



# GORD IN PREGNANCY

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# ARGOMENTI

**DIMENSION OF PROBLEM**

**CLINICAL FEATURES**

**EVALUATION OF GORD IN PREGNANT PATIENT**

**MANAGEMENT OF GORD IN PREGNANCY**

**PHARMACOLOGICAL THERAPY**

**PROGNOSIS OF GORD IN PREGNANCY**

**ACID SUPPRESSION MEDICATIONS  
IN BREAST FEEDING**



# DIMENSION OF PROBLEM



## Dimension of problem

**Gastrointestinal symptoms** ( nausea, vomiting, hyperemesis gravidarum, gastroesophageal reflux disease, constipation, and diarrhea) are one of the **most frequent medical complaints during pregnancy.**

Some women have **gastrointestinal disorders that are unique to pregnancy** and other pregnant women present with **chronic gastrointestinal disorders that require special consideration during pregnancy**

Raja A. et al

2007, *Gastroesophageal reflux disease in pregnancy*  
*Best Practice & Research Clinical Gastroenterology* Vol. 21, No. 5, pp. 793–806



## Incidence

- Gastroesophageal reflux disease (GORD), commonly experienced as **heartburn**, is reported by **40%–85%** women during pregnancy
- The **variation** in the incidence of GORD reported in pregnancy is probably **due to the lack of consensus** over the **definition** of the disease.
- One study noted a **higher incidence** of heartburn in **Caucasians** when compared with **Nigerians** (79% vs 9% respectively).
- Bainbridge et al **found no difference** in the incidence of heartburn in pregnancy between **Caucasian Europeans and Asians**.


Marrero et al studied **607 women** during **various stages of pregnancy** via questionnaire, and found there was an increased **risk of heartburn** with **increasing gestational age, presence of prepartum heartburn and parity, but not race**

Dent J, EL-Serag HB, Wallander MA et al.

2005, *Epidemiology of GORD: a systematic review. Gut* 2005 May; 54: 710–71

# CLINICAL FEATURES

First symptoms of heartburn were reported to occur

- 
- in the **first** trimester in **50% cases**
  - in the **second** trimester in **20%–40%** cases
  - in the **last** term of pregnancy in **10%** cases

**TABLE I. Symptoms of GORD in pregnancy**

<b>Typical symptoms</b>	Heartburn, acid regurgitation and nausea
<b>Atypical symptoms</b>	Dysphagia, globus sensation, non-cardiac chest pain, dyspepsia and abdominal pain
<b>Extra-oesophageal symptoms</b>	Hoarseness, sore throat, sinusitis, chronic dry cough, laryngitis, dental erosions, non-atopic asthma and recurrent aspiration



# CLINICAL FEATURES



Precipitating factors that **aggravate the symptoms** include:

- ingestion of **fatty** or **spicy** food,
- eating soon before **bedtime**, and the
- ingestion of certain foods like **chocolate**, **mints**, **caffeinated beverages** and
- **medications** that **decrease** lower oesophageal sphincter (LOS) **pressure**.

Medications that can **decrease the pressure of the LOS** include **anticholinergics**, **calcium channel antagonists**, **theophylline**, **antipsychotic agents** and **antidepressants**.

Richter JE.

2003, *Gastroesophageal reflux disease during pregnancy. Gastroenterol Clin North Am*; 32: 235–261

# CLASSIFICATION

Typically, **patients themselves determine** whether heartburn and regurgitation are **troublesome**



these have been reported as such when mild symptoms are experienced **2 or more days per week**



or moderate to severe symptoms are experienced **>1 day a week**

*In practice, clinicians may base treatment decisions **on these 2 symptoms alone** without performing further diagnostic tests*



**Vakil N, van Zanten SV, Kahrilas P, Dent J, Jones R**

*2006, Global Consensus Group. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus.*

*Am J Gastroenterol.;101:1900–20*

# PATHOPHYSIOLOGY OF GORD IN PREGNANCY: a multifactorial disease

It involves both **mechanical**  
and **hormonal** factors

The suggested **PREDOMINANT FACTOR** is  
a **DECREASE** in the **LOS** pressure due to a  
progressive rise in **circulating oestrogen**  
and **progesterone**

*Many studies have shown that **LOS** pressure decreases during the course of pregnancy*



# PATHOPHYSIOLOGY OF GORD IN PREGNANCY: a multifactorial disease



Van Thiel et al demonstrated that **resting LOS pressure is lower than normal** during **all three trimesters** of pregnancy, **reaching a nadir at 36 weeks** gestation

The **reduction of LOS pressure** was accompanied by **heartburn** with subsequent **return of normal LOS pressure post-partum**

Van Thiel DH, Gavaler JS & Stremple J.  
1977, *Heartburn of pregnancy. Am J Gastroenterol*; 72: 666–668

# PATHOPHYSIOLOGY OF GORD IN PREGNANCY: a multifactorial disease

- Fisher et al could find **no significant difference** in **LOS pressure before** and **after therapeutic abortion** during the **first 20 weeks** of gestation.
- However, they did notice that the **normal adaptive sphincter responses** to **hormonal** and **pharmacological** agents were **blunted**.
- This suggests that subtle physiological alterations occur in early gestation followed **later** by a measurable **decrease** in **LOS pressure**



# PATHOPHYSIOLOGY OF GORD IN PREGNANCY: a multifactorial disease



Animal and human studies have found that the **increased circulatory level of progesterone** during pregnancy mediates the LOS smooth muscle relaxation.

Although the role of progesterone has been emphasised, **oestrogen is a necessary primer for this action to occur.**

Crystal NB & Richter JE

1998, *Treating GORD during pregnancy and lactation, what are the safest therapy options?* *Drug safety* 1998 Oct; 19(4): 325–337. 15

# PATHOPHYSIOLOGY OF GORD IN PREGNANCY: a multifactorial disease

In the **1970s**, Schulze et al using an animal model of **opossums**, demonstrated that **sequential administration of female sex steroids** inducing a **hormonal pseudo-pregnancy state**, **lowered LOS pressure**

Although the role of progesterone has been emphasised, **oestrogen is a necessary primer for this action to occur.**

Schulze K. Christensen

1977, Lower oesophageal sphincter of the opossum oesophagus in pseudo-pregnancy. *Am J Gastroenterol*; 73: 1082–1085



# PATHOPHYSIOLOGY OF GORD IN PREGNANCY: a multifactorial disease



- Subsequently, others found that **progesterone** in combination with **ethinylestradiol** decreased LOS pressure significantly.
- Fisher et al also reported that a combination of **17-b oestradiol** and **progesterone** profoundly decreased the LOS pressure.

Taken together, these studies indicate **important roles for both progesterone and oestrogen in lowering LOS pressure**, and suggest that their combined actions significantly contribute to this effect

# OTHER FACTOR

- Spence et al<sup>17</sup> hypothesised that the **enlarging gravid uterus causes increased intra-abdominal pressure**, thus compressing the stomach and provoking reflux symptoms
- Although not well understood yet, it is likely that **hormones of pregnancy** may **affect normal function** of the **enteric nerves** and **muscles**, resulting in slower motility throughout the gastrointestinal tract

# PROGESTERONE ROLE

- Studies have shown that **progesterone** has an **inhibitory effect** on the smooth **muscle** of both the **pylorus** and the **small bowel**, which results in decreased GI contractility.
- Other studies **comparing** the gastric emptying rates of **premenopausal women** to **men** and **postmenopausal women** have detected **slower gastric emptying rates**
- There are a few studies evaluating gastric function during pregnancy. However, studies have documented the presence of both **tachygastria** and **bradygastria** in **pregnant women**. Both of these gastric dysrhythmias have been **associated** with reports of **nausea**.

Kock KL et al.

2002, *Gastrointestinal factors in nausea and vomiting of pregnancy. Am J Obstet Gynecol*; 186: S 198-203

# Evaluation of GORD in pregnant patient



## Evaluation

- The symptoms of **heartburn** and **regurgitation** have a sensitivity of **78%** and a specificity of **60%** to diagnose GERD, and typical GERD **can be diagnosed based on these 2 symptoms** without additional diagnostic testing
- **Invasive investigations** such as manometry and pH probes are **rarely** needed, although these **can be safely performed** during pregnancy.
- **Barium** studies **should be avoided** because of radiation exposure to the foetus.
- For **intractable symptoms** or **complications** such as haemorrhage, **upper gastrointestinal endoscopy** may be indicated

Armstrong D, Marshall JK, Chiba N, Enns R, Fallone CA, Fass R.

2004-2005, Canadian Consensus Conference on the management of gastroesophageal reflux disease in adults - update 2004. *Can J Gastroenterol.* 2005



# THE ROLE OF ENDOSCOPY in evaluating GORD in pregnancy

Upper gastrointestinal endoscopy is recommended during pregnancy for the diagnosis of suspected GORD **ONLY when symptoms are SEVERE and refractory to intensive medical therapy** or in the setting of GORD **associated complications** such as haemorrhage

The procedure can be **safely performed** without harm to the mother or foetus by careful **monitoring** of **blood pressure** and **oxygen saturations**.



# THE ROLE OF ENDOSCOPY in evaluating GORD in pregnancy



The choice of **sedation**, for example midazolam and diazepam (category D), fentanyl (category C) and meperidine and propofol (category B) **must be carefully selected**

# MANAGEMENT OF GORD IN PREGNANCY



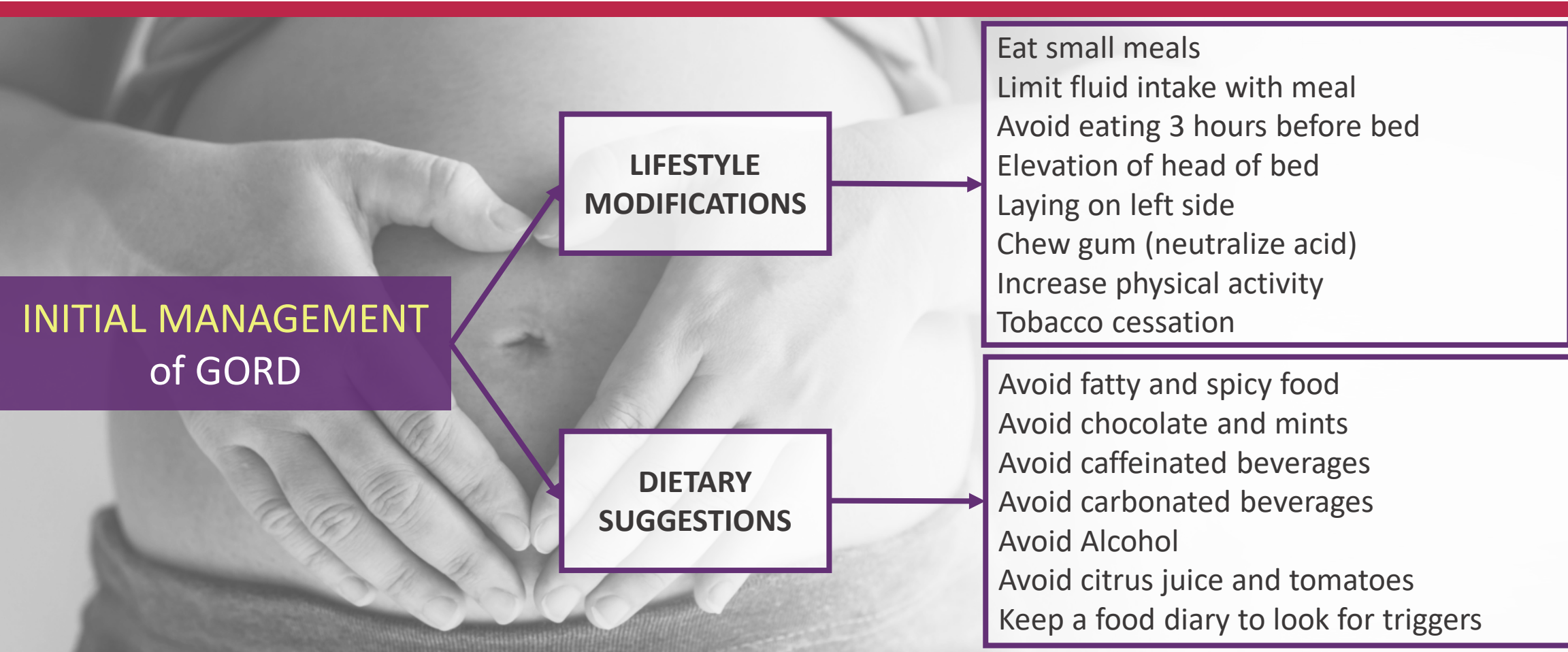
The **OPTIMUM MANAGEMENT** of GORD in pregnant women requires

**special attention and expertise**, since the **effects of medications on the foetus and neonate** must be considered carefully

**Gastroenterologists and obstetricians should participate** in the **SHARED CARE** of pregnant patients with GORD, since this condition can profoundly impair the quality of life of pregnant women



# MANAGEMENT OF GORD IN PREGNANCY



**INITIAL MANAGEMENT**  
of GORD

**LIFESTYLE  
MODIFICATIONS**

Eat small meals  
Limit fluid intake with meal  
Avoid eating 3 hours before bed  
Elevation of head of bed  
Laying on left side  
Chew gum (neutralize acid)  
Increase physical activity  
Tobacco cessation

**DIETARY  
SUGGESTIONS**

Avoid fatty and spicy food  
Avoid chocolate and mints  
Avoid caffeinated beverages  
Avoid carbonated beverages  
Avoid Alcohol  
Avoid citrus juice and tomatoes  
Keep a food diary to look for triggers

**Raja A. et al**

2007, *Gastroesophageal reflux disease in pregnancy*, *Best Practice & Research Clinical Gastroenterology* Vol. 21, No. 5, pp. 793–806,  
doi:10.1016/j.bpg.2007.05.006



# MANAGEMENT OF GORD IN PREGNANCY



When symptoms are **refractory** to these **life-style changes**...

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2007, *Gastroesophageal reflux disease in pregnancy*, *Best Practice & Research Clinical Gastroenterology* Vol. 21, No. 5, pp. 793–806,  
doi:10.1016/j.bpg.2007.05.006

# PHARMACOLOGICAL THERAPY

pharmacological therapy is appropriate



The various **risks and benefit** of medications must be discussed with the patient carefully, in particular the potential for **teratogenicity**

## DEFINITION OF FOOD AND DRUG AGENCY PREGNANCY CLASSIFICATIONS

CLASS	DEFINITION
A	Appropriately designed studies in pregnant women have not demonstrated fetal risk
B	No fetal risk in animal reproduction studies; no well-controlled studies in pregnant women <i>OR</i> Adverse effect in animal studies, but studies in pregnant women failed to demonstrate fetal risk
C	Animal reproduction studies show adverse fetal effect but no well-controlled studies in humans <i>OR</i> No animal reproduction studies and well-controlled studies in humans
D	Evidence of human fetal risk in investigational or marketing experience or studies in humans
X	Animals or humans studies have demonstrated fetal abnormalities <i>OR</i> Evidence of fetal risk based on investigational and/or marketing experience

# PHARMACOLOGICAL THERAPY



DATA



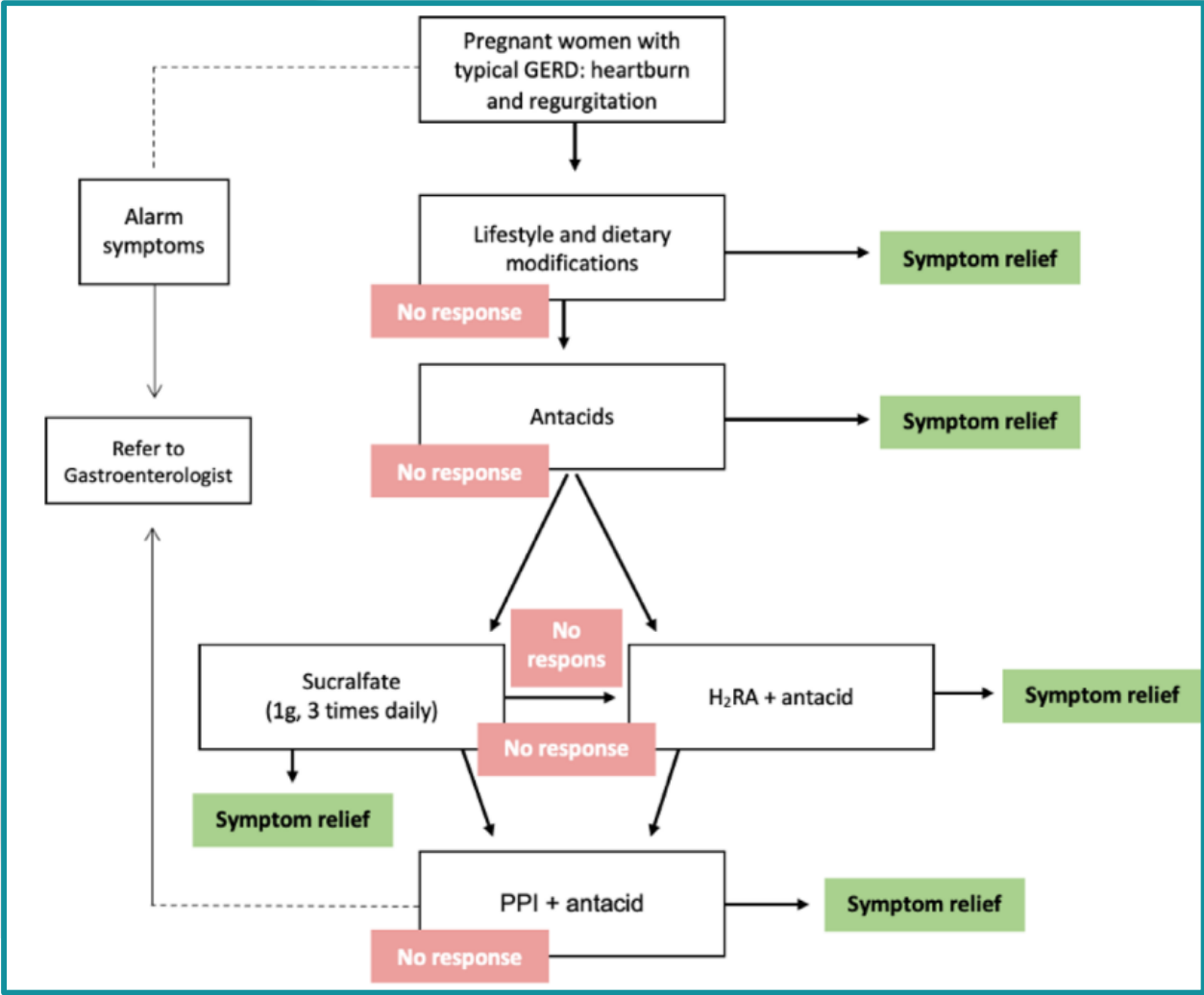
The overall incidence of major foetal congenital malformation in the general population ranges between 1 and 3%.



The critical teratogenic period during pregnancy ranges from day 31 (in a 28-day menstrual cycle) to day 71 from the last menstrual period.

This represents the important phase of organogenesis in the developing embryo. Before this period, **exposure to a potential teratogen usually causes an all-or-none effect** (i.e. the foetus either does not survive or survives without anomalies)

# STEP-UP APPROACH towards management of GORD during pregnancy






# STEP-UP APPROACH towards management of GORD during pregnancy

Ca  
 Al  
Mg

Antacids containing **calcium, aluminum, and magnesium** are recommended as needed as second-line treatment of GERD during pregnancy (**Recommendation Grade B**).



The **preferred choice** of antacids is **calcium-containing** antacids, in normal therapeutic doses, given the beneficial effect of this treatment in the **prevention of hypertension and preeclampsia** (**Recommendation Grade A**).

NaHCO<sub>3</sub>  
 Mg<sub>2</sub>O<sub>8</sub>Si<sub>3</sub>



It is **NOT RECOMMENDED** to use antacids containing **bicarbonate** or **magnesium trisilicate** (**Recommendation Grade C**).

# SUCRALFATE AND ACID-SUPPRESSION THERAPY



If symptoms **persist** with **antacids**, a shift to **Sucralfate** can be reasonable (**Recommendation Grade C**)

If symptoms **persist** with **Sucralfate**, an **H2RA** can be combined with antacids (**Recommendation Grade B**).

If **H2RAs** with **antacids** provide **inadequate** control of symptoms, it is recommended to use **PPIs** along with antacids as rescue medication for breakthrough GORD (**Recommendation Grade C**).

# PROGNOSIS OF GORD IN PREGNANCY

The **outcome** of GORD in pregnancy is **good** but it tends to recur with subsequent pregnancies. **INTENSIVE THERAPY is recommended** in the **POST PARTUM PERIOD** to heal any residual oesophagitis and long-term drug therapy is rarely needed.

# ACID SUPPRESSION MEDICATIONS IN BREAST FEEDING



The **symptoms** of GORD typically **resolve after delivery**.

However, some women continue to have the symptoms and require medications in the post-partum period. Since **many medications** used for the treatment of GORD **are excreted in breast milk**, it is possible that they might be harmful to infants



# ACID SUPPRESSION MEDICATIONS IN BREAST FEEDING



SAFETY OF GORD MEDICATIONS DURING LACTATION		
DRUG	SAFETY	COMMENTS
Antiacids	Yes	Not concentrated in breast milk
Sucralfate	Yes	Minimal, if any, excretion in breast milk
H2RA		
Cimetidine	Yes	American Academy of Paediatrics classified as compatible with breast feeding
Rantidine	Yes	Excreted in breast milk in concentration similar to cimetidine
Famotidine	Yes	Lowest concentrations in breast milk of all H2RAs
Nizatidine	No	Growth depression in pups of lactating rats
Proton-pump inhibitors	No	Little known of excretion in breast milk. Growth depression in pups of lactating rats receiving omeprazole and rabeprazole

GORD, gastro-oesophageal reflux disease; H2RA, histamine-2 receptor antagonist

**Anderson PO.**

*1991, Drug use during breast feeding. Clin Pharm; 10: 594–624*



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