Handläggning vid PUL och behandling av extrauterin tubargraviditet

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ÖVERLÄKARE

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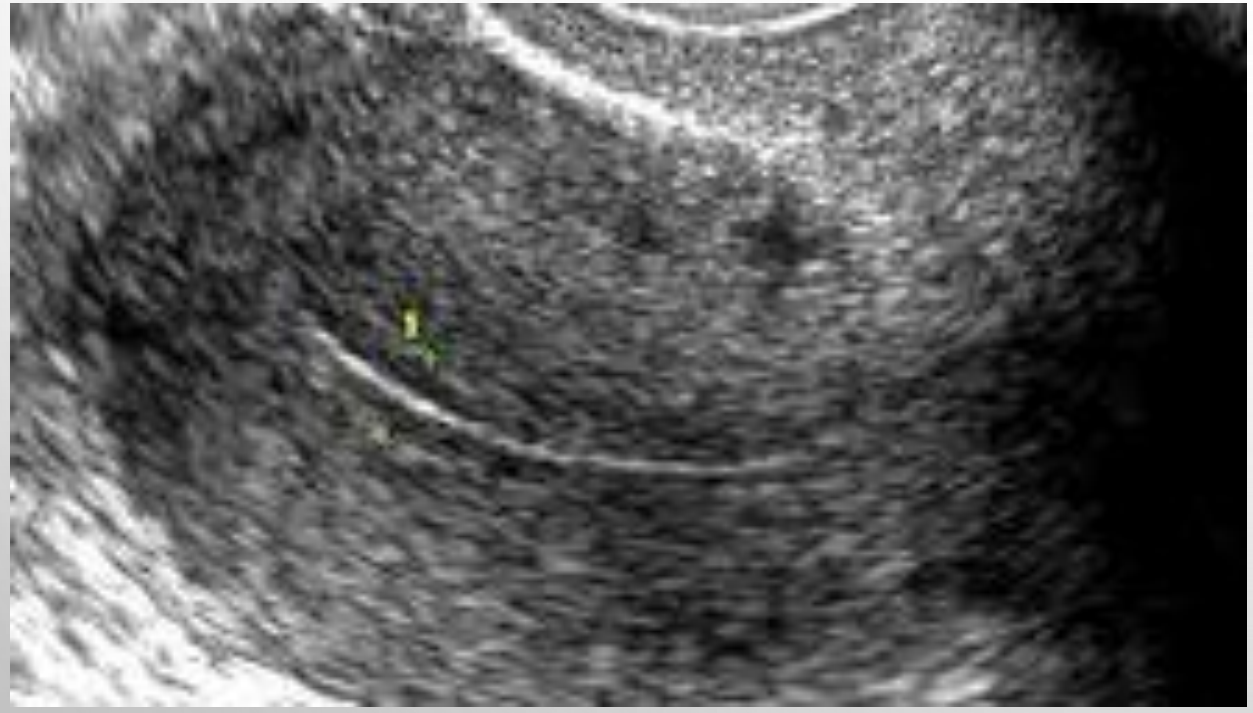
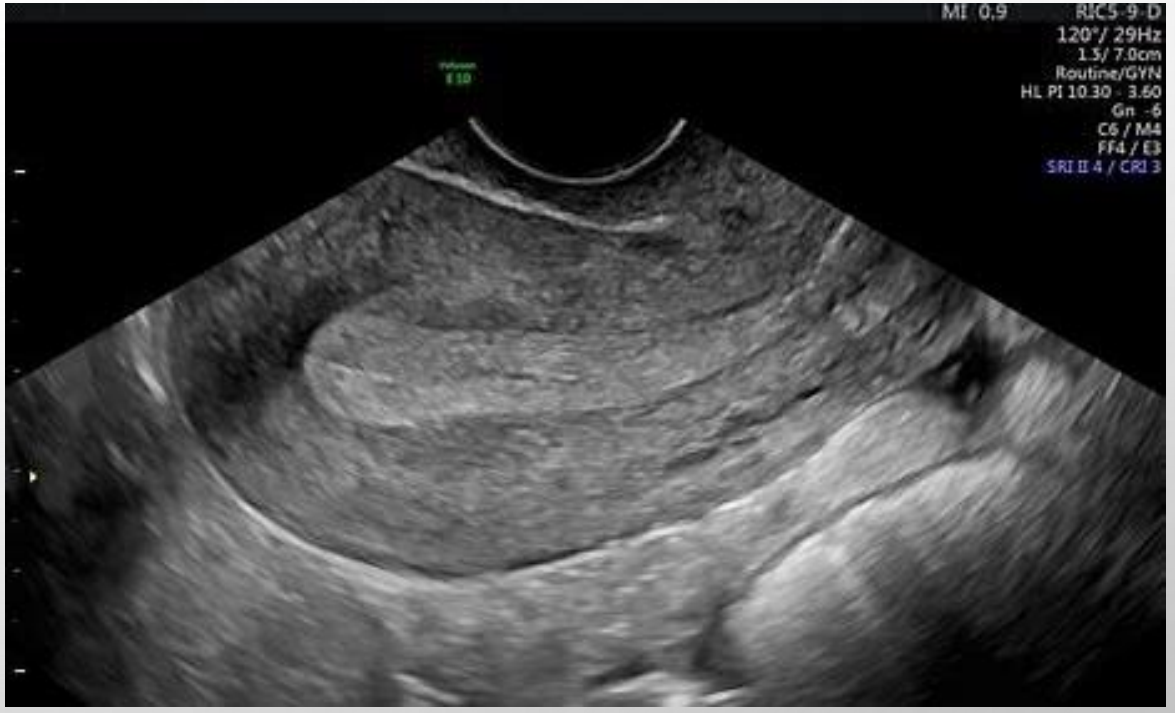
JÄV

JAG HAR INGET JÄV/INTRESSEKONFLIKTER ATT DEKLARERA

GRAVIDITET AV EN OKLAR LOKALISATION (PUL)





HUR VANLIGT ÄR DET MED PUL

- ENLIGT PUBLICERAD DATA VARIERAR 8-31%*

- < 15 % - ACCEPTABEL
- ≥ 15% - ICKE-ACCEPTABEL

JU MER ERFAREN UNDERSÖKARE – DESTO LÄGRE % PUL

CONDOUS ET AL, UOG 2006

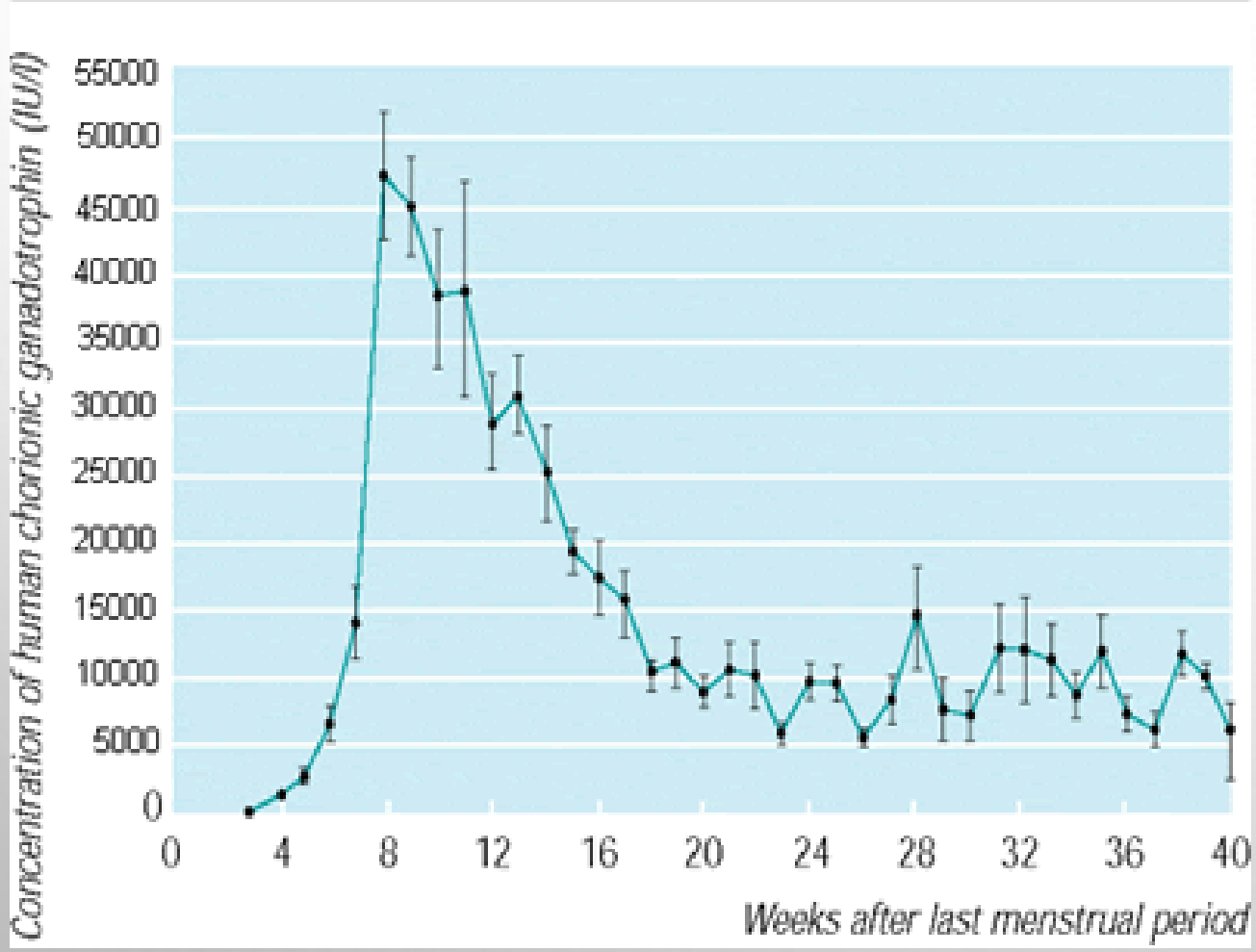
HANDLÄGGNING

- NORMAL INTRAUTERIN GRAVIDITET SYNLIG NÄR HCG ≥1000IU/L (≥1500IU/L)
- **VID NORMAL INTRAUTERIN GRAVIDITET:**
  - HCG DUBBLERAS OM 48 TIMMAR NÄR INITIALT < 1200 IU/L
  - HCG DUBBLERAS OM 72 TIMMAR NÄR INITIALT 1200 – 6000 IU/L

- SYFTET
  - ATT INTE MISSA STORA X
  - MINSKA ANTAL BESÖK

Day et al 2009, Condous et all 2006

HCG



hCG levels during pregnancy (in weeks sincelast menstrual period)	
3 weeks LMP	5 - 50 mIU/ml
4 weeks LMP	5 - 426 mIU/ml
5 weeks LMP	18 - 7,340 mIU/ml
6 weeks LMP	1,080 - 56,500 mIU/ml
7 - 8 weeks LMP	7, 650 - 229,000 mIU/ml
9 - 12 weeks LMP	25,700 - 288,000 mIU/ml
13 - 16 weeks LMP	13,300 - 254,000 mIU/ml
17 - 24 weeks LMP	4,060 - 165,400 mIU/ml
25 - 40 weeks LMP	3,640 - 117,000 mIU/ml
non pregnant	55-200 ng/ml

HANDLÄGGNINGSALTERNATIV

hCG

Progesteron

Model 4

Model 6

HCG

hcg x2 med 48 timmars interval

Ratio 48h/0h

- RATIO < 0.8 = SPONTAN REGRESS 98% PUL, INGEN UPPFÖLJNING

Condous et al, Human Reprod 2007

- NICE/RCOG GUIDELINES
  - RATIO < 0.5 – TA GRAV TEST OM 2 VECKOR
  - RATIO 0.6-1.63 - HÖG RISK FÖR EKTOPISK GRAVIDITET (UL ≤48 H)
  - RATIO >1.63 – IU GRAV, UL OM 1VECKA

HCG OCH UTFALL

- FÖRDUBBLAS EFTER 48 TIMMAR – LEVANDE GRAVIDITET, ULTRALJUD IGEN NÄR ≥1000IU/L
  - INTRAUTERIN GRAVIDITET
  - EXTRAUTERIN GRAVIDITET
- SJUNKER 50% - UTVECKLAS INTE
  - INTRAUTERIN GRAVIDITET (MISSFALL)
  - EXTRAUTERIN GRAVIDITET (TUBARABORT)
- STIGER/SJUNKER SUBOPTIMALT – UTVECKLAS EJ
  - INTRAUTERIN GRAVIDITET
  - EXTRAUTERIN GRAVIDITET

- 30-40% INTRAUTERIN GRAVIDITET
- **8% EKTOPISKA GRAVIDITET**
- 50-60% FÖRSVINNER

INITIAL PROGESTERON

- Progesteron nivå sjunker INNAN hCG sjunker
- Progesteron kan predikera hCG förändring närmaste dagar

- OBSERVATIONSSTUDIE MED INITIAL PROGESTERON (1100 PUL GRAVIDITETER)

  NÄR PROGESTERON < 10 NMOL/L –
  - 98% PUL FÖRSVANN
  - 2% BEHÖVDE INTERVENTION

DAY ET AL 2009,

MODEL 6

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Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.20420

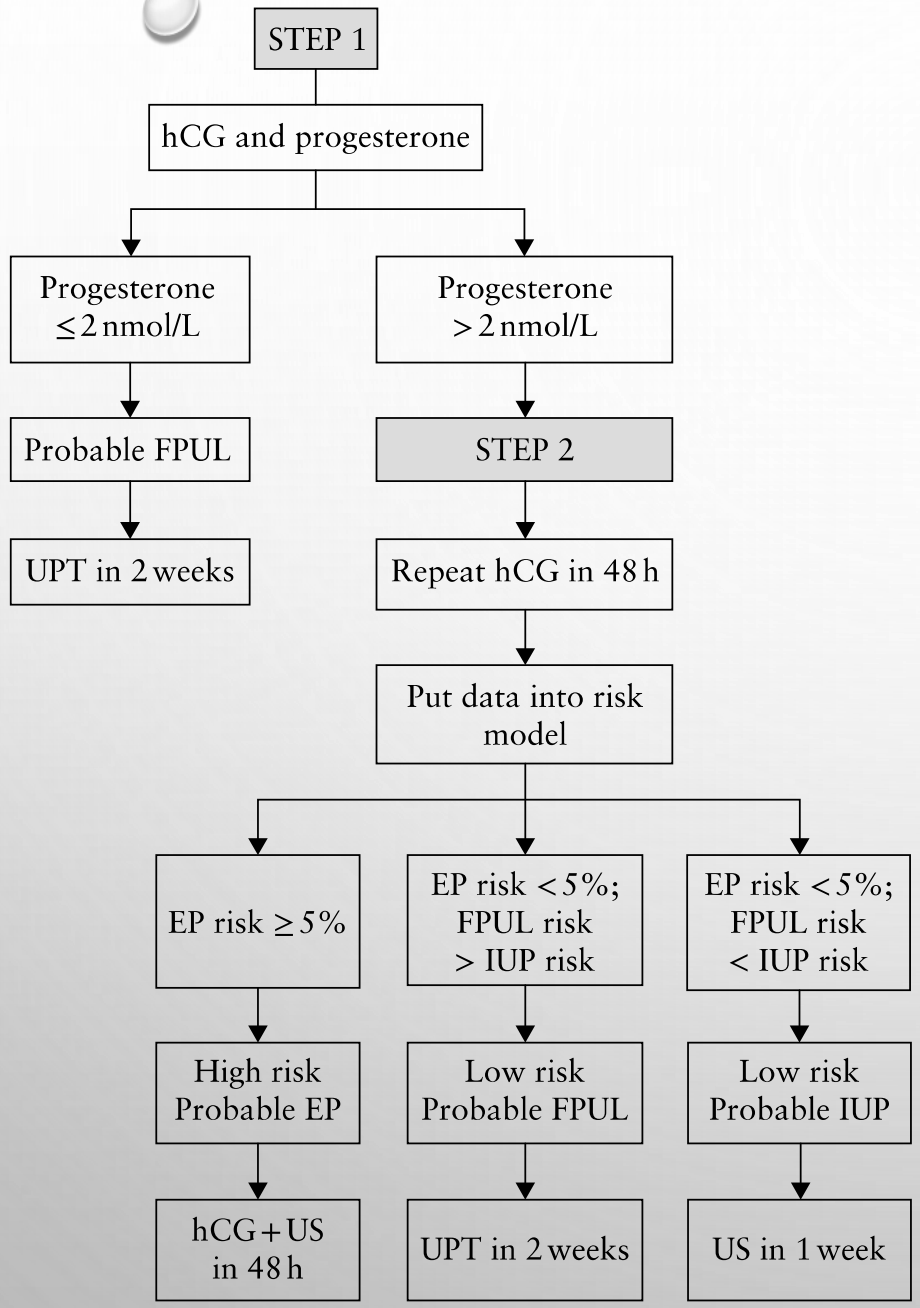
Triaging women with pregnancy of unknown location using two-step protocol including M6 model: clinical implementation study

S. BOBDIWALA[1], E. CHRISTODOULOU[2], J. FARREN[3], N. MITCHELL-JONES[4], C. KYRIACOU[1], M. AL-MEMAR[1], F. AYIM[5], B. CHOHAN[6], E. KIRK[7], O. ABUGHAZZA[8], B. GURUWADAHYARHALLI[4], S. GUHA[4], V. VATHANAN[6], C. BOTTOMLEY[4], D. GOULD[3], C. STALDER[1], D. TIMMERMAN[2,9], B. VAN CALSTER[2,10] and T. BOURNE[1,2,9]

LOGISTISK REGRESSION MODEL M6

- INITIAL PROGESTERON, INITIAL HCG, HCG 48 TIMMAR SENARE
- RÄKNAR SANNOLIKHET FÖR INTRAUTERIN GRAVIDITET, EKTOPISK GRAV, FÖRSVINNANDE GRAV
- RISK FÖR EKTOPISK GRAV ≥5% - UL ≤ 48 H
- 2-STEG STRATEGI
- VALIDERAD INOM KLINISK PRAXIS PÅ 2625 KVINNOR
- BRA UTFÖRLITLIGHET

- BASERAD PÅ 2753 PUL (301 EP)
  - 1449 DEVELOPMENT
  - 1304 VALIDERING



- STEG 1 (INITIAL PROGESTERON) – 16% LÅGRISK PUL
- STEG 2 - 46% LÅGRISK PUL
- STEG1 + STEG 2 – 62% LÅGRISK PUL

EXTERNT VALIDERAD PÅ 2625 PUL

HANDLÄGGNING AV TUBARGRAVIDITET

- VID BEKRÄFTAD TUBARGRAVIDITET
  - KIRURGISK
  - MEDICINSK (METOTREXAT)
  - EXPEKTANS

KIRURGISK HANDLÄGGNING- TUBEKTOMI ELLER TUBOTOMI?

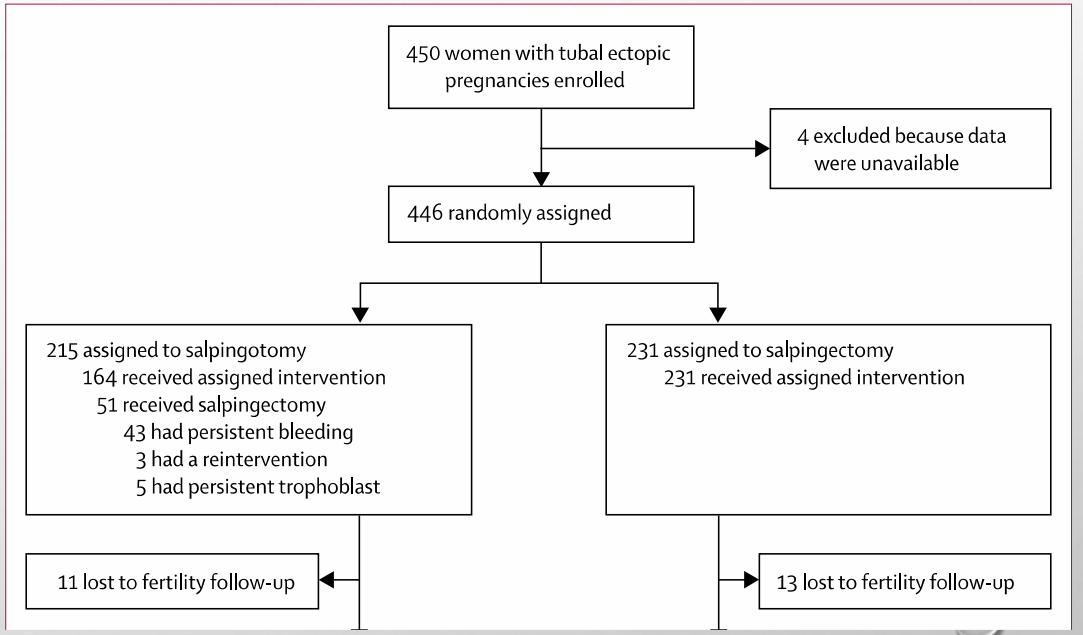
Salpingotomy versus salpingectomy in women with tubal pregnancy (ESEP study): an open-label, multicentre, randomised controlled trial

*Femke Mol, Norah M van Mello, Annika Strandell, Karin Strandell, Davor Jurkovic, Jackie Ross, Kurt T Barnhart, Tamer M Yalcinkaya, Harold R Verhoeve, Giuseppe C M Graziosi, Carolien A M Koks, Ingmar Klinte, Lars Hogström, Ineke C A H Janssen, Harry Kragt, Annemieke Hoek, Trudy C M Trimbos-Kemper, Frank J M Broekmans, Wim N P Willemsen, Willem M Ankum, Ben W Mol, Madelon van Wely, Fulco van der Veen, Petra J Hajenius, for the European Surgery in Ectopic Pregnancy (ESEP) study group**

	Salpingotomy (n=215)	Salpingectomy (n=231)	Relative risk (95% CI)	p value
Persistent trophoblast	14 (7%)	1 (<1%)	15·0 (2·0–113·4)	0·01
Repeat ectopic pregnancy	18 (8%)	12 (5%)	1·6 (0·8–3·3)	0·19
Ipsilateral tube	7 (3%)	3 (1%)	2·5 (0·7–9·6)	0·18
Contralateral tube	8 (4%)	7 (3%)	1·2 (0·5–3·4)	0·69
Persisting pregnancy of unknown location	3 (1%)	2 (1%)	1·6 (0·3–9·5)	0·60
Ongoing pregnancy by:				
Ovulation induction	0	3 (1%)	..	..
Intrauterine insemination	0	1 (<1%)	..	..
In-vitro fertilisation	7 (3%)	2 (1%)	3·8 (0·8–17·9)	0·10

Data are n (%), unless otherwise indicated.

Table 3: **Secondary outcomes**



Interpretation In women with a tubal pregnancy and a healthy contralateral tube, salpingotomy does not significantly improve fertility prospects compared with salpingectomy.

	Salpingotomy (n=215)	Salpingectomy (n=231)
Conversion to open surgery	3 (1%)	3 (1%)
Conversion to salpingectomy	43 (20%)	NA
Blood transfusion	14 (7%)	7 (3%)
Initial admission		
Repeat laparoscopy with salpingectomy for suspected bleeding*	2 (1%)	0
Readmission*		
Repeat laparoscopy with salpingectomy for suspected bleeding	1 (<1%)	0
Repeat laparoscopy with salpingectomy for persistent trophoblast	5 (2%)	0
Other surgical reintervention	4 (2%)	2 (1%)
Readmission only	10 (5%)	3 (1%)

Data are n (%). *Repeat laparoscopy and readmissions were regarded as serious adverse events.

Table 2: **Adverse events**

Diagnosis and Management of Ectopic Pregnancy

Green-top Guideline No. 21

RCOG/AEPU Joint Guideline | November 2016

In the presence of a healthy contralateral tube, salpingectomy should be performed in preference to salpingotomy. [*New 2016*] B

In women with a history of fertility-reducing factors (previous ectopic pregnancy, contralateral tubal damage, previous abdominal surgery, previous pelvic inflammatory disease), salpingotomy should be considered. [*New 2016*] C

METOTREXAT

Human Reproduction Update, Vol.14, No.4 pp. 309–319, 2008 doi:10.1093/humupd/dmn012
Advance Access publication June 2, 2008

Current evidence on surgery, systemic methotrexate and expectant management in the treatment of tubal ectopic pregnancy: a systematic review and meta-analysis

F. Mol[1,2,3], B.W. Mol[1,2], W.M. Ankum[1], F. van der Veen[2] and P.J. Hajenius[1]

- SINGLE DOS METOTREXAT IM (MED EXTRA DOS VB) VAR EFFEKTIV JÄMFÖRT MED LAPAROSKOPISK TUBOTOMI ENDAST VID HCG <1500IU/L

Diagnosis and Management of Ectopic Pregnancy

Green-top Guideline No. 21

RCOG/AEPU Joint Guideline | November 2016

METOTREXAT

A good candidate for methotrexate has the following characteristics:

- haemodynamic stability
- low serum β-hCG, ideally less than 1500 iu/l but can be up to 5000 iu/l
- no fetal cardiac activity seen on ultrasound scan
- certainty that there is no intrauterine pregnancy
- willingness to attend for follow-up
- no known sensitivity to methotrexate.

Success rate of methotrexat vid hCG ≥1500IU/L är 30% (Sowter, 2001)

NICE GUIDELINES - METOTREXAT

NICE[1] recommends that methotrexate should be the first-line management for women who are able to return for follow-up and who have:

- no significant pain
- an unruptured ectopic pregnancy with a mass smaller than 35 mm with no visible heartbeat
- a serum β-hCG between 1500 and 5000 iu/l
- no intrauterine pregnancy (as confirmed on ultrasound scan).

EXPEKTANS

- Patient samarbetsvillig, vill komma på återbesök
- Ingen/Minimal smärta
- Låg/sjunkande hCG (<1000IU/L; <1500IU/L)
- Tubargraviditet <35mm vid TVUL, utan hjärtaktivitet
- Success rate up till 57-100%*

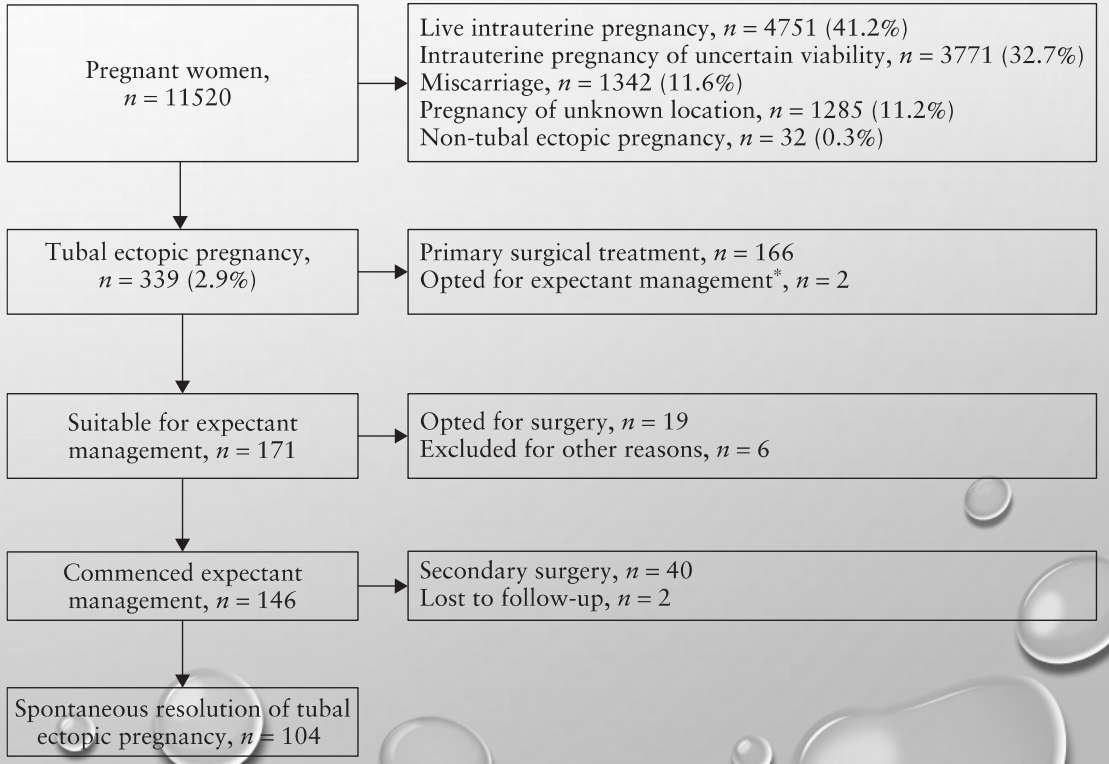
EXPEKTANS

Ultrasound Obstet Gynecol 2013; **42:** 102–107
Published online 27 May 2013 in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.12401

Efficacy and safety of a clinical protocol for expectant management of selected women diagnosed with a tubal ectopic pregnancy

D. MAVRELOS, H. NICKS, A. JAMIL, W. HOO, E. JAUNIAUX and D. JURKOVIC

University College Hospital, Gynaecology Diagnostic and Outpatient Treatment Unit, London, UK



31% av kvinnor med ektopisk graviditet med lyckad expektans handläggning

Diagnosis and Management of Ectopic Pregnancy

Green-top Guideline No. 21

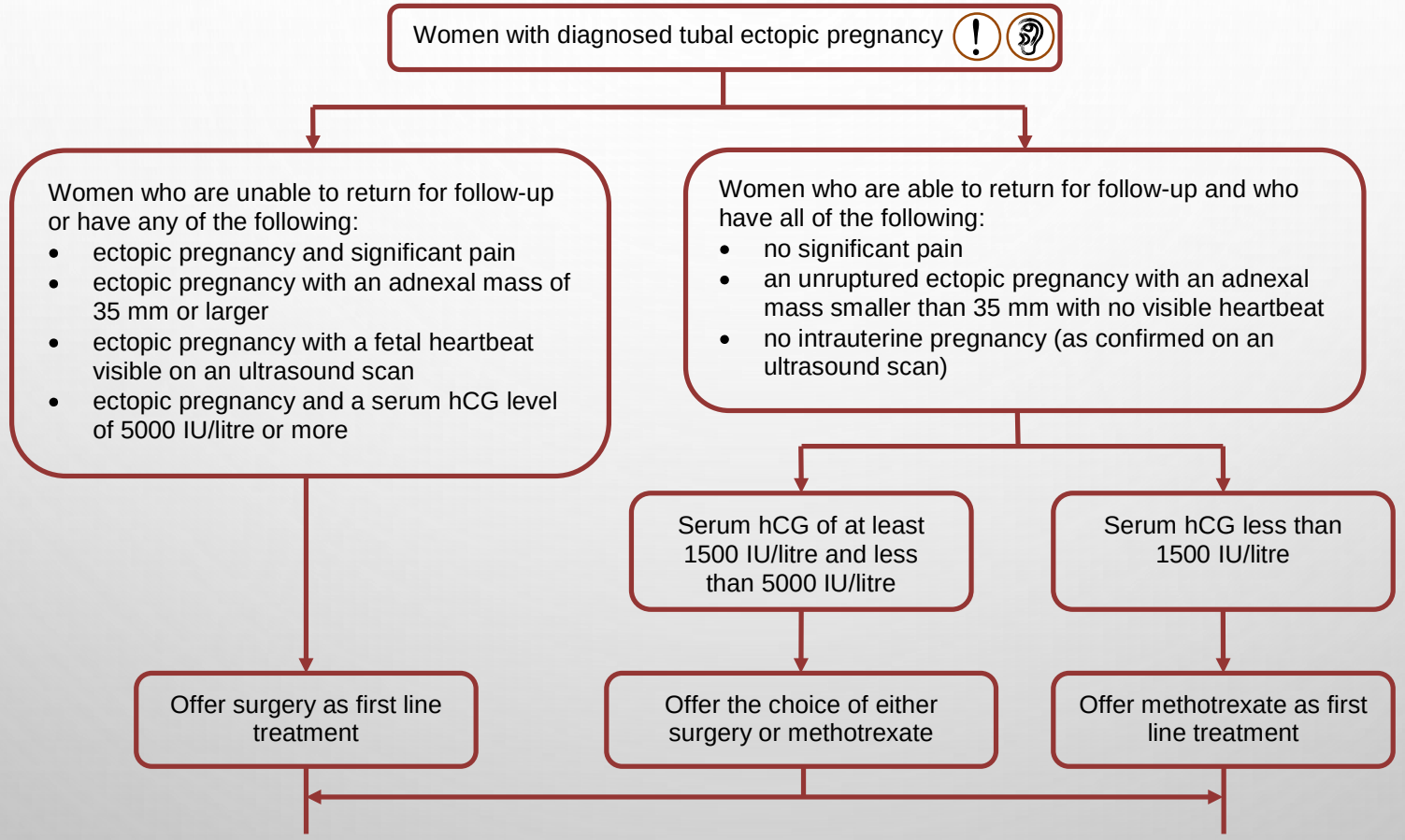
RCOG/AEPU Joint Guideline | November 2016

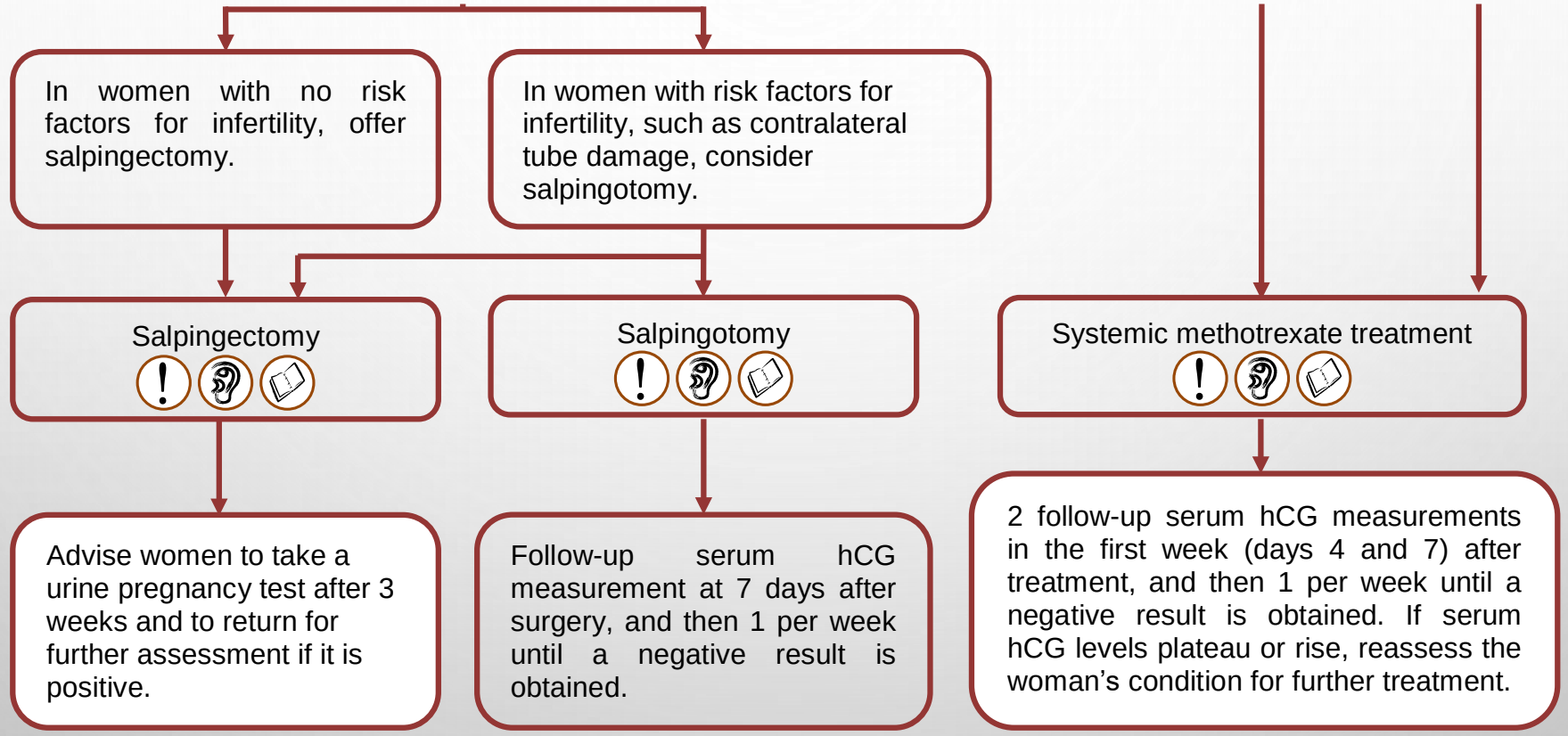
EXPEKTANS

Expectant management is an option for clinically stable women with an ultrasound diagnosis of ectopic pregnancy and a decreasing β-hCG level initially less than 1500 iu/l. B

Expectant management is only suitable for women with low or significantly falling β-hCG levels in whom the addition of methotrexate may not improve the outcome. [*New 2016*] D

H. Ectopic pregnancy




In women with no risk factors for infertility, offer salpingectomy.
In women with risk factors for infertility, such as contralateral tube damage, consider salpingotomy.
Salpingectomy
Salpingotomy
Systemic methotrexate treatment
Advise women to take a urine pregnancy test after 3 weeks and to return for further assessment if it is positive.
Follow-up serum hCG measurement at 7 days after surgery, and then 1 per week until a negative result is obtained.
2 follow-up serum hCG measurements in the first week (days 4 and 7) after treatment, and then 1 per week until a negative result is obtained. If serum hCG levels plateau or rise, reassess the woman's condition for further treatment.

SAMMANFATTNING

- ACCEPTABEL PUL RATE <15%
- MÖJLIGA SCENARIO VID PUL:
  - 30-40% INTRAUTERIN INTRAKAVITÄR GRAVIDITET
  - 8% EKTOPISK GRAVIDITET
  - 50-60% FÖRSVINNER UTAN KÄND LOKALISATION
- HANDLÄGGNING AV TUBARGRAVIDITET – KIRURGISK, MEDICINSK ELLER EXPEKTANS

TACK SÅ MYCKET!