



**Karolinska
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The contraceptive continuum

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and Research Training in Human Reproduction, WHO, Geneva

Disclosures;

Gemzell-Danielsson has been ad hoc advisory board member or invited to give
presentations for Merck (MSD), Bayer, Exelgyn, Actavis, Gedeon Richter, Mithra,
Exeltis, Ferring, Natural Cycles, Gynuity, and HRA-Pharma



Reproductive Health Research
From bench - to bed - to the hands of women
to improve women's health

Effective contraceptive methods and safe abortion are prerequisite for Reproductive Health

”Sexual and reproductive health and rights
constitute fundamental human rights,
form a vital aspect of the women’s empowerment and
are a key to the achievement of gender equality”

Who decides over fertility?



President Donald Trump signs an executive order against abortion in the White House, Jan. 23, 2017, <http://investigatingtrump.com/huffpost-donald-trump-reinstates-ronald-reagans-abortion-global-gag-rule/>

There is no tool for development more effective than empowerment of women

(Kofi Annan)



Swedish Deputy PM Isabella Lövin and her colleagues in a familiar pose.
Photo: Isabella Lövin

Main cause of MM- key interventions

Lancet 2016



Sepsis & other maternal infections

- Tetanus toxoid
- Clean delivery
- Antibiotics
- WASH

Other maternal disorders

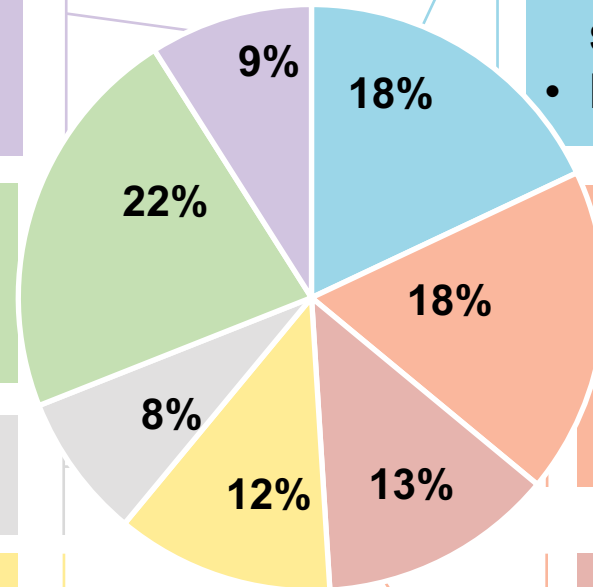
- Caesarean-section
- Other emergency obstetric care

Obstructed labour

- Caesarean-section

Hypertensive disorders

- Early identification & timely delivery
- Magnesium sulphate
- Calcium
- Aspirin
- Anti-hypertensive
- Caesarean-section



Complications of abortion

- Family planning
- Safe abortion services
- Post abortion care

Haemorrhage

- Uterotonics
- Blood transfusion
- Balloon tamponade
- Surgery
- NASG

Indirect causes

- Iron folate supplements
- Malaria intermittent treatment
- Insecticide-treated nets
- Anti-retrovirals

Is there a need for new contraceptive methods?

Globally 225 mill women lack access to effective and acceptable contraception

>40%

Of all pregnancies are
unplanned

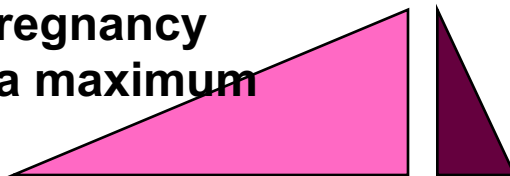
50%

Results in an induced
abortion

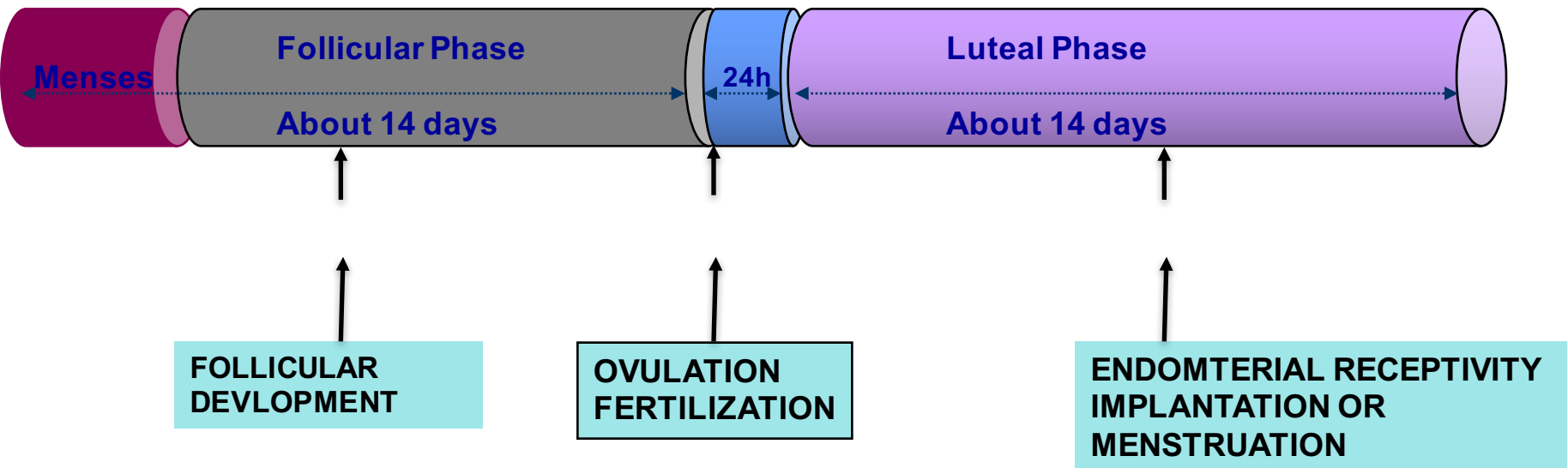


Reproductive physiology –Points for inter(action)

Probability of pregnancy increases until a maximum (30%) LH+0

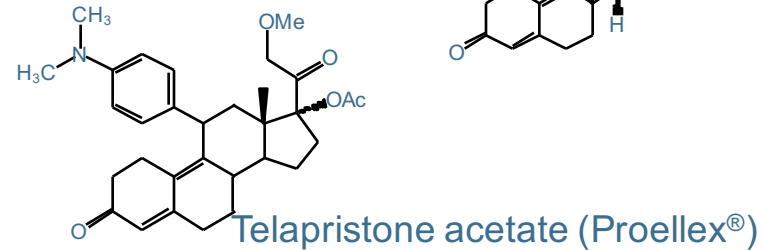
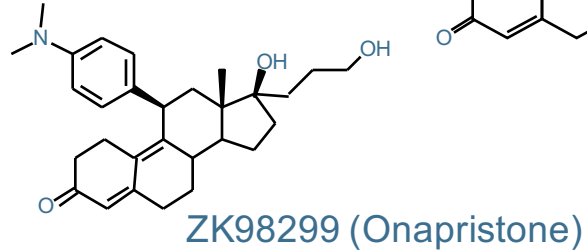
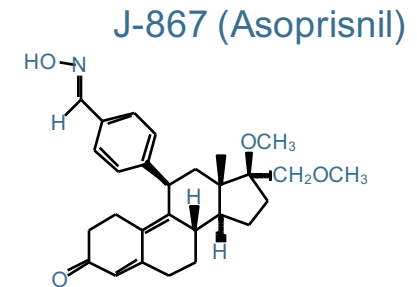
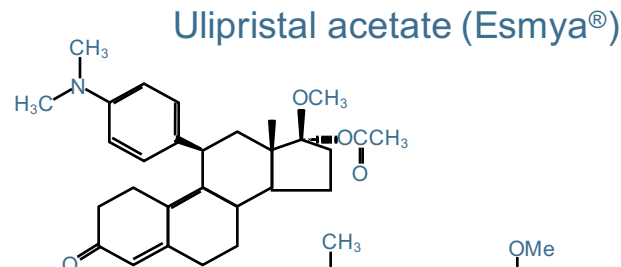
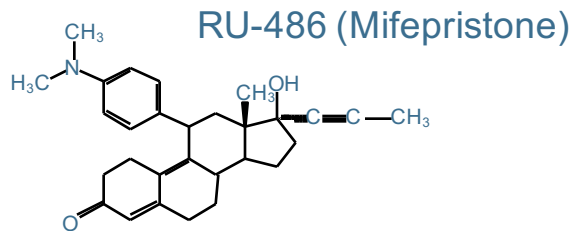


Sharp decline immediately post ovulation, to 0% for any act of intercourse



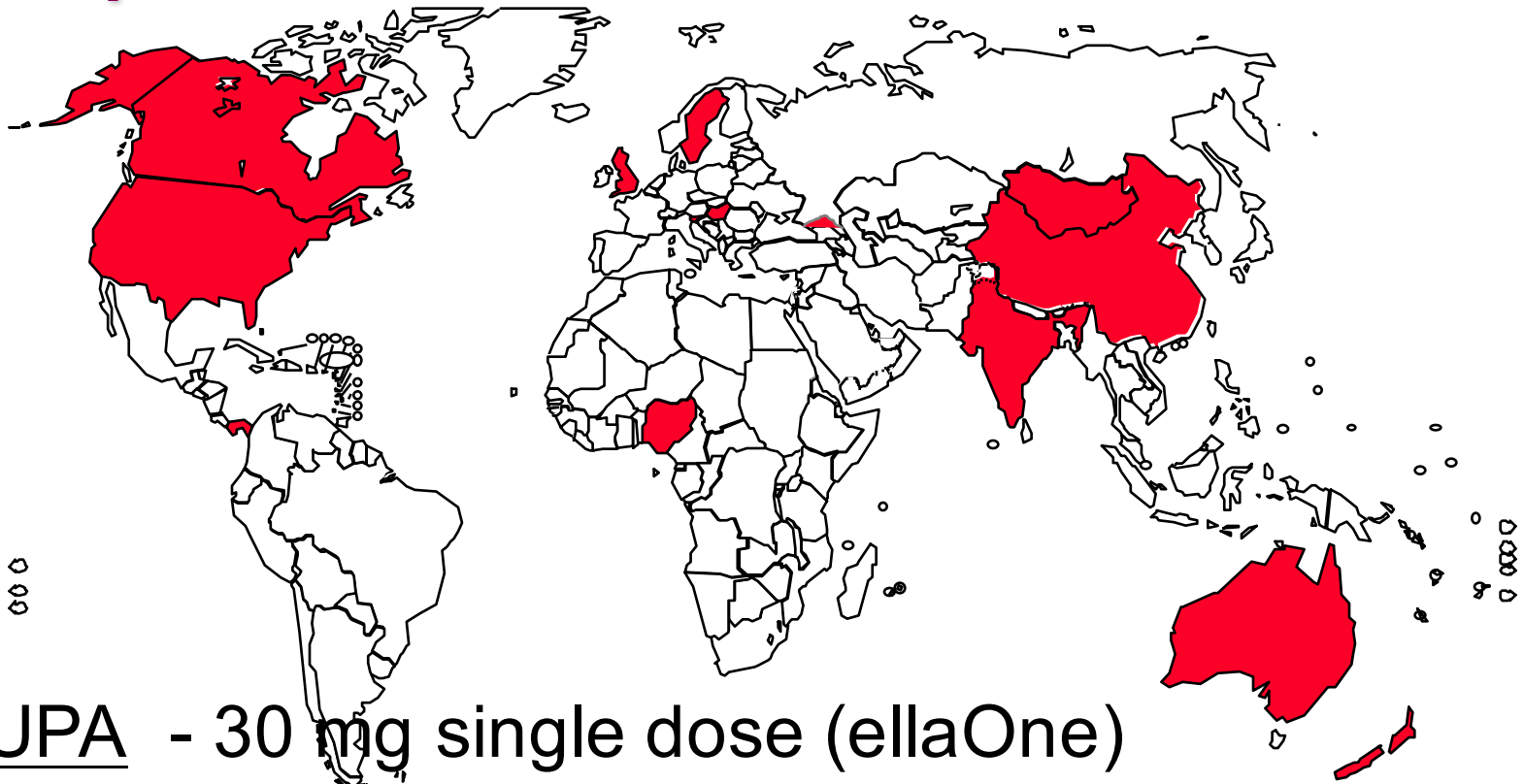
Selective progesterone receptor modulators (SPRM) for contraception and contragestion

- Emergency Contraception → "Regular/ on demand contraception"
 - Inhibition of Ovulation, → Endometrial Contraception → "Menstrual induction" – "contragestion" → VEMA, medical abortion



SPRM: Selective Progesterone Receptor Modulator
UPA: Ulipristal acetate

WHO multicentre trials on Yuzpe vs LNG-EC, and LNG-EC mifepristone

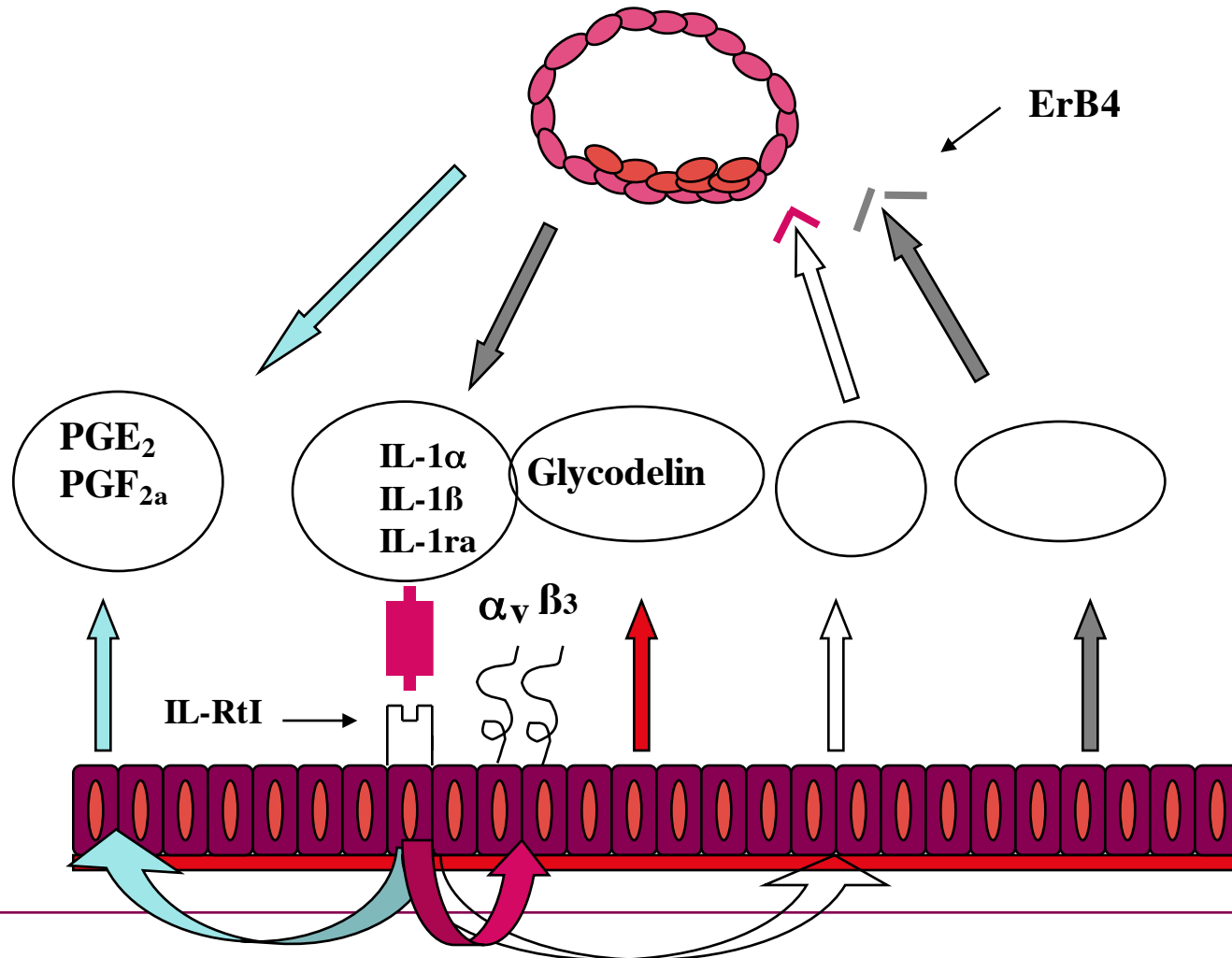


UPA - 30 mg single dose (ellaOne)

Mifepristone (RU486) - ≥ 10 mg, China

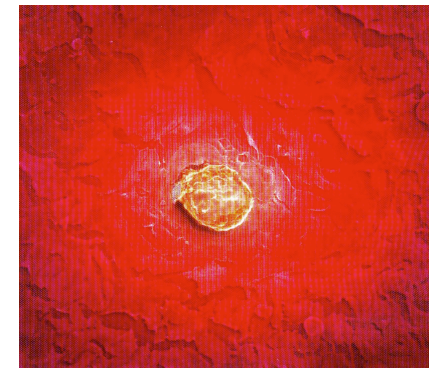
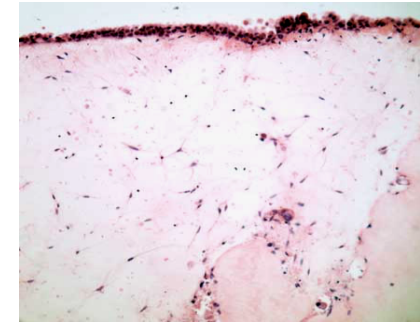
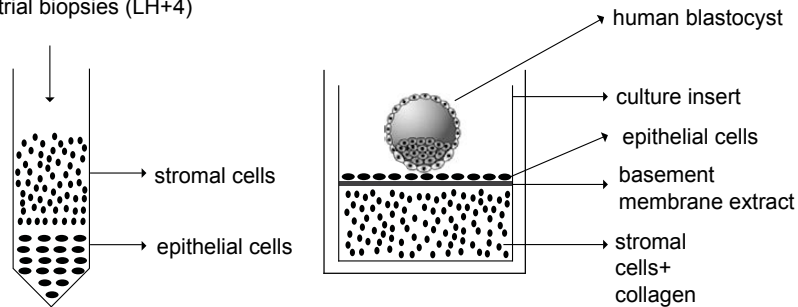
Endometriereceptivitet

Progesteron - ett nyckelhormon för fertilitet

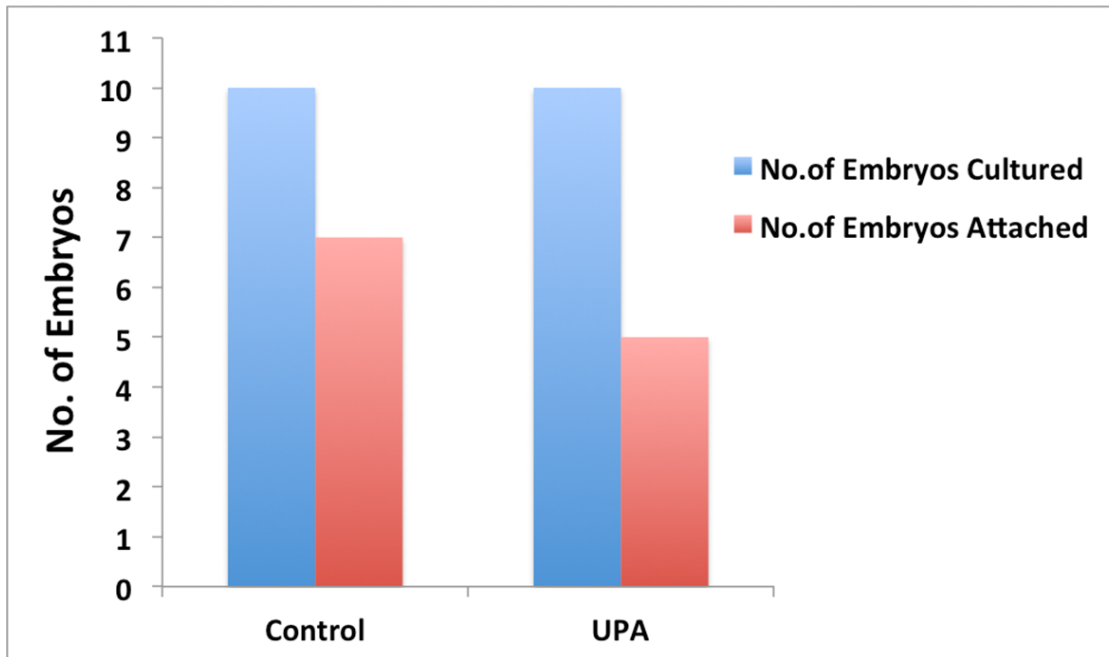


Effects of ECP on the endometrium

endometrial biopsies (LH+4)



Photo; Lennart Nilsson



Effects of mifepristone

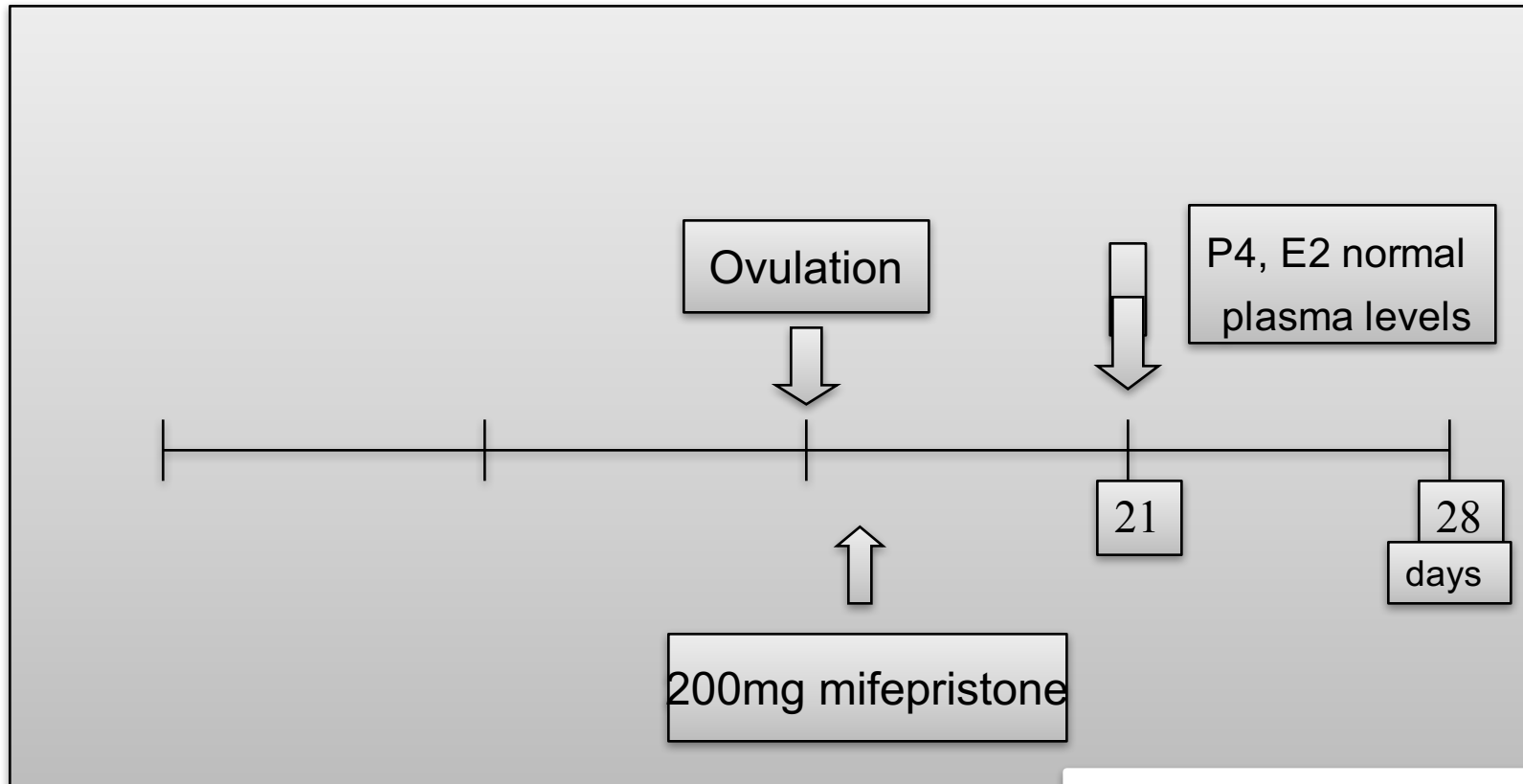
Mifepristone interrupts or inhibits development of the dominant follicle depending on dose and cycle stage

Following treatment in the follicular phase:- If ovulation occurs there is no adverse effect on the postovulatory endometrium

Post ovulatory treatment results in a dose dependent effect on endometrial development and "markers of receptivity"

Endometrial Contraception

/Once-a-month Pill shown to be a highly effective contraceptive method,



Gemzell-Danielsson et al.,
Lancet 1992, Hum Reprod 1993

Effects on embryo development and pregnancy

- No direct effect on human embryos /implantation
- No effect of human pregnancies in vivo or the pregnancy outcome

Lalitkumar et al., 2007, Meng et al., 2008, 2010, Zhang et al., 2009,
Berger et al., 2015

Inhibition of ovulation

SPRM – daily oral administration

Mifepristone continuous low dose

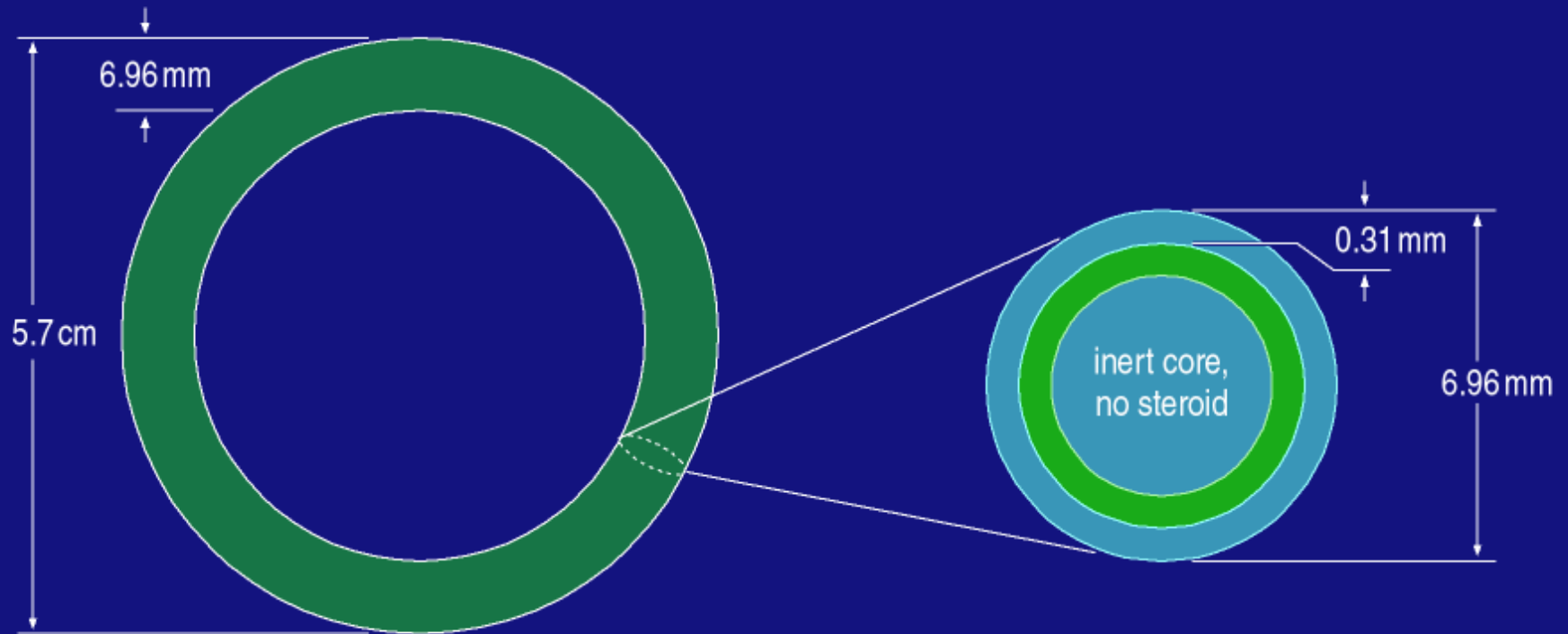
- Disruption of the follicle maturation, inhibition of ovulation
- Non-secretory endometrium
- Amenorrhea
- Well tolerated
- Highly effective contraceptive method (RCT 2 and 5 mg mifepristone/d 120d).

Brown et al., JCEM 2002

UPA. –similar effects

Chabbert-Buffet et al., JCEM 2007

Diagram of CDB-2914 Ring



Vaginal ring dimensions

Cross-sectional view of vaginal ring. The shaded areas are micronized CDB-2914 in silicone matrix.

Once-a-week mifepristone

- Double-blind, RCT with weekly doses of 25 or 50 mg of mifepristone in three centers in China.
- Each study cycle defined as 28 days.
- Outcome measures efficacy, changes of menstrual pattern, side effects.
- No pregnancy (76 women/ 456 cycles)

Pei K, Xiao B, et al., Contraception 2007

Contraception

- Treatment at/ just before expected time of menstruation
- Induction of abortion in pregnant women with very early pregnancy or
- Induction of menstruation

Swahn et al., Hum Reprod 1999,
Xiao B, et al. Contraception. 2003 Dec;68(6):477-82,
CL Li, et al., Hum Reprod, 30:12 ;2794–2801, 2015

VEMA, very early medical abortion

VEMA failure (ie ongoing pregnancy or incomplete abortion)

- NOT more likely in women with no confirmed intrauterine gestation (IUG) vs.confirmed IUG, gestations ≤ 49 days
- Significantly lower rate of treatment for incomplete abortion
- Findings support that VEMA is effective and safe

Recommendation

Avoid unnecessary delay!
Offer medical termination accordingly

The logo consists of three lines of text: "on time", "complete", and "correct". Each line has a green circular icon to its left: a location pin for "on time", a checkmark for "complete", and a thumbs up for "correct".

Bizjak et al., 2017

I need an abortion



I had an abortion



DOI: 10.1111/j.1471-0528.2008.01787.x
www.blackwellpublishing.com/bjog

Short communication

Using telemedicine for termination of pregnancy with mifepristone and misoprostol in settings where there is no access to safe services

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Women have an abortion. No woman dies unnecessarily from an unsafe abortion. If you have your face, share your story and help women around the world find safe abortions. Discuss and support others. Look for support if you have an abortion. Participate to find out also if you did not have an abortion. The portraits to find our

Contraception; regular vs occasional administration

- Once-a-month 200mg mifepristone + 0.4 mg misoprostol po 48h later before or on the day of menstruation,
- Conclusion; not effective enough to be used for menstrual regulation.

- “Late EC” >5 days after a single or several UPSI
- 100 mg mifepristone 48h later 0.4 mg misoprostol po, in the luteal phase of the cycle. u-hCG negative.
- 25 women (2.7%) became pregnant.
- -→could provide an option for preventing unwanted pregnancies in women who are late for EC.

Summary

- The unmet need in contraception remains high
- Today many women are reluctant to use any of the existing contraceptive methods due to side effects or fear of experiencing such effects.
- **New options should be explored to allow women and men all possible options for controlling and preserving their reproductive health and lives.**
- To achieve this we need translational research incl basic research
- Link research to policy, and base policy on evidence
- Room to expand access to SPRMs

WHO Collaborating Centre for Research in

Human Reproduction

Karolinska University Hospital/ Karolinska Institutet

- Research Group on Post-Ovulatory Methods for Fertility Regulation, UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction, WHO, Geneva
- ICCR Population Council, Regine Sitruk-Ware
- Swedish research council
- www.muvs.org



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THANK YOU!

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