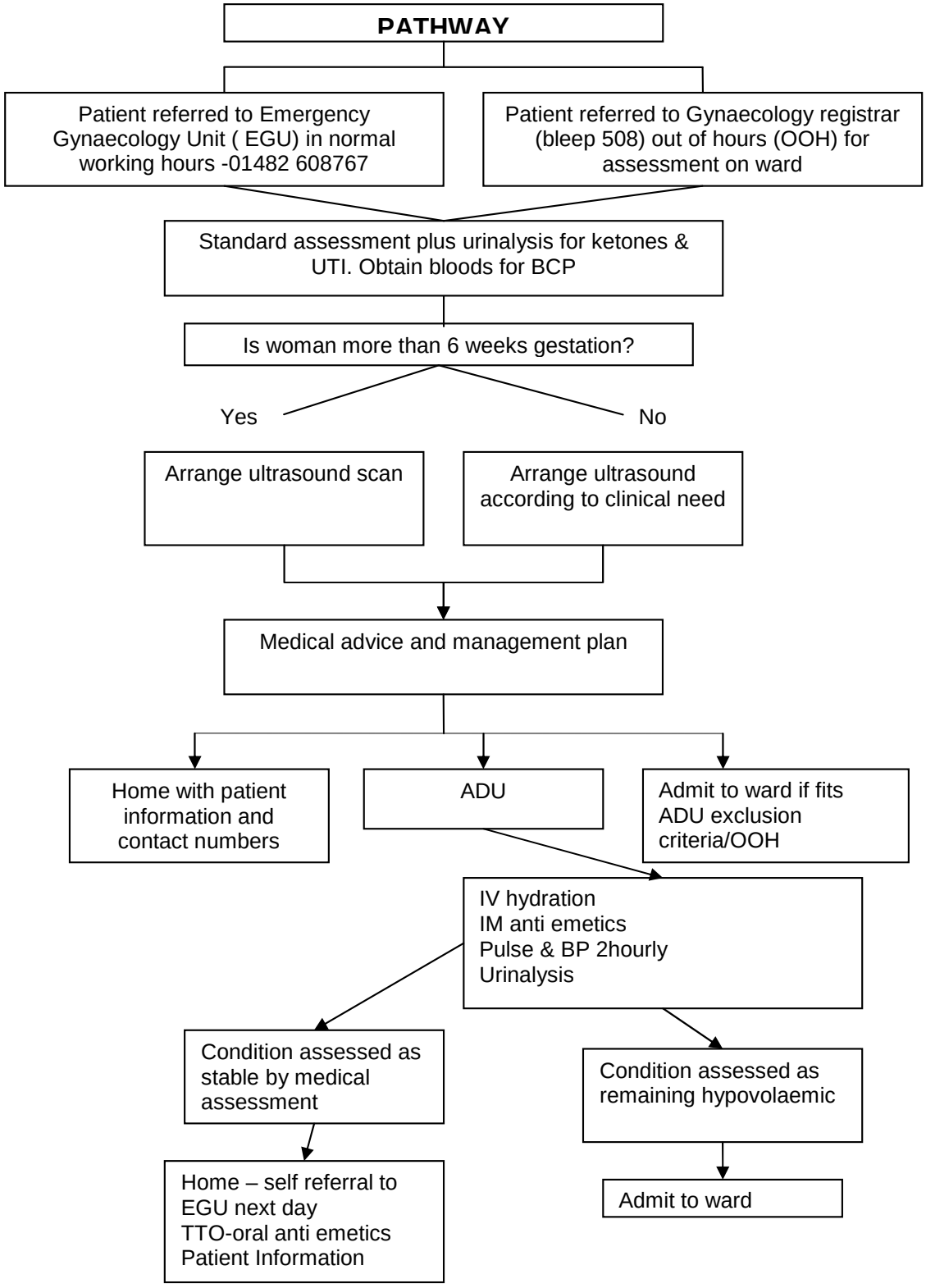
248 - MANAGEMENT OF SEVERE NAUSEA AND VOMITING IN PREGNANCY (HYPEREMESIS GRAVIDARUM)

Broad Recommendations / Summary

The objective of this guideline is to facilitate appropriate assessment and outpatient /inpatient management of women with severe nausea and vomiting (hyperemesis gravidarum) on the Emergency Gynaecology Unit (EGU), Antenatal Day Unit (ADU) and inpatient wards.



248 - MANAGEMENT OF SEVERE NAUSEA AND VOMITING IN PREGNANCY (HYPEREMESIS GRAVIDARUM)

1 PURPOSE / LEGAL REQUIREMENTS / BACKGROUND

This guideline has been developed to provide guidance around the assessment and outpatient/inpatient management of women with severe nausea and vomiting (hyperemesis gravidarum) on the Emergency Gynaecology Unit (EGU), Antenatal Day Unit (ADU) and inpatient wards.

2 POLICY / PROCEDURE / GUIDELINE DETAILS

Nausea and vomiting occur in the majority of pregnancies. Severe nausea and vomiting in pregnancy (hyperemesis gravidarum) is uncommon affecting around 1 in 200 women. Estimates vary depending on how the condition is defined.

Symptoms include:-

- Prolonged and severe nausea and vomiting
- Dehydration
- Ketosis
- Hypotension
- Increased risk of Deep Vein Thrombosis (DVT) (NHS Choices 2012)

Re-hydration is the first line treatment for severe hyperemesis

The objective of this guideline

- To identify women suitable for outpatient management and those requiring admission to a ward.
- To correct hypovolaemia, electrolye imbalance, and ketosis.
- Break the cycle of vomiting and prevent further episodes.
- Psychological support.
- Vitamin supplementation

On preliminary diagnosis of hyperemesis gravidarum in primary care;-

GP or Midwife to refer woman to Emergency Gynaecology Unit (EGU) / Gynaecology ward

Community management patients with nausea and vomiting

Should be encouraged in patients with nausea and vomiting with mild ketone-urea (1-2 +), would benefit with a trial of oral antiemetic's.

OUTPATIENT MANAGEMENT

Inclusion Criteria for outpatient management

Inability to maintain adequate hydration/history of vomiting > 5 times a day
Moderate ketone urea (3 - 4 +)
Patient who continue to have Nausea and Vomiting despite oral antiemetics or are unable to tolerate oral antiemetics commenced by their GP.
Clinical signs of dehydration

Exclusion Criteria for outpatient management

Medical co morbidity i.e. diabetes, thyrotoxicosis, cardiac disease, epilepsy,
Molar pregnancy
Urinary tract infection

Outpatient Management

Initial management on EGU, take patient history of symptoms

Baseline observations: T.P.R, BP, urinalysis
Assess by medical staff
Obtain bloods for FBC & BCP
Arrange scan if appropriate (see pathway)
IV access and treatment to be prescribed on EGU
Transfer to ADU with handover of care from nursing staff to midwives
Assess pulse & BP 2 hourly, document on standard observation chart
Infusion of 1 litre of 0.9% sodium chloride over 2 hours followed by 1 litre of 0.9% sodium chloride over 2-4 hours, prescribed on IV chart.
Promethazine hydrochloride 25mg IM QDS

Discharge Criteria
Re-check ketones after 2 L of IV fluid replacement. If 2+ or less and reasonably well clinically with no tachycardiac >100 or temp >37.5 could be discharged.
Prescribe Promethazine 25mg BD or alternative if this already had and not worked
Ensure direct line for EGU given
Provide a discharge letter for the woman with contact numbers
Provide patient information on management of nausea and vomiting

Exclusion Criteria for Discharge
Remains hypovolaemic (pulse > 100, systolic BP < 80mmHg) following 2 litres of fluid
Pyrexia over 37.5
BCP result outside normal range;-

Sodium	135 -145
Potassium	3.5- 5.5
Creatinine	51-107

INPATIENT MANAGEMENT
If patient does not fit inclusion criteria for outpatient management or patient failing to respond to outpatient management then patient should be admitted for inpatient management

Women require treatment in a psychologically supportive environment by appropriate staff.

Differential diagnosis to be considered
Hyperemesis is a diagnosis of exclusion. Onset is always in the first trimester and other causes of vomiting should be excluded. These include:

Infection UTI, hepatitis

Drug induced Iron supplementation, antibiotics, opiates

Metabolic Thyrotoxicosis, hyperparathyroidism/hypercalcaemia, diabetic ketoacidosis, uraemia, Addison disease

Gastrointestinal Gastroenteritis, reflux oesophagitis, appendicitis, cholecystitis, small bowel obstruction, pancreatitis

Complications
Mallory-Weiss tears of the oesophagus and haematemesis

Weight loss, muscle wasting and weakness

Inadequate nutrition leading to thiamine (vitamin B1) deficiency with risk of Wernicke's encephalopathy

The symptoms of Wernicke's encephalopathy include diplopia, abnormal ocular movements, ataxia and confusion. It can be precipitated in states of thiamine deficiency by IV dextrose so is avoided particularly in the first 24-48hrs of treatment.

Wernicke's encephalopathy is associated with 40% fetal loss.

Hyponatraemia

Plasma sodium of <125 mmol/l can cause lethargy, seizures and respiratory arrest. Rapid reversal and severe hyponatraemia itself can cause central pontine myelinolysis.

Venous thromboembolism due to the combination of pregnancy, dehydration and immobility.

Other vitamin deficiencies include B12 and B6 which can cause anaemia and peripheral neuropathy.

Abnormal biochemistry and recurrent severe hyperemesis is associated with lower birth rates and IUGR.

Initial Assessment/treatment

Baseline observations to be taken and recorded by nursing staff

Review by gynaecology doctor

Bloods for FBC BCP, LFT, TFT to be obtained. (if required to be repeated) G&S only if bleeding. Consider checking calcium and phosphate levels if severe/ recurrent

Dipstix urine & MSU to be obtained

Patient's history, examination and investigations results are recorded on emergency care pathway.

Temporarily discontinue any drugs that may cause nausea and vomiting e.g. iron supplements

USS to be arranged, on either the same or next day when initial management commenced, to assess viability and chorionicity of pregnancy (ideally >8 weeks gestation)

1 Litre 0.9% sodium chloride with 20 mmol KCl or Compound Sodium Lactate solution (Hartmann's solution) over 2-4 hours. If Na is <125 seek consultant advice.

IV fluids may cause osmotic demyelination syndrome, never use double strength saline. Fluid replacement with glucose should be avoided particularly in the first 24-48 hours to avoid the risk of Wernicke's encephalopathy

Monitor fluid balance carefully with strict input / output recordings

Regular antiemetics – see treatment regimens in appendix A. It is acceptable to prescribe the first line antiemetic on a regular basis and the second line prn. If there is no or limited response to therapy after 48 hours of this regime move onto to consider regular 2nd/3rd/4th line therapy giving a minimum of 48hrs to assess effect

Consider the addition of ranitidine or omeprazole

Consider thromboprophylaxis with LMWH and can discontinue thromboprophylaxis when the hyperemesis resolves. [RCOG, 2015]. Therefore every admitted woman with hyperemesis should receive LMWH.

Ongoing management

IV fluid replacement with KCL added, as required, depending on biochemical profile results until tolerating oral fluids and diet. Infusions rates for fluid replacement should run at a minimum of 1 litre fluid over 4-6 hours in first 24 hours. Fluid and electrolyte regimes should be adapted daily according to daily measurements of serum sodium and potassium if further IV rehydration is required.

- Daily weight and urine dipstick
- Daily U+E's whilst having IV fluids
- Encourage fluid and food intake in small frequent amounts
- Folic acid 400mcg daily if first trimester

Thiamine therapy

Routine thiamine supplementation is recommended for women admitted with hyperemeis gravidarum to prevent Wernicke's Encephalopathy.

If able to tolerate oral tablets thiamine hydrochloride tablets should be prescribed 25-50mg TDS

If IV treatment required Pabrinex® (which contains 250mg thiamine per pair of ampoules) can be given once a week. One pair of ampoules should be given diluted in 100ml of Sodium Chloride 0.9% infused over 30 to 60 minutes. Potentially serious allergic reactions may rarely occur during or shortly after parenteral administration. Therefore intravenous administration should be infusion over a minimum of 30 minutes and facilities for treating anaphylaxis (including resuscitation facilities) should be available when parenteral thiamine is administered.

Severe Hyperemesis

The majority of women will improve following rehydration and antiemetics. If no improvement, management needs to be discussed with the consultant. Severe refractory hyperemesis is associated with multiple admissions, psychological morbidity and is a physically a disabling condition impacting on work, time at home and psychological well being. It can be difficult to treat and women may request a termination of pregnancy.

The following may need to be considered:

-Dietician input

-Ondansetron (limited reports available, however no evidence to suggest a teratogenic effect)

-Domperidone

-TPN

-Investigate social situation but do not assume psychological factors are responsible, particularly in cases of severe hyperemesis, which carries a higher rate of morbidity

-Suggested corticosteroid therapy Hydrocortisone 50 mg IV TDS increased every 48 hours if required by 25 mgs upto a maximum dose of 100mgs IV TDS until patient is able to

tolerate oral fluids. When the patient can toterate fluids, Oral Prednisoslone 10 mgs TDS is to replace IV Hydrocortisone and decreased every 48 hours by 5 mgs
(Al-Ozari E, Waugh JJS, Taylor R Termination is not the treatment of choice for severe hyperemesis gravidarum: successful management using prednisolone. Obstetric Medicine 2009; 2: 34- 37)

Discharge

Make sure the woman is drinking and maintaining hydration. ketones 2 or less and pulse rate of <100.

Refer to guidelines and advise the woman regarding 'Outpatient management of hyperemesis at WCH/ HRI' as inpatient management may not be necessary if symptoms recur (those with pre-existing diabetes, thyroid disease or heart disease will not be suitable for this).

If LFTs or TFTs were abnormal ensure follow up is arranged in their consultant led clinic.

Women requesting a termination of pregnancy

Woman with hyperemesis wishing a termination can be referred into the termination service, acknowledging their request for termination. An appointment will not be given to the woman until she has had professional counselling which will be arranged by the Pregnancy Advisory Service.

3 PROCESS FOR MONITORING COMPLIANCE

How often should monitoring take place?	Every three years
Who is responsible for monitoring?	The Gynaecology unit
How will you record your findings	Through audit
Where will you report the findings?	Audit meetings
Who is responsible for developing an action plan?	Health professional undertaking the audit
Who is responsible for implementing these actions?	All consultant gynaecologists
How will you follow up on these actions?	Re-audit
How will lessons be shared locally and if necessary externally?	Audit meeting and conferences

4 REFERENCES

- Boelig RC, Berghella V, Kelly AJ, Barton SJ, Edwards SJ. Interventions for treating hyperemesis gravidarum (Protocol). Cochrane Database of Systematic Reviews 2013, Issue 6
- Jarvis S,Nelson-Piercy C, (2011) Management of nausea and vomiting in pregnancy. British medical Journal (342) 3606
- Neil, A, Nelson-Piercy C, (2003) Hyperemesi gravidarum: Review. The Obstetrician and Gynaecologist; 5:204-7
- http://www.nhs.uk/conditions/morning-sickness/pages/complications.aspx

5 APPENDICES

APPENDIX A : Treatment Regimens

Document Control			
Reference No:	248	**First published:**	August 2009
Version:	3	**Current Version Published:**	February 2016
Lead Director:	Medical Director, Family & Women's Health Group	**Review Date:**	February 2019
Document Managed by Name:	E Morris	**Ratification Committee:**	Health Group Governance
Document Managed by Title:	PDN Gynaecology		
Consultation Process			
The guideline was reviewed by Dr Jo Maolon, and sent to gynaecology and obstetrics guideline groups, clinical areas /consultants /Mr. Maguiness and Mr. Vize			
Key words (to aid intranet searching)			
Hyperemesis, vomiting, pregnancy			
Target Audience			
All staff	**Clinical Staff Only**	Non-Clinical Staff Only	
Managers	Nursing Staff Only	Medical Staff Only	

Version Control			
Date	**Version**	**Author**	**Revision description**
October 2009	V1	Janet Cairns	New guideline
May 2012	V2	Sarah Mableson, Caroline Harrison, Julie Lazenby	Review and update
May 2014	V2.1	Obstetric Guidelines Group	Amendment to monitoring form – frequency of audit
February 2016	V3	E Morris	Update

APPENDIX A : Treatment Regimens:

First line drug therapy: Promethazine

Promethazine Hydrochloride Injection:	25mg IM x FOUR doses in 24 hours = maximum dose.
After 24 hours switch to:	
Promethazine Hydrochloride 25mg tablets	25mg TWICE DAILY = maximum daily dose
Or Elixir 5mg/5ml:	25mg x TWICE DAILY = maximum daily dose.

If there is no response to therapy after 48 hours of regular antiemetics dosing move onto second line therapy

Second line drug therapy: Cyclizine:

Cyclizine Injection**:**	50mg IM or IV THREE times daily (MAX)
After 24 hours switch to:	
Cyclizine 50mg Tablets	50mg THREE times daily (MAX).

If there is no response to therapy after 48 hours of regular antiemetics dosing move onto third line therapy

Third Line Therapy:Prochlorperazine:

Prochlorperazine Injection	12.5mg IM Three times daily (max)
After 24 hours switch to:	Suppository: one 25mg
After 6 hours switch to oral therapy:	
Elixir 5mg/5ml **OR:**	5mls three times daily
5mg Tablets	One tablet three times daily (oral doses can be increased to 10mg TDS)

Note: risk of extrapyramidal side effects

If there is no response to therapy after 48 hours of regular antiemetics dosing move onto fourth line therapy

Fourth Line Therapy: Metoclopramide

Metoclopramide Injection	10mg IM or IV over 1-2 minutes THREE times daily (MAX)

After 24 hours switch to:

Elixir 5mg/5ml	10mls THREE times daily (MAX)
OR:	
10mg Tablets	One tablet THREE times daily (MAX)

NOTE: Caution in patients under 20 yrs as extrapyramidal effects and oculogyric crises may occur. Such side effects subside within 24 hours of stopping the drug

If there is no response to therapy after 48 hours of regular antiemetics dosing move onto fifth line therapy

Fifth Line Therapy: After discussion with Consultant
Corticosteriods:

Corticosteriod Injection:	100mg IV hydrocortisone TWICE daily (equivalent to 50mg prednisolone for ONE day)
After 24 hours switch to oral therapy:	Suppository: one 25mg
40mg od 3/7	Continue to decrease by 5mg increments until
5mg od 3/7	Then decrease by 1mg every 3/7 until
1mg od 3/7	THEN STOP

TOTAL of 36 days steroid therapy

The reduction of the steroid dose can be altered if the patient begins to feel nausea and vomiting recurring. (i.e. if the nausea and vomiting restarts at 5mg od then increase back to 10mg od for 3/7 and reduce slowly

Ondansetron

There has been a recent increase in the use of ondansetron for the treatment of hyperemesis. There is limited data are available on the efficacy of ondansetron in hyperemesis gravidarum and safety data are also limited. Animal studies and small case studies have not demonstrated any teratogenic effect (Mazzotta 2000). Recently, a large retrospective cohort study in Denmark found no association between ondansetron and adverse fetal outcome (Pasternak 2013)