# EARLY PREGNANCY COMPLICATIONS AND FERTILITY INVESTIGATIONS

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# EARLY PREGNANCY COMPLICATIONS

- PV bleeding +/- Pain
- Miscarriage
- Retained products of conception
- Pregnancy of unknown location
- Ectopic pregnancy
- Molar pregnancy
- Hyperemesis gravidarum

# PV BLEEDING +/- PAIN

- TV ultrasound to assess:
  - Location of pregnancy
  - Viability
  - Subchorionic haematoma
  - Cervical length
- Speculum exam
- Anti-D

**Threatened miscarriage**

- Consider Progesterone[1] – vaginal progesterone 400mcg BD until 12 weeks

1. Wahabi HA, Fayed AA, Esmaeil SA, Bahkali KH. Progestogen for treating threatened miscarriage. Cochrane Database of Systematic Reviews 2018, Issue 8. Art. No.: CD005943. DOI: 10.1002/14651858.CD005943.pub5. Accessed 27 June 2024.

# SUBCHORIONIC HAEMATOMA (SCH)

- *Overall risk of miscarriage increases from 9% to 18% with SCH*[1]

- Offer repeat scan in 1-2 weeks for:
  - **< 8 weeks gestation** – *15-20% risk of miscarriage (compared to <4% risk of miscarriage after 8 weeks)*[2]
  - **Size of SCH > 50% of size of gestational sac (GS)** – *23% risk of miscarriage (compared to <11% risk of miscarriage if SCH <50% of size of GS)* [1]
  - History of recurrent miscarriage


1. Tuuli MG, Norman SM, Odibo AO, Macones GA, Cahill AG. Perinatal outcomes in women with subchorionic hematoma: a systematic review and meta-analysis. Obstet Gynecol. 2011 May;117(5):1205-1212. doi: 10.1097/AOG.0b013e31821568de. PMID: 21508763.
2. Heller HT, Asch EA, Durfee SM, Goldenson RP, Peters HE, Ginsburg ES, Doubilet PM, Benson CB. Subchorionic Hematoma: Correlation of Grading Techniques With First-Trimester Pregnancy Outcome. J Ultrasound Med. 2018 Jul;37(7):1725-1732. doi: 10.1002/jum.14524. Epub 2018 Jan 17. PMID: 29341210.

# MISCARRIAGE

ULTRASOUND CRITERIA for Diagnosis of Miscarriage[1,2]:

- Mean sac diameter of gestational sac **(MSD) >25mm with no fetal pole** identifiable
- Crown rump length **(CRL) >7mm with no FHR** visible
- If the above criteria is not fulfilled: **No interval growth**/change in between two scans **>10 days apart**

Refer to EPAS


1. ASUM Guidelines for the Performance of First Trimester Ultrasound (Revised 2014)
2. Abdallah Y, Daemen A, Kirk E, Pexsters A, Naji O, Stalder C, Gould D, Ahmed S, Guha S, Syed S, Bottomley C, Timmerman D, Bourne T. Limitations of current definitions of miscarriage using mean gestational sac diameter and crown-rump length measurements: a multicenter observational study. Ultrasound Obstet Gynecol. 2011 Nov;38(5):497-502. doi: 10.1002/uog.10109. Epub 2011 Oct 13. PMID: 21997898.

# MISCARRIAGE

## Expectant Mx

- 37% success in 1 week
- 75-80% success within 6 weeks[1,2]
- Follow up urine bhCG + phone call in 4 weeks

## Medical Mx

- Mifepristone 200mg oral followed by Misoprostol 800mcg buccal/PV 36-48hrs later
- 83% success in 1 week[3]
- Overall 93% success[1]
- Follow up urine bhCG + phone call in 4 weeks

## Surgical Mx

- 97% success rate[1]
- Recommended if >12weeks by LMP or CRL>30mm (10 week size)


1. Trinder J, Brocklehurst P, Porter R, Read M, Vyas S, Smith L. Management of miscarriage: expectant, medical, or surgical? Results of randomised controlled trial (miscarriage treatment (MIST) trial). BMJ. 2006 May 27;332PMC1471967 (7552):1235-40. doi: 10.1136/bmj.38828.593125.55. Epub 2006 May 17. PMID: 16707509; PMCID:.
2. Butler C, Kelsberg G, St Anna L, Crawford P. Clinical inquiries. How long is expectant management safe in first-trimester miscarriage? J Fam Pract. 2005 Oct;54(10):889-90. PMID: 16202377.
3. Chu JJ, Devall AJ, Beeson LE, Hardy P, Cheed V, Sun Y, Roberts TE, Ogwulu CO, Williams E, Jones LL, La Fontaine Papadopoulos JH, Bender-Atik R, Brewin J, Hinshaw K, Choudhary M, Ahmed A, Naftalin J, Nunes N, Oliver A, Izzat F, Bhatia K, Hassan I, Jeve Y, Hamilton J, Deb S, Bottomley C, Ross J, Watkins L, Underwood M, Cheong Y, Kumar CS, Gupta P, Small R, Pringle S, Hodge F, Shahid A, Gallos ID, Horne AW, Quenby S, Coomarasamy A. Mifepristone and misoprostol versus misoprostol alone for the management of missed miscarriage (MifeMiso): a randomised, double-blind, placebo-controlled trial. Lancet. 2020 Sep 12;396(10253):770-778. doi: 10.1016/S0140-6736(20)31788-8. Epub 2020 Aug 24. PMID: 32853559; PMCID: PMC7493715.



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# RETAINED PRODUCTS OF CONCEPTION

## Expectant Mx

- 88-92% success within 4 weeks (40% in 2 weeks) [1-4]
- *Higher chance of success if there is no vascularity on US (90% vs 60% of spontaneous resolution in 2 weeks)[5].*
- Follow up ultrasound in 4 weeks

## Medical Mx

- Misoprostol 800mcg buccal/PV STAT
- 95% will complete their miscarriage without surgical intervention within 4 weeks (80% within 2 weeks)[3]
- Follow up ultrasound in 4 weeks

## Surgical Mx

- If large volume – D&C under ultrasound guidance
- If very small volume but persistent – hysteroscopic removal


1. Luise C, Jermy K, May C, Costello G and Bourne T Outcome of expectant management of spontaneous first trimester miscarriage: observational study. BMJ. 2002 Apr 13;324(7342):873-5
2. Condous G. The management of early pregnancy complications. Best Pract Res Clin Obstet Gynaecol. 2004 Feb;18:37-57.
3. Ali MK, Emam SM, Abdel-Aleem MA, Sobh AMA. Misoprostol versus expectant management in women with incomplete first-trimester miscarriage after failed primary misoprostol treatment: A randomized clinical trial. Int J Gynaecol Obstet. 2021 Sep;154(3):558-564. doi: 10.1002/ijgo.13652. Epub 2021 Mar 24. PMID: 33615468.
4. Pang MW, Lee TS, Chung TK. Incomplete miscarriage: a randomized controlled trial comparing oral with vaginal misoprostol for medical evacuation. Hum Reprod. 2001 Nov;16(11):2283-7. doi: 10.1093/humrep/16.11.2283. PMID: 11679505.
5. Casikar I, Lu C, Oates J, Bignardi T, Alhamdan D, Condous G. The use of power Doppler colour scoring to predict successful expectant management in women with an incomplete miscarriage. Hum Reprod. 2012 Mar;27(3):669-75. doi: 10.1093/humrep/der433. Epub 2012 Jan 9. PMID: 22232130.



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# PREGNANCY OF UNKNOWN LOCATION (PUL)

- If it is a PUL with pain → Send to ED

- If they are suitable for **outpatient management**:
  1. Perform a serum bhCG at 0hrs and 48hrs (same lab for both bhCG levels)
  2. Advise patient to present to ED if any pain
  3. Refer to EPAS

**48hr bhCG ratio will be calculated = 48hr bhCG/0hr bhCG**

# PREGNANCY OF UNKNOWN LOCATION

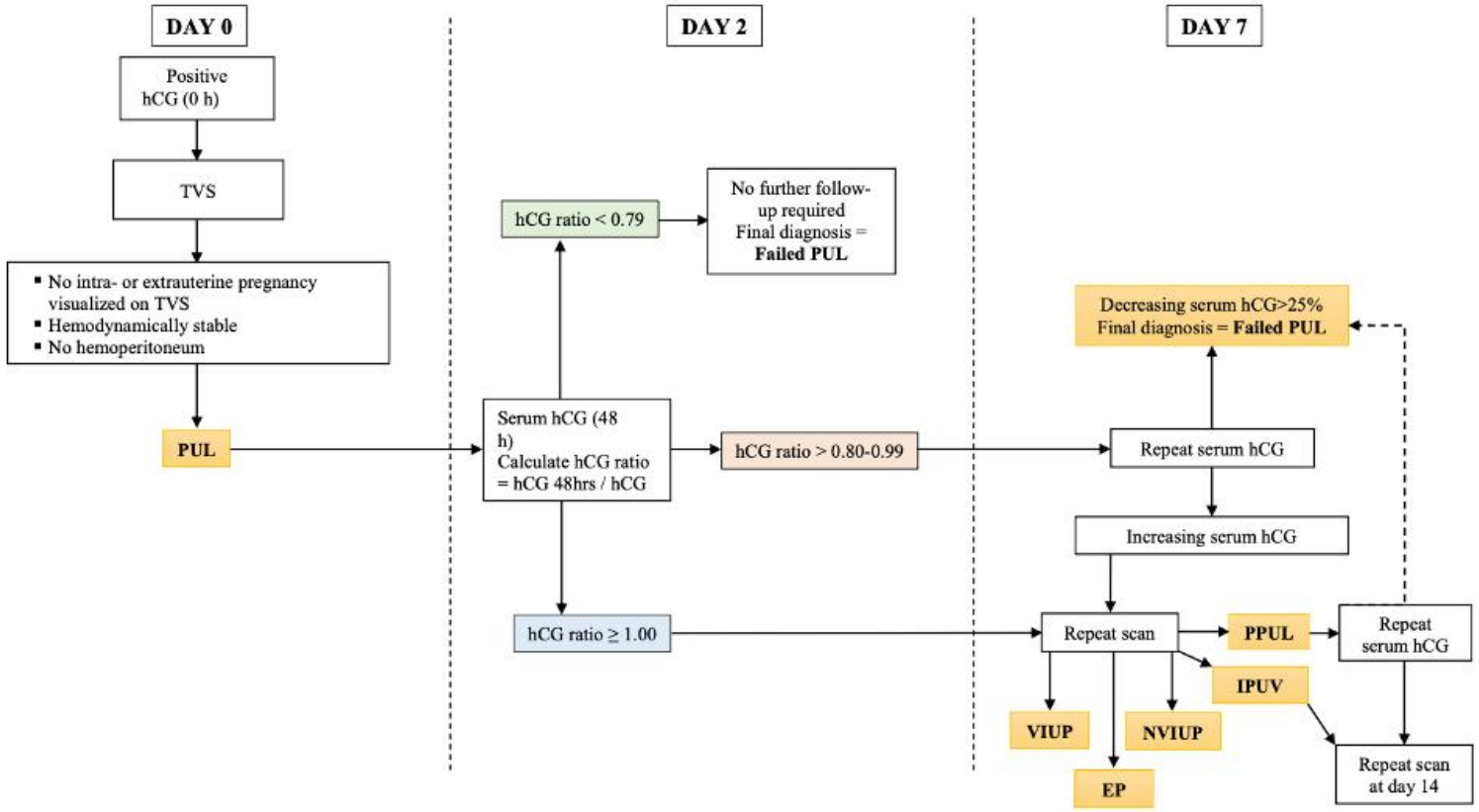


**FIGURE 1** P1 model: Pregnancy of unknown location clinical management flow sheet. EP, ectopic pregnancy; hCG, human chorionic gonadotropin; IPUV, intrauterine pregnancy of unknown viability; IUP, intrauterine pregnancy; NVIUP, non-viable intrauterine pregnancy; PPUL, persisting PUL; PUL, pregnancy of unknown location; TVS, transvaginal ultrasound; VIUP, viable intrauterine pregnancy [Color figure can be viewed at wileyonlinelibrary.com]

*Nadim, B., Leonardi, M., Infante, F., Lattouf, I., Reid, S., & Condous, G. (2019). Rationalizing the management of pregnancies of unknown location: diagnostic accuracy of human chorionic gonadotropin ratio-based decision tree compared to the risk prediction model M4. Acta Obstetricia et Gynecologica Scandinavica. doi:10.1111/aogs.13752*

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# ECTOPIC PREGNANCY

- Unstable, pain or haemoperitoneum on ultrasound → send to ED

- Stable, no pain, minimal free fluid on ultrasound → EPAS
  - Monday-Friday before 3pm – can call EPAS to urgent appointment same day
  - Afterhours
    - Still call/refer EPAS for next available appointment
    - Serum bhCG at 0hrs and 48hrs (same lab for both bhCG levels)

# ECTOPIC PREGNANCY

## Expectant Mx

- Falling bhCG – 48hr ratio <0.8
- Initial bhCG <1500*
- No concern for ruptured ectopic pregnancy
- Patient able to adhere to strict follow up
- *Success rate 72% (up to 96% depending on bhCG)*

## Medical Mx

- 48hr ratio >0.8
- bhCG <5000*
- No absolute indication for surgical management
- No contraindication to MTX
- Patient able to adhere to strict follow up
- *Success rate 90%*

## Surgical Mx

- Haemodynamic instability or significant Hb fall
- Haemoperitoneum with pain
- Live ectopic pregnancy – fetal pole with FHR
- Failed medical management
- Patient preference after careful counselling


1. Kirk E, Van Calster B, Condous G, Papageorghiou AT, Gevaert O, Van Huffel S, De Moor B, Timmerman D, Bourne T. Ectopic pregnancy: using the hCG ratio to select women for expectant or medical management. Acta Obstet Gynecol Scand. 2011 Mar;90(3):264-72. doi: 10.1111/j.1600-0412.2010.01053.x. Epub 2011 Jan 13. PMID: 21306315.
2. Elson CJ, Salim R, Potdar N, Chetty M, Ross JA, Kirk EJ on behalf of the Royal College ofObstetricians and Gynaecologists. Diagnosis and management of ectopic pregnancy. BJOG 2016;.123:e15–e55.



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# MANAGEMENT OF ECTOPIC PREGNANCY

**Expectant Management**

- Weekly bhCGs until negative

**Medical Management**

- Baseline FBC, EUC, LFT to ensure no contraindication
- MTX 50mg/m2 IM injection
- bhCGs Day 1, 4 and 7 of administration
- Aim for >15% drop in bhCG between Day 4 and Day 7
- If successful – weekly bhCGs until negative
- If unsuccessful – repeat TV US + can offer a second dose

# HYDATIDIFORM MOLE

## Partial mole

- When *an ovum gets fertilized by two or more sperm*
- *Usually contain an abnormal or demises fetus*
- *Can be hard to detect on ultrasound*
- *US features: Trophoblastic/placental tissue larger and usually cystic, inappropriately small or hydropic fetus*

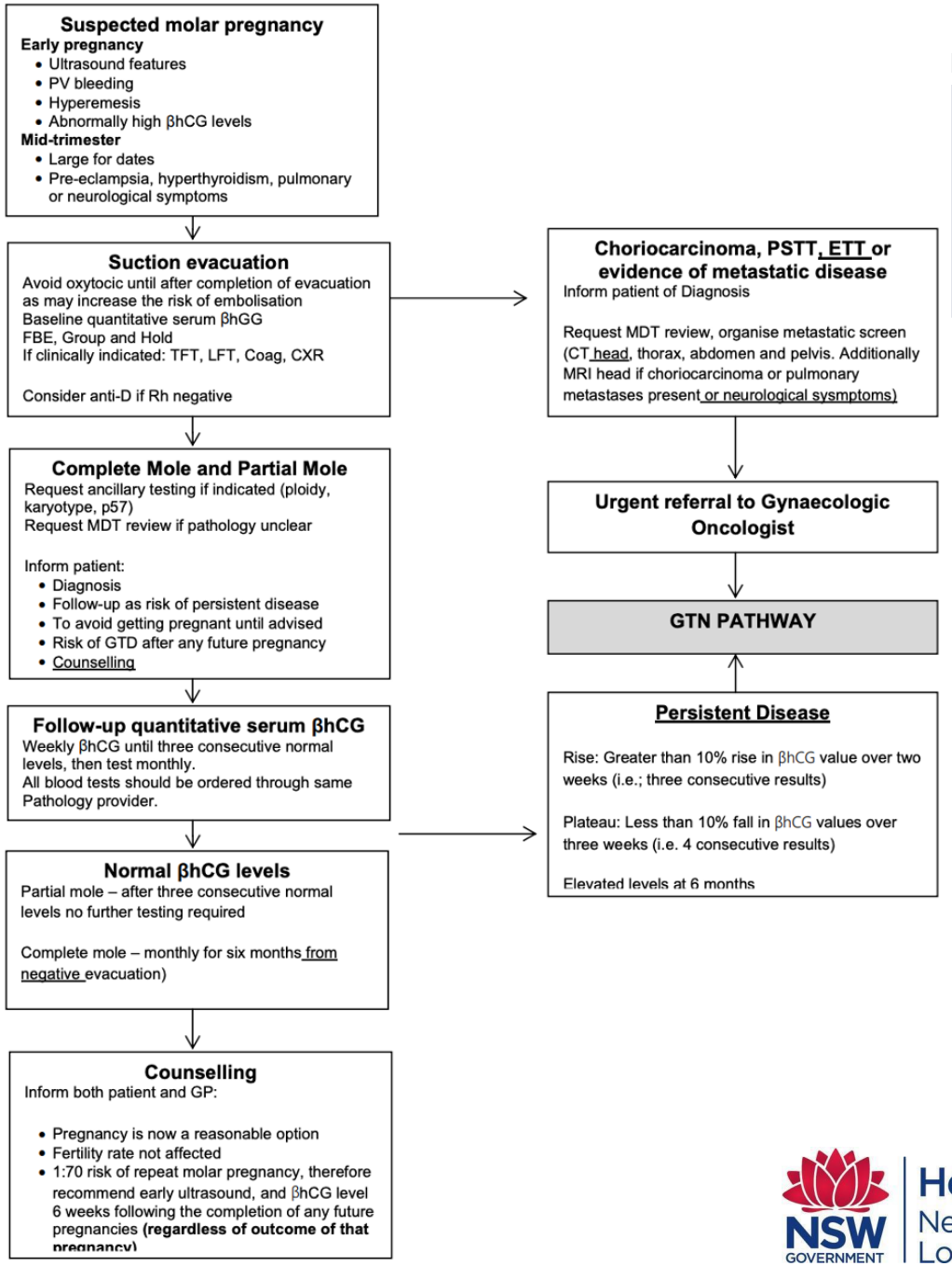
## Complete mole

- *When an ovum contains no maternal genetic material and fertilized by one sperm that replicates or two sperm*
- *No fetus*
- *US features: cystic mass in the uterine cavity "cluster of grapes"*

# HYDATIDIFORM MOLE

- Surgical management required – D&C
- Follow up:
  - **Complete mole**
    - Weekly hCGs until 3x consecutive negative results
    - Then can switch to monthly hCGs until 6 months from negative evacuation
  - **Partial mole**
    - Weekly hCGs until 3x consecutive negative results
    - No further follow up needed thereafter

# HYDATIDIFORM MOLE




*RANZCOG Statement for the management of gestational trophoblastic disease C-Gyn31*

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# HYPEREMESIS GRAVIDARUM

Defined as nausea and vomiting in pregnancy associated with:

- Weight loss >5% of pre-pregnancy weight, not related to other causes
- Objective measure of acute starvation and dehydration such as electrolyte disturbances

PUQE-24 Score

| Pregnancy-Unique Quantification of Emesis (PUQE-24) Scoring | | | | |
|---|---|---|---|---|
| **1. In the last 24 hours, how long have you felt nauseated or sick to your stomach?** | | | | |
| Not at all (1) | 1 hour or less (2) | 2-3 hours (3) | 4-6 hours (4) | >6 hours (5) |
| **2. In the last 24 hours, how many times have you vomited or thrown up?** | | | | |
| I did not vomit (1) | 1-2 times (2) | 3-4 times (3) | 5-6 times (4) | 7 or more times (5) |
| **3. In the last 24 hours, have many times have you had dry retching or dry heaves without throwing up** | | | | |
| None (1) | 1-2 times (2) | 3-4 times (3) | 5-6 times (4) | 7 or more times (5) |
| **PUQE-24 score** | **Mild: 4-6** | **Moderate: 7-12** | | **Severe: ≥13** |

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# RECURRENT MISCARRIAGE

Definition: 3 consecutive pregnancy losses <20 weeks (excluding molar or ectopic pregnancies)

Causes

- Genetic
- Anatomical
- Immune (Antiphospholipid syndrome, SLE, NK cells)
- Thrombophilias
- Hormonal
- Infection

# RECURRENT MISCARRIAGE: INTERVENTIONS

- Supportive care

- Medications:
  - **Unexplained miscarriage**
    - Progesterone – mixed recommendations[1-2]
    - Routine use of Clexane or Aspirin not recommended – nil benefit
  - **Thrombophilia** – Clexane
  - **Antiphospholipid syndrome** – Low dose Aspirin + Clexane


1. Haas DM, Hathaway TJ, Ramsey PS. Progestogen for preventing miscarriage in women with recurrent miscarriage of unclear etiology. Cochrane Database Syst Rev. 2018 Oct 8;10(10):CD003511. doi: 10.1002/14651858.CD003511.pub4. Update in: Cochrane Database Syst Rev. 2019 Nov 20;2019(11). doi: 10.1002/14651858.CD003511.pub5. PMID: 30298541; PMCID: PMC6516817.
2. Shehata, H., Elfituri, A., Doumouchtsis, S.K., Zini, M.E., Ali, A., Jan, H., Ganapathy, R., Divakar, H. and Hod, M. (2023), FIGO Good Practice Recommendations on the use of progesterone in the management of recurrent first-trimester miscarriage. Int J Gynecol Obstet, 161: 3-16. https://doi.org/10.1002/ijgo.14717

# INFERTILITY

- Inability for a couple to fall pregnancy after 12 months of regular unprotected intercourse
- Inability to carry pregnancies to live births

Fecundity:

- Chance of conception in a single menstrual cycle (i.e. monthly success rate):
  - 25% at 25 years of age, 15% at 35, <10% by 37-38
- Within 6 months
  - 75% if 25 years old, 25% if 35-39 years old
- Cumulative pregnancy rate in 1yr - 85%, 2yrs 92%

# FERTILITY INVESTIGATIONS

- Female Factor
  - Ovarian factors/ anovulation
    - Ovulation check – mid luteal serum progesterone, (7 days prior to next expected period), follicle tracking
    - AMH / Antral follicle count
    - Hormonal profile – Day 2-5 of cycle: FSH, LH, E2 (if anovulatory: PCOS testing, TSH, prolactin)
  - Tubal patency – HyCoSy vs laparoscopic dye studies
  - Uterine – pelvic US to assess any anatomical anomalies, endometrial polyps, submucosal fibroids (consider SIS)
  - Endometriosis assessment
  - Prenatal assessment

- Male Factor
  - Semen analysis
    - If abnormal, perform 2nd test in 3 months

# RECURRENT MISCARRIAGE / INFERTILITY

Where to refer – Public options:

- Fertility Clinic Nepean Hospital – Dr Nikhil Patravali
- Recurrent Miscarriage Clinic – Westmead Hospital
  - If no previous livebirth – 2 or more miscarriages
  - If previous livebirth – 3 or more miscarriages
- Westmead Fertility Centre – Westmead Hospital

# EARLY PREGNANCY ASSESSMENT SERVICE

Appointment based service Monday – Friday: 0800 – 1600

- Ran by Consultant, Fellow/Registrar, Midwife

**What the Service Offers:**

- Consultation
- In house ultrasound at time of appointment
- Management
- Follow up
- Referral to longer term follow up if needed

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# EARLY PREGNANCY ASSESSMENT SERVICE

**Who to refer:**

- PV bleeding and/or abdominal pain <20 weeks
- Diagnosed miscarriage or retained products of conception
- Pregnancy of unknown location
- Ectopic pregnancy
- Molar pregnancy
- Unclear diagnosis in pregnancy/second opinion
- Hyperemesis gravidarum

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# EARLY PREGNANCY ASSESSMENT SERVICE

**How to refer:**

- Email: NBMLHD-EPAGSReferrals@health.nsw.gov.au
- Referrals triaged everyday (except weekends)
- Reception open 24/7

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# ACUTE GYNAECOLOGY SERVICE

**Who to refer:**

- Abnormal vaginal bleeding with anaemia
- Concern for malignancy
- Acute abdominal pain <6 weeks duration
- Tubo-ovarian abscess/PID

# QUESTIONS?