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SOCIETY OF OBSTETRIC MEDICINE OF AUSTRALIA AND NEW ZEALAND

GUIDELINE FOR THE MANAGEMENT OF NAUSEA AND VOMITING IN PREGNANCY AND HYPEREMESIS GRAVIDARUM

Executive Summary

2019

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These are the recommendations of a multidisciplinary working party convened by the Society of Obstetric Medicine of Australia and New Zealand. They reflect current medical literature and the clinical experience of members of the working party. The accompanying Executive Summary and Treatment Algorithms (1 and 2) summarise the key recommendations. These should be read in conjunction with this complete guideline which also includes a Patient Information Leaflet and a template for an Individual Patient Management Plan.

The authors declare there are no conflicts of interest.

This guideline has been endorsed by the following organisations:

- *Royal Australian and New Zealand College of Obstetrics and Gynaecology (RANZCOG)*
- *Royal Australasian College of Physicians (RACP)*
- *Australasian College for Emergency Medicine (ACEM)*
- *The Society of Hospital Pharmacists of Australia (SHPA)*
- *New Zealand Hospital Pharmacists' Association (NZHPA)*

This guideline has been officially recognised as an Accepted Clinical Resource by The Royal Australian College of General Practitioners.

Abstract

Objectives: To create an evidence-based guideline for the management of nausea and vomiting of pregnancy (NVP) and hyperemesis gravidarum (HG) based on an understanding of the epidemiology, etiology, pathophysiological mechanisms and appropriate safety data.

Method: Evidence was sought from MEDLINE, EMBASE and PUBMED searches and based on an extensive review of this literature, a fully referenced guideline was written. The evidence was evaluated and recommendations made according to NHMRC principles (1). Where there was insufficient evidence, consensus agreement of the expert guideline group was sought and agreement reached by majority opinion.
From this, a series of recommendations were derived along with potential auditable outcomes to be published as the Executive Summary, to be used in conjunction with the full guideline published on the Society of Obstetric Medicine of Australia and New Zealand (SOMANZ) website.
[https://www.somanz.org/guidelines.asp]

Results: The management of NVP and HG requires appropriate assessment of all pregnant women, relevant investigations and the development of a holistic management plan including pharmacological therapy, fluid and electrolyte treatment and management by the most appropriately trained clinician, preferably in an ambulatory setting. The response to therapy should be monitored with objective and subjective measures using a validated assessment tool and regular clinical review. Multiple antiemetics, along with medication to treat gastro-oesophageal reflux symptoms and improve bowel dysmotility are often required for weeks or months until the natural resolution of NVP or HG. Therapy should be commenced with first line agents and titrated in response to the woman's symptoms.

Gestational hyperthyroxinemia may accompany HG but does not require specific therapy. Regular assessment and management of any associated psychosocial impairment is an important aspect of treatment. The management of NVP or HG should take place in tandem with antenatal care, particularly recognising the increased pregnancy risks associated with HG.

Conclusion: Nausea and vomiting are common symptoms of pregnancy and when symptoms are mild and manageable, no specific investigations or therapy are required. However, clinicians need to ensure that women with more severe symptoms receive appropriate medical and antenatal care, empathy, support and information regarding their condition. Women with previous HG may benefit from pre-conceptual counselling as the risk of recurrence is high and pre-emptive treatment may be beneficial.

Table 1. Definition of recommendations and simplified levels of evidence (1)

RECOMMENDATION	DESCRIPTION
Evidence based (EBR)	Where sufficient evidence was available
Consensus recommendations (CBR)	Where there was insufficient evidence, the expert guideline development group made clinical consensus recommendations
Clinical practice points (CPP)	Important implementation and other issues (such as safety, side effects or risks) arose from discussion of evidence based or clinical consensus recommendations
LEVELS OF EVIDENCE	DESCRIPTION
I	A systematic review of Level II studies
II	A randomised controlled trial
III	Any non-randomised study(ies) including comparative study with concurrent controls, cohort, case-control, historical controls
IV	Case series

What are the definitions of NVP and HG?

There is no accepted definition for NVP nor for the more severe disorder, HG. Although there may be a continuum between these two conditions, it is critical to distinguish HG from NVP as the management and potential maternal and fetal complications differ.

In the absence of accepted definitions for NVP and the more severe disorder, HG, SOMANZ proposes the following definitions:

SOMANZ proposed definitions: **EBR**

Nausea and vomiting of pregnancy:

Nausea, vomiting and/or dry retching caused by pregnancy, with symptoms commencing in the first trimester, without an alternate diagnosis. NVP severity is simply and reliably assessed by answering three questions relating to duration and severity of VP and dry retching symptoms using the Motherisk Pregnancy-Unique Quantification of Emesis and Nausea (PUQE-24) scoring index (Table 2).

Mild: PUQE-24: 4-6

Moderate: PUQE-24: 7-12

Severe: PUQE-24: ≥13

Hyperemesis Gravidarum:

Nausea and/or vomiting caused by pregnancy leading to significant reduction of oral intake and weight loss of at least 5% compared with pre-pregnancy, with or without dehydration and/or electrolyte abnormalities. By definition this condition is considered severe.

All women should be asked about NVP at each visit between 4 and 16 weeks. If present, severity should be assessed by PUQE-24 score, measurement of weight and hydration status.

Table 2. Motherisk PUQE-24 scoring system (2,3)

Total score: mild ≤6; moderate 7 to 12; severe ≥13.

1. In the last 24 hours, for 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 to 6 hours (4)	More than 6 hours (5)
2. In the last 24 hours, have you vomited or thrown up?				
I did not throw up (1)	1 to 2 (2)	3 to 4 (3)	5 to 6 (4)	7 or more times (5)
3. In the last 24 hours, how many times have you had retching or dry heaves without throwing up?				
None (1)	1 to 2 (2)	3 to 4 (3)	5 to 6 (4)	7 or more times (5)

Audit opportunity

- *Proportion of women with symptoms of NVP recorded in the antenatal record*
- *If present, PUQE-24 score and repetition at each visit whilst symptoms persist*
- *Incidence of HG per 1000 deliveries at each institution*

What is the incidence and natural history of NVP and HG?

Nausea and vomiting are common symptoms of pregnancy with the global prevalence estimated risk of any NVP of 69%, and nausea alone 33% (4). The incidence of hyperemesis gravidarum (HG) is much lower than NVP at 1.1%, depending on the definitions used. Both NVP and HG typically have their onset between the 4th and the 10th week of gestation, with the majority experiencing resolution by 20 weeks gestation although up to 24% of women described NVP even in late pregnancy and in approximately 10% of HG patients, symptoms persisted throughout pregnancy (4, 5). The incidence of NVP peaks between 8-16 weeks and starts to fall from 12 weeks (6).

What is the cause of NVP and HG?

The etiology of NVP and HG remains unclear but is likely to be multifactorial. Numerous factors have been implicated, particularly the effect of high levels of Human Chorionic Gonadotrophin (HCG) or specific isoforms of HCG (7). Conditions with higher HCG levels, such as trophoblastic disease and multiple pregnancy, have been associated with increased severity of NVP. Other associations include infection with Helicobacter Pylori, deficiency of trace elements, excess thyroid hormones, gravidity, multiple pregnancy and fetal female sex. Several lines of evidence support a genetic predisposition to NVP and HG with heritability estimates of 73% for occurrence, 51% for duration and 53% for severity of NVP (8).

What investigations are required for women with NVP?

- History and physical examination should be directed towards exclusion of alternate diagnoses, assessment of dehydration and weight/nutritional status.
- Patients with mild-moderate nausea and vomiting of pregnancy (PUQE-24 ≤12) where symptoms are not suspicious for HG or another diagnosis do not need investigation.
- Women with severe NVP (PUQE-24 ≥13) or suspected HG should have the following at first presentation and repeated as per full guideline recommendations:
    1. Sodium, potassium, chloride, bicarbonate, magnesium, urea and creatinine **EBR**
    2. Bilirubin, Alanine Transaminase (ALT), Aspartate Aminotransferase (AST), Albumin **CBR**

3. Obstetric ultrasound to exclude multi-fetal or gestational trophoblastic disease **CBR**
4. Thyroid stimulating hormone (TSH) where indicated CBR [see Full Guideline for further recommendations regarding investigation and treatment of NVP/HG related thyroid disease.] **CBR**

- Patients not requiring admission to hospital or treatment with IV fluids: electrolytes should be remeasured only if their condition deteriorates **CPP**
- Women requiring repeated IV fluids or admission to hospital: electrolytes should be measured daily or less frequently if stable after commencement of therapy **EBR**
- More frequent monitoring of electrolytes (at least daily) is required for women with diabetes or other significant underlying conditions **CPP**

Audit opportunity

- *How many women are weighed when presenting with possible severe NVP/HG?*
- *Assess appropriateness of investigations of women with severe NVP/HG, including physical examination, blood tests and ultrasound*
- *Monitor over-investigation of women with mild-moderate NVP*
- *Proportion of in-patients being treated with IV fluids having daily electrolyte measurements and number of days to achieve normalisation of electrolytes*

Who should care for women with NVP?

All primary carers of pregnant women, particularly midwives and general practitioners (GPs), as well as obstetricians need to take responsibility for ensuring women have access to appropriate advice and care. Women often consult their community pharmacists and they may be an important source of information and advice regarding treatment in mild to moderate cases.

- Maternity caregivers and pharmacists should consult and escalate care as needed to clinicians with experience in managing severe NVP and HG e.g. at tertiary hospitals or via telemedicine. **CBR**
- Clinical assessment and care of women with HG should be undertaken by clinicians with experience in recognising the signs and symptoms of HG, and with expertise in managing this condition effectively. **EBR**
- Consideration should be given to contacting experienced practitioners via an appropriate referral pathway (e.g. tertiary hospital) or via telemedicine. **CPP**
- We recommend consultation with a dietitian for all women requiring inpatient care and for women with protracted symptoms of severe NVP, especially where there is evidence of malnutrition.

Audit opportunity

- *In women with a PUQE-24 score ≥13 or a diagnosis of HG, how many received a consultation with an Obstetrician or Physician?*

Where should management for NVP and HG take place?

- Inpatient management is required at least initially for women with:
    - Severe electrolyte disturbance eg Potassium < 3.0 mmol/L
    - Significant renal impairment or acute kidney injury: Creatinine > 90 mmol/L
    - Concurrent significant co-morbidity e.g. Type 1 diabetes and other high risk conditions (eg short bowel syndrome) or those requiring continuity of essential oral medications (eg severe epilepsy, transplant recipients)
- The lead clinician needs to communicate a clearly documented plan for ongoing management to both the patient (See Individual Patient Management Plan contained in the online Appendix) and treating team members

For the majority of women, NVP with a PUQE-24 score <13 can be managed in the community. In women with severe NVP or HG (PUQE-24 score ≥13), community care alone may be inadequate. **EBR**

- Parenteral fluid resuscitation and anti-emetic therapy may be given at
    - Day Stay facilities: hospital or general practice
    - Hospital in the Home
    - Emergency Room

  if they are unable to tolerate these orally in the community setting (9). **CBR**

  All of these sites should seek to provide management in a comprehensive, empathetic environment with advice from a clinician with expertise in treating NVP and HG.
- Inpatient management should be considered for women with severe NVP or HG (PUQE-24 score ≥13) *not* responsive to ambulatory management. **EBR**
- Inpatient management is required for women with: **EBR**
    1. Severe electrolyte disturbance eg Potassium < 3.0 mmol/L
    2. Significant renal impairment or acute kidney injury: Creatinine > 90 mmol/L
    3. Concurrent significant co-morbidity: Women with Type 1 diabetes and other high risk conditions (eg short bowel syndrome) or those requiring continuity of essential oral

medications (eg severe epilepsy, transplant recipients) who will require initial inpatient management (10)

4. Malnutrition/continuing significant weight loss despite therapy or starvation ketoacidosis
5. Associated conditions requiring inpatient management eg infection, hematemesis

Discharge will be indicated when:

- Appropriate oral pharmacotherapy has been tolerated
- Adequate oral nutrition and hydration has been tolerated
- Management of concurrent conditions is completed

In all cases, the lead clinician needs to communicate a clearly documented plan for ongoing management to both the patient (See Individual Patient Management Plan below) and the treating team members including: **CPP**

- details of therapy
- arrangements for re-assessment including clinical and any diagnostic investigations
- arrangements for ongoing ante-natal care

During outpatient management, women require regular review, at least every 1 to 2 weeks, by their lead clinician to ensure appropriate titration of therapy. **CPP**

Audit opportunity

- *How many women each year received in-patient or day care management for NVP/HG at your institution?*
    - *Were these women appropriately triaged according to PUQE-24 score?*
    - *What proportion of women with NVP managed as in-patients could have been managed at a day-care unit?*
    - *Were discharge criteria described for each in-patient?*
- *Was a clearly documented management plan provided to each patient?*

What is the best treatment for NVP and HG?

Numerous systematic reviews have attempted to assess the heterogeneous and limited high level evidence for the efficacy and safety of treatments for NVP and HG (11-19). In assessing the response to treatment, the fluctuant nature of NVP and the impact of progressive gestation must be considered, as spontaneous resolution is the norm. Similarly, a number of symptoms of normal pregnancy could be misinterpreted as adverse responses to treatment including bowel disturbance,

gastroesophageal reflux, sedation, urinary symptoms as well as vaginal bleeding, abdominal/pelvic pain and miscarriage.

Interventions to improve nausea and fatigue include modification of working patterns, exercise, day time sleeps and an earlier bedtime may benefit some women but the evidence is weak. **CBR**

Diet modification has no proven efficacy for NVP or HG. **EBR**

Although acupuncture, acupressure and hypnosis are safe, they have shown no clinically significant effect for NVP or HG. **EBR**

What medications are effective for treatment of NVP and HG?

The principles of holistic management of NVP and HG must include: **CPP**

- Interventions to reduce nausea, retching and vomiting
- Management of associated gastric dysmotility ie gastroesophageal reflux and constipation
- Maintenance of hydration, fluid and electrolyte replacement
- Maintenance of adequate nutrition including provision of vitamin supplements where required
- Psychosocial monitoring and support
- Monitoring and prevention of side effects and adverse pregnancy and fetal outcomes

Considerations for treatment choices in NVP and HG:

- Establish targets for symptom relief ie ability to eat and drink adequately without necessarily complete resolution of NVP **CPP**
- Discontinue prenatal multivitamins if they are contributing to NVP: the two critical micronutrients which should be continued if at all possible are iodine (150 mcg per day) and folate (at least 400 mcg per day) **EBR**
- The timing of administration of pharmacological therapy should reflect the woman's symptom pattern **CPP**
- All routinely prescribed antiemetics are more effective than placebo (11). When comparing 4 commonly used antiemetics (ondansetron versus metoclopramide versus promethazine or prochlorperazine), there was no difference in response in terms of time from administration to discharge (20). There is no convincing evidence of superiority of any particular drug (21). **EBR**
- The choice of antiemetic should be individualised, based on the woman's symptoms, previous response to treatment and potential side effects (Table 3a, 3b, 3c, 4) **EBR**

    - Mild-moderate initial treatment: Start with ginger ± B6, add oral antihistamine or dopamine antagonist if needed
    - Moderate-severe NVP, inadequate response to initial treatment or excessive sedation: consider add/substitute oral serotonin antagonist at least during daytime. Add acid suppression therapy. Manage/prevent constipation with laxatives. If not tolerating oral treatment, substitute with IV/IM equivalent if available.
    - Refractory NVP or HG: consider corticosteroids in addition to other antiemetics. Intensify acid suppression. Continue laxatives as needed.
- When selecting pharmacotherapy for NVP and HG, the prescriber need to make a rational assessment of maternal and fetal benefit versus risk. The woman must be appropriately counselled prior to the commencement of therapy. **CBR** Any potential increase in the risk of congenital malformation needs to be compared with the background rate of congenital malformations which was 3.1% in 2002–2003 (22).
- There is inconsistent evidence regarding the risk of congenital malformation with the use of ondansetron and corticosteroids in the first trimester **EBR**
    - Ondansetron is therefore recommended for second line use
    - Corticosteroids have generally been used after other antiemetic therapies have failed or are inappropriate and should be reserved for more severe NVP or HG
- Oral therapy is usually commenced first and parenteral or subcutaneous treatment reserved for refractory cases (Table 5). Rectal therapy may have a role but no options are currently available.
- Written instructions should be given regarding titrating therapy (up and down) as symptoms fluctuate, deteriorate or improve (see Individual Management Plan below)
- Regular review of therapy is required in all cases: the natural history of NVP and HG is for spontaneous resolution
- Many women with vomiting in pregnancy experience symptoms of gastroesophageal reflux (GER) as well, and the presence of such symptoms is associated with more severe NVP (23). The treatment of GER has been associated with reduced PUQE-24 scores and improved quality of life scores (24).Treatment with antacids, histamine 2 antagonists or proton-pump inhibitors should be added in all women with severe NVP or HG (Table 5). **EBR**
- Prescribe laxatives in all women with constipation or at risk of constipation (eg from serotonin antagonists) **CBR**
- Assess women with NVP and HG for ptyalism and consider treatment if severe or debilitating **CBR**

Table 3a, 3b,3c : Oral antiemetic medications for mild-moderate NVP (25).

Dosing: BD- twice a day, TDS-three times per day, QID-four times per day, max-maximum recommended total daily dose.

Note: *Do not combine these agents with similar mechanism of action and side effects [S]-sedating, preferably use nocte only.

Table 3a HERBAL/VITAMIN	GINGER	VITAMIN B6 (PYRIDOXINE)
Mechanism of action	Improvement in gastrointestinal motility: weak effect on cholinergic M3 receptors and serotonergic 5-HT3 and 5-HT4 receptors in the gut	Water soluble vitamin, inhibits H1 receptor, acts indirectly on vestibular system, some inhibition of muscarinic receptors to decrease stimulation of vomiting centre
Evidence for efficacy	↓N but not V Superior to placebo Equal to Vitamin B6, dimenhydrinate, metoclopramide, doxylamine, P6 (LOE- II)	↓N but not V Less effective than dimenhydrinate (LOE- I)
Recommended/max dose	Use standardised products rather than foods: up to 1200 mg/day split doses eg 250 mg QID	10 to 25 mg 3-4x/day Up to 200 mg/day Or 37.5 mg combined with ginger 600 mg up to 2x/day
Side effects	Inability to tolerate treatment, sedation and heartburn	Sensory neuropathy has been reported with chronic intake of pyridoxine at doses >500 mg/day
Risk of teratogenesis	No increase	No increase
Practice points	Theoretical but unproven risk of bleeding risk by decreasing platelet-aggregation. May inhibit the growth of Helicobacter Pylori	More effective when used in combination eg with doxylamine or dicyclomine (equivalent to metoclopramide)

Table 3b HISTAMINE/DOPAMINE ANTAGONISTS	DOXYLAMINE[S]/DIMENHYDRINATE[S] DIPHENHYDRAMINE[S]/CYCLIZINE[S]/ PROMETHAZINE[S]	METOCLOPRAMIDE
Mechanism of action	Indirectly affect the vestibular system, decreasing stimulation of the vomiting centre	Dopamine and serotonin receptor antagonist which stimulates upper gastrointestinal motility and acts on CNS vomiting centre
Evidence for efficacy	DOXYLAMINE: ↓N compared with placebo, with or without pyridoxine (LOE II) DIMENHYDRINATE/DIPHENHYDRAMINE/ CYCLIZINE: (LOE-III)	Equal to ondansetron for N but less effective for V (LOE-II)
Recommended/max dose	DOXYLAMINE*: 6.25-25 mg TDS, max 50 mg/day DIPHENHYDRAMINE*: 25-50 mg TDS, max 150 mg/day DIMENHYDRINATE*: 25 to 50 mg TDS, max 100 mg/day CYCLIZINE*: 12.5-50 mg TDS, max 150 mg/day PROMETHAZINE*: 25 mg TDS, max 75 mg/day	10 mg TDS, max 30 mg/day
Side effects	Sedation, anticholinergic effects	Less sedation, akathisia, depression. Rare: tardive dyskinesia with chronic use
Risk of teratogenesis	No increase	No increase
Practice points	Doxylamine and dimenhydrinate are available as non-prescription sleeping tablets or travel sickness tablets. Dimenhydrinate is often combined with caffeine and hyoscine. Safety data on combination indicates no concerns. Best reserved for evening dosing	

Table 3c PHENOTHIAZINES*	PROCHLORPERAZINE[S]	CHLORPROMAZINE[S]
Mechanism of action	Central and peripheral dopamine antagonists	
Evidence for efficacy	Superior to placebo for NVP (LOE-I)	(LOE-III)
Recommended dose	5-10 mg TDS, max 30 mg/day	10-25 mg TDS
Side effects	Sedation, akathisia, anticholinergic effects, hypotension Rare: dystonias, tardive dyskinesia with chronic use	
Risk of teratogenesis	No increase	
Practice points	Best reserved for evening dosing	

Table 4: Oral antiemetic medications for severe NVP and HG (25).

	ONDANSETRON	CORTICOSTEROIDS
Mechanism of action	Central (medullary vomiting centre) and peripheral (small bowel) serotonin receptor blocker	Antiemetic effect on the chemoreceptor trigger zone in the brainstem
Evidence for efficacy	Superior to combination doxylamine/B6 for reduction in N and V Superior to metoclopramide for reduction of V but not N in HG	Improved sense of wellbeing, appetite and increased weight gain in HG patients No difference in days of hospital admission or readmission rates compared to placebo Equal to promethazine with fewer side-effects (LOE-I) Superior to IV metoclopramide (LOE-I)
Recommended dose	4-8 mg up to TDS	Prednisone 40-50 mg/day. (May be commenced as hydrocortisone 100 mg IV BD)
Side effects	Constipation, headache, dizziness	Potential Cushing's syndrome, mood disturbance, hypertension, hyperglycemia
Risk of teratogenesis	Conflicting data but does not appear to increase overall risk of birth defects	Possible increased risk of oral clefts when used < 10 week's gestation, but data are weak
Practice Points	No sedation Expensive Available as tablets, wafers and oral dispersible formulations Ensure concurrent management of constipation-bowel obstruction has been reported	Consider withholding until after 10 weeks gestation if alternate therapy an option Restrict to refractory cases

Table 5: Parenteral/subcutaneous antiemetics (26, 27)-for additional information see Tables 3a, 3b, 3c and 4.

	Dosage (Max daily dose)	Comments
METOCLOPRAMIDE	10 mg IV TDS (0.5 mg/kg to max 30 mg/day) Or 1.2 to 1.8 mg/hour intravenously by infusion Or Subcutaneous infusion 20-40 mg/day	Slow IV over 2-20 min Sedation
CYCLIZINE	50 mg slow IV BD-TDS	Severe sedation
DROPERIDOL	0.5 to 1 mg/hour (25 mg/day)	Sedation
PROMETHAZINE	25 mg IM or IV TDS-QID (100 mg/day)	Sedation
PROCHLORPERAZINE	5 to 10 mg IV TDS-QID	Sedation
ONDANSETRON	4-16 mg IV TDS SC infusion 16-28 mg/day	Avoid in women with pre-existing QT prolongation
METHYLPREDNISOLONE	16 mg TDS for 48 to 72 hours	
HYDROCORTISONE	100 mg IV BD	

Table 6: Acid suppression for symptoms of gastroesophageal reflux (22,23, 28,29).

Therapy	Dose	Risk	Comment
First line: Antacids containing magnesium, calcium, or aluminium	As required for mild symptoms	No increase in congenital malformations	Constipation or diarrhoea in high doses.
Second line: H2 antagonists	RANITIDINE 150-300 mg BD FAMOTIDINE 20 mg OD or BD	No increase in congenital malformations	Well tolerated
Third line: Proton-pump inhibitors	OMEPRAZOLE 20 mg OD-BD LANSOPRAZOLE 15 mg OD-BD RABEPRAZOLE 20 mg OD-BD ESOMEPRAZOLE 40 mg OD-BD PANTOPRAZOLE 40 mg OD-BD	No increase in congenital malformations	Well tolerated

When should intravenous fluid and parental feeding be used for management of NVP and HG?

- Consider early treatment with IV fluids for women with dehydration or uncontrolled vomiting, including prior to the development of electrolyte deficiency. **EBR**

  IV fluids have been shown to reduce vomiting (30) and are therefore valuable for both outpatient and inpatient management of the symptoms of HG and severe NVP as well as associated dehydration and electrolyte disorders.

  The prescription of IV fluid therapy should take into account the degree of dehydration and any electrolyte disturbances (Table 7). If dextrose based solutions are used, IV thiamine must be administered prior as Wernicke's encephalopathy may be precipitated in women with thiamine deficiency (31).
- Should ongoing fluid administration be required, fluid balance (input and output) should be monitored for the duration of the treatment cycle. IV fluid resuscitation with or without electrolyte (potassium, magnesium and phosphate) replacement should be prescribed as required. **CPP**
- IV fluid therapy should preferably be administered in an outpatient setting where available as this has been associated with equivalent patient satisfaction outcomes and lower total hospitalisation days (32,33). **EBR**
- Clear pathways for access to outpatient fluid therapy can give women a sense of control over their symptoms which can be very helpful.
- HG leads to dehydration, fluid and electrolyte abnormalities, and inadequate nutrition. In severe cases, if antiemetic and steroid therapy has failed, nutritional support via enteral or parenteral routes may be required to adequately restore hydration, correct electrolyte imbalance and maintain nutrition.
- Due to their associated complications, cost burden, and high rates of patient dissatisfaction, the use of enteral and parenteral nutrition should be a last resort and trialled only if women are failing to respond to oral feeding and antiemetic therapy. Enteral nutrition would preferentially be recommended over TPN. **CBR**
- Patients commencing enteral or parenteral nutrition are at high risk of refeeding syndrome and need to be monitored closely, with a slow introduction of supplementation. **EBR**

Table 7: Recommendations for parenteral replacement of IV fluids and electrolytes K: potassium, Mg: magnesium (34)

Type of fluid	Quantity/Rate	Comments
0.9% sodium chloride	1-2 L. Initial rate 1L/hour	Further IV fluids should be given at a rate of 1L/1-2 hours or slower to correct dehydration and electrolytes (see below)
4% dextrose and 0.18% sodium chloride or 5% dextrose	1 L. Initial rate 1L/2 hours.	Consider as an option if minimal oral intake, starvation or uncontrolled nausea and only after correction of thiamine deficiency and exclusion of hyponatremia
Add electrolytes as required		
Potassium chloride	30-40 mmol/L. Maximum infusion rate 10mmol over 1 hour	Administer with caution as per local protocol. Preferred product is premixed 30mmol potassium chloride in 1 L bags of 0.9% sodium chloride. Use large peripheral vein or central venous access only.
Magnesium sulphate	10-20 mmol/day over 20-40 minutes	Dilute with 100ml 0.9% sodium chloride. Use large peripheral vein or central venous access only.

When should termination of pregnancy be considered for NVP or HG?

Occasionally, failure of response to comprehensive treatment of HG may be life threatening, and in this instance, termination of pregnancy may be the only option for prolongation of the woman's life. In less severe cases, a decision for termination of pregnancy may be made after comprehensive management, including anti-emetics and corticosteroids have been trialled and the option of enteral or parenteral feeding has been considered. This management should include appropriate psychiatric and psychological care and support in a multidisciplinary environment. Failure of therapy should be clearly documented prior to consideration of medically-indicated termination of pregnancy (35, 36). **CBR**

What role does psychosocial assessment and support play in the management of NVP?

Women with severe NVP or HG have greater levels of depression and worsening symptoms are associated with greater severity and duration of both depression and anxiety.

- Women with HG or severe NVP should be screened for depression and associated mental distress at first presentation with a validated tool and this should be repeated as indicated, particularly if symptoms are severe and prolonged. **CBR**

Women with elevated screening scores should be referred to a mental health professional. Social isolation is a major risk factor; social work review and support should be assessed in each case and whether responsibilities can be delegated to another member of the family (37).

- HG has a substantial financial impact upon the individual and upon the economy (38).

How should NVP/HG associated gestational hyperthyroxinemia be managed?

- Do not measure TFTs in women with nausea and vomiting of pregnancy and no diagnostic criteria for HG. **CBR**
- TSH should be measured in women with HG or NVP refractory to treatment or in women with signs and/or symptoms of thyrotoxicosis. If TSH is below the normal gestational corrected reference range, additional investigations should be performed to exclude an alternate cause. Management of women who have gestational hyperthyroxinemia is supportive as the condition is self-limiting and anti-thyroid medications are not required. Specialist referral is not required. **EBR**

What impact does NVP and HG have on pregnancy and neonatal outcome?

- Mild-moderate NVP without features of HG is associated with a favourable effect on the rate of miscarriage, congenital malformations, prematurity and childhood performance intelligence quotient (39).
- Women with severe NVP or HG should be considered at high risk of adverse maternal and fetal outcomes and require quality, evidence based medical and antenatal care in an appropriate setting. **EBR**
- Women with HG were found to have high rates of post-traumatic stress syndrome, with a number of associated negative outcomes including inability to breastfeed, marital problems, financial problems, and inability to self-care (37).
- HG has also been associated with placental dysfunction as evidenced by an increased risk of small baby or preterm birth (40) and preterm preeclampsia, a threefold increased risk of placental abruption and an increased risk of an SGA newborn (41). It is unclear whether HG is associated with an increased risk of stillbirth (40, 42).
- Women with HG should have fetal growth surveillance in the third trimester of pregnancy. **EBR**

Audit Opportunity

- *Audit the rate of pregnancy, fetal and neonatal complications in women with severe NVP or HG*

What is the recurrence risk of NVP and HG?

As NVP is such a common symptom, the risk of recurrence is very high (43). Women with severe NVP or HG should be counselled that the risk of recurrence in future pregnancies is high: up to 83% for NVP and 15-26% for HG. **EBR**

What is the role of preconceptual counselling for NVP and HG?

In subsequent pregnancies, early or even pre-emptive commencement of antiemetic therapy should be considered in women with previous severe NVP or HG. **CBR**

Although there is no trial data to inform this area of practice, preconceptual counselling can provide information and reassurance to a woman previously affected by NVP or HG. It also allows planning for early, effective management if symptoms of NVP or HG occur.

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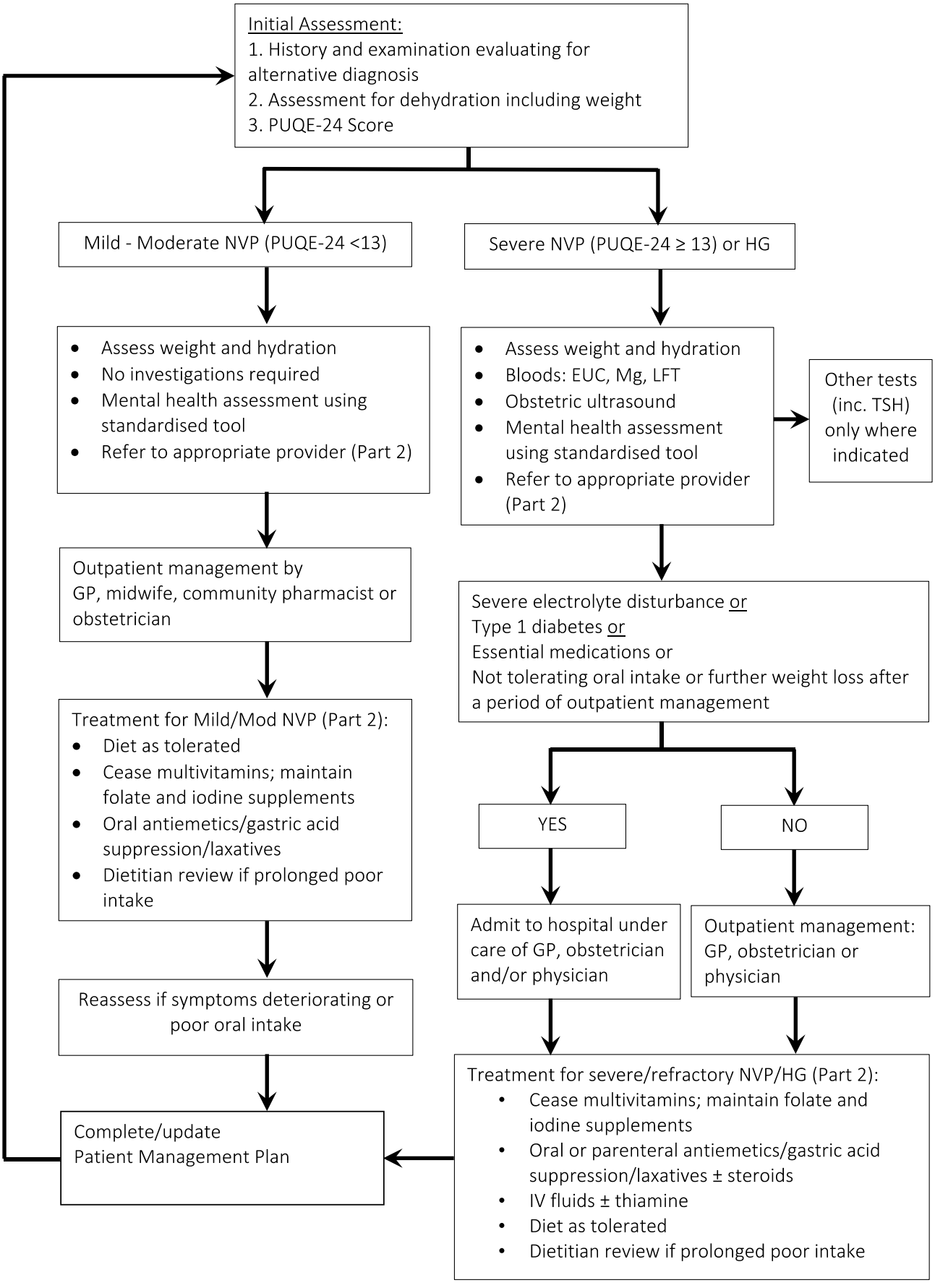
Appendices

SOMANZ Management of NVP/HG (Part 1)



SOMANZ Management of NVP/HG (Part 2)

	MILD PUQE-24: <7	MODERATE NVP (PUQE-24: 7-12)	SEVERE NVP (PUQE-24: ≥13) or HG Outpatient management	REFRACTORY SYMPTOMS or in HOSPITAL
General	Diet as tolerated Cease multivitamins (particularly those containing iron); maintain folate and iodine supplements If an antiemetic is ineffective, at maximal dose, discontinue before commencing an alternate agent. If an antiemetic is partially effective, optimise dosage and timing, and only add additional agents after maximal doses of the first agent have been trialled. Add laxatives as required (eg docusate 120 mg 1-2 BD with or without macrogol containing laxatives 1-2/daily)			
Investigations	Nil	Nil	Electrolytes, LFTs: repeat if persistent vomiting or requiring repeated IV fluids TSH if clinically indicated Obstetric US	Repeat electrolytes, LFTs if persistent vomiting or requiring IV fluids
Medications	Pyridoxine 10-50 mg QID PO or Ginger 200-600 mg TDS PO or Ginger plus Pyridoxine PO	One of the following PO up to TDS. Metoclopramide* 10 mg Prochlorperazine* 5 mg Doxylamine* 6.25-25 mg Promethazine* 25 mg or Ondansetron 4-8mg To avoid sedation and for prolonged use ie more than 5 days, preferentially use ondansetron during the day	Ondansetron 4-8 mg PO/IV BD-TDS and Consider night time dosing with either: Metoclopramide* 10 mg PO/IV or Prochlorperazine* 5-10 mg PO/IV or Doxylamine* 6.25-25 mg PO or Cyclizine 12.5-50 mg PO/IV and Consider prednisone: commence 40-50mg OD or hydrocortisone 100mg IV BD and wean prednisone over 7-10 days to minimal effective dose. May need to continue until symptoms resolve.	As for severe NVP/HG Convert to parenteral: IV/IM or subcutaneous treatment if not tolerating oral Convert back to oral equivalent when suitable.
Additional treatment		H2 antagonist PO BD eg Ranitidine 150-300 mg IV fluids 1-3 x per week as required	Cease H2 antagonist and substitute PPI PO BD eg esomeprazole or rabeprazole 20 mg IV fluids 1-3 x per week as required: add IV thiamine if poor oral intake or administering dextrose.	Continue PPI PO or IV if not tolerated. Continuous IV fluid and electrolyte replacement. Add IV thiamine if poor oral intake or administering dextrose Consider total parenteral nutrition
Treatment supervision and site	GP, midwife, obstetrician or community pharmacist Outpatient	GP or obstetrician Outpatient/Day Stay/Emergency Room	Obstetrician and/or physician Outpatient/Day Stay/Emergency Room	Obstetrician and physician Admit to hospital

OD: once a day, BD: twice a day, TDS: three times a day, QID: four times a day, PO: oral, IV: intravenous, H2: histamine 2, PPI: proton pump inhibitor, TSH: thyroid stimulating hormone.
Electrolytes: sodium, potassium, chloride, bicarbonate, magnesium, urea and creatinine, LFTs: Bilirubin, Alanine Transaminase, Aspartate Aminotransferase, Albumin.

SOMANZ
SOCIETY OF OBSTETRIC MEDICINE OF AUSTRALIA AND NEW ZEALAND

Sickness and Vomiting in Pregnancy

Patient information

Many pregnant women feel sick (nausea) or vomit during early pregnancy. This can vary from mild when it can be considered a normal part of pregnancy. If you can continue to eat and drink even with the sickness, this is considered reasonably normal. The exact cause of the sickness is not known but is probably due to the hormonal changes of early pregnancy.

It can occur more commonly in some families (genetic tendency), if you have twins or triplets, if your baby is a girl and if you had sickness and vomiting in your previous pregnancies. We don't really understand why some women suffer more, but the most important thing to know is that it's not your fault and it doesn't mean there is anything wrong with your pregnancy.

In this leaflet we answer some common questions about nausea and vomiting in pregnancy and provide some guidance for where you can get more information and help if you need it.

Although it is often called morning sickness, symptoms can occur at any time - not just in the morning. It usually starts from the early part of pregnancy and settles between 12 and 16 weeks. Rarely, women have some sickness throughout their entire pregnancy.

Even mild sickness and vomiting in pregnancy can be difficult to cope with. It can affect your mood, your work, your home situation and your ability to care for your family. If sickness and vomiting are really interfering with your life, particularly your ability to eat and drink, you should seek help from your doctor or midwife.

What is hyperemesis gravidarum?

If you have severe sickness and vomiting for more than a few days, you may find it hard to drink anything leading to dehydration (lack of fluid in your body) and difficulty eating enough food, causing weight loss and vitamin deficiencies. This severe sickness and vomiting in pregnancy is known as **hyperemesis gravidarum**.

If you have these symptoms, even for more than a few days, you need urgent, expert medical help. Treatment is effective and protects you and your baby from complications. You should see your family doctor (GP), obstetrician or attend the Emergency Room at your local hospital for advice and help.

Do sickness and vomiting affect the baby?

Not usually. The baby gets nourishment from your body's reserves even though you may not eat well when you are vomiting. The effort of retching and vomiting does not harm your baby. In fact, some studies have shown that having sickness and vomiting in early pregnancy is a good indication that your pregnancy is healthy and will have a successful outcome.

Your baby may be affected if you develop hyperemesis gravidarum and become very ill with lack of fluid in the body (dehydration) which is not treated. In this case, the most likely problem is that your baby will have a low birth weight when he or she is born. However, not all babies born to women with hyperemesis gravidarum have a low birth weight.

Do I need any special tests?

If you have mild feelings of sickness (nausea) and vomiting during pregnancy, you do not usually need any specific tests or investigations.

Sometimes your doctor or midwife will suggest some tests:

-
- If your symptoms become more severe.
- If you are not able to keep any food or fluids down.
  If you start losing weight.

Investigations may include blood or urine tests to look for a another cause for your nausea and vomiting or to check how your body is coping.

What can I do to help relieve sickness and vomiting?

In most cases, as the symptoms are often mild, no specific treatment is needed. However, there are certain things that you may like to try to help relieve your symptoms. They include the following:

- Eating small but frequent meals may help. Some people say that sickness is made worse by not eating anything at all. If you eat some food regularly, it may help to ease symptoms. Eat whatever you can, when you can. Don’t worry too much about a balanced diet at this time. There may be some foods you really want and others you can’t stand. Cold meals may be better if nausea is associated with food smells.

- Ginger. Some studies have shown that taking ginger tablets or syrup may be effective for relieving feelings of sickness (nausea) and vomiting in pregnancy. However, care should be taken, as the quality of ginger products varies. Before you take a ginger product, you should discuss this with a pharmacist, midwife or GP. Food containing ginger may also help.
- Avoiding triggers. Some women find that a trigger can set off the sickness. For example, a smell or emotional stress. If possible, avoid anything that may trigger your symptoms.
- Having lots to drink to avoid lack of fluid in the body (dehydration) may help. Drinking little and often rather than large amounts may help to prevent vomiting. Try to aim to drink at least one to two litres of some sort of fluid each a day.
- Rest. Make sure that you have plenty of rest and sleep in early pregnancy. Being tired is thought to make nausea and vomiting during pregnancy worse.

Note: generally, you should not use over-the-counter remedies for sickness and vomiting whilst you are pregnant unless recommended by your doctor, midwife or pharmacist.

When are anti-sickness medicines needed?

Anti-sickness medicine may be necessary and recommended if your symptoms are persistent and severe, or do not settle with the above measures. Although it is generally recommended to avoid medicines when you are pregnant, certain medicines have been used for a number of years to treat feelings of sickness and vomiting in pregnancy and are considered safe. Some of the more commonly used medicines are pyridoxine (vitamin B6), doxylamine, promethazine, cyclizine and prochlorperazine and there is no evidence that they harm a developing baby. If these are not helpful, metoclopramide, ondansetron, ranitidine and sometimes prednisolone may be used.

Always discuss with your doctor, community pharmacist or midwife before taking an anti-sickness medicine when you are pregnant.

They should inform you about any possible concerns regarding using medicines for sickness and vomiting during pregnancy. Feel free to ask them any questions you have before taking medicine in pregnancy.

It is best to use medication for the shortest time possible. For some women, medication may be needed for several weeks or even months until symptoms settle.

What if these treatments do not work very well?

A small number of women need to be seen at the hospital or Day Hospital facility to be given fluids by a drip. Admission to Hospital is sometimes needed if you do not respond to medication or can't keep it down. You may need to be admitted to hospital if you lose weight or can’t keep enough fluid down and become too dry (dehydrated).

Other causes of vomiting

Remember, not all vomiting may be due to the pregnancy. You can still get other illnesses such as a tummy bug (gastroenteritis) or food poisoning. Sometimes a bladder or kidney infection can cause vomiting in pregnancy. You should see a doctor urgently if you develop any symptoms that you are worried about, particularly any of the following symptoms:

-
- Very dark urine or not passing any urine for more than eight hours.
- Stomach pains.
- High temperature (fever).
- Pain on passing urine.
- Headache not responding to paracetamol.
- Runny stools (diarrhoea).
- Yellow skin (jaundice).
- Severe weakness or feeling faint.
- Blood in your vomit.
  Repeated, unstoppable vomiting.

Where can I get more information?

The following sites may be helpful if you want more information or support:

-
  SOMANZ Guideline for the management of nausea and vomiting in pregnancy.
- https://www.somanz.org/Index.asp
- Hyperemesis Gravidarum Australia: https://www.hyperemesisaustralia.org.au
  Pregnancy Sickness Support UK: https://www.pregnancysicknesssupport.org.uk/
- American College of Obstetrics and Gynecology: Morning Sickness: Nausea and Vomiting of Pregnancy: https://www.acog.org/Patients/FAQs/Morning-Sickness-
- Nausea-and-Vomiting-of-Pregnancy
  Various online forums and blogs are available for women to share their experiences. We cannot recommend individual sites as they do not contain supervised content.

Sickness in Pregnancy Plan

Date: _____
Doctor: _____
Contact: _____

Patient Label

My medications for sickness, vomiting and acid reflux				
	Morning	Middle of day	Evening	Bedtime
For sickness or dry heaves (nausea or vomiting or retching)				
For stomach acid (reflux)				
For constipation				
Other				

If you feel worse:

_____

_____

_____

If you feel better:

_____

_____

_____

Would you like to tell us how you're going?

Eating and drinking:

_____

_____

_____

_____

Work or study:

_____

_____

_____

_____

Family:

_____

_____

_____

_____

Mood:

_____

_____

_____

_____

_____

Did you have drip (IV) fluids this week? If so, when? Did it help?

_____

_____

_____

_____

_____