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Dipartimento di Scienze Ginecologiche e della Riproduzione Umana
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Direttore Prof. Giovanni Battista Nardelli

DIAGNOSIS OF ECTOPIC PREGNANCY AFTER EMERGENCY CONTRACEPTION

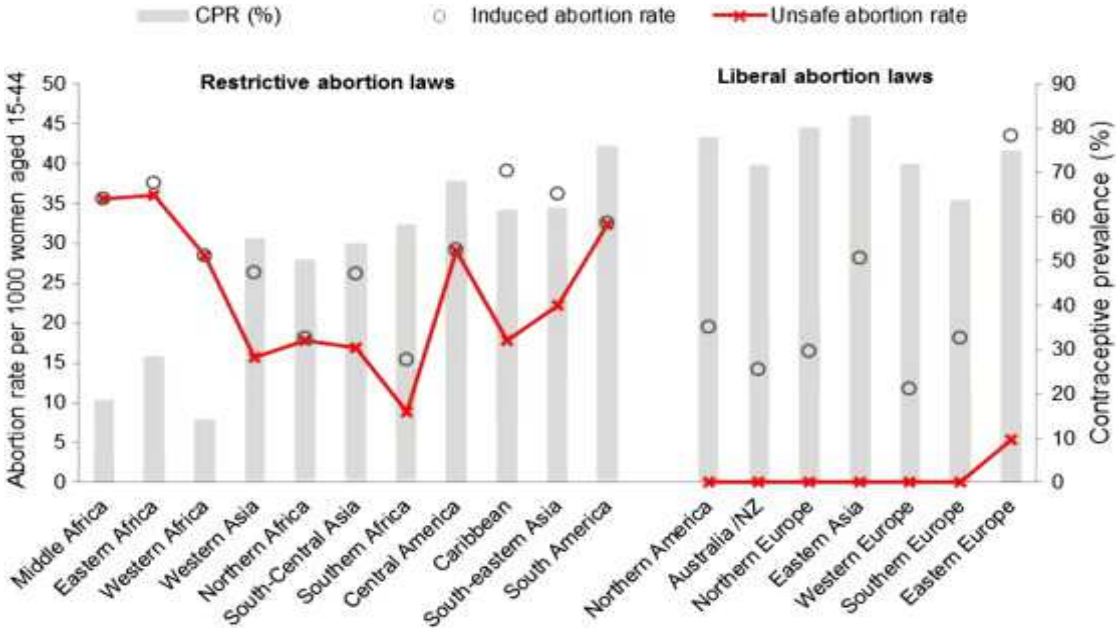
- ***Dott.ssa Martina Bertin***

EMERGENCY CONTRACEPTION: WHY?

Unplanned and undesired pregnancies constitute an important worldwide. It was estimated that **43.8 million induced abortions** (i.e., 28 per 1000 women of reproductive age between 15 and 44) occurred globally in 2008, of which about 49% were unsafe.

Li H-WR, et al., Emergency contraception, Best Practice & Research Clinical Obstetrics and Gynaecology (2014), http://dx.doi.org/10.1016/j.bpobgyn.2014.04.011.

The available evidence indicates that overall induced abortion rates are lower where abortion laws are liberal (12-19 per 1000 women of reproductive age); only in Eastern Europe and Eastern Asia, two subregions with a long history of reliance on abortion as a method for fertility regulation, are induced abortion rates higher.

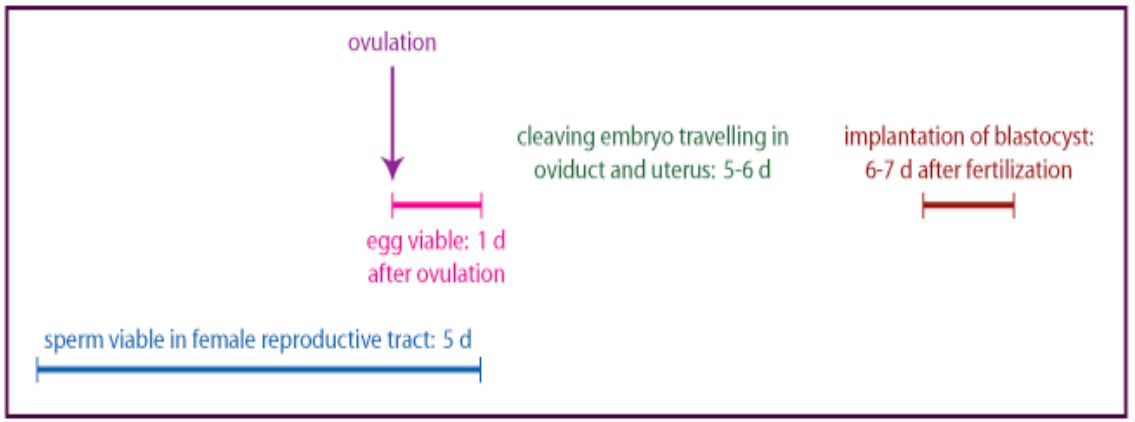


Shah IH et al. Access to safe abortion: progress and challenges since the 1994 International Conference on Population and Development (ICPD).Contraception. 2014 Apr 13. pii: S0010-7824(14)00155-3. doi: 10.1016/j

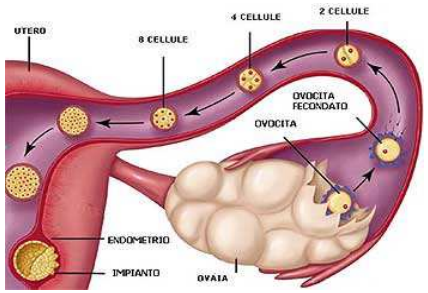
EMERGENCY CONTRACEPTION: WHAT IS THIS?

Emergency contraception (EC), or post-coital contraception, refers to methods of contraception that can be used to prevent pregnancy in the few days after intercourse. It is intended for emergency use following unprotected intercourse, contraceptive failure or misuse (such as forgotten pills), rape or coerced sex.

The possible targets for postcoital contraception are:
- sperm transportation,
- follicular development,
- ovulation,
- fertilization,
- embryo development,
- endometrial receptivity,
- implantation
- corpus luteum.



EMERGENCY CONTRACEPTION: WHEN?



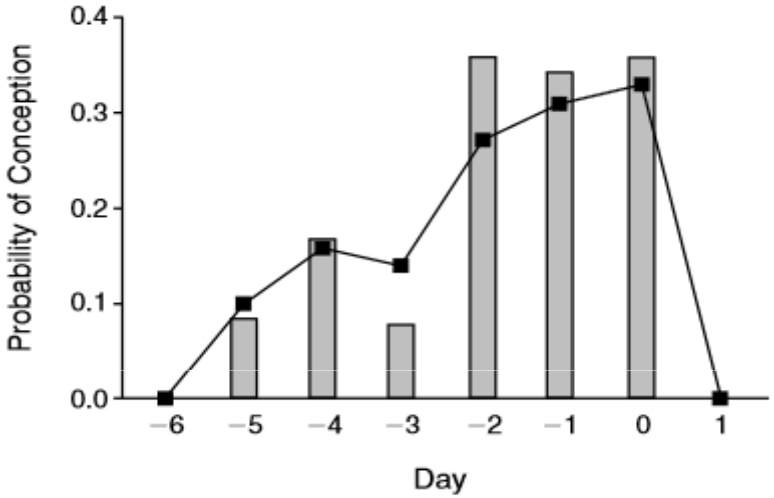


Figure 2. Probability of Conception on Specific Days near the Day of Ovulation.

The bars represent probabilities calculated from data on 129 menstrual cycles in which sexual intercourse was recorded to have occurred on only a single day during the six-day interval ending on the day of ovulation (day 0). The solid line shows daily probabilities based on all 625 cycles, as estimated by the statistical model.

"(….) all conceptions resulted from intercourse that occurred during a **six-day interval ending on the day of ovulation**."

Wilcox AJ. et al. Timing of sexual intercourse in relation to ovulation. Effects on the probability of conception, survival of the pregnancy, and sex of the baby N Engl J Med 1995; 333:1517-1521.

EMERGENCY CONTRACEPTION: WHO?

- Almost 70% of all women requesting EC were aged **between 18 and 25 years**. Some 80% of all women were in a stable relationship with their partner, with fewer than 20% having had an occasional intercourse (..)

-Concerning the reasons for requesting EC, **condom breakage or slipping** was the most frequently cited (64%), followed by totally unprotected intercourse (28%), failed withdrawal (5%) and forgetting one or more pill (only 1.1%).

- More than one-third of the women interviewed had previously used an emergency contraceptive modality; although no one did so more than four times.

Bastianelli C et al. Reasons for requesting emergency contraception: A survey of 506 Italian women. The European Journal of Contraception and Reproductive Health Care, 2005, Vol. 10, No. 3 : Pages 157-163

EMERGENCY CONTRACEPTION

There are two methods of emergency contraception:
1) emergency contraception pills (ECPs)
2) copper-bearing intrauterine devices (IUDs).

WHO recommends **levonorgestrel** for emergency contraceptive pill use. Ideally, this progestogen-only method should be taken as a single dose (1.5 mg) within five days of unprotected intercourse.

WHO recommends that a **copper-bearing IUD**, as an emergency contraceptive, be inserted within five days of unprotected intercourse. This may be an ideal emergency contraceptive for a woman who is hoping for an ongoing, highly effective contraceptive method.

http://www.who.int/mediacentre/factsheets/fs244/en/

EMERGENCY CONTRACEPTION

Table 1 Methods of emergency contraception in the UK

Method	Class	Products	Recommended dose/use	Indications
Copper-bearing intrauterine device (Cu-IUD)	Intrauterine contraceptive method	Various types licensed for contraception	IUD retained until pregnancy excluded (e.g. onset of period) or for licensed duration of IUD (5–10 years)	Within the first 5 days (120 hours) following first UPSI in a cycle or within 5 days from the earliest estimated date of ovulation
Levonorgestrel (LNG)	Progestogen hormone	Levonelle One Step® (P) Levonelle1500® (POM)	1.5 mg single oral dose	Licensed for use within 72 hours of UPSI or contraceptive failure
Ulipristal acetate (UPA)	Progesterone receptor modulator	ellaOne® (POM)	30 mg single oral dose	Licensed for use within 120 hours of UPSI or contraceptive failure

EC, emergency contraception; P, pharmacy medicine; POM, prescription-only medicine; UPSI, unprotected sexual intercourse.

PROGESTOGEN EC: CONTRAINDICATIONS

Although the Centers for Disease Control and Prevention (CDC) and the World Health Organization's (WHO) Medical Eligibility Criteria for Contraceptive Use applies **contraindications** to daily use of hormonal contraceptives in some women based on their medical history*, these contraindications do not apply to women seeking emergency contraception..*

…In particular, cardiovascular disease, thrombophilic disorders, migraine, liver disease, and breastfeeding are considered conditions where the advantages of using **the method generally outweigh the theoretical or proven risks**…

CDC. U.S. Medical Eligibility Criteria for Contraceptive Use, 2010. Classification for emergency contraception. http://www.cdc.gov/mmwr/pdf/rr/rr59e0528.pdf

PROGESTOGEN EC: CONTRAINDICATIONS

LNG emergency contraception may be less effective or not effective in **overweight and obese women**. Product labeling for LNG EC is being updated with clinical trial information suggesting the contraceptive may be less effective in women 75 to 80 kg and not effective in women >80 kg and 80 kg correlates with BMI of about 30 kg/m^2 [obese category].

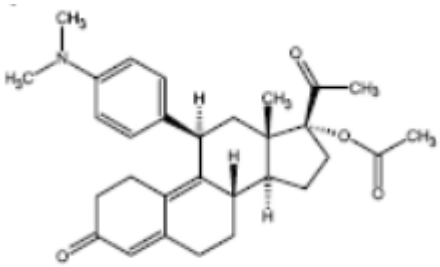
Overweight and obese women should be counseled about potentially reduced or absent efficacy of levonorgestrel emergency contraception as BMI increases above the normal range or at weights ≥75 kg, and **they should be offered a copper-releasing IUD as first-line therapy to prevent pregnancy**

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2014/01/news_detail_002010.jsp&mid=WC0b01ac058004d5c1.

ULIPRISTAL EC

Ulipristal acetate is a **selective progesterone receptor modulator** with antagonistic and partial agonistic effects (a progesterone agonist/ antagonist) at the progesterone receptor, thereby preventing the binding of progesterone. Ulipristal is a single pill containing **30 mg of ulipristal acetate** and is indicated up to 120 hours after unprotected intercourse.

Unlike with hormonal emergency contraception, existing pregnancy must be excluded before prescribing ulipristal because of the risk of fetal loss if used in the first trimester of pregnancy.



$C_{30}H_{37}NO_4$

Table 3: Summary of Clinical Trial Results for Women Who Received a Single Dose of ella (30 mg Ulipristal Acetate)

	Open-Label Study 48 to 120 Hours *	Single-Blind Comparative Study 0 to 72 Hours *
	N = 1,242	N = 844
Expected Pregnancy Rate **	5.5	5.6
Observed Pregnancy Rate ** (95% confidence interval)	2.2 (1.5, 3.2)	1.9 (1.1, 3.1)

* Time after unprotected intercourse when **ella** was taken
** Number of pregnancies per 100 women at risk for pregnancy

http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/022474s000lbl.pdf

ULIPRISTAL EC

Gynecological Endocrinology, 2012; Early Online: 1–6

ISSN 0951-3590 print/ISSN 1473-0766 online
DOI: 10.3109/09513590.2012.662546

informa
healthcare

REVIEW

Nowadays which emergency contraception? Comparison between past and present: latest news in terms of clinical efficacy, side effects and contraindications

Salvatore Gizzo MD[1], Tiziana Fanelli MD[1], Stefania Di Gangi MD[1], Carlo Saccardi MD,PhD[1,2], Tito Silvio Patrelli MD,PhD[2], Alessandra Zambon MD[1], Anis Omar MD[1], Donato D'Antona MD[1] & Giovanni Battista Nardelli MD[1]

Review

Reproductive Sciences
2014, Vol. 21(6) 678-685

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Ulipristal Acetate: Critical Review About Endometrial and Ovulatory Effects in Emergency Contraception

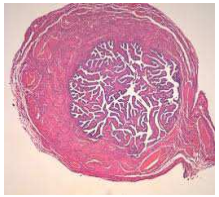
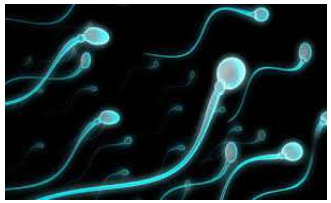
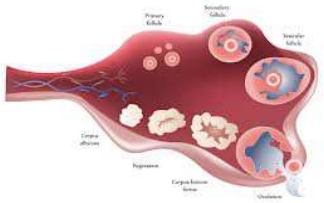
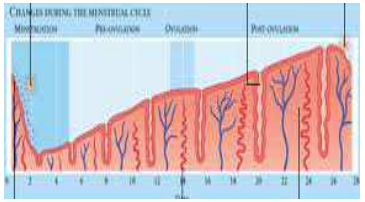
Bruno Mozzanega, MD[1], Salvatore Gizzo, MD[1], Stefania Di Gangi, MD[1], Erich Cosmi, MD[1], and Giovanni Battista Nardelli, MD[1]

http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/022474s000lbl.pdf

ULIPRISTAL EC

There have also been preliminary in vitro data indicating that UPA at pharmacological concentrations could inhibit human **sperm hyperactivation**, as well as ciliary beating and muscular contraction in the human **fallopian tube**.

Li H-WR, et al., Emergency contraception, Best Practice & Research Clinical Obstetrics and Gynaecology (2014), http://dx.doi.org/10.1016/j.bpobgyn.2014.04.011

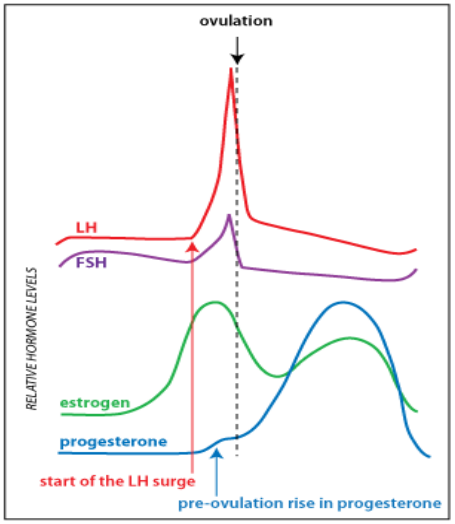
"…UPA effectiveness <u>does not decrease depending on which of the 5 days it is taken after unprotected intercourse</u>…This appears surprising if we assume that UPA effectiveness is due to an **anti-ovulatory action** which decreases as LH levels approach to peak..This suggests that the effectiveness of UPA relies on its **endometrial effect.** The inhibitory effect of UPA acts directly on the endometrial tissue through its inactivation of progesterone receptors. Thus, evidence shows that UPA endometrial effects can **interfere with embryo implantation**"

Mozzanega B et al. Ulipristal acetate in emergency contraception: mechanism of action. Trends Pharmacol Sci. 2013 Apr;34(4):195-6.

LEVONORGESTREL EC

The precise mode of action of levonorgestrel (LNG) is incompletely understood but it is thought to work primarily by **inhibition of ovulation**. Administration of LNG appears to prevent follicular rupture. LNG taken prior to the luteinising hormone surge has been shown to result in ovulatory dysfunction in the subsequent 5 days, by which time any sperm in the reproductive tract will have become non-viable.

FSRH Clinical Effectiveness Unit Guidance (August 2011) Emergency Contraception



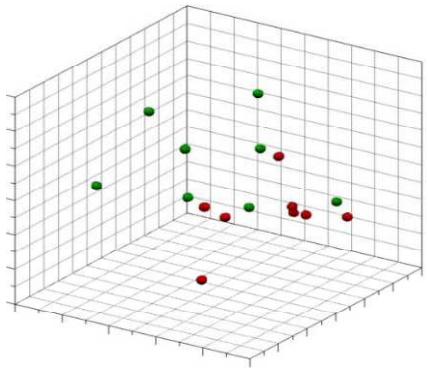
It works by delaying or inhibiting ovulation via the same mechanism (**negative feedback inhibition of gonadotropin secretion**) as conventional hormonal contraception.

In a study in which LH levels were measured (as a marker for ovulation), it was found that LNG EC only worked when taken before the LH surge.

LNG EC ENDOMETRIAL EFFECTS

Deleterious effects of LNG impairing endometrial receptivity to subsequent implantation have not been found either in vivo or in vitro. LNG caused minimal changes in **transcripts levels** and, considering their nature and magnitude, it is unlikely that they would interfere with endometrial receptivity.

Vargas MF. et al. Effect of single post-ovulatory administration of levonorgestrel on gene expression profile during the receptive period of the human endometrium Journal of Molecular Endocrinology (2012) 48, 25–36.



Multicriteria analysis (MCA) of samples obtained during placebo- and LNG-treated cycles showing there were no remarkable differences between placebo- and LNG-treated cycles with respect to the global gene expression profile.

Following the repeated oral treatment, the immunoreactivity of both **progesterone receptor** (PR)-A and PR-B declined in glandular epithelium (P = 0.03 and P = 0.02, respectively) (…) However, levonorgestrel did not cause any significant endometrial changes.

Meng CX et al. Effects of oral and vaginal administration of levonorgestrel emergency contraception on markers of endometrial receptivity. Hum Reprod 2010;25:874–83.

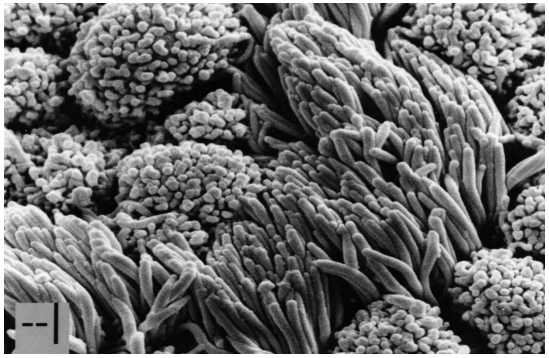
LNG EC TUBAL EFFECTS 1

Progesterone has been shown to **regulate tubal transport** of the zygote in vitro. Both muscular contractions and cilia activity are involved in the transportation. Cilia from the human fallopian tube beat significantly slower after treatment with high doses of progesterone, an effect that could be reversed by mifepristone.

A. Christow et al. Effect of mifepristone and levonorgestrel on expression of steroid receptors in the human Fallopian tube. Mol Hum Reprod, 8 (2002), 333–340

Treatment with LNG (1.5 mg) on day LH peak + 2 did not affect the distribution of progesterone or estrogen **receptors** in the human fallopian tube in vivo.

DB Smotrich et al. Immunocytochemical localization of growth factors and their receptors in the human pre-embryos and fallopian tubes. Hum Reprod, 11 (1996),184–190



LNG EC TUBAL EFFECTS 2

Serum peak levels of LNG following the administration of 1.5-mg LNG are relatively high **(35–40 nmol/L).**

An in vitro study describes that high dose of LNG (≥20 nmol/L) significantly **decreases tubal motility**.

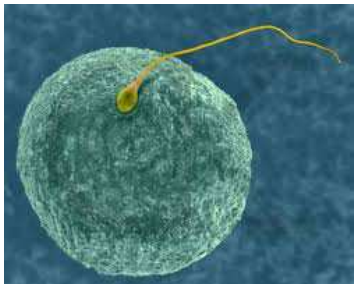
Pharmacokinetics of LNG shows that the serum level of hormone is above this threshold **from 1 to 6 h after the intake of 1.5-mg LNG**. Moreover, it is of paramount importance that the tubal musculature is exposed to LNG only for some minutes in a laboratory study, whereas its action lasts more than 5 days in vivo.

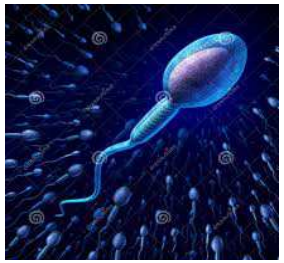
Devoto L et al. Pharmacokinetics and endometrial tissue levels of levonorgestrel after administration of a single 1.5-mg dose by the oral and vaginal route. Fertil Steril 2005;84:46–51.

LNG EC SPERM EFFECTS

In vitro data indicate that LNG in doses relevant for EC has no direct effect on sperm function.

WSB Yeung et al. The effects of levonorgestrel on various sperm functions. Contraception, 66 (2002), pp. 453–457





LNG in a similar dose to that observed in serum following oral intake for EC had no effect on the number of motile spermatozoa recovered from the human fallopian tubes in vitro, their adhesion to the tubal epithelium, distribution or acrosome reaction rate.

A. Hermanny et al. In vitro assessment of some sperm function following exposure to levonorgestrel in human fallopian tubes. Reprod Biol Endocrinol, 10 (2012), p. 8

LNG did not impair the cervical mucus either because viable spermatozoa were found in the genital tract 36–60 h after coitus and 24–48 h after LNG intake

do Nascimento AJJ et al. In vivo assessment of the human sperm acrosome reaction and the expression of glycodelin-A in human endometrium after levonorgestrel-emergency contraceptive pill administration. Human Reproduction 2007, 22, 8 pp. 2190–2195

LNG EC and PREGNANCY RATE

The risk of pregnancy with LNG was **4.12%.** A single dose of 1.5 mg LNG could reduce the pregnancy rate to **0.7%.**

Sarkar NN. The emergency contraceptive drug, levonorgestrel: a review of post-coital oral and peri-coital vaginal administration for prevention of pregnancy. J Obst Gynaecol. 2011;31(8):703-7.

Expected and observed pregnancies after LNG-EC administration before the day of ovulation (days −5 to −1), on the day of ovulation (day 0) and thereafter

Time of LNG-EC administration	Number of women	Pregnancies expected/ observed
Preovulatory days −5 to −1	103	16.0/0*
Postovulatory day 0 or +	45	8.7/8**

Expected pregnancies were calculated according to the probabilities estimated by Wilcox et al. [10] for each fertile day of the menstrual cycle. Fisher's Exact Test: *p>.0001; **p=1.00.

The **ratio observed/expected pregnancies** is an accepted means to define the efficacy of LNG-EC. The efficacy when used before ovulation was 100%. On the contrary, when used after ovulation has occurred, the number of observed and expected pregnancies is not statistically different, indicating that no reproductive process subsequent to ovulation is interfered with by LNG-EC.

Noé G et al. Contraceptive efficacy of emergency contraception with levonorgestrel given before or after ovulation. Contraception. 2011 Nov;84(5):486-92.

LNG EC and ECTOPIC PREGNANCY

Data from 136 studies on LNG revealed that 3 of 307 **(1%)** were ectopic, a rate which does not exceed the rate in the general population.

K. Cleland et al. Ectopic pregnancy and emergency contraceptive pills: a systematic review Obstet Gynecol, 115 (2010), pp. 1263–1266

In this review **five cases of ectopic pregnancy** were reported among 45,842 women and it did not look as if ectopic pregnancy was as common as seen in previous studies.

Cheng L et al. Interventions for emergency contraception. Cochrane Database of Systematic Reviews 2008, Issue 2. Art. No.: CD001324

In women treated with LNG-EC, the rate of ectopic pregnancy does not exceed the rate observed in the general population, suggesting that embryo transport is not delayed by this treatment.

CASE REPORT

- V.A. 19 years old, italian white women
- P0 G0
- FAMILY HISTORY: ndp
- MEDICAL HISTORY: no previous surgery, no pathologies, no current therapy, never used E/P, no smoke, already taken EC without problem, Leiden Factor V heterozigosis.

LMP 24/02/2014 (regular menstruations)

On evening of 07/03/2014 she had an unprotected sexual intercourse (UPSI) **(day 12 of the menstrual cycle)**. ..Patient came to Padua ER the morning after it for prescription of EC..

CASE REPORT

REGIONE VENETO
AZIENDA OSPEDALIERA DI PADOVA
SERVIZIO DI PRONTO SOCCORSO E ACCETTAZIONE
Responsabile Dott. Franco Tosato
VERBALE DI PRONTO SOCCORSO

Cartella DEA :2014 / 14913 , 08/03/2014 09:49

Assistito/a [redacted]
Sesso F **nato/a il** 29/05/1994
a DOLO
Tess.San: 260432837 **CF:** [redacted]
Residenza: SAONARA
Via: [redacted] 15 **tel:** 8790994

Codice Triage di ingresso: BIANCO
Motivo di ingresso:
Modalità di arrivo: DEAMBULANTE
Provenienza: SOLO
Operatore al triage: A062498

APERTURA - 08/03/2014 ore 10:56

Dr. CASTIGLIONE GIULIA dal 08/03/2014 10:57

08/03/2014 10:57 Anamnesi/E.O.: La paziente riferisce rapporto non protetto alle ore 19 circa di ieri. Ultime mestruazioni in data 24/02 u.s. APR: nega patologie di rilievo. Non assume terapia continuativa. Nega allergie a farmaci. Nega fumo. Ha gia assunto in altra occasione questo farmaco senza complicanze. Riferisce (e confermato dai bioumorali consultabili su e-health) mutazione in eterozigosi del fattore V di Leiden. Indagini eseguite per trombofilia nel gentilizio

08/03/2014 10:58 VISITA MEDICA DI PRONTO SOCCORSO

CHIUSURA - 08/03/2014 ore 11:14
Esito: DIMISSIONE
Diagnosi: CONTRACCEZIONE D'EMERGENZA IN PAZ CON ETEROZIGOSI PER FATTORE V DI LEIDEN
Note: SI PRESCRIVONO CALZE ELASTOCOMPRESSIVE PER PROFILASSI ANTITROMBOTICA PER ALMENO UN PAIO DI SETTIMANE. SI PRESCRIVE ~~NORLEVO 1.5 MG 1 CP~~ SUBITO. TORNA IN PS SE GONFIORE AD UN ARTO O MANCANZA DI RESPIRO. Il/la paziente dichiara di essere informato/a sui pericoli, potenzialmente anche letali, cui si espone la decisione di assumere tale farmaco. Firma del paziente _____ Al momento della firma il/la paziente risulta in grado di intendere e volere e di assumere decisione consapevole. Firma del Medico
_____

CASE REPORT

EC has been correctly assumed, without episodes of vomiting or diarrhea.

Persistent spotting the days following EC assumption.
….but she did not ask for a ob/gyn consultation…

…after three week she was assuming AB for temperature and cold.. she complained of suddenly **right groin pain radiating to the right leg** so she went to Padua ER..

No risk factors for ectopic pregnancy were identified (no history of salpingitis, previous tubal surgery, previous ectopic pregnancy or intrauterine device use).

CASE REPORT

REGIONE VENETO
AZIENDA OSPEDALIERA DI PADOVA
SERVIZIO DI PRONTO SOCCORSO E ACCETTAZIONE
Responsabile Dott. Franco Tosato
VERBALE DI PRONTO SOCCORSO

Cartella DEA :2014 / 22964 , 11/04/2014 09:29

Assistito/a [redacted]
Sesso F **nato/a il** 29/05/1994
a DOLO
Tess.San: 260432837 **CF** [redacted]
Residenza: SAONARA
Via [redacted] 15 **tel:** 8790994

Codice Triage di ingresso: BIANCO
Motivo di ingresso: ALTRO
Modalità di arrivo: DEAMBULANTE
Provenienza: SOLO
Operatore al triage: A063462

APERTURA - 11/04/2014 ore 10:14
Dr [redacted] dal 11/04/2014 10:16

11/04/2014 10:16 CREATININEMIA, D-DIMERO (EIA), SODIO (P), EMOCROMO, PTT, PT, PROTEINA C REATTIVA, POTASSIO (P), GLICEMIA, AZOTEMIA, CLORO (P)

11/04/2014 10:17 Anamnesi/E.O.: Paziente di 19 anni,, riferisce dolore all'inguine dx irradiato all'arto inferiore dx da stamattina , riferisce di aver preso la pillola del giorno dopo il 08/03, da allora spotting.Riferisce di essere heterozygote per V fattore di leiden - Da 3 gg in terapia antibiotica con amoxicilinia ac. clavulanico per odinofagia e febbre di 38.0^C. EO: ABC ispettivo nei limiti, eupnoica, addome trattabile, non segni clinici di TVP. In ecoscopia addominale ndp, non versamento intraperitoneale- vescica poco distesa. Ecoscopia venosa: asse femoro-poplitea bene comprimibile bilateralmente.

11/04/2014 10:17 PRELIEVO DI SANGUE VENOSO, VISITA MEDICA DI PRONTO SOCCORSO
11/04/2014 10:19 ESAME URINE, TEST DI GRAVIDANZA
11/04/2014 11:37 Visita ginecologica
Dr [redacted] dal 11/04/2014 12:29

CHIUSURA - 11/04/2014 ore 15:59
Esito: DIMISSIONE
Diagnosi: ALGIE PELVICHE IN GRAVIDA
Note: Trattenuta in regime di ricovero presso la Clinica ostetrica

…Urine pregnancy test positive!!

CASE REPORT

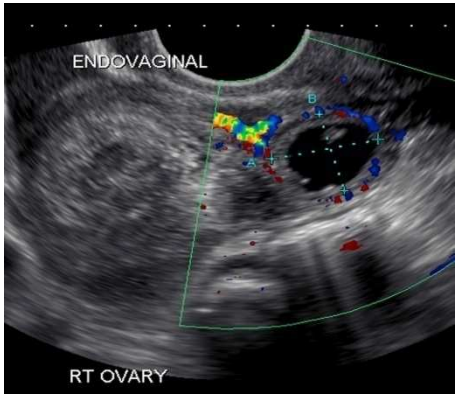
Blood test at admission to ER

Prelievo del *: 11/04/2014 10:30.* ASSIPCA : 46827901
Referto del : 11/04/14 11:10. Data di Nascita : 29/05/1994
Referto pronto il : 12/04/14 ***Riferimento*** *: 4045301749*
Ric/Ref *: 2014 / 022964-DEA_AO*
Note dal richiedente:

Costituente	Risultato	Unita'	Int. di Riferimento	Ris. Prec.
EMATOLOGIA E COAGULAZIONE				
CITOMETRIA				
B-LEUCOCITI	*8,28*	x10.9/L	4,40 - 11,00	
B-ERITROCITI	*4,77*	x10.12/L	4,31 - 5,10	
B-EMOGLOBINA errore totale ≤2,0%	*135*	g/L	123 - 153	
B-EMATOCRITO	*0,403*		0,360 - 0,450	
MCV	*84,7*	fL	80,0 - 96,0	
MCH	*28,3*	pg	26,0 - 33,0	
MCHC	*334*	g/L	320 - 360	
B-PIASTRINE	*172*	x10.9/L	150 - 450	
P-TEMPO DI PROTROMBINA				
-ATTIVITA' PROTROMBINICA	*88*	%	75 - 112	
- RATIO NORMALIZZATO	*1,02*	INR	0,88 - 1,13	
Terapia con antagonisti vit. K		obiettivo terapeutico		
- a media intensita'		2,50	2,00 - 3,00	
- ad alta intensita'		3,50	3,00 - 4,50	
P-APTT	*28*	s	22 - 32	
P-FDP D-DIMERO	*162*	ug/L	fino a 225	
COSTITUENTI BIOCHIMICI				
P-GLUCOSIO	** 5,7*	mmol/L	3,7 - 5,6	
	103	mg/dL		
		alterata a digiuno:	5,7 - 6,9	
		gravidanza:	3,7 - 5,1	
P-UREA	*4,10*	mmol/L	2,50 - 7,50	
P-CREATININA	** 51*	umol/L	53 - 97	
	0,56	mg/dL		
errore totale ≤7,0%				
P-SODIO	*139*	mmol/L	136 - 145	
P-POTASSIO errore totale ≤5%	*3,9*	mmol/L	3,4 - 4,5	
P-CLORO	*107*	mmol/L	96 - 108	
S-PROTEINA C REATTIVA	** 30,00*	mg/L	0,00 - 6,00	

Plasmatic bHCG was 1021 U/L at access to Ob/Gyn Unit

CASE REPORT



REGIONE VENETO
AZIENDA OSPEDALIERA DI PADOVA

SALA OPERATORIA: 05120D SALA OPERATORIA D - CLINICA OSTETRICA **n° pr. 2014/240**
REPARTO GIURIDICO: 018405 CLI. GINEC. OSTETR. S.O.

INTERVENTO: Ordinario [X] Urgente [X] Ambulatoriale [ ] D.S. [ ]

DATA: 11/04/2014 Inizio intervento h 17:50 Fine intervento h: 18:10

[redacted] Data di nascita **29/05/1994** Nosologico 2014 / 18126

INDICAZIONE DIAGNOSTICA: GRAVIDANZA TUBARICA

INTERVENTO SINTETICO: SALPINGECTOMIA DESTRA

PRIMO OPERATORE [redacted]
SECONDO OPERATORE
INFERMIERE STRUMENTISTA
OSS
ALTRI OPERATORI:
TIPO ANESTESIA ANESTESIA GENERALE

DIAGNOSI FINALE: GRAVIDANZA TUBARICA

INTERVENTO/I (ICD9-CM):
6662 SALPINGECTOMIA CON RIMOZIONE DI GRAVIDANZA TUBARICA
5421 LAPAROSCOPIA

DESCRIZIONE INTERVENTO :
LPS OPERATIVA: SALPINGECTOMIA DESTRA
Introduzione dell'ottica mediante Optiview ed induzione di pneumoperitoneo. Introduzione di 2 accessi ancillari per transilluminazione e visione diretta. All'ispezione addomino-pelvica si reperta emoperitoneo (circa 100 cc). La salpinge destra appare ectasica ed iperemica, come da gravidanza tubarica. Ovaio destro, utero ed annesso di sinistra nella norma. Previa aspirazione dell' emoperitoneo, nell' impossibilita di eseguire terapia conservativa si procede a coagulazione e sezione della salpinge destra e nel suo tratto istmico e del mesosalpinge; asportazione della salpinge destra mediante endobag senza rottura ne spillage e suo invio per esame istologico. Accurato controllo dell' emostasi e lavaggi ripetuti della cavita' addominopelvica. Sutura della cute a punti staccati con filo non riassorbibile. Perdite ematiche: tracce.

Surgery: laparoscopic right salpingectomy (minimum hemoperitoneum)

CASE REPORT

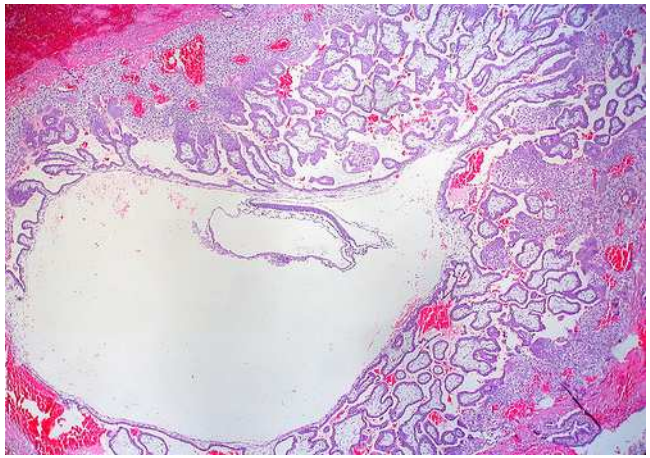
Prelievo del	***: 12/04/2014 07:00.***	ASSIPCA	: 46827901
Referto del	: 12/04/14 10:23.	Data di Nascita	: 29/05/1994
Referto pronto il	: 15/04/14	***Riferimento***	***: 4042710114***
Ric/Ref	***: 2014 / 018126-RIC_AO***		

Note dal richiedente:

Costituente	Risultato	Unita'	Int. di Riferimento	Ris. Prec.
EMATOLOGIA E COAGULAZIONE				
PROFILO EMATOLOGICO				
Citometria:				
B-LEUCOCITI	***7,46***	x10.9/L	4,40 - 11,00	
B-ERITROCITI	**** 4,30***	x10.12/L	4,31 - 5,10	
B-EMOGLOBINA errore totale <2,0%	***124***	g/L	123 - 153	
B-EMATOCRITO	**** 0,354***		0,360 - 0,450	
MCV	***82,3***	fL	80,0 - 96,0	
MCH	***28,8***	pg	26,0 - 33,0	
MCHC	***350***	g/L	320 - 360	
RDW	***11,9***		11,2 - 15,6	
B-PIASTRINE	***165***	x10.9/L	150 - 450	
Conteggio Differenziale dei Leucociti:				
B-NEUTROFILI	***5,44***	x10.9/L	1,80 - 7,80	
	72,9	%		
B-LINFOCITI	***1,20***	x10.9/L	1,10 - 4,80	
	16,1	%		
B-MONOCITI	***0,79***	x10.9/L	0,20 - 0,96	
	10,6	%		
B-EOSINOFILI	***0,01***	x10.9/L	0,00 - 0,50	
	0,1	%		
B-BASOFILI	***0,02***	x10.9/L	0,00 - 0,20	
	0,3	%		
ORMONI				
S-HCG (Gonad.Corion.Umana)	**** 520,6***	U/L	0,0 - 5,0	
Commento: **Dalla 5a alla 7a settimana**			**1.000- 100.000**	

Blood test at day 1 after salpingectomy

CASE REPORT



REGIONE DEL VENETO

AZIENDA OSPEDALIERA PADOVA

UNITÀ OPERATIVA DI ANATOMIA PATOLOGICA

Direttore Prof. Massimo Rugge

UNIVERSITÀ DEGLI STUDI PADOVA

Accettazione 14/04/2014
Refertazione 24/04/2014
Cod. Paziente 46827901

SALA OPERATORIA D - CLINICA OSTETRICA

[redacted]

Referto n° 14-17549
Pag. 1/1
Data di nascita 29/05/1994

DESCRIZIONE MACROSCOPICA

Reperto macroscopico (campione pervenuto fissato in formalina) [IRC]:
Materiale inviato in esame come "Salpinge destra".
Salpinge della lunghezza di cm 5, con lume ectasico e a contenuto emorragico.
Il materiale inviato si processa *in toto* per esame istologico (1-9).

Informazioni cliniche (come segnalate in richiesta):
- Salpingectomia destra per gravidanza extrauterina. 6^ S.G. +4 gg. PARA 0000.

DIAGNOSI

Salpinge con ectasia del lume in rapporto ad impianto gravidico con cellule del trofoblasto e villi coriali e con angiectasie e diffuso infarcimento emorragico della parete (1-9).

CASE REPORT

- Patient was well, no fever or vaginal bleeding was remarked and she was discharged on third day after salpingectomy.

- She continued AB for 7 days at home.

- bHCG dosage was repeated at 7 and 24 days after surgery and both them were under 20 U/L.

ECTOPIC PREGNANCY

Clinical manifestations typically appear **six to eight weeks after the last normal menstrual period**, but can occur later.
Normal pregnancy discomforts (eg, breast tenderness, frequent urination, nausea) are often present in addition to the symptoms described below:

- Abdominal pain
- Amenorrhea
- Vaginal bleeding

These symptoms can occur in both ruptured and unruptured cases.

Ectopic pregnancy should be suspected in any women of reproductive age with these symptoms, especially those who have risk factors for an extrauterine pregnancy However they are the same as those associated with threatened abortion, which is far more common.

Ankum WM et al. Risk factors for ectopic pregnancy: a meta-analysis. Fertil Steril. 1996;65(6):1093.

ECTOPIC PREGNANCY

Risk factors for ectopic pregnancy

Degree of risk	Risk factors	Odds ratio
High	Previous ectopic pregnancy	9.3-47
	Previous tubal surgery	6.0-11.5
	Tubal ligation	3.0-139
	Tubal pathology	3.5-25
	In utero DES exposure	2.4-13
	Current IUD use	1.1-45
Moderate	Infertility	1.1-28
	Previous cervicitis (gonorrhea, chlamydia)	2.8-3.7
	History of pelvic inflammatory disease	2.1-3.0
	Multiple sexual partners	1.4-4.8
	Smoking	2.3-3.9
Low	Previous pelvic/abdominal surgery	0.93-3.8
	Vaginal douching	1.1-3.1
	Early age of intercourse (<18 years)	1.1-2.5

ECTOPIC PREGNANCY

The most common extra-uterine location is the fallopian tube (98 percent of all ectopic gestations). The prevalence of ectopic pregnancy among women who go to an emergency department with first trimester bleeding, pain, or both ranges from 6 to 16 percent.

The overall incidence of ectopic pregnancy increased during the mid twentieth century, approximately almost **20 per 1000 pregnancies.**

This rising incidence is strongly associated with an increased incidence of pelvic inflammatory disease

Murray H. et al. Diagnosis and treatment of ectopic pregnancy. CMAJ. 2005;173(8):905.

ECTOPIC PREGNANCY

The differential diagnosis of lower abdominal pain in women includes urinary tract infection, kidney stones, diverticulitis, appendicitis, ovarian neoplasms, endometriosis, endometritis, leiomyomas, pelvic inflammatory disease, and pregnancy-related conditions.

Vaginal bleeding also has several pregnancy-related and nonpregnancy-related etiologies.

A pregnancy test is important in premenopausal women who present with abdominal pain or vaginal bleeding in order to guide the direction of further evaluation

This combination of TVUS and hCG will permit a definitive diagnosis in almost all cases at a very early stage of pregnancy.

Gabrielli S et al. Accuracy of transvaginal ultrasound and serum hCG in the diagnosis of ectopic pregnancy. Ultrasound Obstet Gynecol. 1992;2(2):110.

ECTOPIC PREGNANCY

The **discriminatory zone** is based upon the correlation between visibility of the gestational sac and the hCG concentration. It is defined as the serum hCG level above which a gestational sac should be visualized by ultrasound examination if an intrauterine pregnancy is present. In most institutions, this serum hCG level is **1500 or 2000 IU/L with TVUS** (the level is higher [6500 IU/L] with TA ultrasound). However, a single serum hCG measurement does not usually distinguish between ectopic and intrauterine pregnancy so that it is mandatory to repeat the dosage of hCG.

Kadar N et al. Discriminatory hCG zone: its use in the sonographic evaluation for ectopic pregnancy. Obstet Gynecol. 1981;58(2):156.

In one representative study, 185 of 188 (98 percent) intrauterine pregnancies in women with hCG above 1500 IU/L were visualized.

Barnhart KT et al. Diagnostic accuracy of ultrasound above and below the beta-hCG discriminatory zone. Obstet Gynecol. 1999;94(4):583.

LITERATURE REVIEW

Randomised, double-blind trial in 10 countries.

4136 healthy women with regular menstrual cycles, who requested EC within 120 h of one unprotected coitus, to one of three regimens: 10 mg single dose mifepristone; 1·5 mg single-dose levonorgestrel; or two doses of 0·75 mg levonorgestrel given 12 h apart.

Of 4071 women with known outcome, **pregnancy rates** were:

-1·5 % (21/1359) in those given mifepristone,

-1·5 % (20/1356) in those assigned single-dose levonorgestrel,

-1·8% (24/1356) in women assigned two-dose levonorgestrel.

The RR of pregnancy for single-dose levonorgestrel compared with two-dose levonorgestrel was 0·83 (95% CI 0·46–1·50), and that for levonorgestrel (the two regimens combined) compared with mifepristone, 1·05 (0·63–1·76). Mifepristone and levonorgestrel do not differ in efficacy. A 1·5 mg single levonorgestrel dose can substitute two 0·75 mg doses 12 h apart.

von Hertzen H. et al. Low dose mifepristone and two regimens of levonorgestrel for emergency contraception: a WHO multicentre randomised. Lancet. 2002 Dec 7;360(9348):1803-10.

LITERATURE CASE REPORT 1

A 27-year-old white woman, G1, PARA 0, presented at our clinic because of lower abdominal pain and prolonged vaginal bleeding during the previous 4 weeks.

No risk factors for ectopic pregnancy were identified (no history of salpingitis, previous tubal surgery, previous ectopic pregnancy or intrauterine device use, and Chlamydia trachomatis DNA screening proved negative). She had regular menstruations. She had an unprotected intercourse 6 weeks before the consultation (**day 13 of the menstrual cycle**). She took 1.5-mg LNG (Norlevo®) 5 h after this unplanned interaction. She reported no vomiting or irregular spotting after the ingestion of the medication but noted mild abdominal pain. On day 28 of the same menstrual cycle, she experienced light vaginal bleeding, which she interpreted as menstrual bleeding.

Transvaginal ultrasound revealed a complex hypoechogenic tubal mass sized 3.5×2.7 cm and pelvic fluid suspected to be blood were demonstrated. The serum β-human chorionic gonadotrophin level was 3927 IU/L.

Kozinszky Z. et al. Ectopic pregnancy after levonorgestrel emergency contraception Contraception 83 (2011) 281–283

LITERATURE CASE REPORT 2

25-year-old nulliparous woman with acute onset of pain in her lower abdomen. A urine pregnancy test was positive.

Her menstrual cycle was every 30 days, and her last menstrual period was 6 weeks prior to presentation. She had light vaginal bleeding 2 weeks earlier, which was interpreted by her as menses, following which **spotting persisted**. She did give a history of a ruptured condom approximately **10 days after her last normal period** and took two doses of 750 mcg of LNG, 12 h apart. There was no history of repeat unprotected intercourse, and no risk factors for ectopic pregnancy were identified.

A transvaginal sonogram revealed no gestational sac in the endometrial cavity, with no adnexal mass and minimal free fluid in the pelvis. Serum beta-human chorionic gonadotrophin (β-hCG) was 3816.8 mIU/mL.

Ghosh B. et al. Ectopic pregnancy following levonorgestrel emergency contraception: a case report. Contraception 79 (2009) 155–157

LITERATURE CASE REPORT 3

The patient was a 24-year-old unmarried female, G1 P0, and a normal menstrual period of 28 days. After a single unprotected intercourse **in her follicular phase (day 11),** she had taken 750 μg levonorgesterol (Norlevo™) 16 hour and 28 hours later.
Three weeks later, on the 15th of May, 2009, she was first seen in our hospital. Her complaints were lower abdominal pain and light vaginal bleeding.

The patient's level of serum β-human chorionic gonadotropin (β-hCG) was 2980 mIU/ml. Transvaginal ultrasound showed a complex structure of 3x3x4.3 cm in diameter in her left tube, with no evidence of intrauterine pregnancy. A diagnosis of ectopic pregnancy was made

Kaymak O. et al. Ectopic pregnancy following levonorgestrel emergency contraception: a case report. J Turkish-German Gynecol Assoc 2010; 11: 168-9