VOMITING IN PREGNANCY
(including Hyperemesis Gravidarum)

BACKGROUND

- Nausea and vomiting (NVP) are both normal in early pregnancy affecting up to 50-80% of pregnant women.[1] Symptoms usually begin between weeks 4 to 6 and peak severity is around week 11.[8]
- Nausea and vomiting persisting beyond 20 weeks can be normal, but this is seen in only 1-3% of pregnancies. Therefore symptoms persisting beyond this point should prompt a search for alternative diagnoses.[1]
- Nausea and vomiting that starts at or beyond 12 weeks gestation are unlikely to be caused by pregnancy.[1] Therefore symptoms developing beyond this point should prompt a search for alternative diagnoses.
- Hyperemesis gravidarum occurs in 0.3-1.3% of pregnancies. Defined as severe intractable vomiting resulting in a state of nutritional deficiency. It is characterised by dehydration, ketosis, electrolyte imbalance and weight loss of more than 5%.[1]
- Risk factors for hyperemesis gravidarum include multiple gestation, molar pregnancies and history of hyperemesis in previous pregnancy.[2]
- Hyperemesis gravidarum is on rare occasions associated with maternal complications such as Wernicke's encephalopathy due to thiamine deficiency and fetal growth restriction.[1]

ASSESSMENT

- **The aim of the initial assessment is to identify one of the following groups**
  - Nausea and vomiting in the first trimester of pregnancy (normal)
  - Nausea and vomiting beyond the 20th week of pregnancy
  - Hyperemesis gravidarum
  - Exclude other causes
- **If marked hypovolaemia start IV fluids (Normal Saline or Hartmann's)**

COMPLETE ASSESSMENT

- History
- Vomiting or ptyalism (inability to swallow saliva); duration, amount
- Food/fluid intake
- Urine output
- Weight loss
- Previous admissions for vomiting in early pregnancy
- Details of this pregnancy, gestation, scans to date, etc.
- Details of any prior treatment (eg. from GP)
- Mental health assessment

MOTHERISK PUQE-24 SCORING SYSTEM

Pregnancy-Unique Quantification of Emesis and Nausea

Mild ≤ 6 Moderate 7-12 Severe ≥ 13

1	2	3	4	5
In the last 24 hours, for how long have you felt nauseated, or sick to your stomach?				
Not at all	1 hour or less	2-3 hours	4-6 hours	More than 6 hours
In the last 24 hours, have you vomited or thrown up?				
I did not throw up	1-2	3-4	5-6	7 or more
In the last 24 hours, how many times have you had retching or dry heaves without throwing up?				
None	1-2	3-4	5-6	7 or more

EXAMINATION – LOOK FOR EVIDENCE OF DEHYDRATION AND/OR OTHER CAUSES

- Pulse, temp, blood pressure both lying and standing
- Skin turgor
- Mucous membranes
- Weight
- Abdominal examination – to exclude other intra-abdominal causes

INVESTIGATIONS – TO ASSESS SEVERITY OF PROBLEM AND/OR OTHER POTENTIAL CAUSES

Urine

- Dipstick for ketones which is used as marker for the degree of dehydration but is no longer a reliable marker of severity; increased specific gravity
- Microscopy, culture and sensitivity – to exclude UTI

Bloods

- FBC – increase in Hct from haemoconcentration, if high WCC be suspicious of alternative pathology
- U+Es – hyponatraemia, hypokalaemia, low serum urea, metabolic hypochloraemic alkalosis
- LFT's – raised transaminases, should improve with resolution of vomiting
- Magnesium and phosphate – due to the risk of refeeding syndrome
- TFT's – biochemical hyperthyroidism with a suppressed TSH and sometimes raised thyroid hormone levels is common in hyperemesis. If not accompanied by any of the other usual signs and symptoms of thyrotoxicosis, observation rather than treatment is appropriate and the thyroid function tests usually return to normal after the vomiting has settled. **Thyroid function should only be tested in patients who meet the criteria for hyperemesis gravidarum or who have signs or symptoms of thyrotoxicosis.**[14]

Ultrasound

- Exclude multiple gestation or trophoblastic disease (only needs to be done once) no need for hCG levels

DIAGNOSIS

- **Likely normal** – nausea and vomiting, no dehydration or ketonuria
- **Mild to moderate** – nausea and vomiting, signs of dehydration 0 or 1+ ketones
- **Moderate** – nausea and vomiting, signs of dehydration, 2+ ketones, moderate
- **Hyperemesis gravidarum** – a diagnosis of exclusion. Nausea and vomiting unresponsive to other therapy, weight loss of more than 5%, biochemical abnormalities.[1]

DIFFERENTIAL DIAGNOSIS

Other causes of vomiting in pregnancy to consider: [8]

Infection	• Urinary tract infection • Ear infection • Hepatitis	
Drug induced	• Iron supplementation • Antibiotics	
Metabolic	• Thyrotoxicosis • Hyperparathyroidism/hypercalcemia • Diabetic ketoacidosis • Uraemia • Addison's disease	
Gastrointestinal	• Gastro-oesophageal reflux H. pylori • Appendicitis • Cholecystitis • Small bowel obstruction • Pancreatitis	• Gastroenteritis • Peptic ulcer disease • Cholelithiasis • Constipation
Central nervous system	• Pseudomotor cerebri • Vestibular lesions • Migraine headaches • Tumours	
Genitourinary	• Kidney stones	
Endocrine	• Porphyria	
Pregnancy related conditions	• Acute Fatty Liver • Pre-eclampsia • Degenerating uterine leiomyoma	

MANAGEMENT MILD/MODERATE VOMITING

Aim to rehydrate and control nausea as a day case in GAU. Rehydration can be carried out at the 24-Hour Surgery, Burwood, Oromairaki or Rangiora Hospitals.

DISCHARGE CRITERIA

- Oral medications tolerated
- Oral intake has been tolerated – nutrition and hydration.
- Treatment of concurrent conditions has been completed and ongoing plan of care initiated.

DIETARY AND LIFESTYLE ADVICE RE. NON-PHARMACOLOGICAL MEASURES[2]

- Rest
- Small amounts of fluid frequently
- Small frequent meals and snacks
  - Eat something bland before getting out of bed
  - Choose high protein foods
- Avoid smells or foods that trigger symptoms
- Ginger capsules
- Wrist acupressure (some women find this helpful – there is no evidence of harm, however, evidence is limited)
- Avoid brushing teeth for > 1 hour after vomiting or eating

SUPPORTIVE TREATMENT OPTIONS FOR MILD/MODERATE VOMITING IN PREGNANCY

IV fluids	0.9% Sodium Chloride or Hartmann's Solution with: **Potassium, magnesium and phosphate additives if needed**
Folic Acid tablets	5 mg daily until 13 weeks of pregnancy in moderate to severe cases
Multivitamin tablets	Iodine 150 mcg and folate 800 mcg should be continued. Consider ceasing iron-containing supplements which may exacerbate symptoms. Avoid vitamin supplements that contain Vitamin A. Please note that the Pharmac funded multivitamin contains 860 micrograms of Vitamin A from retinol, and although this amount is below the upper limit, it is not recommended in pregnancy. If patients can't tolerate a pregnancy multivitamin or can't afford the cost, ensure that they are prescribed iodine 150 microgram tab daily and folic acid on discharge Note that Elevit is high in iron so may exacerbate symptoms

Thiamine supplement	Oral: 50 mg once a day* or IV: 100 mg in 100 mL over 30 minutes *In severe cases or if Wernickes Encephalopathy is suspected, higher doses of thiamine are required. Those at risk include weight loss of ≥ 5% in the past month, or little or no nutrition intake for ≥ 5 days. See Hospital HealthPathways – refeeding syndrome for further information.
Pyridoxine tablets	25 mg three times a day
Management of gastric dysmobility	eg. gastro-oesophageal reflux, constipation

IV REHYDRATION

With 0.9% Sodium Chloride (sodium chloride 0.9%, sodium content = 150 mmol/L) or Hartmann's solution (sodium chloride 0.6%, sodium content = 131 mmol/L).

Double strength saline solution should be avoided even in cases of severe hyponatraemia, rapid correction of sodium depletion may cause central pontine myelinolysis.

Potassium supplementation is usually required with each bag of sodium chloride, particularly if there is continued vomiting. Potassium Chloride is available in premixed bags containing 30 mmol/L potassium chloride in 0.9% sodium chloride or alternatively potassium dihydrogen phosphate 1 mmol/mL may be added to 0.9% sodium chloride infusion bags (max. concentration 40 mmol/L max infusion rate = 20 mmol/hr).

Solutions containing dextrose should be avoided (eg. dextrose-sodium chloride solution) because they do not contain enough sodium and may precipitate re-feeding syndrome which may be associated with Wernicke's encephalopathy.

Fluid and electrolyte regimens must be adapted daily and titrated against daily measurements of serum sodium and potassium, calcium, magnesium and phosphate.[8]

SUPPLEMENTATION

Commence folic acid supplementation 5 mg per day until 13 weeks gestation.

Multivitamins containing iron can worsen nausea, vomiting and constipation. This includes the pregnancy multivitamin 'Elevit®'.

A multivitamin can be recommended for patients to try; however it should be ceased if it worsens symptoms. Multivitamins with Vitamin A from retinol should be avoided in pregnancy therefore use only pregnancy specific multivitamin preparations.[11]Consider Vitamin D supplements for women at risk of Vitamin D deficiency (Women of South Asian, African, Caribbean or Middle Eastern family origin, living south of Nelson during winter and spring, limited sun exposure, dark skin or cover the skin for religious/medical purposes).[11]

THIAMINE

Thiamine deficiency has been reported in as many as 60% of hyperemesis patients.[12]

Routine thiamine supplementation is advisable for all pregnant women admitted with prolonged vomiting to prevent re-feeding syndrome and Wernicke's encephalopathy.

If the woman is able to tolerate tablets, thiamine can be given as thiamine hydrochloride tablets 50 mg daily and given prior to starting feeding. If intravenous treatment is required, this is given as thiamine 100 mg diluted in 100 mL of 0.9% sodium chloride and infused over 30–60 minutes, given weekly.[8]

Higher doses of thiamine are required if there is risk of refeeding syndrome. Those at risk include weight loss of ≥ 5% in the past month, or little or no nutrition intake for ≥ 5 days. See Hospital HealthPathways – refeeding syndrome for further information.

PYRIDOXINE

Studies have shown that pyridoxine improves mild to moderate nausea but does not significantly reduce vomiting[3] – (vitamin B6) 25 mg orally three times a day.

GASTRO-OESOPHAGEAL REFLUX

Treatment of concurrent gastro-oesophageal reflux can be used as adjunctive therapy. Heartburn and reflux have been shown to exacerbate nausea and vomiting in pregnancy so managing these conditions, by making dietary changes or using medications, may help improve symptoms. Antacids containing aluminium or calcium are safe and preferable to those containing bismuth or bicarbonate, which may have adverse fetal/neonatal effects.[3]

ANTACIDS [3]

DRUG	DOSAGE
Antacids containing magnesium, calcium or aluminium	10-20 mL PRN
Omeprazole	10-20 mg daily

ANTIEMETICS

Antiemetics should be offered to women whose nausea and vomiting in pregnancy interferes with normal functioning. In hyperemesis gravidarum, offer antiemetics to women who fail to respond to intravenous hydration and electrolyte replacement. Clinicians should use drugs with confirmed safety profiles in a regimen that they feel comfortable prescribing.[1] The table below shows possible antiemetic regimens in order of suggested use. In severe cases, combinations of antiemetics and parenteral treatment are necessary.

LAXATIVES

Physiological changes of pregnancy together with dehydration, reduced oral intake and side effects from medications can contribute to constipation, which in itself can contribute to nausea. Prevention with laxatives should be considered.[14]

ANTI-EMETICS [1, 7]

	DRUG	DOSAGE	COMMENTS, SAFETY DATA
First-line therapy	Ginger	200-600 mg TDS PO	Considered safe in pregnancy
	Pyridoxine B6	10-50 mg QID PO	Considered safe in pregnancy
Second-line therapy	Cyclizine	Oral: 25 to 50 mg every 8 hours IV: 12.5 to 50 mg every 8 hours	Side effects such as sedation and dry mouth can occur. Limited animal studies demonstrating risk of malformation, no evidence in human studies.
	Metoclopramide	Oral: 10 mg every 8 hours IV: 10 mg every 8 hours	Side effects such as restlessness, drowsiness and rarely dystonic reactions can occur. Limited animal studies demonstrating risk of malformation, no evidence in human studies.
	Prochlorperazine	Oral: 5-10 mg every 8 hours IM: 12.5 mg every 6-8 hours	Side effects such as sedation, dizziness, dry mouth and dystonia can occur. Animal models demonstrated potential harmful effects without evidence in human studies.
	Promethazine	Oral: 10-25 mg every 4 hours, as needed IV: 12.5-25 mg every 4 hours, as needed (max 100 mg daily)	Side effects such as sedation and dry mouth can occur. Animal models did not demonstrate teratogenicity. No data in humans.
Third-line therapy	Ondansetron	Oral & IV: 4-8 mg every 8 hours under specialist recommendation	Recent retrospective studies have demonstrated a small increase in cleft palate defects and cardiac abnormalities, in use in the first trimester, however recent meta-analysis has not shown this increase to be statistically significant.[15] Constipation is a common side effect.

A note on use of medications in pregnancy

The FDA has removed the standard 'ABCDX' categories in 2015 and now recommend assessing on a case-by-case basis.

The first point of reference should be NZF and if insufficient, use the Health NZ Waitaha Canterbury Medicines Information Service.

THROMBOPROPHYLAXIS

Ensure risk assessment for venous thrombosis is carried out and considering prescribing prophylactic low molecular weight heparin while dehydrated, unwell, or immobile is important.[1]

DIETITIAN REFERRAL FOR MILD TO MODERATE AND HYPEREMESIS GRAVIDARUM

Refer to dietitian if:

- ≥ 5% weight loss (after rehydration) or BMI < 18.5
- Previous moderate or severe hyperemesis that required nutrition support
- Severe or persistent hyperemesis and/or no weight gain in 2nd trimester
- Medications are optimised and still eating < 50% of normal

MANAGEMENT OF HYPEREMESIS GRAVIDARUM

- Manage as per mild/moderate vomiting as above, plus
- **If ketotic and unable to maintain hydration – admit as an inpatient**
- Nutrition – feed as tolerated once thiamine and electrolytes replacements have commenced. Some advocate withholding food to 'rest' the gastrointestinal tract, but this has never been formally evaluated.[1]
- Refer to dietitian (as above)
- Social support – consider social work referral
- Corticosteroids may be considered for women with intractable nausea and vomiting[3] in discussion with relevant O&G SMO. Use of glucocorticoids before 10 weeks gestation has been associated with an increased risk of cleft lip and palate and is not recommended. [5]
  - Prednisolone 40-50 mg orally in divided doses or hydrocortisone 100 mg twice daily is a suggested regimen.[13]
- Enteral and parenteral nutrition – consider in cases unresponsive to other management, discuss with dietitian and relevant O&G SMO[4]
  - Refer to hospital guideline *Enteral Feeding in Hyperemesis Gravidarum patients* for criteria and processes.
  - Parenteral nutrition should be used as a last resort via PICC.

COMPLICATIONS

- **Electrolyte/volume depletion**
  - **Hyponatraemia**
    Plasma sodium < 120 mmol/L can lead to lethargy, seizures and respiratory arrest. Caution with replacement is required due to the risk of central pontine myelinloysis.
- **Malnutrition/dehydration**
  - **Other nutritional deficiencies**
    Such as B12 and B6 deficiency leading to anaemia and sequelae
- **Aspiration pneumonia**
- **Mallory-Weiss tears syndrome or gastro-esophageal laceration syndrome**
  Bleeding from tears in the mucosa at the junction of the stomach and oesophagus, usually caused by severe retching, coughing, or vomiting and presenting with haematemesis
- **Oesophageal perforation** (pain is a prominent feature)
- **Wernickes encephalopathy**
  A syndrome characterised by ataxia, ophthalmoplegia, nystagmus, confusion, and impairment of short-term memory often resulting from inadequate intake or absorption of thiamine (vitamin

B1). If thiamine is deficient, intravenous dextrose or glucose may precipitate Wernickes encephalopathy.

Untreated can lead to coma and death. Thiamine is required immediately whenever the diagnosis of Wernickes encephalopathy is entertained.

If suggestion or concern of Wernickes commence immediate treatment as below and contact on-call obstetric physician for further advice.

A suggested treatment regimen is:

- Thiamine 500 mg intravenous (IV), infused over 30 minutes, repeated three times daily for two consecutive days and 500 mg IV or IM once daily for an additional five days.[6]
- Oral thiamine 50 mg three times a day and
- Multivitamin supplementation Elevit with Iodine 1 tablet daily are recommended thereafter as long as the patient remains at risk.

- **Re-feeding syndrome**
  Defined as the potentially fatal shifts in fluids and electrolytes that may occur in malnourished patients. The hallmark biochemical feature is hypophosphataemia and may also feature abnormal sodium and fluid balance, changes in glucose, protein, and fat metabolism; thiamine deficiency; hypokalaemia and hypomagnesaemia. See Hospital HealthPathways – Refeeding syndrome for the re-feeding management guidelines for recommended thiamine doses, and electrolyte replacement. Contact dietitian to start feeding.[9]
- **Psychological effects**
  The condition may exacerbate underlying mental health conditions but can also cause significant distress by its own account which can lead to depression. Mental health should be assessed and referral to support services provided as necessary.

  Evidence suggests that the present of at least three support persons is protective against NVP.
- **Venous thromboembolism**
  Dehydration, immobility and hospital admission contribute to this risk, therefore VTE prophylaxis should be considered.

PATIENT INFORMATION

Patient information on vomiting in pregnancy is available on PRISM and www.healthinfo.org.nz:

Hyperemesis Gravidarum (Ref.2402440)

Hyperemesis Gravidarum Food Ideas (Ref.2406514)

Patients can be given a health info card: search – *nausea and vomiting pregnancy*.

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