

# **A LITERATURE REVIEW OF PREGNANCY SICKNESS**

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## **A. DESCRIBED CLINICAL FEATURES OF NAUSEA AND VOMITING OF PREGNANCY (NVP) AND HYPEREMESIS GRAVIDARUM (HG)**

### **Contents**

#### **Item**

1. **Incidence of NVP.**
2. **Features of the nausea of NVP** (a) Percentage of women with NVP who have nausea only; (b) episodic nature of nausea in pregnancy; (c) regular daily pattern of NVP; (d) severity of nausea; average duration of days of nausea per pregnancy; average duration in hours of nausea per pregnancy. Numbers of women with NVP classified by total hours of nausea; (e) nausea the most distressing symptom of NVP; (f) Hyperemesis Gravidarum develops from NVP; (g) the nausea of NVP is unusual compared to nausea in other conditions.
3. (a) Incidence of vomiting in early pregnancy; (b) severity of vomiting occurring daily; (c) total number of vomits in each woman; (d) significance of vomiting in relation to nausea positive correlation; (e) incidence of vomiting alone without nausea.
4. **Analysis of time of onset of NVP from first day of last menstrual period (LMP)** (a) mean day of onset of NVP; (b) early onset of NVP; (c) late onset of NVP; (d) onset of vomiting; (e) time of onset of NVP and HG in relation to their severity; (f) peak time of NVP from LMP.
5. **Cessation of NVP from first day of last period (LMP).**
6. **Percentage of women, who deliver a singleton normal infant, who have no NVP.**
7. **Time of day of NVP.** (a) Exclusively morning or evening; (b) NVP before and after midday; (c) morning sickness is a misnomer; (d) time of day for vomiting in NVP.
8. (a) Variation of severity of NVP from pregnancy to pregnancy in the same women; (b) symptoms of NVP can recur similarly from one pregnancy to the next in the same women; (c) there is a 50-66% chance symptoms of NVP will be similar in succeeding pregnancies; (d) a lower incidence of recurrent HG in succeeding pregnancies is also recorded; (e) three recent papers a higher rate for recurrent HG 70-80% in succeeding pregnancies in the same woman is recorded.
9. **Hyperemesis Gravidarum.** (a) Incidence of HG; (b) time from LMP until admission to hospital due to HG; (c) length of stay in hospital for HG; (d) re-admission to hospital for HG; (e) prompt recovery after therapeutic abortion or after delivery for HG and NVP patients; (f) the significance of HG in early pregnancy.
10. **NVP in animals.**

## Chapter A

### 1. INCIDENCE OF NAUSEA AND VOMITING IN PREGNANCY (NVP)

1.	57% of 100 pregnancies	G G Robertson (2)
2.	50% of 385 pregnancies	J P Semmens (3)
3.	71% of 100 pregnancies	J H Medalie (4)
4.	72.9% of 7,027 Gravidi	J M Brandes (5)
5.	83% of 300 women had NVP in one pregnancy	A M Barnie- Adshead (not published)
6.	70% of all 948 pregnancies	A Jarnfelt-Samsioe (6)
7.	72% of 6,376 pregnancies	S Kullander (16)
8.	72% of 214 pregnancies	R E Little (38)
9.	89.4% of 414 pregnancies	F D Tierson (21)
10.	81% of 363 pregnancies	R Gadsby (50)
11.	76% of 500 women	I D Vellacott (27)
12.	85% of 1,000 patients experienced nausea	S A Whitehead (40)
13.	72% of 68 patients experienced nausea	A Jarnfelt-Samsioe (32)
14.	71% of 7,767 women nauseated during pregnancy	D B Petitti (51)
15.	69% of 903 pregnant women had NVP	M M Weigel (44)
16.	74.9% of 1,453 women had NVP	R K Chin (63)
17.	79% of 1,513 women had nausea	L Meyer (45)
18.	73.3% of 86 women had nausea	C Fitzgerald (15)
19.	69.8% of 998 women incidence of NVP	R Boneva (67)
20.	71.2% of 3,029 women incidence of NVP (controls)	R Boneva (67)
21.	85.3% incidence of at least mild NVP in 129 women	S R Crystal (77)
22.	74% of 160 women reported nausea	R Lacroix (80)
23.	67.4% of 193 women reported NVP	S Emelianova (83)
24.	70.9% of 825 women in study reported NVP	M M Weigel (31)
25.	71.7% nauseated of 1,284 control women in study	L Fenster (43)
26.	79% of 3675 pregnant women had NVP	B Kallen (132)

Total women in 26 references 39,710. Those with NVP 29,145.

Percentage of pregnant women who have NVP 73.4%.

Range 50% to 85%

### 2. FEATURES OF THE NAUSEA OF NVP

#### 2a. PERCENTAGE OF WOMEN WITH NAUSEA ONLY

NVP	Vomited	Nausea only	Women in study	Ref
74%	37%	37%	160	(80)
67%	22%	45%	193	(83)
75%	63%	12%	1,453	(63)
85%	40%	45%	129	(77)
76%	32%	44%	500	(27)
74%	37%	37%	234	(21)

81%	52%	29%	363	(50)
69%	46%	23%	903	(44)
71%	47%	24%	825	(31)
79%	38.2%	39.2%	3,675	(132)

Total number of women in ten references: 8,435.

Total number of women with nausea only: 2,629.

Percentage of women who had nausea only: 32%.

Percentage of women with vomiting only (no nausea): 0.64%. (RI 3e)

2b. **EPISODIC NATURE OF NAUSEA IN PREGNANCY**

1. 85% of pregnant women with nausea have two episodes per day and 56% have three episodes of nausea per day. 292 women in the study had nausea. (50)
2. 70% of episodes of nausea lasted 1 - 4 hours. (50)
3. 65.9% of subjects stated that the episodes of nausea lasted 2-4 hours. 78 women in study. (23)
4. NVP had a habit of coming and going in waves. 27 women in study. (103)
5. The nurse practitioner may suggest keeping a diary listing the time of onset and length of each episode. (107)
6. When nausea is at it's worse women may have from one up to 5 separate episodes of nausea per day (very occasionally more than 5) (50) not published.
7. To assess at which week of pregnancy women experience the longest episodes or nausea, the percentage of all episodes which lasted four or more hours was calculated for each women for each week. Week 9 was the median week at which the longest episodes formed the greatest percentage of all episodes (intraquartile range 7-10 weeks) (50) not published.
8. Women with NVP who have nausea only in the morning have a mild form of the illness.
9. When symptoms of NVP improve the episodes become shorter and less frequent so that they often become once daily in the morning. (50) not published.

**Summary**

Symptoms of NVP usually occur in at least two daily episodes, the majority of each episode lasting 1-4 hours per day.

2c. **REGULAR DAILY PATTERN OF NVP**

1. Observations of individual daily diaries appeared to suggest that during the period of maximum symptoms there was a consistent pattern of the daily timing, frequency and duration of episodes. 292 women in study had NVP. (50)
2. Nausea and vomiting during pregnancy are fairly stable in terms of their intensity in each individual. The ratings for mean nausea intensity among women with nausea were fairly constant, not only in the first trimester when they ranged from 1.4 to 2.1 on a five point scale, but throughout pregnancy and although the prevalence of nausea during pregnancy is considerably decreased by the third trimester, in those still experiencing such, the intensity stayed fairly constant (1.9) until nausea ended. (80)

3. These waves of NVP occurred at predictable times. 27 women in study. (103)
4. Some variations in daily nausea patterns were seen. Whereas some women demonstrated predictable patterns others demonstrated variation in time of occurrence of nausea. 17 women kept daily diaries of nausea symptoms for seven days. (98)

**Summary**

During the period of maximum symptoms there was usually a consistent pattern of daily episodes.

2d.

**SEVERITY OF NAUSEA**

**AVERAGE DURATION OF DAYS OF NAUSEA PER PREGNANCY**

1. The median number of days of nausea per pregnancy in 292 women suffering from nausea was 41 days (inter-quartile range 38 to 56 days). (50)
2. From the time that daily self-recording began (mean of 8.3 weeks from LMP), nausea lasted a mean on 34.6 days (range 1-114 days). 118 women reported NVP in this study. (80)
3. A finding was that 23% of our study has uninterrupted daily nausea for an average of 44.6 days, while 20% who had one complete day of interruption of their nausea symptoms averaged 24.7 days with nausea (80). 160 women in study.
4. 46% of women experienced NVP for six weeks or less.  
35% for seven to ten weeks.  
19% for more than 11 weeks.  
55 women in study, 37 had NVP. (110)
5. Among 3675 women who completed questionnaires, the average length of reported problems was 9.2 weeks (64 days), 8.2 weeks with only nausea, 9.5 weeks with occasional vomiting and 12.3 weeks when daily vomiting was reported. (132)

**Summary**

Number of women in 5 studies 4433.

Average duration of nausea per women with NVP 45 days = 6.5 weeks. Inter-quartile range 5-12 weeks.

**AVERAGE DURATION IN HOURS OF NAUSEA PER PREGNANCY**

6. The median number of hours of nausea per pregnancy in 292 women suffering from nausea was 56 hours (inter-quartile range 22 to 139 hours). (50)

7. **Numbers of women with NVP classified by total hours of nausea**

<b>Hours of Nausea</b>	<b>Total No. Of Women</b>	<b>Percentage of Total With Nausea</b>	
0.1 - 16	57	19.5%	
16.1 - 33	48	16.3%	35.8%
33+ - 66	58	19.7%	
66+ - 100	37	12.6%	32.1%

100+ - 199.9	45	15.3%	
200+ - 299.9	18	6.1%	21.4%
300+ - 399	11	3.75%	
400+ - 499	5	1.7%	
500+ - 599	7	2.3%	
600+ - 699	3	1.0%	
700+	3	1.0%	9.7%
	<u>292</u>	<u>99.2%</u>	

Total number of women with NVP in study = 292.

71 women, 19.5% had no NVP.

Total in study; 363 women. Gadsby (Not Published)

### **Summary**

For women who have NVP approximately 20% have nausea lasting 100-300 hours and a further about 10% have nausea lasting 300-700 hours per pregnancy.

#### **2e. NAUSEA THE MOST DISTRESSING SYMPTOM OF NVP**

1. Nausea was the most common symptom experienced. Vomiting was frequently experienced but did not cause as much distress. Clearly nausea would be the most troublesome symptom experienced by women in terms of its duration and intensity, with the day to day constancy becoming wearisome. 593 women with nausea and/or vomiting in study. (81)
2. Relief occurred if nausea was reduced or relieved. Vomiting was not the most distressing symptom. 27 women in study. (103)
3. Nausea was more prominent than vomiting. 56 women had NVP mainly of moderate severity. (13)
4. Nausea occurs in 99% of pregnant women who have NVP. Vomiting occurs in 49% of women who have NVP. Therefore, nausea is the more frequent symptom. (Information from this Review).
5. Nausea is the main symptom effecting the quality of life of the women in this study. 500 women in this study. (114)
6. Our data shows that vomiting and retching are strongly interrelated, whereas nausea is perceived differently. Most women report that persistent nausea negatively affects their quality of life, whereas vomiting often signals relief of symptoms. (120)
7. In this study three times more women reported that nausea (and not vomiting) was their most bothersome symptom. (3201 callers to a health-line in Canada who had NVP in a previous pregnancy). (89)

### **Summary**

Nausea in the most distressing of symptoms of NVP i.e. vomiting, retching or nausea. (81) (103)

(13) (This review) (114) (120) (89)

Total: Seven References

#### **2f. HYPEREMESIS GRAVIDARUM DEVELOPS FROM NVP**

1. There is no clear-cut division between morning sickness and what is excessive vomiting

of pregnancy. It is only a matter of degree and both conditions should be treated. Probably the only value of drug therapy is at the stage of morning sickness when anti-emetics or mild sedatives may counter the feeling of nausea and prevent the woman from developing excessive vomiting and entering the vicious cycle of dehydration, starvation and electrolyte imbalance. (75)

2. Each year a significant number of women are admitted to hospital for hyperemesis gravidarum. Early recognition and management therefore have a significant effect on the quality of life during pregnancy, as well as a financial impact on the health care system. Management of this problem is multi-faceted. It includes early recognition, dieting and lifestyle advice as well as pharmaceutical and alternative forms of therapeutic interventions. (92)
3. In deciding whether or not to initiate anti-emetic treatment, consideration should be given to the impact NVP is having on the woman's life. Treatment may be appropriate for less severe NVP that does not necessarily cause dehydration and/or malnutrition. (89)
4. The value of drug treatment, if any, is at the stage of intractable vomiting when any of the stated anti-emetics, eg, antihistamines or phenothiazines, may be used to counter the feeling of nausea. If one can control the symptoms at this stage then it is likely that a large number of women can be prevented from developing excessive vomiting which, if prolonged, leads to hyperemesis gravidarum. (101)
5. On June 9th 1983, Bendectin, widely used throughout the world to treat nausea and vomiting during pregnancy, was voluntarily removed from the market by the manufacturer Merrill Dow. At the time, the company faced 327 pending US product liability suits - eventually all lawsuits, which went to court, were dismissed. The company estimated that the drug was used in 33 million pregnancies by 1983. A generic version, Diclectin, which contains Doxylamine (an antihistamine with antinauseant properties) and Pyridoxine (Vit B6), has been available in Canada since 1983 with gradually increasing sales. Bendectin was shown to be an effective drug by default, as lack of use of the drug resulted in a measurable increase in rates of hospitalisation for the symptoms of excessive vomiting during pregnancy, which it was designed to control. (93)
6. Benefits of recommendations. Nausea and vomiting of pregnancy (NVP) has a profound effect on women's health and quality of life during pregnancy, as well as a financial impact on the health care system, and its early recognition and management are recommended. Cost including hospitalisation, additional office visits and time lost from work may be reduced if NVP is treated early. (115)

## **SUMMARY**

HG develops from NVP. (75) (92) (101) (93) (89) (115) Total: Six References

### 2g. **THE NAUSEA OF NVP IS UNUSUAL COMPARED TO THE NAUSEA ASSOCIATED WITH OTHER CONDITIONS**

1. Fifty percent of women with NVP find their nausea is improved by eating food. (RI 39)
2. Women with NVP can also experience hunger (RI 39). Hunger can co-exist with NVP (103) or hunger can make NVP worse (54) or hunger can contribute to NVP (109).
3. Food cravings in pregnancy are associated with a higher incidence of NVP. (27)(40) (77) (RI 37)
4. NVP and HG are more common in non-smokers than in those women who smoke cigarettes. (RI 16)

## SUMMARY

The unusual nausea of NVP suggests a different (possibly hormonal) cause for the nausea of NVP compared to nausea associated with other conditions.

### 3a. INCIDENCE OF VOMITING IN EARLY PREGNANCY

- |  |                       |
|--|-----------------------|
| 1. Vomiting occurred in 162 of 500 patients: 32.4%   | Vellacott (27)        |
| 2. Vomiting occurred in 190 of 363 women: 52.3%  | Gadsby (50)           |
| 3. Vomiting in 234 out of 414 women: 56.5%   | Tierson (21)          |
| 4. 104 women in study: 50% vomited   | Jarnfelt-Samsioe (19) |
| 5. 9,098 women in study: 4,472 vomited: 55%  | Klebanoff (18)        |
| 6. 903 women in study: 46% vomited   | Weigel (44)           |
| 7. 1,453 women in study: 63.5% vomited   | R Chin (63)           |
| 8. 129 women in study: 40.3% vomited   | Crystal (77)          |
| 9. 160 women in study: 60 (37.5%) reported vomiting<br>50.8% of those who had nausea vomited | Lacroix (80)          |
| 10. 193 women in study: 22.3% vomited  | Emelianova (83)       |
| 11. 825 women in study: 47.3% vomited  | Weigel (31)           |
| 12. 1,513 women: 46% vomited   | Meyer (45)            |
| 13. 3,675 women: 1406 vomited (38.3%)  | Kallen (132)          |

Total women in 13 references 19,330. Total who vomited 9,095.

Range 22.3% - 63.5% vomited. On average 47.1% of pregnant women vomited.

### 3b. SEVERITY OF VOMITING

#### **Vomiting Occurring Daily**

- |  |                       |
|--|-----------------------|
| 1. Vomiting occurred daily in 99 out of 500 women: 18.4%.<br>A further 62 women vomited at least once per week.<br>42.3% of those women with nausea vomited. | Vellacott (27)        |
| 2. 33% suffered from moderate nausea with occasional vomiting, and in 17% nausea was severe with daily vomiting. 62 women in study.                          | Jarnfelt-Samsioe (19) |
| 3. Daily vomiting in 1,000 women: 20.8%.<br>52% of women vomited.  | Whitehead (40)        |
| 4. Among 3,675 women who completed NVP questionnaires, 1406 (38.3%) vomited, 938 (25.6%) reported occasional vomiting and 468 (12.7%) daily vomiting.        | Kallen (132)          |

#### Summary

Total number of women in 4 studies 5127.

Total number of women who vomited daily 777.

Percentage of women who vomited daily in 4 studies 15.1%.

3c. **TOTAL NUMBER OF VOMITS IN EACH WOMAN**

1. Total of 10 or less vomits in 92 out of 363 women: 25% Gadsby (50)
2. Total of 40 or more vomits in 36 out of 363 women: 9.9% Gadsby (50)
3. Max number of vomits in one woman's pregnancy: 258 Gadsby (50)
4. 160 women in study, vomiting occurred an average of 9.8 times per pregnancy. Lacroix (80)
5. Vomiting occurred on a mean of 5.6 days for the 60 women who vomited. 160 women in study. Lacroix (80)

**Summary**

Women who vomit in pregnancy 25% have less than 10 vomits per pregnancy, about 10% have more than 40 vomits per pregnancy.

3d. **SIGNIFICANCE OF VOMITING IN RELATION TO NAUSEA  
A POSITIVE CORRELATION**

1. Women experiencing severe vomiting i.e. 40 or more vomits per pregnancy, had significantly more hours of nausea than those with less severe vomiting, i.e. 10 or less vomits per pregnancy. The mean hours of nausea for those with severe vomiting was 136 hours, compared to those with less severe vomiting 41 hours. Mann Whitney U test  $P < 0.001$ . Therefore, measuring severe nausea is equivalent to measuring severe vomiting. 363 women in study. (50)
2. Significant correlation between severity of reported nausea and vomiting ( $r = 0.53$   $P < 0.001$ ). 129 women in study. (77)
3. 33% suffered from moderate nausea with occasional vomiting and in 17% nausea was severe with daily vomiting. 62 women in study. (19)

**Summary**

Significant correlation between severity of nausea and severity of vomiting.

3e. **NUMBER OF WOMEN WHO VOMIT WITHOUT ANY NAUSEA**

1. All women who reported vomiting reported nausea as well. 1,000 women in study. (40)
2. No-one had vomiting only. 363 women in study. (50)
3. 12 women (2.8%) had vomiting but did not have accompanying nausea. 414 women in study. (21)

Percentage of pregnant women with vomiting only (no nausea) 0.64%

4. **ANALYSIS OF TIME OF ONSET OF NVP FROM FIRST DAY  
OF LAST MENSTRUAL PERIOD (LMP)**

4a. **MEAN DAY OF ONSET OF NVP FROM LMP**

1. Sickness of pregnancy sets in around the 40th day - Soranus, AD100. (10)
2. 363 women in study, mean day of onset of nausea, day 39 from LMP. (50)
3. Symptoms of NVP began typically at four to six weeks gestation, 825 women in study. (31)
4. The mean and median week of onset of nausea among women who ever had nausea was the 6th week of gestation. No significant difference in mean days of onset for women with nausea only, compared with women who had nausea and vomiting. 414 women in study. (21)
5. 71% of 43 women with HG started symptoms prior to the sixth week from LMP. (7)
6. Mean day of onset of NVP  $5.6 \pm 1.7$  weeks of gestation. 260 women in study. (91)
7. Mean day of onset of NVP 5.5 weeks. 27 women in study. (103)
8. The mean gestational age at onset was 5.7 weeks. 160 women in study. (80)

**Summary**

The mean day of onset of NVP day 39 from LMP. (Five references)

4b. **EARLY ONSET OF NVP**

1. 8% of 500 women developed NVP before their first missed period. (27)
2. 20% of 414 women developed NVP before fourth week of gestation. (21)
3. 13.3% of 363 women developed NVP on or before day 28 from LMP. (50)
4. 16.2% of 43 patients with hyperemesis gravidarum started symptoms before day 28 from LMP i.e. before a missed period. (7)
5. 12.3%, 37 in 300 women, started NVP before they missed a period.  
(Barnie-Adshead, not published)

Total number of women in five references = 1620.

Number whose NVP started before day 28 from LMP, 215 = 13.2%.

4c. **LATE ONSET OF NVP**

1. 94% of 363 women started nausea on or before day 56 from LMP. (50)
2. Nearly 80% of 414 women started nausea by day 56 from LMP. (21)
3. 87% of 500 women, nausea and vomiting had commenced by the eighth week of pregnancy. (27)
4. 11.6% of 43 women with HG started symptoms after eighth week of pregnancy. (7)
5. Eight of 118 (6.7%) of women noted nausea beginning during or after week 10. 160 women in study. 90% of women destined to have NVP reported its onset by the eighth week of pregnancy. 160 women in study. (80)
6. NVP began at less than six weeks from LMP for 90% of women and by the eighth week of pregnancy NVP had begun for all women. 593 women in study. (81)
7. 86.4% started NVP by day 56 from LMP. 55 women in study, 37 experienced NVP. (110)

**Summary**

90% of women who will get NVP start before day 56 from LMP. (Seven references)

4d. **ONSET OF VOMITING**

1. Vomiting began as early as a gestational age (from LMP) of four weeks. (80)
2. Forty per cent of total women in study (414) were experiencing vomiting by the eighth week (up to day 56 from LMP) compared to 70% experiencing nausea. (21)
3. 91.5% of 414 women had developed vomiting by 12th week of pregnancy. (21)

**Summary**

Vomiting often begins one or two weeks after nausea of NVP.

4e. **TIME OF ONSET OF NVP IN RELATION TO SEVERITY OF SYMPTOMS**

1. Average number of hours of nausea for those women whose symptoms started on or before day 28 from LMP = 144.3 hours. (Total number of hours of nausea = 4,770 in 33 women).  
Average number of hours of nausea for those women whose symptoms started on or after day 50 from LMP = 57.6 hours. (Total number of hours of nausea = 1,787 in 31 women).  
Women whose NVP starts early, on or before day 28 from LMP, have more hours of NVP than those who start later, after day 50 from LMP. This result may be expected because whether nausea starts early or late from LMP, the symptoms cease at approximately the same time. (50)
2. Neither the time of onset during pregnancy, nor loss of weight indicates the severity of hyperemesis gravidarum nor affords a safeguard to its prognosis. 43 women with hyperemesis gravidarum in study. (7)
3. Women who had early onset of vomiting or nausea after conception were more likely to experience daily sickness symptoms compared to those women who reported that the onset of their symptoms occurred later than seven weeks (i.e. after day 49) gestational age. 1,000 women in study. (Early onset worse symptoms). (40)
4. NVP started at the same stage of gestation, 5.6 weeks, even though symptoms of NVP for the women in this study were more severe than the average in the population. 260 women in study population. (91)

**Summary**

Time of onset of NVP not related to the severity of symptoms. (7) (91)      Total 2 Refs.  
Early onset of NVP associated with longer hours of nausea. (50) (40)      Total 2 Refs.

4f. **PEAK TIME OF NVP FROM LMP**

1. In order to compare the symptoms of one woman's pregnancy with that of another, the week of peak symptoms was plotted. The peak incidence was in weeks 7-9, median week 9 from LMP, inter-quartile weeks 8-10 after rising sharply from week 6. The tail-off is more gradual. (50)
2. The distribution of the proportion of women with nausea each week of gestation shows the peak at eight weeks, reflecting that fact that most women who ever had nausea had begun having symptoms by the eighth week and very few had ceased having symptoms by then. (21)  
The distribution of the population of women having vomiting in each week of gestation

- peaked at about the same time as for nausea, but the peak was flatter for vomiting, reflecting the somewhat higher variance in week of onset of vomiting. (21)
3. Although gestational age at which nausea was reported to be most severe varied, the weeks of peak severity occurred at 11 and 13 weeks from LMP. 160 women in study. Week 11 from LMP was the week in which the highest proportion women, 40%, had nausea. (80) Week 11 was also the peak week for vomiting. (80).
  4. For the purpose of studying the variation in the weekly rate of N/V, the data from medical records was used to determine the weekly acute nausea prescription rates. The rates for weeks 5-6 are based on small numbers; from week eight onward throughout the third lunar month, (12 weeks), the rate is almost constant. There is a slight suggestion of a small peak between 10 and 11 weeks from LMP. Thereafter, the rate declines rapidly. 4,172 women entered the study within 12 weeks from LMP. (5)
  5. The patients in the trial had symptoms of relatively acute onset which were mainly of moderate severity. The treatment of nausea and vomiting most commonly started one or two weeks after the first symptoms commenced. 28 women. (17)
  6. Symptoms of NVP peaked in intensity between 8-12 weeks of gestation. 825 women in study. (31)
  7. Of women who completed the questionnaire (1,000 women in study) before 12 weeks of pregnancy (17% i.e. 170) 65% reported reduction in frequency of vomiting and 62% of nausea. (40)
  8. Only 9.3% of women experience NVP which gets worse by more than seven hours per week after the end of week nine (day 63) from LMP. (50)

### **Summary**

The evidence of these papers shows weeks 7-13 from LMP to be the weeks of maximum NVP. Most authors give a tighter two week period within this range. We believe weeks 7-9 from LMP to be the period of maximum NVP. (50)

### **5. CESSATION OF NVP FROM FIRST DAY OF LAST PERIOD (LMP)**

27% of women's symptoms had ceased by the end of the 10th week From LMP. (50)	363 women
27% of women's symptoms had ceased by the 12th week. (27)	500 women
60% of women's symptoms had ceased by the end of the 12th week. (50)	
70% of women's symptoms had ceased by the 13th week. (23)	78 women
80% of women's symptoms had ceased by the end of the 14th week. (50)	
50% of women's symptoms resolved by the 14th week. (80)	160 women
91% of women's symptoms had ceased by the end of the 16th week. (50)	
95% of women's symptoms had ceased by four months. (19)	104 women
87% of women's symptoms had ceased by the end of the 20th week. (40)	1,000 women
75% of women's symptoms had ceased by the 20th week. (21)	414 women
90% of women's symptoms resolved by the 22nd week. (80)	160 women
81% of women's symptoms had ceased by the 26th week. (15)	86 women
Mean day NVP ceased $16.9 \pm 3.1$ weeks of gestation. (91)	260 women

## Summary

Mean week for cessation of NVP end of week 12 (50); by the 14th week (80).

These results for cessation of NVP are variable. Range from 9 studies: 91% of women's symptoms ceased by the end of the 16th week from LMP. 90% of women's symptoms resolved by the 22nd week.

## OTHER FACTORS CONCERNING CESSATION OF NVP

- 1a. 29.3% of women's NVP appeared to stop suddenly, that is they reported 14 or more hours of nausea in the week prior to cessation. (50)
- 1b. Most women find that morning sickness disappears at right about the three month mark. It's a truly magical feeling the day you wake up and go to the kitchen eagerly thinking of breakfast. It happens just like that - one day you are miserable and the next you've never felt better.  
Iovine Vicki. The Best Friends Guide to Pregnancy 'Morning Sickness' - pages 35-39.
- 2a. NVP did not disappear at 12 weeks but rather tapered off throughout the early second trimester or continued into the 5th month particularly if severe. 27 women in study. (103)
- 2b. Nausea persisted significantly longer among women whose nausea was accompanied by vomiting than among women with nausea alone. (21)
- 2c. The percentage of women experiencing vomiting decreased by 20% during the 17-20 week interval and only 9% of women complained of vomiting, unassociated with fever or diarrhoea, after 20 weeks. 8019 women in study, 4517 women vomited. (18)
3. Cessation of NVP occurred at approximately the same day from LMP whether the symptoms began early, before day 28 from LMP, or later, after day 49 from LMP, or severely or mildly, that is those women who had less than 36 hours of nausea in all seven day periods up to day 49 from LMP (mildly) or those women who experienced more than 36 hours of nausea in any seven day period up to day 49 from LMP (severely). (50)
4. A finding was that 23% of this study has uninterrupted daily nausea for an average of 44-46 days, while 20% who had one complete day of interruption of their nausea averaged 24.7 days with nausea (80). 160 women in study.

## Summary

1. NVP will stop suddenly in about 30% of women but will taper off for the remaining 70%.
2. A complete day of no NVP symptoms is an encouraging sign that cessation will not be too long delayed.
3. Early symptoms of NVP are not an indication of how long NVP will last from LMP. Obviously, on average ladies whose symptoms start early, before day 28 from LMP will have more hours of nausea, than those whose symptoms start late after day 49 from LMP as in both situations NVP stops at about the same time from LMP.

6. PERCENTAGE OF WOMEN, WHO DELIVER A SINGLETON  
NORMAL INFANT, WHO HAVE NO NVP

1.	17% of 948 pregnancies	(6)
2.	10.6% of 414 pregnancies	(21)
3.	16.7% of 300 women with no NVP in any pregnancy	(A M Barnie-Adshead not published)
4.	24% of 500 pregnancies	(27)
5.	19% of 363 pregnancies	(50)
6.	28% of 199 women in study	(11)
7.	27% of 7,027 gravidas	(5)
8.	27.8% of 1,008 patients	(46)
9.	26.7% of 86 women	(15)
10.	24.8% of 1,453 women with singleton pregnancy	(63)
11.	14.7% of 129 women	(77)
12.	29.0% of 7,767 pregnancies	(51)
13.	32.6% of 193 women	(83)
14.	26.4% of 160 women	(80)
15.	29% of 100 pregnancies	(4)
16.	20.9% OF 3,675 women	(132)

Total number of women in studies 24,322.

Total number of women with no symptoms 6,234.

On average 25% of women who deliver a singleton normal infant had no symptoms of NVP.

## 7. TIME OF DAY FOR NVP

### 7a. EXCLUSIVELY IN THE MORNING

- 19% of sufferers complained of NVP confined to the morning (500 women in the survey). (27)
- 17% of women with nausea reported the symptoms occurred exclusively in the morning. 10% reported that they never had symptoms in the morning but only at other times of day. This survey disputes the concept of morning sickness. 1,000 women in the survey. (40)
- 4% had symptoms only in the morning. 1% had symptoms only in the evening, 95% had symptoms before and after midday. The condition should be called 'pregnancy sickness' not 'morning sickness'. 363 women in study. (50)
- In a group of 80 women only 10% experienced predominantly morning sickness.  
Barnie-Adshead 1978 (not published)
- Although 80.2% of women reported nausea in the morning, nausea limited to morning only occurred in only 1.8% of affected women. These figures suggest that the term morning sickness is misleading and should be avoided when one is referring to nausea and vomiting during pregnancy. 160 women in study. (80)
- The largest proportion of women had nausea throughout the day (68 women - 58%). Only 13 women (11%) had symptoms only in the morning. 46 women (39%) who participated had constant nausea. Number of women in study 117. (118)

Total number of women with only morning sickness - 304.

Total number of women in studies - 2220.

Percentage of women with morning only sickness - 13.6%.

7b. **NVP BEFORE AND AFTER MIDDAY**

1. 41% of patients experienced NVP before midday.  
49% of patients experienced NVP after midday.  
95% before and after midday.  
363 women in study. (50)
2. The more usual pattern was for symptoms to persist throughout the day. Morning 80%, afternoon 45%, evening 55% and night 15%. 500 women in study. (27)
3. Although the early morning was the most common time for symptoms of NVP, 20% of the subjects stated they were most likely to experience NVP in the evening. Another 20% stated they were nauseated the entire day. 78 patients. (23)
4. The maximum incidence of NVP was in the period up to 10:00 hours, with the next highest incidence between 10:00 and 13:00 hours. 56 patients. (17)
5. Of all the women who reported nausea, 57% (n = 477) said the symptoms occurred in the morning and at other times during the day. 1,000 women. (40)
6. 61% of women experienced NVP which recurred intermittently throughout the day. 80 women in study. Barnie-Adshead, 1978 (not published)
7. Nausea and vomiting during pregnancy lasted until the afternoon in 3.7%, until after suppertime in 4.7% and all day long in 80%. The 10 remaining women reported no morning nausea but had nausea at various other times during the day. 160 women in study. (80)
8. About 50% (92 patients) experienced the peak of nausea in the morning. (19)
9. NVP symptoms occur with equal probability throughout normal working hours; 40-45% of women experience nausea at least once each 4 hour period from 07:00 - 23:00.  
Morning sickness is actually a complete misnomer. (86)
10. In the present sample if NVP were present, it lasted all day, and for some also all night.  
Morning sickness is an inappropriate name for NVP. 27 women in study. (103)
11. Percentage of hours in the day in which nausea was experienced during a seven day period:-

7am - 10am	43.2%
11am - 2pm	42.0%
3pm - 6pm	43.9%
7pm - 10pm	40.3%
11pm - 2am	8.3%
3am - 6am	4.9%

19 women in study. (98)  
Nausea was not significantly more prevalent in the morning hours compared to other times during the waking hours, 7am - 10pm. (98)
12. NVP occurred at the following times during the day:-  
Morning for 29.4% of women.  
Later in the day 10.8%.  
All day long 24.3%.  
Varied times throughout the day 35.1%.  
55 women in study. (102)
13. Occurrence of nausea during 24 hour period:-  
On rising 21.4%.

Morning and/or evening 28.5%.  
Intermittently during the day 31.0%.  
At night 7.1%. (112)

NVP most commonly occurs before and after midday.  
(50) (27) (23) (17) (40) (Barnie-Adshead) (80) (19) (86) (103) (98) (102) (112)  
Thirteen References

7c. **AUTHORS STATE NVP SHOULD NOT BE CALLED MORNING SICKNESS**

1. The traditional label of morning sickness does not hold true for this study. Less than 20% of sufferers with NVP complained of symptoms only in the morning. (27)
2. In this study only 4% of women had only morning sickness. The episodic nature of pregnancy sickness is rarely described. Perhaps a more appropriate description of the condition would be episodic daytime pregnancy sickness. (50)
3. An analysis of the time of day at which women felt nauseated or vomited clearly shows that the term morning sickness is a misnomer. (40)
4. Only 10% of patients had predominantly morning sickness, whereas 61% of patients experienced nausea and vomiting recurring throughout the day. The condition is better described as pregnancy sickness. 80 patients in the study. (Barnie-Adshead 1978 not published).
5. Nausea and vomiting during pregnancy lasted all day in 80% of women. These figures suggest that the term morning sickness is misleading and should be avoided when one is referring to nausea and vomiting during pregnancy. (80)
6. NVP symptoms occur with equal probability throughout normal working hours. 40-45% of women experience nausea at least once each four hour period from 07.00 - 23.00 hours. Morning sickness is actually a complete misnomer. (86)
7. Continued references to nausea and vomiting of pregnancy as morning sickness may be confusing for women pregnant for the first time, and experiencing the symptoms at other times of the day. The results of this study support findings of previous investigators, who noted that morning sickness is too narrow a descriptive term for the experiences of nausea and vomiting of pregnancy. (98)
8. In the present sample, if nausea and vomiting were present, it lasted all day and for some also all night. Morning sickness is not an appropriate name for nausea and vomiting of pregnancy. (103)

**Summary**

Pregnancy sickness should not be called morning sickness.  
(50) (27) (40) (Barnie-Adshead - not published) (80) (86) (98) (103)  
Eight References

**Summaries for 7a, 7b and 7c stated together to show that morning sickness is the wrong name for the condition of pregnancy sickness**

- 7a. NVP occurring exclusively in the morning. Only 13.6% of women.  
(27) (40) (50) (Barnie-Adshead) (80) (118) Average of Five References
- 7b. NVP most commonly occurs before and after midday.

(17) (19) (23) (27) (40) (50) (Barnie-Adshead - not published) (80) (98) (102) (103) (86) (112)  
Total: Thirteen References

7c. Pregnancy sickness should not be called morning sickness.

(27) (40) (50) (Barnie-Adshead - not published) (80) (86) (98) (103)

Total: Eight References

7d. **TIME OF DAY FOR VOMITING IN NVP**

1. 31% of women vomited exclusively in the morning. 41% vomited at other times during the day. 1,000 women; 206 vomited. (40)
2. 53% of episodes of vomiting occurred between 6am and 12 noon.  
46% of episodes of vomiting occurred after midday.  
363 women in study, 190 vomited. (50)  
Total number of women who vomited, 396. Number of women who vomit before midday, 166. Vomiting occurred in 42.6% before midday.

8a. **VARIATION IN SEVERITY OF NVP FROM PREGNANCY TO PREGNANCY IN THE SAME WOMAN**

1. Some women who have no symptoms of nausea and vomiting in one pregnancy shall be violently attacked with it in another. - Smellie, 1779. (From Ref 10).
2. Frequency and duration of NVP vary greatly in individuals, as well as in different pregnancies in the same individual. (1)
3. The multipara numbered 63 between them gave a history of 175 previous pregnancies. The syndrome of NVP was not necessarily a constant feature of successive pregnancies in the same woman. (2)
4. A woman could be very sick in one pregnancy and yet have been less affected or even not affected at all in a previous or in a subsequent pregnancy. (41)
5. Of 55 women in this study, 18 had no NVP in the current pregnancy but 5 (27%) of these 18 women had distress with NVP in a previous pregnancy. (102)

8b. **SYMPTOMS OF NVP CAN RECUR SIMILARLY FROM ONE PREGNANCY TO THE NEXT IN THE SAME WOMAN**

1. Prior nausea on parity residuals were positively associated with nausea ( $P < 0.001$ ) and vomiting ( $P < 0.001$ ) in the current pregnancy indicating a strong tendency for NVP to recur across pregnancies. Decreased prior nausea was associated with lower risk of current NVP. (31) The division of this continuous variable into discrete intervals revealed that the association of nausea in a prior pregnancy with NVP in the current pregnancy was a pattern that was most apparent in the very low risk of current NVP for women with infrequent nausea in previous pregnancies. (31)
2. A history of nausea during previous pregnancy was associated with an increased risk of NVP during current pregnancy. 825 women in study. (78)
3. The present study confirms the significant relationship between pregnancy nausea in the current pregnancy and the occurrence of pregnancy sickness in a previous pregnancy. 363 women in study ( $P = 0.005$ ). (53)

4. Women with nausea during a previous pregnancy were significantly more likely to report NVP during the index pregnancy  $P < 0.001$  and to have higher scores on the overall nausea index  $P = < .01$ . McGill Nausea Questionnaire used. 160 women in study. (80)
5. Vomiting in one pregnancy is highly associated with vomiting in the subsequent pregnancy ( $P < 0.001$ ) after adjustment for age and smoking for each pregnancy. 9,098 pregnancies; 4,517 vomited. (18)
6. For women with a normal first pregnancy, the risk of HG in the second pregnancy was very similar to the overall population risk in the first pregnancy. 0.7% developed HG in the second pregnancy. 0.9% in the first. No convincing protective effect of a former normal pregnancy was observed. (148)

8c. **THERE IS A 50-66% CHANCE THAT SYMPTOMS OF NVP WILL BE SIMILAR IN SUCCEEDING PREGNANCIES IN THE SAME WOMAN**

1. Of the 57 women who were multiparous and who had had over 100 hours of nausea, 36 (63%) stated they had similar symptoms in a previous pregnancy. Of 41 women who were multiparous and had no nausea in the current pregnancy, 24 (59%) stated they had no or only slight symptoms in a previous pregnancy. These figures suggest about 1/3 of women will have varying NVP in their pregnancies, whereas about 2/3 will have similar NVP in successive pregnancies. (50)
2. A third to half of multipara admitted to hospital with hyperemesis gravidarum in this series had been treated in hospital with this condition in previous pregnancies. Of the 106 treated in their second pregnancy, 50 had been treated in their first. There were 82 patients in their third pregnancy. 44 had been treated in both and 11 in one previous pregnancy (67%). (9)
3. The number of women who had very bad nausea or sickness in their first pregnancy (longer than 3/12 or very severe in the first 3/12) 99 out of 300 = 33%. The number of women who had similar severe symptoms in their second pregnancy 51 in 99 = 51% (Barnie-Adshead, not published).
4. First pregnancy no vomiting in 314 patients but of these, 54% vomited in their second pregnancy. (18)

8d. **RECURRENCE RATE OF HYPEREMESIS GRAVIDARUM IN SUCCEEDING PREGANANCIES 70 – 80 %**

1. Multiparous hyperemetic subjects were more likely to have suffered from hyperemesis in a previous pregnancy than multiparous control subjects. 13/16 (81.2%) v 3/16 (18.8%). (113)
2. 10 out of 14 (71.4%) multipara with severe HG had a previous pregnancy affected by HG. (121)
3. The control group of 35 women who had severe nausea and vomiting in their previous pregnancy exhibited the expected 80% rate of recurrence of severe nausea and vomiting in a successive pregnancy. (122)
4. Of the 545 Women with at least 2 pregnancies 453 (83.1%) reported at least 1 recurrence of HG (808 Women from 23 Countries located the survey of Women with HG through an internet search regarding HG). (145)
5. Among women who had HG in their 1<sup>st</sup> pregnancy 15.2% developed HG in their 2<sup>nd</sup> pregnancy. Women without HG in their 1<sup>st</sup> pregnancy 0.7% developed HG in 2<sup>nd</sup> pregnancy. A women is 26 times more likely to have a recurrence of HG in 2<sup>nd</sup> pregnancy if she had HG in her 1<sup>st</sup> pregnancy than the woman who did not have HG in her 1<sup>st</sup> pregnancy. (148).

6. Among 504 informative women 331 reported more than one pregnancy and among these Women 307 (96%) reported at least one recurrence, with 84% (1104 pregnancies out of 1309 Pregnancies) reported to be HG pregnancies. (152).
7. 26.6% patients with hyperemesis gravidarum in their second or subsequent pregnancy admitted to hospital because of hyperemesis gave a history of admission in a previous pregnancy with a similar diagnosis. (10) Incidence of hyperemesis gravidarum in first pregnancy is 0.14% - 1.3% of births (RI 9a)

8e. **A LOWER INCIDENCE OF RECURRENT HG IN SUCCEEDING PREGNANCIES IS ALSO RECORDED**

1. 26.6% patients with hyperemesis gravidarum in their second or subsequent pregnancy admitted to hospital because of hyperemesis gave a history of admission in a previous pregnancy with a similar diagnosis. (10)

**Summary**

NVP can vary in severity from one pregnancy to the next in the same woman.

(1) (2) (10) (41) (102)

Total: Five references

Symptoms of NVP can recur similarly from one pregnancy to the next in the same woman. (31) (53)

(78) (80) (18)

Total: Five References

There is a 50-66% chance that symptoms of NVP will be similar in succeeding pregnancies. (9) (50)

(Barnie-Adshead, not published) (18)

Total: Four References

In seven recent references the recurrence rate of HG for succeeding pregnancies in the same woman is recorded between 70% and 80%. (113) (121) (122) (145) (148) (152) (10)

Total: Seven References

9. **HYPEREMESIS GRAVIDARUM**

9a. **INCIDENCE OF HYPEREMESIS GRAVIDARUM (HG)**

The definition of HG varies in the published literature. Fairweather's definition (10) is the one most widely used (i.e in nine studies), which states, persistent vomiting before the 20th week of gestation and of such severity to require hospital admission unassociated with coincidental medical conditions. Other authors have added in their separate definitions of HG, weight loss of more than 5% of pre-pregnancy weight (42), ketosis and/or electrolyte imbalance especially hypokalaemia. (75)

1. 1:150 pregnancies 43 patients with HG 0.66%
2. 0.68% of 12,675 deliveries developed moderately severe or severe vomiting
3. 0.88% of 453 patients with HG
4. 0.39% of births
5. 0.14% of births

C H Peckham (7)

D Reid (1)

J Fitzgerald (9)

D Fairweather (10)

Cleveland, USA 1958-1964

Tokyo, 1961-1969 (10)

- |     |  |   |
|-----|--|---|
| 6.  | 0.32% of births  | Registrar General for Wales and England 1958 (10) |
| 7.  | 0.55% of 363 pregnancies   | R Gadsby (50)                                     |
| 8.  | 0.54% of 82 patients in HG   | R Chin (26)                                       |
| 9.  | 0.3% of 3,068 women with HG  | B Kallen (29)                                     |
| 10. | 0.3% of pregnancies: 30 women with HG  | Fischer-Rasmussen (36)                            |
| 11. | 0.35% of pregnancies: 46 women with HG   | I Tsang (61)                                      |
| 12. | 0.63% of live births: 164 women with HG  | A Bashiri (64)                                    |
| 13. | There seems little doubt severe vomiting during pregnancy is now relatively uncommon with an incidence probably as low as 0.1% | D Fairweather (10)                                |
| 14. | 0.3% of 1,453 women with singleton pregnancies   | R K H Chin (63)                                   |
| 15. | 0.79%, 1,027,213 births. 8,186 were preceded by hospital admission for hyperemesis gravidarum                                  | J Askling (66)                                    |
| 16. | 0.52% treated for HG, 86 with HG in study population of 16,398   | M A Klebanoff (20)                                |
| 17. | Thirty-nine women had been hospitalised because of HG (1.3%). 2906 women in the study population reported NVP                  | B Kallen (132)                                    |
| 18. | 0.9% of women had HG in first pregnancy. 547238 Norwegian women in study   | Trogstad (148)                                    |

In 17 references range 0.14% - 1.3% of births.

9b. **TIME FROM LMP UNTIL ADMISSION TO HOSPITAL DUE TO HYPEREMESIS GRAVIDARUM**

1. The peak incidence of admission for hyperemesis gravidarum is between 8-12 weeks, (57% of the total 217 women), while only 5% were admitted before eight weeks of gestation. (10)
2. Time of admission to hospital varied from 4 weeks to over 20 weeks, the average being 10.4 weeks. 71% of patients were under three months pregnant. 43 patients in study. (7)
3. Mean gestational age at initial admission to hospital was  $11.1 \pm 3.9$  weeks in the severe hyperemesis gravidarum group and  $9.5 \pm 2.6$  weeks in the mild hyperemesis gravidarum group ( $P < 0.5$ ). 98 women with severe hyperemesis gravidarum. 40 women with mild hyperemesis gravidarum in study. (62)
4. 86 women admitted to hospital with hyperemesis gravidarum. Gestation on admission.

Weeks	Number of Patients
<6	1
6-10	41
10-14	31
14-20	9

(26)
5. Admission to hospital in weeks from LMP.

Weeks	Total	Percentage
4-8	18	20.7%
8-12	50	57.5%
12-16	10	11.5%
16-20	1	1.1%

(69)
6. Mean week for first admission for hyperemesis gravidarum week 10. 25 women with HG in study. (94)

7. 50 women with hyperemesis gravidarum divided into two groups. 25 women in each. Gestational age at first hospitalisation in weeks.  
Group A ( $11.2 \pm 3.17$ )                      Group B ( $11.5 \pm 2.96$ )                      (105)  
Patients were admitted to Groups A or B according to the different treatment they received.
8. 46 women admitted to hospital with hyperemesis gravidarum. All diagnoses were made prior to 13 weeks gestation, range 6-13 weeks. Mean = 9 weeks. (61)
9. The mean gestational age for admission due to hyperemesis gravidarum was  $11.0 \pm 2.7$  weeks for 56 women in Group A and  $10.8 \pm 2.7$  weeks in 54 women in Group B. (116)  
Patients were admitted to Groups A or B according to the different treatment they received. (116)
10. Mean gestational age for admission to hospital with hyperemesis gravidarum  $8.7 \pm 0.7$  weeks. 10 patients. (117)
11. Women with hyperemesis gravidarum weight loss of more than 5% and severe enough to require admission to hospital in accordance with the criteria of Fairweather gestational age  $10.2 \pm 2.3$  weeks, n = 8. (134)
12. The average gestational age of first treatment for HG = 8.6 weeks. (152)

**Summary:**     Mean weeks for hospital admission for hyper emesis gravid arum are 10-11 weeks from LMP.

9c.     **LENGTH OF STAY IN HOSPITAL FOR HYPEREMESIS GRAVIDARUM PATIENTS**

1. Forty-six patients with hyperemesis gravidarum. Mean hospital stay 1.8 days, range 1-10 days. (61)
2. It will be noted that nearly half of the patients were discharged in a week or less and that over two-thirds were well enough to go home by the tenth day, leaving less than one-third who were under treatment for more than 10 days. (14)
3. Average hospital stay 12.8 days per patient, 89 women with HG admitted to hospital. (69)
4. The majority of hyperemesis patients failing conservative therapy, stay 5 to 9 days in hospital and are then discharged to a home total parenteral nutrition programme. (73)
5. 50 women with HG divided into two groups of 25. Besides usual treatment one group received Diazepam 10mg bd by iv infusion then 5mg bd for 7 days. The mean hospital stay was shorter in the Diazepam group.  $1.5 \pm 1.9$  v  $5.6 \pm 1.6$  days. (105)
6. Annually in the United States more than 50,000 women are hospitalised with the diagnosis of hyperemesis gravidarum, with an average hospital stay of 4 days per patient.  
Paper dated 2000. (106)
7. There was no significant difference in the average total length of hospital stay between Group A ( $9.4 \pm 5.8$  days) and Group B ( $7.2 \pm 5.8$  days). Both groups HG; Group A n = 30, Group B n = 34. Group A weight loss > 5% of pre-pregnancy weight. Group B maintained at least 95% of their pre-pregnancy weight. (42)
8. Length of stay in hospital for various pregnancy related conditions for women who had a live birth n = 3003. Hyperemesis Gravidarum 337 women.  
Mean length of stay 3.0 days. (128)
9. 1825 women in study. Among the 84.4% of hospitalisations for which length of stay was known, the median length of stay for hyperemesis gravidarum was 3 days. (129)
10. Of 109 women with hyperemesis gravidarum, 39 (28%) were admitted on multiple occasions. The average length of stay was slightly longer for the women admitted on

multiple occasions.  $5.5 \pm 6.0$  v  $4.2 \pm 2.4$  days  $P < 0.05$ . (33)

11. Mean length of stay in hospital for 130 pregnancies 3.7 days. (150) after treatment with metoclopramide and diphenhydramine combination.

**Summary:** The average length of stay in hospital for HG is between 3 and 4 days.

9d. **RE-ADMISSIONS TO HOSPITAL DUE TO HYPEREMESIS GRAVIDARUM**

1. 25% of patients required re-admission to hospital due to recurrence of symptoms, but the author goes on to say that some patients may have been discharged originally too soon. (10)
2. 360 women during 12 years, 1925-1936. Were admitted to wards because of vomiting that seems intractable enough to require hospitalisation. 29 (8.0%) readmitted one or more times because of recurrent symptoms. (14)
3. Of 140 patients with hyperemesis gravidarum, 70 (50%), were admitted on only a single occasion accounting for 32% of the 320 admissions. 39 (28%) were admitted on multiple occasions and were responsible for 51% of admissions ( $2.9 \pm 1.1$  admissions per patients range 2-6). 31 patients were lost to follow-up or elected to have a therapeutic abortion. (33)
4. 42 women with hyperemesis gravidarum, 29 were admitted once (69%), 13 were admitted twice or more (31%). (76)
5. 25% (10); 28% (33), 31% (76) of women were readmitted to hospital on one or more occasions due to HG. In about 25% of women, the condition recurs when treatment is stopped. However, oral methylprednisolone treatment does reduce the need for readmission to hospital for HG. (99)
6. Evaluation of efficacy of methylprednisolone (MSPS) versus placebo (PCO) in HG. 14 women in MPS group. 11 in PCO group. MPS group 12, 4mg tabs for 3 days then 10 day taper decreasing 1 tab per day. Recurrence of vomiting after randomisation occurred in 4 (29%) and 8 (73%) MPS and PCO respectively.  $P = 0.05$ . Readmissions for repeat treatment occurred in 1 (7%) MPS and 4 (36%) PCO respectively. A short course of MPS in patients with HG decreases the likelihood of a recurrence of vomiting and readmission for HG. (94)
7. A randomised controlled trial comparing oral methylprednisolone (M) and oral promethazine (P). 40 patients enrolled over 11 months, 20 in each group. M = 16mg, P = 25mg three times daily, both for 3 days. M tapered over 2 weeks, P dose maintained unchanged for two weeks. Patients who continued to vomit after 2 days had study medication discontinued. 3 in group M and 2 in group P failed treatment. No women in M group but 5 in 17 (29.4%) in P group were readmitted for HG within 2 weeks of discharge. ( $P = 0.0001$ ). (95)
8. Re-admission to hospital due to recurrence of HG 19.2% after treatment with metoclopramide and diphenhydramine combination. 130 pregnancies study. (150)
9. The number of women requiring a second admission due to renewed symptoms was less in the Diazepam group, 4% than the other group, 27%. The difference was significant. 50 women with HG. (105)
10. The length of stay in hospital and the number of admissions required are not good indications of the severity of the condition. (28)

11. Of the 19 (35%) of women in each group, Group A and Group B who needed readmission to hospital, 11 in Group B and 8 in Group A were readmitted within 2 weeks of their first admission. (116)
12. It has been found that patients have a high relapse rate if they are discharged too soon. Ideally, the patient should show consistent weight gain and not just cessation of vomiting and re-hydration. (126)

### **Summary**

About 25% of women with HG require readmission to hospital. This percentage is greatly reduced if Methylprednisolone or Diazepam are used for treatment of HG.

#### 9e. **PROMPT RECOVERY AFTER THERAPEUTIC ABORTION OR AFTER DELIVERY FOR HYPEREMESIS GRAVIDARUM AND NVP PATIENTS**

1. 32 patients were subjected to therapeutic abortion. Of those, 23 recovered promptly. (The other nine may have had super-added infection - raised temperature and died). (14) (1938 paper)
2. One patient's condition was so serious as to warrant induction of therapeutic abortion, which was followed by prompt recovery. (7) (1929 paper).
3. NVP goes off immediately (within three or four hours) after termination of pregnancy in over 90% of women whose termination took place usually at 9-10 weeks from LMP (Kumar and Barnie-Adshead - not published). 1980.
4. In those women whose hyperemesis continues throughout pregnancy, the nausea lifts within a minute or two of the placental circulation closing down. (Professor R. Taylor Personal Communication).
5. Patient's statements about cessation of pregnancy sickness.  
 "Symptoms generally disappear as soon as the baby is born or even before I went into labour and ate two cooked meals straight away. After the birth I could eat anything".  
 'Beyond Morning Sickness' by Liz Frazer.  
 Mother and Baby Journal October 2005, Page 42. 11/10/2005.

#### 9f. **THE IMPORTANCE OF HYPEREMESIS GRAVIDARUM IN EARLY PREGNANCY**

1. The hospitalisation ratios for leading obstetric and non-obstetric causes of hospitalisation listed as primary diagnoses. Although pre-term labour was listed most frequently (35%) as the principle diagnosis with a ratio of 4.6 hospitalisations per 100 deliveries, most admissions were not directly labour related diagnoses. Other specific conditions with ratio > 1.0 hospitalisations/100 deliveries were genito-urinary tract infections 1.2, vomiting 1.1. All other conditions have a ratio of <1.0. (119)
2. Hyperemesis gravidarum is the most common indication for hospital admission during the first part of pregnancy and is second only to pre-term labour as the most common reason for hospitalisation during pregnancy. (124)
3. Women who have a live birth, 45,166 in study population, were primarily hospitalised for pre-term labour 24%, hyperemesis gravidarum 9.3%, hypertension 9.1%, kidney disorders 6% and prolonged premature rupture of membranes 6%. (128)
4. Overall 26.8 of women, 1825 women in study population, were hospitalised antenatally. Of the estimated 702 antenatal hospitalisations 44.0% were related to pre-term labour, 10.3% to pre-eclampsia, 5.5% to hyperemesis and 4.7% to urinary tract or

kidney infections.

From conception - 19 weeks gestation, 30.2% of admissions were due to hyperemesis, the highest figure for any condition.

5. Annually in the United States, more than 50,000 women are hospitalised with the diagnosis of hyperemesis gravidarum. (106)
6. Finished admission episodes for a primary diagnosis of excessive vomiting in pregnancy (ICD-9 643, ICD-10 021) NHS hospitals in England 1989/90 - 2003/04. This is based on ICD-9 code 643 for the years 1989/90 to 1994/95 and ICD-10 code 021 for the years 1995/96 - 2003/04.

<u>YEAR</u>	<u>FINISHED ADMISSION EPISODE</u>	<u>YEAR</u>	<u>FINISHED ADMISSION EPISODE</u>
1989/90	8,637	1997/98	16,369
1990/91	9,607	1998/99	17,618
1991/92	11,959	1999/00	17,453
1992/93	12,543	2000/01	19,244
1993/94	13,421	2001/02	19,156
1994/95	14,067	2002/03	20,299
1995/96	14,991	2003/04	22,181
1996/97	14,722		

Source Hospital Episode Statistics (H.E.S). Department of Health 22 Feb 2005.  
Personal Communication. London SE1 6LH

The increase in finished hospital admission episodes for excessive vomiting of pregnancy in England increased by 2 ½ times between 1989/90 and 2003/04.

An approximate estimate of the cost of Hyperemesis Gravidarum to the National Health Service in England for the year 2003/04 may be 22,181 finished hospital episodes multiplied by the estimated cost of each admission at £470 per day, multiplied by the average length of stay in hospital per patient at 3.5 days (item 9c of this review) = **£ 36,481,745**. This figure does not take account of the financial implication of time lost from paid employment for approximately 30% of working women (item 41 of this review) due to severe nausea and vomiting of pregnancy, or the cost of consultations with Midwives and General Practitioners before admission.

7. Finished Admission Episodes of Excessive Vomiting in Pregnancy NHS Hospitals in England. Code ICD-10-021.

#### **Financial Years 2004/05 - 2005/06**

2004 - 2005 23,738  
2005 - 2006 25,685

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There has been an almost three-fold increase in hospital admission for excessive vomiting in pregnancy in England in the years from 1989/90 until 2005/06. The authors of this review consider

the principal cause of this increase to be the lack of early treatment of NVP in England during those years. Similar comments by eight authors (R142a).

Finished admission Episodes of Excessive Vomiting in Pregnancy NHS Hospitals in England. Code ICD-10-201.

### **Financial Year 2006-2007**

2006-2007 25,420

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8. Charges for inpatient management of HG total more than 18 million dollars per year in California alone. California performed 13% of all live births in the U.S.A. in 1999. Thus nationally we can estimate that approximately 200,000,000 dollars is charged annually for inpatient treatment of hyperemesis gravidarum. (149)

### 10. **SYMPTOMS OF NVP IN ANIMALS**

1. It is generally agreed that hyperemesis gravidarum complicates only pregnancies of human beings. Fairweather. (10)
2. Veterinary surgeons and farmers find no comparable vomiting in pregnant animals. (85)
3. Private communication, Royal College of Veterinary Surgeons, Welcome Library, 7<sup>th</sup> December 1971.  
We have checked through various books on reproduction, plus our subject files on periodicals' articles published over the last five years, but we have been unable to find any references to pregnancy sickness in the bitch or in any other animal.
4. Private communication, The Zoological Society of London, N R Brambell, Curator of Mammals, 15<sup>th</sup> March 1972.  
We have not seen vomiting in apes or monkeys here. Whether they suffer from nausea at this time is hard to say, but from their general behaviour we see no signs that might be due to nausea.
5. We searched widely for information on NVP in non-human mammals. We found only suggestive evidence for these species. Female domestic dogs typically exhibit a sharp drop in food consumption during weeks three to five of their nine week gestations (three references). Captive Rhesus macaques also exhibit a decrease in appetite during weeks three to five of their 23 week gestation (one reference). Captive chimpanzees – the pregnant female may initially experience morning sickness and irregularities in appetite (one reference). We were unable to locate any other mention of morning sickness in wild or captive chimpanzees. (86)

### **SUMMARY**

Animals do not suffer from vomiting due to pregnancy.

Total: five references