 8 years prior and treated with chemotherapy. She had been

In case 2, the patient was already at the highest risk of VTE according to the Caprini risk assessment, but was not given chemoprophylaxis by the operating surgeons. The patient had a major surgery lasting 3 hours (three points), a history of previous malignancy (two points), and was on a Nuvaring at the time of surgery (one point). This gives the

Add 2 points for each of the following statements that apply:

☐ Age 61–74 years _____

☐ Current or past malignancies (excluding skin cancer, but not melanoma) **X**

☐ Planned major surgery lasting longer than 45 minutes (including laparoscopic and arthroscopic) **X**

☐ Non-removable plaster cast or mold that has kept you from moving your leg within the last month _____

☐ Tube in blood vessel in neck or chest that delivers blood or medicine directly to heart within the last month

For women only: Add 1 point for each of the following statements that apply:

☐ Current use of birth control or Hormone Replacement Therapy (HRT) _____

☐ Pregnant or had a baby within the last month _____

☐ History of unexplained stillborn infant, recurrent spontaneous abortion (more than 3), premature birth with toxemia or growth restricted infant. _____

☐ Spinal cord injury resulting in paralysis _____

☐ Experienced a stroke _____



Add up all your points to get your total Caprini DVT Risk Score

What does your Caprini DVT Risk Score mean?

- Risk scores may indicate your odds of developing a DVT during major surgery or while being hospitalized for a serious illness.

- Studies have shown if you have 0–2 risk factors, your DVT risk is small. This risk increases with the presence of more risk factors.

For more information call ISMS at 1-800-782-4767, ext. 1678

www.isms.org

Special Topic

Contraceptive Vaginal Rings: Do They Pose an Increased Risk of Venous Thromboembolism in Aesthetic Surgery?

Robert J. Paresi Jr., MD, MPH; Robert S. Myers, MD;
and Alan Matarasso, MD



CONCLUSION

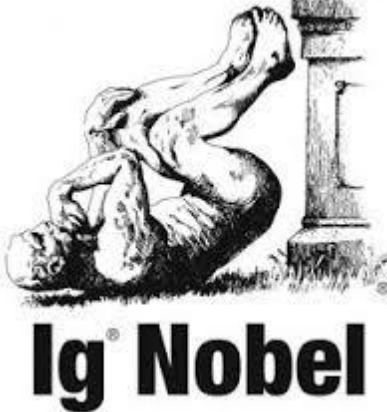
We report two cases of venous thromboembolism in patients having aesthetic surgery while on Nuvaring. The authors recommend that until the exact potential risk of VTE associated with Nuvaring is elucidated, surgeons should specifically query aesthetic surgery patients as to its use and discontinue its use from 4 weeks preoperatively to 2 weeks postoperatively.

***RISKY MINIMIZED
BY PRESCRIBING
SAFER choice
TO “SAFER” WOMEN
AND
GOOD MONITORING***

False Alarms and Pseudo-Epidemics

The Limitations of Observational Epidemiology

David A. Grimes, MD, and Kenneth F. Schulz, PhD, MBA



Exposure	Outcome	Explanation
Cigarette smoking	Increased risk of suicide	Smoking associated with factors predisposing to mental state that increases suicide risk ^{27,28}
Beta-carotene	Reduced risk of lung cancer	Information bias and residual confounding ²⁹
Menopausal estrogen therapy	Reduced risk of coronary artery disease	Selection bias: women who chose to use estrogen were at lower risk for coronary artery disease ³¹
Reserpine therapy	Increased risk of breast cancer	Flawed case-control studies; findings not replicated by later, larger studies ²⁰
Drinking coffee	Increased risk of pancreatic cancer	Gravely flawed case-control study; finding refuted by later studies ^{13,20}
Induced abortion	Increased risk of breast cancer	Information bias; under-reporting of abortion among healthy control individuals ^{13,32}
Antihistamine and vitamin B6 (pyridoxine/doxylamine) exposure	Increased risk of birth defects	Junk science ³⁵
IUD use	Increased risk of salpingitis and infertility	Wrong comparison groups, information bias (systematic overdiagnosis in IUD users), failure to control for confounding by STD ⁶³
Oral contraceptive use	Increased risk of pituitary adenoma	Confounding by indication ³⁷



An initiative of the ABIM Foundation

Five Things Physicians and Patients Should Question

Don't require a pelvic exam or other physical exam to prescribe oral contraceptive medications.

Hormonal contraceptives are safe, effective and well-tolerated for most women. Data do not support the necessity of performing a pelvic or breast examination to prescribe oral contraceptive medications. Hormonal contraception can be safely provided on the basis of medical history and blood pressure measurement.

Don't routinely order thrombophilia testing on patients undergoing a routine infertility evaluation.

There is no indication to order these tests, and there is no benefit to be derived in obtaining them in someone that does not have any history of bleeding or abnormal clotting and in the absence of any family history. This testing is not a part of the infertility workup. Furthermore, the testing is costly, and there are risks associated with the proposed treatments, which would also not be indicated in this routine population.

American College of
Medical Genetics and
Genomics

Don't order MTHFR genetic testing for the risk
assessment of hereditary thrombophilia.



Ride a motorbike for 1 minute



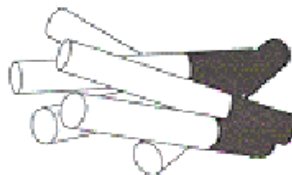
Rock climb for 1.5 minutes



Stay alive for 5 minutes
if over 65 years old



Drive for 1 hour



Smoke 6 cigarettes in 5 hours
(if a 20-a-day smoker, age 35)



Take pill for 1 month
(non-smoker)

La via vaginale: dalla teoria alla pratica



contraccettiva



Possibilità di uso come terapia



Possibilità di uso continuativo



Prescrizione come momento di Educazione alla sessualità



CONQUISTA IRRINUNCIABILE



CONQUISTA RISCHIOSA ?



Tenta di uccidere il marito con il veleno sulla vagina

► RIO DE JANEIRO

Grazie per l'attenzione

insolito, ha interrotto subito il Corso in ospedale. È stato sottoposto a una gastrectomia, che ha evidenziato la presenza di alcuna sostanza velenosa.

La vicenda però sembra ancora tutta da chiarire. Secondo i medici, la donna cercava di uccidere il marito cospargendo di veleno la propria vagina. Il tentativo non è riuscito.