

NAUSEA AND VOMITING OF PREGNANCY

**CLINICAL INFORMATION ABOUT NAUSEA AND
VOMITING OF PREGNANCY ITS RELATION TO VARIOUS
ASPECTS OF WOMEN'S PERSONAL AND OBSTETRIC
HISTORIES AND OTHER SIGNIFICANT FACTORS
RELATED TO NAUSEA AND VOMITING OF PREGNANCY
OR HYPEREMESIS GRAVIDARUM**

A LITERATURE REVIEW

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THEME WORDS:

NAUSEA VOMITING PREGNANCY HYPEREMESIS GRAVIDARUM

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INTRODUCTION TO A LITERATURE REVIEW OF NAUSEA AND VOMITING OF PREGNANCY

DESCRIBED CLINICAL FEATURES OF NAUSEA AND VOMITING OF PREGNANCY (NVP) AND HYPEREMESIS GRAVIDARUM (HG)

The object of this review is to describe the clinical features of nausea and vomiting of pregnancy (NVP), so that this overlooked, under researched and poorly treated condition can be better understood as a significant medical problem. Using criteria quoted later in this introduction we have culled 159 papers from Medline studies published during the last 35 years under the headings of Nausea and Vomiting of Pregnancy or Hyperemesis Gravidarum (HG) and related papers. NVP has clinical features that can be defined, and NVP can be related to personal and obstetric factors effecting the lives of women during their pregnancies.

The incidence of NVP in normal singleton pregnancies is reported to occur in 73.4% of 39,710 pregnant women. (Review Index RI, 1). Group Literature Review Index references are abbreviated to RI plus number. Individual Review references pages 108-124 are shown in plain brackets.

Nausea is reported in all women who have NVP except for 0.64% who have vomiting alone (RI 3), making nausea the most frequent symptom. 32.0% of 8435 pregnant women had nausea only (RI 2a).

EPISODIC NATURE OF NAUSEA

NVP follows a well-defined episodic pattern. 85% of women with NVP have at least two symptom episodes per day (RI 2b), with 70% of episodes lasting 1-4 hours (50). These episodes of nausea have a consistent daily pattern of timing, frequency and duration during the peak symptoms of each individual pregnancy (RI 2c). Recording the pattern of these episodes using a structured daily diary enables women to predict when they will be able to take nourishment at symptom-free intervals each day.

Severity of nausea in a study of 363 women, 292 of whom had NVP, the mean number of hours of nausea per pregnancy was 56 hours and this symptom lasted for a median of 41 days (almost 6 weeks) (50). In 36% of women who had NVP, the nausea lasted for up to 33 hours per pregnancy, but 21% had nausea which lasted for 100-300 hours and a further 10% from 300-700 hours, a thoroughly distressing and depressing experience (RI 2d).

Vomiting is also a significant symptom of NVP, occurring in 47.1% of 19,330 pregnant women (RI 3a) with about 10% of pregnant women experiencing 40 or more vomits during their pregnancy (RI 3c), but women describe nausea as the more distressing symptom (RI 2e).

Absence of NVP. 25% of 24,322 pregnant women who deliver a singleton normal infant did not have any NVP (RI 6). These papers specifically reported the women did not have any NVP, whereas the pregnant women with no NVP which could be inferred from RI 1 mentioned in paragraph 2 above (26.6%), no NVP was not specifically reported.

ONSET, PEAK AND CESSATION OF NVP

The mean day of onset of NVP is day 39 from LMP. (All day dates that are given in this introduction are measured from the first day of the last menstrual period (LMP)). However 13% of pregnant women start NVP before day 28, which can be the first symptom of their pregnancy. 90% start NVP before day 56, that is the end of week 8 (RI 4). The weeks of peak incidence, that is the weeks when the maximum number of women were experiencing these symptoms, were weeks 7-9. The symptoms rise sharply from week 6 and tail off gradually after week 10 (50). Cessation of NVP was not so well defined as the onset of symptoms (RI 5). The range was 91% of women's NVP ceased by the end of the 16th week in our study (50), but 90% resolved by the 22nd week in another study (80). In our study (50) the mean day of cessation was 84 and occurred at approximately the same day whether NVP began early or late or began severely or mildly, suggesting that possibly a second factor is responsible for the cessation of the condition, a view that is supported by statements of Weigel, M. (31). NVP will stop suddenly in around 30% of women but will taper off gradually after week 12 in the majority (RI 5). About 10% of women find that their NVP symptoms get worse after week 9 (50)

TIME OF DAY OF NVP, MORNING SICKNESS IS THE WRONG NAME FOR PREGNANCY NAUSEA AND VOMITING

Several authors consider the name morning sickness to be inaccurate (RI 7c). Nausea and Vomiting of pregnancy gives a simple, and far better description of the condition. The symptoms only occur exclusively in the morning in about 14% of women who have NVP (RI 7a), a mean figure of five studies, and symptoms occur after midday in approximately 70% of women with NVP (RI 7b). Dilorio (98) makes the relevant statement that continued references to NVP as morning sickness may be confusing for women pregnant for the first time, when they experience the symptoms at other times of the day. Moreover, frustration can ensue when attempts to seek suggestions for relief from healthcare professionals and self-help books lead only to interventions for morning sickness. In addition, if a woman suffers only from morning sickness she does not have the more severe or most severe symptoms of NVP. In fact the name morning sickness may give the impression that NVP only occurs in the morning, and is therefore not a significant problem. One employer of a lady who rang our support line (pregnancysicknesssupport.org.uk) said "if you got up one hour earlier in the morning the condition would be better by the time you came to work". We wish to join the chorus of eight authors in this review asserting that the condition should be called pregnancy sickness or even better, nausea and vomiting of pregnancy rather than morning sickness (RI 7c).

RECURRENCE OF NVP IN SUBSEQUENT PREGNANCIES

Probably one of the questions healthcare professionals will be asked most frequently on the subject of NVP is, “what is the likelihood of similar symptoms of NVP recurring in subsequent pregnancies?” (RI 8). There is surprisingly and disappointingly very little useful information in the literature that sheds light on this problem. There is no doubt that the severity of NVP can vary from one pregnancy to the next in the same individual woman (RI 8a), but that does not answer the question. The best answer that can be given at present, from our own studies and six other investigations, is that about half to two thirds of women will have similar NVP in successive pregnancies, whether these symptoms have been severe or mild in the previous pregnancy (RI 8c). Obviously this leaves one third to one half of women who will have varying degrees of pregnancy nausea and vomiting symptoms in the pregnancies subsequent to their first. This may mean worse symptoms in subsequent pregnancies after little or no trouble in the first pregnancy, or better symptoms after very troublesome pregnancy sickness in a previous pregnancy. Weigel (31) has stated that the recurrence of NVP pattern is most apparent in women who will have a very low risk of recurrent NVP after infrequent nausea in previous pregnancies. More recent reports suggest that hyperemesis gravidarum has a recurrence rate between 70% and 80% in further pregnancies for the same woman (RI 8C).

HYPEREMESIS GRAVIDARUM (HG)

HG is pregnancy sickness at its most severe. It occurs in about 1% of pregnancies range 0.14% to 1.3% in 16 references (RI 9a). HG develops from NVP in six references (RI 2f). The definition of HG used in nine papers in this review which was written by Fairweather in 1968 states, vomiting occurring in pregnancy starting before the 20th week of gestation, and of such severity to require the patient’s hospital admission, without coincidental medical conditions (10). Other important additions to this definition from various authors include maternal weight loss of more than 5% of pre-pregnancy weight, dehydration, ketonuria, and electrolyte imbalances, most significantly hypokalaemia, and readmissions to hospital for HG (9d). The mean weeks for hospital admission for HG were 10-11 from LMP (RI 9b). The length of stay in hospital for HG varied greatly in different hospitals from 1.8 days to 12.8 days per patient. Annually in the United States more than 50,000 women are hospitalised with the diagnosis of HG with an average hospital stay of 4 days per patient (RI 9c). Readmission to hospital for HG in the current pregnancy again varied for different centres between 8.0% and 31% of patients. After a therapeutic abortion recovery from HG occurred promptly (RI 9e) and after delivery the nausea lifts within a minute or two of the placental circulation closing down (RI 9e).

The importance of Hyperemesis Gravidarum is shown by the incidence of Finished Admission Episodes of Excessive Vomiting in Pregnancy NHS hospitals in England, Years 2004/2005 to 2005/2006 - Hospital Episode Statistics 2004/5 23,738; 2005/6 25,685. “Copyright © 2007 re-used with permission of the information centre. All rights reserved” (RI 9f). When compared to a similar figure for the year 1989/90 of 8,637 finished admission episodes for excessive vomiting in pregnancy shows a nearly threefold increase. The authors of this review agree with eight authors (R142a) and suggest the most significant cause of this increase is the lack of safe pharmacological treatment given for NVP in early pregnancy in England during those years 1989/90 to 2005/6 (RI 42a).

The estimated cost of treating Hyperemesis Gravidarum in 2003/4 by the National Health Service in England 36,481,745 pounds. In California alone the estimated cost of treating Hyperemesis Gravidarum was 18 million dollars in 1999 and in Canada from the perspective of society Hyperemesis Gravidarum cost approximately 653 Canadian dollars per woman week in 2007 (three references RI 9f).

COMPARISON OF NVP WITH VARIOUS FACTORS IN WOMEN'S OBSTETRIC AND PERSONAL HISTORIES

110, marked in references with an asterisk, of the 159 papers assembled in this review relate symptoms of NVP to significant factors in women's personal and obstetric histories, including the findings of our own study (53). The results from each group of papers can be conflicting so that they do not give a definitive answer for the subject, for example, the woman's age did not relate to NVP in 11 references, whereas women of younger age (up to 26 years) were more likely to have increased NVP in another 11 references (RI 18). O'Brien (48) suggests that discrepancies in results of research findings for NVP may be accounted for by the method used to investigate NVP. In this respect, Chin (63) reporting on the symptoms of NVP, states recollection of symptoms and events may be inaccurate. Weigel (78) writes, differences among previous studies of NVP may be due to the following:- population differences; methods of selection; different classification system for NVP and for foetal outcome; or failure to control confounding variables.

The studies used in this review for comparing NVP with various factors in women's personal and obstetric histories do have different methodologies, particularly two. First, the mean time from LMP that information was first collected, the majority of studies collect retrospective information, relying upon memory which is imperfect. Secondly, the method of grading symptoms of NVP. The grading of NVP should be specific, one example being the hours of each day nausea lasted which can be accurately measured using a structured daily diary. This will avoid vague grading such as comparing (1) no NVP with (2) nausea only, or (3) nausea and vomiting. We would suggest that future studies/papers should aim to have the following criteria for the comparing of NVP with any other factors. (1) A well-defined basic population with clearly defined limited exclusions. (2) Be prospective rather than retrospective. (3) If retrospective, include the day from the LMP that information was first collected. (4) Specific grading of NVP with the use of a structured daily diary kept by the pregnant woman of her NVP. (5) An initial questionnaire to obtain relevant personal and obstetric information completed with a trained medical professional. (6) An ultrasound scan to confirm stage of gestation and the expected date of confinement. (7) Regular follow-up consultations with the medical professional at least once per fortnight until NVP symptoms have ceased for two weeks, and thereafter the facility for further contact to be made if NVP recurs. (8) A post-natal questionnaire completed by the medical professional from hospital or community medical records, confirmed by an interview with the infant's mother. (9) The use of modern statistical methods.

A similar problem of methodology can arise with the studies of Hyperemesis Gravidarum. Here the first problem is the definition of HG. Some papers do not define HG, indeed the diagnosis may only be severe vomiting (66). When multi-centre information concerning women with HG are brought together into one study, the diagnosis of HG did vary considerably between centres (29). The definition used by Fairweather and modified by other authors quoted in RI 9 may be acceptable. Four authors have compared mild HG and severe HG. Mild HG referred to those women simply admitted to hospital with HG. Severe HG was defined as admission to hospital accompanied by either loss of more than 5% of pre-pregnancy weight (42) or one of the following:- ketonuria, electrolyte disturbances (28) (62), or single compared to multiple admissions for HG in the current pregnancy (33). The other standard criteria for the comparison of HG with any other obstetric or personal factor should be the same as those for a NVP study.

These suggested criteria for comparison of NVP with any other obstetric or personal factor have only been completed by two authors in this review. However, all the information obtained throws some light on the specific subject being studied. Therefore, the information should not be ignored but used profitably, especially where a majority report the same result. We agree with the statement of Pettigrew “A stainless steel law of systematic reviews also generally applies that is, the more rigorous the review, the less evidence there will be to prove a point”. (111)

The objectives of the studies in this review were either to find some clues to the aetiology of NVP, or to find an association between NVP with conditions that might arise later in pregnancy or at its outcome. In the summary of results of references in this review (RI 44) the probability of NVP was found to be independent of (not related to) a woman’s marital status (RI 11), a wanted or unwanted pregnancy (RI 12), her ethnic origin (RI 13), pre-pregnancy motion sickness (RI 15), alcohol consumption (RI 17) although there are well known dangers to the foetus for women drinking alcohol during pregnancy, maternal age (RI 18), parity (RI 19), women’s initial body weight (RI 20), pre-pregnancy diabetic state (RI 22), pre-eclamptic toxemia in the current pregnancy, delivery before 37 weeks (RI 30), birth weight of the baby (RI 32), and any specific fetal abnormality (RI 35).

The probability of NVP or HG was higher (or greater) (RI 44) when the woman had NVP in a previous pregnancy (RI 1, 8b, 8c) was a non-smoker (RI 16), had nausea when previously taking an oral contraceptive (RI 21), with a hydatidiform mole (RI 24), with a twin pregnancy (RI 33), with an increase of food cravings (RI 37) and aversions (37a) and with excessive caffeine intake (RI 38). The probability of NVP was lower (the only negative association) for spontaneous abortion (RI 26). However, the present review has shown that 25% of women who have a normal singleton delivery also have no NVP (RI 6). Therefore, the absence of NVP should not be viewed as a negative consideration for the outcome of a pregnancy. On the other hand, provided a hydatidiform mole or twin pregnancy are excluded by an ultrasound scan, the presence of NVP, even severe NVP or HG may be viewed as an encouraging sign for a successful outcome of the pregnancy.

Hyperemesis Gravidarum alone, but not NVP other than HG, was associated with a three-fold increased risk of HG when the woman's mother had suffered from HG (RI 14) with young age, up to 25 years (RI 18), nulliparity (primiparity in earlier papers) (RI 19), a previous unsuccessful pregnancy (abortion, stillbirth or neo-natal death) (RI 25), reduced maternal weight gain in the current pregnancy (RI 27) and a reduced sex ratio (female excess) of offspring (RI 31). It is difficult to explain the reason that only HG should be associated with these pregnancy related subjects but it may be of interest to the clinician. Severe HG, included loss of 5% or more of pre-pregnancy weight or multiple admissions for HG, can be associated with intra uterine growth retardation (RI 29), reduced birth weight of the baby (RI 32), but not with delivery before 37 weeks of gestation (RI 37).

OTHER SIGNIFICANT INFORMATION RELATING TO NVP AND HG

Natural Ways to Improve NVP

Eating during nausea free episodes, which can be anticipated by using a structured daily diary, especially eating immediately she feels hungry, or nibbling food even if she feels nauseous. Nausea improved after eating in 55% of women and improved after frequent small meals in 61% of women (RI 39). The usual advice of small meals often is still important but eating as soon as the nausea goes off is even more relevant. Stop eating as soon as she feels full, don't eat the last crust. Let them eat their cravings, for women with severe NVP will still have cravings (RI 37), or whatever she fancies with certain important exceptions such as pâté, liver, soft cheeses, under cooked eggs and peanuts. Whether she can eat or not encourage plenty of drinks in small frequent quantities avoiding all alcoholic drinks or more than a total of 3 cupfuls of either tea or coffee per day (RI 38).

Rest (RI 39) The experience of ladies with severe NVP shows that rest, lying down to avoid positional changes especially after meals or when feeling nauseous is the second most important way of naturally relieving the nausea.

Minimising all odours (RI 39 & RI 40) is also so important for her. Associated with her nausea increased or altered olfactory sensation (sense of smell) is her problem (RI 40). The most troublesome odours are fried or fatty cooking smells and other cooking odours. Even usually inoffensive odours such as perfumes or deodorants can be most troublesome. Some women experience increased sensitivity to many different odours causing them to make statements such as "I can smell odours in a room nobody else can smell". (RI 40)

Adverse effects of severe NVP on the quality of women's lives. As yet no acceptable method for analysis of descriptive papers has been identified. Therefore, all the papers describing the clinical features of NVP (RI 1-9), the time lost from work (RI 41) and the adverse effects of the mother-to-be's quality of life (RI 42) and early treatment of NVP is advisable (RI 42a), were accepted for analysis. Certainly the studies related to these two latter subjects are retrospective, sometimes the severe symptoms occurred a long time earlier, and may be considered subjective depending upon the woman's reaction to her NVP. These studies also contain the reports of a selected group of women suffering from the more severe symptoms of NVP. Nevertheless, they are significant because they give a relevant picture of the adverse effect NVP has on the mother-to-be's lifestyle, a most important but often neglected subject.

These women with severe NVP reported the following adverse effects to their lives (RI 42), 52% said they felt depressed always or most of the time; 40% said NVP had an adverse effect on the relationship with their partner; 50% of women feared that NVP would harm their baby. Even mild to moderate NVP caused depression most of the time in 21% of women (RI 42). NVP can impose substantial lifestyle limitations on pregnant women, interfering with cooking, shopping and interaction with their children (81). Severe NVP caused 14% of women to state they would be less likely to consider having more children (91), and 25-59 legal abortions per year in England and Wales from 1979 to 1992 were performed due to “excessive vomiting of pregnancy” (100). This figure in 2002 - 2006 was less than 10 annually in England (R142). The authors of eight studies have stated that the time lost from work due to NVP is significant (RI 41), in fact it has been estimated that 8.5 million hours per year in England and Wales are lost from paid employment due to pregnancy nausea and vomiting (50) (RI 41). Early treatment can prevent more serious complications including hospitalisation (115)(124) (RI 42a).

These facts and figures show the distress nausea and vomiting of pregnancy can cause. NVP is an under-researched and poorly treated condition. Further investigation into its aetiology, and safe effective treatment which is currently available, and extensively used in Canada, please see our website www.pregnancysicknesssupport.org.uk given early in the condition (R142a), can be of great benefit to women suffering from NVP.

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

- | | | |
|-----|---------------------------------------------------|---------------------------------------|
| 1. | 57% of 100 pregnancies | GG 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 NVP | 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%	1453	(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%	3675	(132)

Total number of women in ten references: 8435.

Total number of women with nausea only: 2639.

Percentage of women who had nausea only: 32%

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

2b. EPISIODIC 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) Research article.
6. When nausea is at its worst 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 of nausea the percentage of all episodes which lasted four or more hours was calculated for each woman for each week. Week 9 (from LMP) 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. (50)
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.
10. Nausea at group time 1n = 306 gestation age approx. 9 weeks and group time 2n = 231 gestation age mean 12.8 weeks. 30-40% experienced nausea either all the time or more than once per day. (156)

Summary

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

Pooled Population in 4 studies 934 women.

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 has 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) 160 women in study
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. 4 references pooled population 496 women.

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). 160 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.

Item 2d continued....

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**

Hours of Nausea	Total No. Of Women	Percentage of Total With Nausea
0.1 – 16	57	19.5%
<u>16.1 – 33</u>	<u>48</u>	<u>16.3%</u> 35.8%
33+ - 66	58	19.7%
<u>66+ - 100</u>	<u>37</u>	<u>12.6%</u> 32.1%
100+ - 199.9	45	15.3%
<u>200+ - 299.9</u>	<u>18</u>	<u>6.1%</u> 21.4%
300+ - 399	11	3.75%
400+ - 499	5	1.7%
500+ - 599	7	2.3%
600+ - 699	3	1.0%
700+	<u>3</u>	<u>1.0%</u> 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)

8. In about 35% of women who have NVP the nausea and vomiting are clinically significant resulting in lost work time and negatively affecting family relationships. (160)

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 47% 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
4377 women in 7 studies.

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. 55% of women with NVP find their nausea is improved by eating food. (RI 39) 8 references with 2254 with NVP, 1248 nausea improved after eating.
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)
5. Increased nausea may be associated with greatly increased olfaction, even, for example when no one else can detect a noticeable odour in the room.
Personal communication to Bernie-Adshead RI 40.

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
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) |
| 14. Group time 1n = 306 gestational age approx. 9 weeks
and group time 2n = 231 gestational age 60% of women
did not vomit. | Swallow (156) |

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%.
A further 62 women vomited at least once per week.
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%.
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 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 ($r \pm 0.53$ $P < 0.001$). 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 in pregnancy. Pooled population in 3 studies 554.

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%

Pooled population in 3 studies 1777.

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 ± 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)

Pooled population 2092 women in 7 studies.

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%.

ITEM 4, continued....

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)
Pooled population in 7 studies 2036 women.

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)

ITEM 4e, continued....

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 gradual after week 10. (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)

TAIL OFF OF NVP

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)
9. When comparing group time 1n = 306 gestation approx. 9 weeks with group time 2n = 231 gestation time mean 12.8 weeks a significant reduction was noted in severity of reported nausea. No significant difference in vomiting was noted. (156)

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)

Pooled population of 9 studies 6729 women.

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

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

Summary

Pooled population in 9 studies 3125 women

Mean week for cessation of NVP end of week 12 (50); by the 14th week (80) or by the 13th week. (23) Pooled population 738

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)

ITEM 5, continued....

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 12-14 weeks mean day 84 (50).

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

	<u>Reference Number</u>
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	(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**

1. 19% of sufferers complained of NVP confined to the morning (500 women in the survey). (27)
2. 17% of women with nausea reported the symptoms occurred exclusively in the morning. 10% reported that they never had symptoms in the morning. This survey disputes the concept of morning sickness. 1,000 women in the survey. (40)
3. 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)
4. In a group of 80 women only 10% experienced predominantly morning sickness.
Barnie-Adshead 1978 (not published)
5. 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)
6. 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)

ITEM 7b, continued....

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) 5432 women in study
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) 42 women in this study

NVP most commonly occurs before and after midday.

(50) (27) (23) (17) (40) (Barnie-Adshead) (80) (19) (86) (103) (98) (102) (112)

Thirteen References

Pooled population in 13 studies 7904 women.

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) 500 women
2. In this study only 4% of women had only morning sickness. The episodic nature of pregnancy nausea and vomiting is rarely described. Perhaps a more appropriate description of the condition would be episodic daytime pregnancy sickness. (50) 363 women
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) 1000 women
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) 160 women
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) 5432 women
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) 19 women
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) 27 women

Summary

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

Eight References

Pooled population in 8 studies 7581 women

Item 7, continued....

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 nausea and vomiting 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 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)

Summary

Total number of women who vomited, 396. Number of women who vomit before midday, 166. Vomiting occurred in 42.6% before midday, 57% after mid-day.

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. 547,238 singleton pregnancies registered with their first and second deliveries between 1967 and 1998. Norwegian women. (148)

Item 8, continued....

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)

Summary Total 818 women in 4 studies

8d. **RECURRENCE RATE OF HYPERMEMESIS GRAVIDARUM IN SUCCEEDING PREGNANCIES 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 1st pregnancy (n = 4796) 15.2% developed HG in their 2nd pregnancy. Women without HG in their 1st pregnancy 0.7% developed HG in 2nd pregnancy. A woman is 26 times more likely to have a recurrence of HG in 2nd pregnancy if she had HG in her 1st pregnancy than the woman who did not have HG in her 1st 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 pregnancy is 0.14%-1.3% of births (RI 9a).

Summary Pooled population in 6 studies 7038 women.

Item 8, continued....

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% C H Peckham (7)
2. 0.68% of 12,675 deliveries developed moderately severe or severe vomiting D Reid (1)
3. 0.88% of 453 patients with HG J Fitzgerald (9)
4. 0.39% of births had HG D Fairweather (10)
Cleveland, USA 1958-1964
5. 0.14% of births had HG in one centre Tokyo, 1961-1969 (10)
6. 0.32% of births had HG Registrar General for Wales
and England 1958 (10)
7. 0.55% of 363 pregnancies had HG R Gadsby (50)
8. 0.54% of 82 patients with HG R Chin (26)
9. 0.3% of 3,068 women had HG B Kallen (29)
10. 0.3% of pregnancies: 30 women had 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 had HG 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 18 references range 0.14% - 1.3% of pregnant women suffered from HG.
Pooled population 13,489 pregnant women had HG.

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 ± 3.9 weeks in the severe hyperemesis gravidarum group and 9.5 ± 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 ± 3.17) Group B (11.5 ± 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 ± 2.7 weeks for 56 women in Group A and 10.8 ± 2.7 weeks in 54 women in Group B. 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 ± 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 ± 2.3 weeks, n = 8. (134)
12. The average gestational age of first treatment for HG = 8.6 weeks. 1224 women with HG in this study (152).

Summary: Mean weeks for hospital admission for hyperemesis gravidarum 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 ± 1.9 v 5.6 ± 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 ± 5.8 days) and Group B (7.2 ± 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 ± 6.0 v 4.2 ± 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 ± 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 in study. (150)

Item 9d, continued....

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.
6. Post termination some women expressed a lingering depression and anxiety, although nausea was usually reported to disappear quickly. One woman stated that her symptoms of NVP were completely resolved upon waking after her termination. (145)

9f. **THE IMPORTANCE OF HYPEREMESIS GRAVIDARUM IN EARLY PREGNANCY INCIDENCE AND COST**

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 ration 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 $26.8 \pm 1.6\%$ 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. (129)
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

Item 9f, continued....

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

“Copyright © 2007, Reused with the permission of the Information Centre. All rights reserved”. 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)
9. From the perspective of society the total cost per woman week was \$132, \$335, \$653 per woman with mild, moderate or severe NVP respectively. \$ = Canadian Dollars
The majority of cost items (see table 3 of article) showed an increase with increasing severity of NVP. (153)

10. **SYMPTOMS OF NVP IN ANIMALS**

1. It is generally agreed that hyperemesis gravidarum complicates only pregnancies in 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, 7th 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, 15th 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

B. FACTORS IN A WOMAN'S PERSONAL HISTORY RELATED TO NVP OR HG

11. MARITAL STATUS IN RELATION TO NAUSEA AND VOMITING IN PREGNANCY (NVP)

Marital status refers to married or unmarried women only.

1. Marital status has no bearing on occurrence of hyperemesis gravidarum. (10)
Three separate references from 10 and Fairweather's own series.
2. In this group of hyperemesis patients, about 10% of the total were unmarried and this is about the same ratio as the unmarried group bears to the whole clinic (396 patients). (14)
3. Vomiting was not more common in women whose partners were not cohabiting.
4,517 women vomited, 3,502 did not vomit. (18)
4. The correlation between marriage and increased pregnancy nausea was $P=0.013$ which just failed to meet our criteria of $P=0.01$. (363 women). (53)
5. No statistical difference in marital status between the two groups, i.e. those with or without symptoms. (500 women). (27)
6. Marital status was similar for patients with hyperemesis gravidarum, 193 in the study and the general population 13,053. (61)
7. 95.4% of 87 patients with hyperemesis gravidarum were married. (69)
8. The percentage of women married at LMP increasing from the group with no vomiting, to a maximum in the group using anti-emetic drugs. ($P<0.001$). (16)
9. a. Married admission for hyperemesis $870 = 72.6\%$ } Total number of admissions
b. Not married admission for hyperemesis $329 = 27.4\%$ } for HG 1270 (158)

Summary

No association between marital status and NVP.

(10 with three references) (14) (27) (18) (53) ▲ (61)

Total: Six References

More married women have HG (69) (158)

Total: Two References

Married women more NVP (16)

Total: One Reference

▲ P value recorded

12. **WANTED AND UNWANTED PREGNANCIES IN REALTION TO NVP**

1. Women who wanted the pregnancy were more likely to experience NVP than those who did not want the pregnancy. 78 women. (23)
2. Planned pregnancies had a higher incidence of nausea. 1,000 women. (40)
3. Nausea is more prevalent among those whose pregnancy is planned. 1,513 women. (45)
4. Women with wanted pregnancies were more likely than those with unwanted pregnancies to report pregnancy symptoms which include amenorrhoea, morning sickness and breast tenderness. 99 women. (52)
5. The percentage of women with wanted pregnancies is significantly lower among women who report not having NVP than among women who report this complaint. 4,954 women. (16)
6. Women having both nausea and vomiting during the first trimester reported significantly more unplanned unwanted pregnancies than women experiencing nausea only or no symptoms. 86 women. (15)
7. 80% of unwanted pregnancies (25 legal abortions) have nausea, 70% in total study population of 948 pregnancies had NVP. (6)
8. No difference in NVP among planned and unplanned pregnancies. 9,098 women, 4,517 vomited, 3,502 did not vomit. (18)

Summary

Wanted pregnancy more NVP. (23) (40) (45) (52) (16) Total: Five References

Unwanted pregnancy more NVP. (15) (6) Total: Two References

No difference in NVP between wanted and unwanted pregnancies. (18)
Total: One Reference

13. ETHNIC ORIGIN IN RELATION TO NVP

1. Colour and race do not significantly influence the incidence of hyperemesis gravidarum. Three references and the author's own experience. (10)
2. Afro-Caribbean patients (71%) had symptoms of NVP compared to 78.5% of Caucasians. 500 women. (27)
3. The percentage of women who were nauseated was not significantly associated with race, 7,767 women. (51)
4. Racial status was similar for hyperemesis patients 193, and the general population. 13,053 women. (61)
5. 47 Negro women had the same incidence of pregnancy sickness as Caucasians. (Barnie-Adshead, not published).
6. Vomiting compared to non-vomiting was more common in 'Blacks' than 'Whites'. Highly significant. 8,019 women, 4,517 vomited, 3,502 did not vomit. $P < 0.001$. (18)
7. In general it may be said that coloured women are apt to be afflicted more often in hyperemesis than white women of the same social class. 43 women with hyperemesis gravidarum. (7)
8. Low incidence of NVP has been reported among Eskimos and Native African Tribes (Review Article). (24)
9. The incidence of NVP is similar in both Eastern and Western populations. 1,453 women with singleton pregnancies. (63)
10. White ethnicity was associated with increased vomiting. 825 women in study population. (78)
11. Hospitalisations were higher for black than white women for vomiting. White women 1.1 hospitalisation/100 deliveries; black women 1.7 hospitalisation/100 deliveries. Information gained from approximately 274,000 records sampled from 978 hospitals between 1991-1992. (119)
12. Of all the societies available in the Human Relation Area Files (1980) the 30 societies having information on morning sickness, eight (27%) reported no morning sickness. All the geographical areas are represented in the sample of 30 societies. The authors give the reason as a stable diet of maize in these eight societies, rather than genetic make-up of families. (110)
13. Black and Asian Women have less NVP than Caucasians in the 1st trimester of pregnancy. (146).
14. In Norway, Pakistani women have been 3.7 times more likely to report HG than ethnic Norwegians. A larger study showed that women born in Pakistan had more than twice higher risk of developing HG than women born in Norway. 798311 Norwegian, 3927 Pakistani women in study. (151)

Summary

No difference in incidence of NVP with ethnic origin. (10) (27) (51) (61) (B-A) (63)	Total: Six References
NVP more likely in Negros. (18) (7) (119)	Total: Three References
Low incidence of NVP in Eskimos and native African tribes.	One Reference
White ethnicity was associated with increased vomiting. (78)	One Reference
Stable diet of maize associated with no NVP. (110)	One Reference
In Norway Pakistani women 3.7 times more likely to report HG than ethnic Norwegians (150)	One Reference

14. GENETIC FACTORS IN RELATION TO NVP

1. NVP is more than twice more common in women who have monozygotic (one egg) twins than in women who have dizygotic (two egg) twins, which suggests there is a maternal genetic factor responsible for NVP. Information from 2,655 twin pairs who each had a pregnancy. This included 830 monozygotic female, 902 dizygotic female, 459 monozygotic male and 464 dizygotic male twin pairs. (47)
2. There was an association between the women in our clinic suffering nausea and vomiting and their mother having experienced pregnancy sickness ($P>0.0001$). 343 out of 518 said their mother was sick. (40)
3. Women whose mothers had trouble with NVP were significantly more likely to have NVP themselves ($P>0.001$). 363 women in study population. (53)
4. 202 of the women studied whose sisters who had themselves been pregnant. The results show that women whose sisters had been nauseous in pregnancy were statistically more likely to be so themselves ($P<0.001$). The results concerning mothers were similar but narrowly failed to match statistical significance. (27)
5. Whether mothers of the study subjects had had nausea during pregnancy was not related to the study subjects' current experience with nausea and to their scores in the overall nausea index. 160 women in study. (80)
6. Different partners have no impact on NVP. Paternal contribution to placental function does not affect NVP. (142)
7. 28% (348/1224) of participants reported that their mother had experienced severe NVP or HG while pregnant with them. A strong family history of HG (two or more affected relatives) was reported by 109/1224 (9%). 1224 women who completed an online survey administered by the Hyperemesis Education and Research (HER) Foundation www.helper.org between 2003 – 2006. (152)
8. 504 participants reported on the pregnancy history of 721 sisters prevalence of HG (HG specifically mentioned) was 19% 137/721 affected sisters. (152)
9. The risk of hyperemesis for a pregnant woman is three-fold if the woman's mother had ever experienced hyperemesis in a pregnancy. (157)
HG is more strongly influenced by the maternal genotype than fetal genotype, though environmental influences along the maternal line cannot be excluded as contributing factors. (157)

Summary

Women whose mother suffered from NVP more likely to have NVP themselves.

(27) ▲ (40) ▲ (53) ▲

Total: Three References

Women whose sisters had NVP more likely to have NVP.

(27)

Total: One Reference

Maternal genetic factor responsible for NVP. (47) (53) (152)(157) Total: Four References

Mothers' NVP not related to study subjects' experience of NVP. (80)

Total: One Reference

Paternal contribution does not affect NVP. (142)

Total: One Reference

▲ P value recorded.

15. **PRE-PREGNANCY MOTION SICKNESS IN RELATION TO NVP**

1. Women who reported occurrences of travel sickness (n = 131) within 3/12 before pregnancy were more likely to vomit. 1,000 women in study population. Whitehead. (40)
2. Women who generally suffered from travel sickness showed a difference in total hours of nausea which just failed to reach statistical significance at the 0.01 level. The women were asked if they had generally or ever suffered from travel sickness. Those who replied 'generally' had a median total hours of 58 hours of nausea compared to 33 hours for those who did not generally so suffer. (Mann-Whitney U Test P=0.032). This was not true for those who had 'ever' suffered travel sickness compared to those who had 'never' so suffered. P = 0.32. 363 women in study population. Gadsby. (53)
3. There was no difference in emesis rate in patients who suffered from motion sickness in the non-pregnant state compared to those who do not. 90 women in study population. (19)
4. A history of nausea while travelling was unrelated to NVP or intensity of NVP. 160 women in study. (80)
5. However, motion sickness was aggravated during pregnancy in emetic women. (19)
6. What makes NVP worse?. Factors which interfere with the ability to use relief measures for NVP, travel (particularly to work). (109) 19 women in study kept diaries for seven days.

Summary

Women who suffered from pre-pregnancy travel sickness get more NVP.

(40) (53) ▲

Total: Two References

No difference in emesis rate, those who did or did not have

Pre-pregnancy travel sickness. (19) (80)

Total: Two References

Travel sickness worse during pregnancy. (19) (109)

Total: Two References

▲ P value recorded.

16. **NAUSEA AND VOMITING OF PREGNANCY IN RELATION TO SMOKING CIGARETTES IN THE CURRENT PREGNANCY**

1. Smokers had significantly less NVP than non-smokers, 52% versus 79%. 210 patients. (38a)
2. Nausea and vomiting of pregnancy (NVP) reported less frequently by women who were simultaneously both regular smokers and drinkers of alcohol, especially if these habits existed prior to pregnancy. (38b)
3. Non-smokers are statistically more likely to have nausea and vomiting than smokers. 151 of the women studied were smokers, 500 in study. (27)
4. There was a negative correlation between nausea and smoking. 855 singleton deliveries. (6)
5. Women who smoked cigarettes had a lower median number of total hours of nausea compared to women who did not smoke (18 hours versus 45 hours Mann-Whitney U Test P=0.004). 363 women in study. (53)
6. Smoking, and to a lesser extent alcohol intake, are related to a decreased risk of nausea and vomiting. 1,513 women in study. (45a)
7. Women who gave up smoking during pregnancy reported more nausea and vomiting than those who continued to smoke. (45b)
8. Smokers had lower scores than non-smokers for nausea and vomiting. The difference between the two groups approached significance. 100 women in the study. P=0.013. (48)
9. Vomiting more likely to occur in non-smokers. Among women who never smoked, 58% vomited, whereas 46% of current smokers vomited. 4,517 women vomited, 3,502 did not. P<0.001. (18)
10. Women with hyperemesis less likely to smoke in pregnancy. 78 women in study. (23)
11. Women with hyperemesis gravidarum were less likely to smoke during pregnancy (O.R. = 0.6). 419 women with hyperemesis gravidarum. 836 who did not vomit. (22)
12. Of 74 patients admitted with hyperemesis gravidarum, none were smokers. (28)
13. Smoking was not associated with either nausea or vomiting during pregnancy or with scores on the overall nausea index. 160 women in study, 19 smoked cigarettes. (80)
14. A risk factor for taking Meclozine by 16,536 women in the first 12 weeks of pregnancy was not to smoke. Meclozine was mainly taken for NVP. (133)
15. Admission for HG

Smoking during pregnancy

	Number	%	
Yes	261	21.4	Total admission for HG 1270
No	961	78.6	Total women in study 156,091 (158)

Summary

Nausea and vomiting of pregnancy including hyperemesis gravidarum more common in non-smokers. (6) (18) ▲ (22) ▲ (23) (27) (28) (38) ^a_b(45) ^a_b (48) (53) ▲ (133) (158)

Total: Fourteen References

Smoking cigarettes not associated with NVP. (80)

Total: One Reference

▲ P or O.R. value recorded.

Pooled population of pregnant women in 11 studies 29,937

PLEASE NOTE

BERNSTEIN L, PIKE MC, LOBO RA, DEPUE RH, ROSS RK, HENDERSON BE. Cigarette smoking in pregnancy damages placental cells.

Brit J. Obstet Gynaecol 1989;96;92-96.

17. **NVP IN RELATION TO DRINKING ALCOHOL**

1. For non-smokers, alcohol use was unrelated to the occurrence of NVP. 210 women in study. (38)
 - a. Change in alcohol consumption in early pregnancy was unrelated to NVP for smokers and non-smokers alike. 210 women in study. (38)
 - b. For smokers, regular drinking before pregnancy was significantly related to the occurrence of NVP, with less than half of women who smoked and drank regularly in this period reporting NVP. Of the 210 subjects in the study population 72% experienced NVP. (38)
2. Women who were ethnically white, of white-collar or professional occupation and who consumed alcohol prior to conception were at decreased risk of NVP. 825 women in study. (31)
3. There was no correlation between emesis and alcohol use. Roughly three-quarters of the women in the study (102 study population) report no or little alcohol use in pregnancy. (19)
4. Alcohol consumption not associated with NVP or with scores on the overall nausea index. 160 women in study. (80)
5. Alcohol consumption was associated with lower risk of nausea and of nausea and vomiting. 1,513 women in study. (45)

Summary

Alcohol consumption not related to NVP. (38) (19) (80) Total: Three References

Alcohol consumption decreased risk of NVP. (31) (45) Total: Two References

18. **AGE IN RELATION TO NVP**

1. Vomiting compared to no vomiting was more common among younger women. Vomiting present in 69%, 54% and 38% of women aged less than 20, 20-34 and 35+ years respectively. 8,019 women, 4,517 vomited, 3,502 did not vomit. (18) ▲ $P < 0.001$.
2. Younger age was significantly associated with risk of hyperemesis gravidarum (HG). 419 women with HG, 836 women who did not vomit. (22)
3. Younger age is significantly associated with an increased risk of hyperemesis gravidarum. 78 women in study. (23)
4. The incidence of hyperemesis gravidarum is highest in the pregnant women between 21-25 years if age. 15,099 single pregnancies, 86 with hyperemesis gravidarum. (26)
5. The greatest percentage of 87 HG patients occurred between age 21-25 years, 31%. (69)
6. A shift towards younger women in HG. 3,068 women with HG. (29)
7. A negative correlation was noted between the Rhodes INV scores and age, i.e the higher the score, the lower the age. 100 women. (48)
8. Younger women were significantly ($P=0.05$) more likely to be nauseated than older women. 7,767 pregnancies. (51)
9. Hyperemesis gravidarum is more prevalent among younger women. Average age HG 26.6 years. Average age controls 27.7 years, $P < 0.05$. HG 164 women control 209 women. (64)
10. The age of women who do not report morning sickness is significantly higher than in that of women with morning sickness. 6,376 pregnancies, 894 anti-emetics. (16)
11. Younger women experience more severe episodes of morning sickness. 129 women in study. (77)
12. Like others we found that the frequency of NP (nausea during pregnancy) decreased with age. 4,029 women in study. (67)
13. 35 years and older was associated with decreased nausea ($P < 0.05$) and vomiting ($P < 0.001$) in the current pregnancy. 825 women in study. (31)
14. NVP is not related to the patient's age. 855 singleton deliveries. (6)
15. Age is not related to the symptoms of hyperemesis gravidarum, 43 cases of vomiting of pregnancy admitted to hospital. (7)
16. Nausea is not as common in the women between 25-29 years as in the younger and the older age groups. 90 women. (19)
17. Age was found to have no statistical significance as far as comparing those with NVP to those with no NVP was concerned, 500 women, 120 no NVP. (27) ▲
18. The mean age of 46 patients with severe hyperemesis, 26 patients with mild hyperemesis and a control group were not different. 8,802 in control group. (28)
19. There was no significant correlation between the incidence of nausea with age. 1,000 women. (40)
20. No significant correlation between NVP and age. 363 women. (53)

Item 18, continued....

21. Age was similar for those women who developed hyperemesis gravidarum, 193, and the general population. 13,053 women. (61)
22. Greater maternal age did not produce a marked increase in risk of vomiting in the present study. 1,867 women with single live births, 1,666 no vomiting, 201 severe vomiting. (65)
23. Age did not differ among the four groups.
 - Group 1: Those with no symptoms, 361 women.
 - Group 2: Those with nausea but no vomiting. 165 women.
 - Group 3: Those with vomiting. 922 women.
 - Group 4: Those with hyperemesis gravidarum. 5 women.1,452 women with singleton pregnancies. (63)
24. The woman's age was not predictive of nausea and vomiting during pregnancy. 160 women in study. (80)
25. There was a clear cut maternal age effect with a decline in the rate of NVP with age. The major increase in risk occurred in women aged younger than 25 years. 3,675 women in the study. 2,906 reported NVP. (132)
26. Risk factors for taking Meclozine in early pregnancy. Young maternal age. This effect was possibly due to NVP. 16,536 women used Meclozine in the first 12 weeks of pregnancy. (133)
27. Maternal age at delivery
Admissions for HG

	N	%
<20 yrs	153	12.1
20-29 yrs	823	64.8
30-34 yrs	226	17.8
35-49 yrs	68	5.4

Total number of admission for HG (n 1270) (158)

Summary

Women of younger age (up to 26 years) likely to have increased symptoms of NVP particularly hyperemesis gravidarum. 33,939 women in studies.

(18) (22) (23) (26) (69) (29) (48) (51) ▲ (64) ▲ (67) (77) (132) (133)

Total: Thirteen References

(Of this 13, the following refer to HG):- (22) (23) (26) (69) (29) (64)

Women of older age less likely to have NVP or HG (16) (31)(158) Total: Three References

Women's age not related to NVP. 28,258 women in studies.

(6) (7) (19) (27) ▲ (28) (40) (53) (61) (63) (65) (80)

Total: Eleven References

(Of this 11, the following refer to HG):- (7) (28) (61) (63)

▲ P value recorded.

19. **PARITY IN RELATION TO NVP**

1. Vomiting compared to no vomiting was more common among primigravida. 8,019 pregnancies, 4,517 vomited, 3,502 did not vomit. $P = 0.02$. (18)
2. Nulliparity was significantly associated with increased risk of hyperemesis. 419 women with hyperemesis, 836 women did not vomit. (22)
3. Hyperemesis gravidarum. 51 Nulliparous, 30 para 1, 1 para 2. (26)
4. There was a higher proportion of primigravida in the hyperemetic group. 72 hyperemetic women. (28)
5. A shift towards para 1 is seen in hyperemesis. 3,068 women with hyperemesis gravidarum. (29)
6. Nulliparous women reported more severe vomiting or retching symptoms. 100 women in the study population. (48)
7. Less women with hyperemesis gravidarum who were para 3 or greater. 193 women with hyperemesis gravidarum. (61)
8. Hyperemesis gravidarum more prevalent among women with fewer pregnancies. Average number pregnancies HG = 2.8. Average number of pregnancies control $3.60 < 0.01$. Hyperemesis 164, controls 209 women. (64)
9. Primigravida did not produce a marked increase in risk of vomiting in this study. 1,867 women in study. 1,666 no vomiting, 201 severe vomiting. (65)
10. Multigravida suffered from emesis gravidarum at a higher rate than did primigravida. 90 women in study population. (19)
11. Women of higher parity were significantly ($P < 0.05$) more likely to be nauseated than primigravidas. 7,767 pregnancies in study population. (51)
12. 72.4% of HG 'cases' were multipara. 87 women with HG in study, records from 1921-1937 in Baltimore University Hospital. (69)
13. Women who experience morning sickness, 67%, had a greater number of previous pregnancies, 2.0 ± 1.7 , than those who had no morning sickness, 1.4 ± 1.4 . 180 women in study. (104)
14. The woman's parity was not related to NVP. 100 women in study. (4)
15. Incidence of nausea did not appear to be higher in first pregnancy, when white population was considered ($P = < 0.02$). (10)
16. There was no correlation between the incidence of nausea and parity. 1,000 women in study population. (40)
17. No relation between NVP and parity. 363 women in study population. (53)
18. The parity did not differ among the four groups. Group (Gr) 1 No symptoms; Gr2 Nausea only; Gr3 Vomiting; Gr4 HG. 1,453 women with singleton pregnancies in study. (63)
19. Parity not associated with NVP. 825 women in study. (31)
20. The number of previous children of the study subjects was unrelated to the study subjects' current experience with nausea and to their scores on the overall nausea index. (McGill Nausea Questionnaire). 160 women in study. (80)
21. Twenty patients were admitted with hyperemesis gravidarum to Tygerberg Hospital over a 1 year period. Sixty percent of the group were primigravid. (125)

Item 19, continued....

- 22. Women expecting their first baby (parity 0) had a decreased risk of NVP.
3,675 women in study.
2,906 reported NVP. (132)
- 23. Women who used Meclozine in the first 12 weeks of pregnancy, 16,536 were less often of parity 1 (their first child). Meclozine was mainly used for NVP. (133)
- 24. Admission for HG

Parity	n	%
0	618	48.7
≤ 1	652	51.3

Total number of admissions for HG 1270 (158)

Summary

Primigravida (or in more recent references nulliparity) relative to increased NVP.
(18) (22) (26) (28) (29) (48) (125). All seven references refer to HG.
12,596 women in six studies. Total: Seven References

The greater the gravida the less likely to have HG.
(61) (64) ▲
Both references refer to HG.
566 women in six studies. Total: Two References

Multigravida more NVP than primigravida.
(19) (51) ▲ (69) (104) (133)
One of these references refers to HG (69).
24,660 women in five studies. Total: Five References

No relationship between nausea and parity.
(4) (10) ▲ (40) (53) (63) (31) (80)(158)
Of these eight, only (63) refers to HG.
11,848 women in seven studies. Total: Eight References

Primigravida no marked increase in vomiting. (65) Total: One Reference

Primigravida (parity 0) decreased risk of NVP. (132) Total: One Reference
▲ P value recorded.

20. NVP IN RELATION TO WOMEN'S INITIAL WEIGHT

1. Vomiting is more likely to occur in patients weighing 77.1kg (170lbs = 12st 1lb) or more. 8,019 pregnancies, 4,517 reported vomiting, 3,502 did not vomit. (18) ▲ P=0.003.
2. Maternal risk factor is high body weight in hyperemesis. 419 women with hyperemesis, 836 did not vomit. (22)
3. Pre-pregnant weight of the group experiencing no nausea or vomiting was lower than that of the groups with nausea, and nausea and vomiting. 414 women, 44 women had no NVP. (21)
4. No relation between NVP and woman's weight. 363 women in study. (53)
5. Weight was found to have no statistical significance in comparing those with symptoms to those with no symptoms. 500 women in study, 124 had no symptoms. (27) ▲
6. Body mass index was not significantly associated with nausea or vomiting or retching subscales. 100 women in study population. (48)
7. The woman's weight was not predictive of nausea and vomiting in pregnancy. 160 women in study. (80)
8. Our results show small pre-pregnancy body weight is a significant variable for hyperemesis gravidarum during pregnancy. (154) 3350 singleton deliveries in study. Small pre-pregnancy habitus increased the risk of hyperemesis gravidarum. (154)
9. Risk for hospital admission for hyperemesis gravidarum was greater in under-weight than in ideal weight women. No significant association was seen among over-weight women. The risk was decreased among obese women. 24,485 women in study. (155)
10. Pre-pregnancy weight (Kg)
Admissions for HG

	n	%
<60	502	45.5
60-69	279	25.3
70-79	153	13.9
≥80	169	15.3

(60Kg = 9st 4lb)
Total number with HG = 1270 (158)
11. Pregnancy weight in protocol group
HG in 130 pregnancies $66.66 \pm 18.69\text{Kg} = 146.6\text{lbs} - 10.5\text{st}$
And in control treated group for HG pre-pregnancy weight of 99 patients
 $62.74 \pm 10.40\text{Kg} = 138.0\text{lbs} = 9.8\text{st}$
Both groups within satisfactory pregnancy weight. (150)

Summary

Heavier women more likely to have NVP. (18) ▲ (21) (22)
9,688 women in three studies. Total: Three References

No relation between body weight and NVP. (27) ▲ (48) (53) (80) (150)
1,123 women in four studies. Total: Five References

Low initial body weight associated with HG (154) (155) (158)
Total: Three References

21. **NVP IN RELATION TO PREVIOUS NAUSEA WHEN TAKING THE CONTRACEPTIVE PILL**

1. Of those who had taken the contraceptive pill, the ones in whom it caused nausea were more likely to have nausea and vomiting of pregnancy. $P < 0.05$. Study population 500 women. (27)
2. Strong correlation between those who had nausea with the pill and those who had NVP. The patients who did not tolerate oral contraceptives suffered NVP at a considerably higher frequency, $P < 0.001$, and also the longer the duration, $P < 0.01$, was striking. 855 singleton pregnancies. (6)
3. In the present study 33% ($n = 19$) did not tolerate the drugs (oral contraception) for various reasons (nausea, bleeding disorders, weight increases or tendency to depression) and these women showed a remarkably higher frequency of emesis gravidarum. 68 pregnant women in study population. (32)
4. Among the 45 women who reported sickness whilst they had been taking oral contraceptives there was a higher incidence of pregnancy vomiting ($P < 0.05$). 1000 women in study population. (40)
5. Increased incidence of nausea when taking an oral contraceptive failed to reach statistical significance at the $P = 0.01$ level. Differences in the median total hours of nausea found for the group who complained of suffering nausea when taking an oral contraceptive, compared to those who had no nausea with this treatment, was 58.8 hours compared with 35.5 hours (Mann-Whitney U Test, $P = 0.12$). 363 women in study population. (53)
6. A history of nausea while using oral contraceptives was unrelated to NVP or to intensity of nausea scores. 160 women in study. (80)

Summary

Women who reported sickness when taking oral contraceptives more likely to have NVP. (27) ▲
(6) ▲ (32) (40) ▲ (53) ▲ Total: Five References

A history of nausea when taking an oral contraceptive was unrelated to NVP. (80)
Total: One Reference

▲ P value recorded

22. **PRE-PREGNANCY DIABETES IN RELATION TO NAUSEA AND VOMITING IN PREGNANCY**

1. No correlation between nausea of pregnancy and diabetes. 855 singleton deliveries, no record number of diabetics in the study. (6)
2. Vomiting was not more common among diabetics. 4,517 women vomited, 3,502 did not vomit. Number of diabetics not stated. (18)
3. The incidence of impaired glucose tolerance or gestational diabetes mellitus was not different between vomiting and non-vomiting patients. 1,453 patients with singleton deliveries, impaired glucose tolerance 42, gestational diabetes mellitus 14. (63)
4. There was no statistical difference in women with gestational diabetes between those with hyperemesis gravidarum and controls. Hyperemesis 7.9% 13/164; controls 17/209 8.1%. (64)
5. A maternal pre-pregnancy existing diagnosis of diabetes was less frequent than in the 540,660 births in the study when women had used meclizine. 16,536 women 3.0% used meclizine mainly for NVP. (133)

Summary

No difference in nausea and vomiting of pregnancy in pre-pregnancy diabetic women compared to normal controls. (60) (18) (63) (64) Total: Four References

NVP less common in diabetic women. (133) Total: One Reference

GESTATIONAL DIABETES

Total pregnancies in study
No admission for HG
n = 154,821

Total pregnancies in study
Admitted for HG
n = 1,270 (0.82%) (158)

Gestational Diabetes

Total number in study
No admission for HG
3957 (2.6%)

Number admitted for HG
25 (0.63%)

(158)

C. **OBSTETRIC CONDITIONS RELATED TO NVP OR HG**

23. **HYPEREMESIS GRAVIDARUM AS A CAUSE OF MATERNAL MORTALITY**

1925-1936 15 deaths of out 396 cases of hyperemesis gravidarum. (14)

In the whole North West Scotland there were 14 maternal deaths due to hyperemesis gravidarum between 1931 and 1940. There was one such death between 1940 and 1956. (9)

Lupzic Clinic, Pokorny, showed falling maternal mortality due to hyperemesis gravidarum:

1900-1924	2.8%
1925-1936	0.75%
1937-1954	0.28%
1955-1959	0.0%

(10)

Results from the treatment of moderately severe and severe cases of vomiting of pregnancy at the Boston Lying-in Hospital:

Years	Deliveries	Maternal Deaths	Percentage
1930-1933	12,675	7	0.047%
1934-1937	14,600	0	

(1)

In Britain the maternal mortality from hyperemesis fell from 159 per million total births in the years 1931-1940 to three per million total births between 1951 and 1960. (75)

Summary

Maternal mortality due to hyperemesis gravidarum became extremely rare after 1955.

24. HYPEREMESIS GRAVIDARUM AND HYDATIDIFORM MOLE

1. Hyperemesis gravidarum occurred in 26% of patients who had a complete hydatidiform mole, study population not included. (25)
2. 8% of patients, 6 out of 74 with complete hydatidiform mole, presented with hyperemesis gravidarum. (55)
3. 6% of women with hydatidiform mole presented with hyperemesis gravidarum. (Papua New Guinea). 37 women with hydatidiform moles. (56)
4. 23% of 39 women with hydatidiform mole presented with hyperemesis gravidarum (Guadalajara). (57)
5. Three out of 15 patients (20%) with hydatidiform mole presented with weight loss due to hyperemesis. (Barnie-Adshead, 1980, not published).
6. Six out of 40 women (15%) with hydatidiform mole presented with nausea and vomiting. (58)
7. Frequency of most common symptoms occurring prior to evacuation in patients with molar pregnancies (347 patients, 50=14%) excessive nausea and vomiting. (59)
8. Roughly 10% of 196 patients with hydatidiform mole are hospitalised with severe vomiting and weight loss. (60)
9. Hyperemesis gravidarum occurs in nil of 69 patients with trophoblastic disease. (26)

Summary

Hyperemesis gravidarum is more common in hydatidiform moles than in normal singleton pregnancies. (25) (55) (56) (57) Barnie-Adshead (58) (59) (60)
680 moles in 7 references

Total: Eight References

Hyperemesis gravidarum is no more common in trophoblastic disease. (26)

Total: One Reference

24a. NV AND CHORIOCARCINOMA

“Very raised serum and cerebrospinal fluid levels of human chorionic gonadotrophin occur with choriocarcinoma in the absence of nausea and vomiting, provided there are no gastrointestinal or cerebral metastases”. - Personal communication, Bagshawe, K D 1995.

25. **HYPEREMESIS GRAVIDARUM (HG) AND NAUSEA AND VOMITING IN PREGNANCY (NVP) AFTER PREVIOUS UNSUCCESSFUL PREGNANCY (MISCARRIAGE, STILLBIRTH OR NEONATAL DEATH)**

1. In no fewer than 41% of 207 HG patients is there a history of previous unsuccessful pregnancy. In a control population 1,719 cases (13.6%) gave a history of previous unsuccessful pregnancy. (10)
2. Among 2,500 patients evaluated in the general clinic population there were 432 multiparas with previous abortions of whom 229 vomited (53.1%). Among the remaining 2,078 patients, 707 vomited (34%). The difference between these two percentages is statistically significant ($t=7.3$). (3)
3. 86 women with hyperemesis gravidarum: the number of these women having a past history of abortion (24.4%) is much higher than would be expected from the general obstetric population (10%). (26)
4. 27.4% - 52/190 women with hyperemesis gravidarum reported a spontaneous abortion in a previous pregnancy compared to 17.3% 36/209, in the control group ($P<0.05$). (64)
5. Vomiting compared to non-vomiting was not more common among women experiencing prior fetal loss. 4,517 vomited, 3,502 did not vomit. (18)
6. No obvious correlation between emesis gravidarum and a history of previous unsuccessful pregnancy (previous abortion, ectopic pregnancy, etc) was found. 62 women complained of NVP, 28 no NVP. (27)
7. The numbers of previous pregnancies, miscarriages and terminations were not significant comparing those with the symptoms of NVP to those with no symptoms. 500 women, 380 had NVP. (27)
8. No significant association between duration of nausea and previous miscarriage. 363 women, 292 had NVP. (53)

Summary

Increased NVP or HG associated with previous unsuccessful pregnancy.

(10) (3) (26) (64) ▲ Three of these references refer to HG.

Total: Four References

Previous unsuccessful pregnancy not related to NVP. (18) (19) (27) (53)

Each of these references refers to NVP.

Total: Four References

▲ P value recorded

26. NVP IN RELATION TO MISCARRIAGE IN THE CURRENT PREGNANCY

1. The significant relationship between NVP and miscarriage is a reverse one i.e. the more severe the nausea and vomiting the less tendency to abort. 100 women, 11 miscarried. (4)
2. Gravidae who do not experience NVP in the first trimester have higher abortion rates. 1,910 normal births, 27.1% no NVP, 126 miscarriages, 46.5% no NVP. (5)
3. There is a lower frequency of NVP in pregnancies resulting in spontaneous abortion. 855 singleton deliveries, 56 abortions. Frequency of emesis in pregnancies with different outcomes, Infants 70%, Spontaneous Abortions 50%. (6)
4. Hyperemesis gravidarum patients did not have any increased incidence of spontaneous abortion compared with the general obstetric population. (10)
5. Women who do not suffer nausea in early pregnancy experience abortion rates nearly three times as high as gravidas who experience NVP in early pregnancy. 4,277 gravidas. (12)
6. A deficit of prescriptions of anti-histamine (anti-emetic drugs) in women whose pregnancies ended in abortion was found in the Royal College of General Practitioners' Research Unit Outcome of Pregnancy study, conducted between 1967 and 1968, suggesting that emesis gravidarum is associated with a good prognosis for pregnancy. 9,147 pregnancies. (D M Fleming, personal communication).
7. 591 (11.9%) patients used anti-emetics out of a total patient population of 4,954 who had living normal infants, but of 423 women who later had a miscarriage, only 22 (5.2%) used anti-emetics. (16)
8. Among pregnancies carried to at least 14 weeks there were 153 miscarriages (3.4%) among the vomiting group total vomiting 4,517 pregnancies, and 184 (5.3%) among the non-vomiting group, total 3,502 pregnancies in the non-vomiting group. (18)
9. Women with no symptoms of NVP experienced a significantly greater proportion of fetal deaths. 414 pregnancies, 44 women had no NVP. (21)
10. Women with hyperemesis (419) had fewer spontaneous abortions than women who did not vomit (836). 6/419 (1.43%) hyperemesis, 25/836 (2.99%) controls. (22)
11. A statistical re-analysis confirmed the decreased risk of miscarriage associated with gestational NVP. The meta-analysis also revealed that 150 additional possibly unreported studies with contradictory evidence would be required to refute this observed association. Meta-analysis included 7 studies based on 18,464 pregnancies of 17,760 women. (30)
12. The analysis indicated that vomiting was associated with decreased risk of miscarriage ($P < 0.001$) 873 women in the study delivered a singleton birth, 31% had no NVP. There were 32 women in the miscarriage group, 20 (62.5%) had no NVP. (44)

Item 26, continued....

13. 32 women miscarried and were therefore excluded from the main study. Of those 32 miscarriages, 50% were associated with no symptoms of pregnancy sickness, whereas of 363 women in the main study, 19.6%, had no NVP (Gadsby, 1993, not published).
14. The risk of spontaneous abortion was higher in women who were not nauseated at all during pregnancy. 1,553 (a 20% sample of 7,767 pregnancies) singleton live births 29.9% no NVP. 450 miscarriages 41.1% no NVP. (51)
15. In the 164 women in the study with hyperemesis gravidarum the risk of spontaneous abortion was 3.1% compared to a prevalence of 15% in previously reported populations ($P < 0.001$). Thus hyperemesis gravidarum would appear to be a protective factor for spontaneous abortion. (64)
16. 30 women with hyperemesis gravidarum causing a weight loss of greater than 5% of their pre-pregnancy weight had a spontaneous abortion rate of 2 (6.6%) compared to prevalence of 15% in the previously reported populations. (42)
17. Women with spontaneous abortions: 52% nauseated, 46.4% no nausea; 607 women had spontaneous abortions. Controls 1,284 women: 71.7% nauseated; 28.3% not nauseated. (43)
18. For the 160 women who completed the study, 74% reported nausea. Of the 20 who miscarried and for whom data are available ($n=14$), 70% reported nausea. (80)

Summary

There is a lower occurrence or severity of NVP in pregnancies resulting in spontaneous abortion. (4) (5) (6) (10) (12) Fleming (16) (18) (21) (22) (30) (42) (43) (44) Gadsby (51) (64) [▲] (80)
1,863 miscarriages involved in these 18 studies. Total: Eighteen References

MORE DETAILED SUMMARY OF NVP AND HG IN RELATION TO MISCARRIAGE

1. Women with HG have a lower risk of abortion. (22) (42) (64)
- 1a. Women with HG did not have any increased incidence of spontaneous abortion. (10)
2. Increased NVP is associated with less risk of miscarriage. (4) Fleming (16) (30)
3. Increased risk of miscarriage with no NVP. (5) (12) (18) (21) Gadsby (44) (51)
4. Lower frequency of NVP in pregnancies resulting in abortion. (6) (43) (80)

[▲] P value recorded

PLEASE NOTE

On average 25% of women who deliver a single normal infant have no symptoms of NVP. (RI 6)

27. **REDUCED MATERNAL WEIGHT GAIN IN CURRENT PREGNANCY RELATED TO NVP AND HYPEREMESIS GRAVIDARUM**

1. Women admitted repeatedly with hyperemesis have a more severe nutritional disturbance associated with significantly reduced maternal weight gain. 140 patients with HG, 70 admitted on only one occasion, 39 admitted on multiple occasions. 31 patients lost to follow-up. (33)
2. Women with hyperemesis gravidarum tended to gain less weight during pregnancy. 419 women with hyperemesis gravidarum. 836 women who did not vomit. (22)
3. No relation between maternal weight gain and NVP, 363 women. (53)
4. The weight gain during pregnancy for women with no NVP, nausea only and vomiting of pregnancy was not too different. 414 women, 44 had no NVP. (21)
5. Of 555 women in Cohort B (those specially requesting advice regarding the management of nausea and vomiting in pregnancy), 9.3% reported weight loss associated with vomiting in pregnancy. There was a significant correlation between maximal number of daily episodes of vomiting and maximal weight loss ($r=0.25$ $P<0.0001$). Women with one episode of vomiting per day experienced an average of 1.5kg weight loss and those with 10 episodes per day reported a mean weight loss of 6kg. (83)
6. Group A mothers (Hyperemesis Gravidarum with weight loss greater than 5% pre-pregnancy weight) gained 9.6 ± 2.4 kg and Group B mothers (HG with less than 5% pre-pregnancy weight gain) 13.7 ± 3.2 kg. $P<0.05$. (42)
7. The adverse infant outcomes associated with hyperemesis are the consequence of and mostly limited to, women with poor maternal weight gain. (158)
Compared to women without hyperemesis $n=127,835$, infants born to women with hyperemesis and with low pregnancy weight gain <7 kg [15.4lb] $n=144$ were more likely to be low birth weight, small for gestational age (SGA) born before 37 weeks of gestation and have a 5 minute Apgar score of less than 7.
The outcomes among infants born to women with hyperemesis with weight gain of 7kg or more $n=885$ were not different from the outcomes among women without hyperemesis. (158)

Summary

No difference in maternal weight gain in relation to NVP. (53) (21)

Total: Two References

Hyperemesis associated with reduced weight gain. (33) (22) (83) (42) (158)

Total: Five References

28. **PRE-ECLAMPTIC TOXAEMIA IN THE CURRENT PREGNANCY IN RELATION TO NVP OR HG**

1. No correlation between nausea and pre-eclamptic toxemia. 853 singleton deliveries. (6)
2. There is no difference in emesis gravidarum between patients with oedema and those without it. Oedema was reported in 30 patients. In late pregnancy, 5 patients developed proteinuria, 4 of them had suffered from emesis gravidarum in early pregnancy. 102 women in study. (19)
3. There was no association between hours of nausea and pre-eclamptic toxemia in current pregnancy. P=0.89. 363 women. (53)
4. The incidence of pre-eclampsia was not different between vomiting and non-vomiting patients. 3.0% PET with no NVP 361 women. 3.9% PET with vomiting. 922 women. (63)
5. Vomiting was not more common in women with proteinuria 2+ or greater. 4,517 women vomited, 3,502 women did not vomit. (18)
6. It would not appear that patients suffering from hyperemesis have any greater risk of developing toxemia in late pregnancy than does the general obstetric population. (10)
7. There was no significant difference in the incidence of eclampsia in the current pregnancy between women with hyperemesis and controls. 164 women with hyperemesis gravidarum, 209 controls. (64)
8. Even after controlling for chronic hypertension a modest association between severe vomiting and pre-eclampsia was still present. 1,867 subjects with single births. 1,666 had no vomiting, 201 with severe vomiting. Definition of severe vomiting not included. (65)
9. 24 women with eclampsia in 1,379 deliveries, 6 (25%) had hyperemesis gravidarum. Definition of HG not included. (68)
10. Maternal diagnosis of pre-eclampsia was less frequent when the woman had used meclizine. 16,536 women used meclizine in the first 12 weeks of pregnancy. Meclizine was mainly used for NVP. (133)

Summary

Women with pre-eclamptic toxemia no increase in NVP. 23,457 women in 8 studies with NVP
(6) (10) (18) (19) (53) ▲ (63) (64) (133) Total: Eight References

Modest association between severe vomiting and pre-eclampsia. (65)
Total: One Reference

High incidence of hyperemesis gravidarum in eclamptic patients. (68)
Total: One Reference

29. INTRA-UTERINE GROWTH RETARDATION IN RELATION TO NVP OR HG

1. The foetuses of gravidas admitted for hyperemesis gravidarum are not at increased risk for growth retardation. 193 patients with hyper emesis gravidarum. 13,053 pregnant women in the study population. (61)
2. There was no significant difference in the incidence of intra-uterine growth retardation between women with hyperemesis gravidarum (164) and the control group (209). (64)
3. Women with hyperemesis gravidarum causing loss of greater than 5% of their pre-pregnancy weight, Group A (n=30), we compared to women with symptoms of nausea and vomiting but maintaining at least 95% of their pre-pregnancy body weight. Group B (n=34). Baby's growth retardation occurred in Group A. (42)
4. A modest association between severe vomiting and small for gestational age infants was identified in the present study. 201 women with severe vomiting, compared to 1,666 women with no vomiting. (65)
5. 18% of infants in the multiple admissions group were small for gestational age as compared to 7% in the single admissions group. This difference approached but did not achieve statistical significance. (33) A small for gestational age infant was diagnosed on the basis of weight <10% of age using the Brenner growth curve. (33)
6. No significant association ($P<0.05$) of freedom from nausea with intra-uterine growth retardation. 7,767 pregnancies, 2,253 pregnancies with no nausea. (51)
7. Compared to women without hyperemesis n=127,835 infants born to women with hyperemesis and with low pregnancy weight gain n=144 are more likely to be low for gestational age. (158)

Summary

A. Severe hyperemesis gravidarum association with intra-uterine growth retardation.

Total 235 women with hyperemesis. (33) (42) (65) (158)

Total: Four References

B. Hyperemesis gravidarum not associated with intra-uterine growth retardation.

Total 359 women with hyper emesis. (61) (64)

Total: Two References

C. No association between freedom from nausea and intra-uterine growth retardation.

2,253 pregnancies no nausea. (51) ▲

Total: One Reference

▲ P Value Recorded

Severe hyperemesis defined as loss of greater than 5% of pre-pregnancy weight or multiple admissions to hospital for HG.

30. **LENGTH OF PREGNANCY < 37 WEEKS IN RELATION TO NVP OR HG**

1. Women experiencing vomiting were less likely to experience delivery before 37 weeks. (P=0.004). Women who vomited carried their pregnancies approximately 1.5 days longer on average before and after adjustment. (P<0.001). Total vomiting group 4,517 pregnancies and 3,502 pregnancies in the non-vomiting group. (18)
2. 30 hyperemesis patients mean gestational age of delivery 39.9 weeks. (36)
3. Pregnancy outcomes between hyperemesis gravidarum patients and the general population were similar in the two groups 38 weeks. The percentage of infants born before week 37 of gestation was 22% in the general population, similar to 23% in the hyperemesis group. 193 women with hyperemesis gravidarum. 13,053 pregnant women in study population. (61)
4. Babies of gravidas admitted for hyperemesis gravidarum are not at increased risk of prematurity i.e. < 37 weeks. 138 patients with HG. Mild HG = n 40, 7 delivered before 37 weeks = 17.5%. Severe HG n = 98, 11 delivered before 37 weeks = 11.2%. Controls n = 12,335, delivered before 37 weeks, 1,370 (10.7%). (62)
5. Maturity at delivery the same for patients with vomiting and those with no vomiting. No vomiting 38.9 ± 3.3 weeks. Vomiting 39.4 ± 0.8 weeks. 526 women with no vomiting, 927 women with vomiting. (63)
6. There was no statistical difference in the length of gestation between patients with hyperemesis gravidarum and the control group. Hyperemesis 164 patients 38.8 weeks. Controls 209 patients, 39.1 weeks. (64)
7. All infants of mothers with severe hyperemesis gravidarum (n=9) were 38 weeks or beyond at delivery. (73)
8. Gestational age at birth, 38.7 ± 2.7 weeks. 162 patients treated for HG over three years. (82)
9. The mean gestation at delivery in the three groups (severe HG n=46, mild HG n=26 and controls n=8,802) was not different. Controls n 8,802, 39.4 ± 1.9 weeks. Severe HG n 46, 38.9 ± 2.4 weeks. Mild HG n 26, 39.2 weeks. (28)
10. There were no significant differences in gestational age at delivery, both 39.2 + 39.5 weeks. 64 women with HG n = Group A 30, n = Group B 34. (42)
11. Patients with HG admitted to hospital once or those admitted more than once showed no difference in gestational age at delivery. Single admission n = 70 women, 38.9 ± 2 weeks. Multiple admission n = 39 women, 38.3 ± weeks. (33)
12. No correlation between nausea and pre-term labour. 855 singleton deliveries. (6)
13. NVP not related with length of gestation. 873 women in the study. 69% had NVP. (44)
14. Our observations indicate that nausea and vomiting of pregnancy does not imply an excessive risk of pre-term birth. 309 singleton pregnancies. (13)
15. Moderate increase in somewhat shorter pregnancies, 36-40 weeks, in hyperemesis gravidarum. But not for very short pregnancies (below 36 weeks). The excess for < 38 weeks gestation is statistically significant. (P<0.001). 3,068 women with hyperemesis. (29)

Item 30, continued....

- 16. Pre-term birth occurred at a reduced rate after meclizine use. 16,536 women used meclizine in the first 12 weeks of pregnancy mainly for NVP. (133)
- 17. 17 Patients with hyperemesis gravidarum in the study. Apart from one premature delivery at 33 weeks, all patients gave birth between 38 and 41 weeks of gestation. (125)
- 18. Compared to women without hyperemesis n=127,835 infants born to women with hyperemesis and with low pregnancy weight gain below 7kg [15.4lb] n=144 were more likely to be born before 37 weeks.

(158)

Total: One Reference

Summary

Women with HG or NVP not likely to experience delivery before 37 weeks – Total 19,646 pregnancies with 886 pregnancies with NVP or HG

(6) (18) (28) (33) (36) (42) (44) (61) (62) (63) (64) (73) (82) (13) (133) (125)

Total: Sixteen References

Moderate increase in somewhat shorter pregnancies in hyperemesis gravidarum. (29)

Total: One Reference

There is therefore no association between HG or NVP and premature labour, unless the woman with HG also has low pregnancy weight gain below 7kg (158). One reference.

31. SEX OF NEWBORN IN RELATION TO NVP OR HG

1. No significant difference in emesis rate could be ascribed to the sex of the newborn. 102 women. (19)
2. In all results concerning the outcome of pregnancy, including the male-female ratio of the offspring, the two groups (those with and those without emesis) showed no significant difference. 500 women, 124 had no symptoms. (27)
3. The percentage of women nauseated during pregnancy was 70.1% in those who delivered a boy and 73.3% in those who delivered a girl, a difference that was not statistically significant. 7,767 pregnancies. (51)
4. There was no association between hours of nausea and sex of the baby. 363 women. (53)
5. There was no statistical significance in the gender of the offspring between the women with hyperemesis gravidarum (164 women) and the control group (209 women). (64)
6. In hyperemesis gravidarum there were fewer male infants. 3,068 women with hyperemesis gravidarum. Nearly one million births. (29)
7. There was a significant correlation between participants who later gave birth to girls and the vomiting or retching subscale ($P=0.015$). These women experience more severe vomiting or retching than those bearing male infants. $P<0.03$. The nausea subscale was not significantly correlated with gender of the infant. 100 women in study. (48)
8. There was a significant correlation between women who later gave birth to girls and the vomiting and retching subscale. 66 women with hyperemesis gravidarum. (49)
9. Although the male to female ratio of all births was 51.4/48.6, the ratio among mothers admitted to hospital for hyperemesis gravidarum during the first trimester was 44.3/55.7 $P<0.000001$ compared with all births. 1,027,213 births, 8,816 (0.79%) were preceded by a hospital admission for hyperemesis gravidarum. (66)
10. The occurrence of nausea and vomiting did not predict the sex of the child. 160 women in study. (80)
11. Pregnant women hospitalised for hyperemesis gravidarum in the first trimester had a 50% increased odds of having a female infant compared with controls (OR 1.5, 95% CI 1.4, 1.7). Women hospitalised for three or more days had the greatest odds of having a female infant compared with control women. (OR 1.8, 95% CI 1.5, 2.0). 2,110 women hospitalised for hyperemesis gravidarum. 9,783 pregnant women without hyperemesis gravidarum. (127)
12. Admission for Hyperemesis.

	n	%
Male	578	45.5
Female	692	54.5

Total number of admissions for HG = 1270 (158)
13. One hundred (60.2%) Asian women admitted with HG had female offspring compared with 2311 (48.5%) female babies in our control group who gave birth in 2003 $p=0.004$ O.R. 1.6, 95% CL 1.2 – 2.2. Female fetal sex was significantly associated with high urea and severe ketonuria. (159).

Summary

No association between sex of newborn in mothers with NVP.

(19) (27) (51) (53) (64) (80)

Total: Six References

Infant girls more common when mother has hyperemesis gravidarum or severe NVP.

(29) (48) ▲ (49) (66) ▲ (127) (158) (159)

Total: Seven References

Pooled population 15,430 pregnancies

▲ P Value Recorded

32. NVP OR HG IN RELATION TO BIRTH WEIGHT OF BABY

1. Infants of vomiting mothers were not more likely to be of low birth weight than were infants of non-vomiting mothers in either the crude or adjusted analysis. Birth weight < 2,500g p=0.45, the mean birth weight of infants born to mothers both with and without vomiting was 3,203g. 4,517 women reported vomiting and 3,502 women did not vomit by 16 weeks. (18)▲
2. There were no differences in birth weights between the two groups, those with NVP or those with no symptoms. 62 women complained of emesis gravidarum. 28 had no symptoms of NVP. (19)
3. NVP not related to birth weight. 873 women in study, 602 women (69%) had NVP. (44)
4. No significant relationship was found between infant birth weight and any of the subscales, i.e. nausea, vomiting or retching. Pregnancy resulted in a live birth for 100 women. (48)
5. NVP not related to birth weight. 363 women with normal live singleton deliveries. 292 women had NVP. (53)
6. Our observations indicate that nausea and vomiting of pregnancy does not imply an excess risk of low birth weight. 309 singleton pregnancies. (13)
7. Birth weight, 3,286 ± 659g. 162 patients treated for HG over three years. (82)
8. Birth weights of babies the same for all four groups of NVP. 1,453 women with singleton pregnancy - Gr1 No symptoms; Gr2 Nausea only; Gr3 Vomiting; Gr4 HG. (63)
9. The occurrence of nausea and vomiting did not predict the birth weight of the child. 160 women in study. (80)
10. No difference in birth weight for babies with morning sickness, 3,289 ± 553gms (67%) and mothers with no morning sickness, 3,179 ± 466gms (33%). 180 women in study. (104)
11. There is certainly no suggestion that the patient who suffers from hyperemesis gravidarum is likely to produce an underweight baby. 105 hyperemesis gravidarum cases. (10)
12. Average birth weight of 30 babies delivered to women with hyperemesis gravidarum. Average weight: 3.585 kgm = 7.8 lbs. (36)
13. Pregnancy outcome between hyperemesis gravidarum patients and the general population was similar for birth weight. 193 hyperemesis gravidarum patients, 13,053 women in study population. (61)
14. The mean birth weights were 3.100, 3.093, 3.160 kgms in the mild hyperemesis gravidarum, severe hyperemesis gravidarum and control groups respectively. 40 patients were diagnosed as having mild hyperemesis gravidarum and 98 as having severe hyperemesis gravidarum. 12,335 patients were defined as controls. (62)
15. There was no statistical difference in the average birth weight of the baby between women with hyperemesis gravidarum (164) and the control group (209). 3.1229 kgms hyperemesis gravidarum, 3.1429 kgms control. (64)
16. The birth weights of infants (n=9) with hyperemesis gravidarum attained, and slightly surpassed, the mean birth weight for gestational age. (73)

Item 32, continued....

17. The mean birth weight of the babies in the severe hyperemetic group was significantly lower than in both the mild hyperemesis gravidarum group ($P < 0.05$) and the control group ($P < 0.001$). Total hyperemesis gravidarum patients 74. 48 patients had severe hyperemesis gravidarum, one required termination, one molar pregnancy. 72 hyperemesis gravidarum patients in study population. Control group 8,802 consecutive deliveries. HG classified as severe if one or more of the following conditions was present: Ketonuria 3+ on Ketostix, increase in serum creatinine, electrolyte imbalance or increase haematocrit (> 0.43). (28)
18. In hyperemesis gravidarum increased incidence of low birth weight. 3,068 women with hyperemesis gravidarum in nearly one million births. (29)
19. Women with hyperemesis gravidarum causing a loss of greater than 5% of their pre-pregnancy weight, Group A $n=30$, were compared to women with symptoms of nausea and vomiting, but maintaining at least 95% of their pregnancy weight Group B, $n=34$. Group A babies significantly smaller with respect to birth weight expressed as a percentage for gestational age. (42)
20. Hyperemesis gravidarum. A comparison of single and multiple admissions. Women admitted repeatedly have babies with reduced neonatal birth weights. $2,806g \pm 676g$ compared to $3,071g \pm 477g$. Study population 140 patients, 70 were admitted on only one occasion. 39 women (28%) were admitted on multiple occasions. 31 patients were lost to follow up or elected to undergo a therapeutic abortion. (33)
21. 7.9% of gravidas who did not experience NVP were delivered of low birth weight babies, whereas only 5.6% of the N & V group had low birth weight, significant. 1,910 women experienced no N & V. 5,111 experienced N & V. (5)
22. Low birth weight associated with absence of NVP. 199 women who bore single live children, 72% experienced NVP. (11)
23. A larger proportion of low birth weight infants were delivered of women having no symptoms of NVP. 414 women, 44 women had no NVP (10.6%). (21)
24. Pregnancy outcome of 17 patients with hyperemesis gravidarum. Mean birth weight was $3,176 \pm 539$ gm. All babies weighed > 2500 gm. (125)
25. Compared to women without hyperemesis ($n=127,835$) infants born to women with hyperemesis and low weight gain < 7 kg [15.4lb] $n=144$ were more likely to be low birth weight.

Summary

NVP not related to birth weight of baby. (13) (19) (44) (48) (53) (63) (80) (82) (104)

Total: Ten References

Hyperemesis gravidarum associated with average birth weight babies.

(10) (36) (61) (62) (64) (73) (125)

Total: Seven References

Hyperemesis Gravidarum increased incidence of low birth weight babies.

(18)

Total: One Reference

Severe Hyperemesis gravidarum associated with low birth weight babies.

(28) [▲] (29) (33) (42) (158)

Total: Five References

No NVP associated with low birth weight babies. (5) (11) (21)

Total: Three References

[▲] P value recorded

33. **TWINS IN RELATION TO NVP OR HG**

1. Incidence of hyperemesis gravidarum in single pregnancies (90,153 pregnancies) was 3.58 per thousand. Incidence of hyperemesis gravidarum in twin pregnancies (986 twin pregnancies) 14.2 per thousand. A very highly significant relationship ($P=0.001$) between multiple pregnancy and hyperemesis gravidarum. (10)
2. We certainly have a high incidence of hyperemesis gravidarum among our patients with twin pregnancies, 25.9 per thousand for twins compared to 5.1 per thousand for singletons. (15,099 single pregnancies and 193 twin pregnancies in the study). (26)
3. 2.2 x risk of hyperemesis gravidarum in twins ($P=<0.001$), 118 twin pregnancies in this study. (29)
4. Hyperemesis gravidarum was statistically more common in twin pregnancies. (86 twin pregnancies in the study). ($P<0.001$). (18)
5. In multiple gestations (83 twin and one triplet pregnancies) 73 (86.9%) suffered from nausea and vomiting. This difference between single, as opposed to multiple gestation, is statistically significant ($P=<0.01$). (5)
6. Higher frequency of NVP seen in study for twin pregnancies. Eight twins, seven (87.5%) had NVP. 71% NVP in study population. (6)
7. Of the blacks studied, 24 had twins. 18 (75%) of them maintained that they were very sick in that pregnancy. (41)
8. Twinning rate was increased when the woman had used meclizine. 16,536 women used meclizine in the first 12 weeks of pregnancy. Meclizine was mainly used for NVP. (133)

Summary

Increased incidence of hyperemesis gravidarum in twin pregnancies.

▲ (10) ▲ (18) ▲ (26) (29) ▲

Total: Four References

Increased incidence of NVP with twin pregnancies.

(5) (6) (41) (133)

Total: Four References

} 1498 twin pregnancies in 8 references

▲ P value recorded

* **Being a twin does not make one more liable to NVP. Information from 2,655 twin pairs who have each had a pregnancy. (47)**

34. **PLACENTAL WEIGHT IN RELATION TO NVP**

1. Positive correlation for increased nausea was found with heavier placental weight (P=0.005). 363 women in study. (53)
2. The placental weight of subjects who had morning sickness was higher than those who had none. (P<0.002). 33% of women had no symptoms. 180 women in study. (104)
3. No obvious correlations between emesis gravidarum and placental weight were found. (NVP n=62, no NVP n=28). (19)
4. NVP not associated with placental weight. 873 women in the study, 69% had NVP. (44)
5. There was no difference in placental weight between patients with vomiting and patients with no vomiting. 1,453 formed the study population. 63% vomited, 12% did not vomit. (63)

Summary

Increased nausea associated with heavier placentae. (53) ▲ (104) ▲

Total: Two References

NVP not associated with placental weight. (14) (44) (63) Total: Three References

▲ P value recorded

PLACENTAL PATHOLOGY IN RELATION TO NVP

No statistical difference between women with hyperemesis gravidarum (n=164) and controls (n=209) in terms of placental pathology. (64)

Pathologic reviews of placentas from women receiving total parenteral nutrition with fat emulsions during the study period showed no gross abnormality.

Nine women with hyperemesis gravidarum. (73)

35. **HYPEREMESIS GRAVIDARUM OR NVP IN RELATION TO FETAL ABNORMALITY**

35a. **FETAL ABNORMALITY ASSOCIATED WITH HYPEREMESIS GRAVIDARUM (Six References)**

1. Studies into 60,000 births in Leipzig Clinic found deformed children after hyperemesis exceeded the mean (Noack, 1963). He noted that these observations were made during a period when drugs now suspected of causing deformities had not yet come on the market. From Ref (10)
2. 98 cases of hyperemesis gravidarum, 6.1% deformity. In the same clinic the overall incidence of deformity 0.65%, 1949-56. Mey R. Ref from (10).
3. 165 patients with hyper emesis, 8.3% incidence of deformity. Total births in the same clinic, 0.98% incidence of deformity. 1949-59. Holbein, 1961. Ref from(10).
4. Doring and Hossfeld reported that 4% of infants of 649 women with hyperemesis were malformed, while the control group without hyperemesis (8,422 women) showed only 1.5% malformation rate. 1964. Ref from (29).
5. Fairweather points out that the definition of what constitutes a deformity clouds observations of the incidence of fetal deformity in hyperemesis. 1968. (10)

35b. **SPECIFIC FETAL ABNORMALITY ASSOCIATED WITH HYPEREMESIS GRAVIDARUM**

1. Congenital Dislocation of the Hip (CDH). 6,376 pregnancies in study population, 894 women used anti-emetics. 37 women had babies with CDH and 13 of these took anti-emetic drugs compared to the expected four. (16)
2. Hip Dysplasia. 3,068 hyperemetic women in study population. 60 infants with CDH compared to the expected 47. (29)
3. Undescended Testicles. 2,068 hyperemetic women, 21 infants had undescended testicles. This figure was roughly twice the expected one, but this diagnosis in the newborn period is uncertain. (28)
4. No significant increase in congenital hernia or undescended testicles in the vomiting n=9,255 compared to the non-vomiting group n=7,143. (20)
5. Down's Syndrome. 3,068 hyperemetic women, nine women had a baby with Down's Syndrome. Three times the expected number. (29)
6. Cleft Palate deformity. Peer and Stream reported on 228 cases of cleft palate which showed that in 10% of cases the mother had suffered from hyperemesis in pregnancy. Ref from (10)

Item 35b, continued....

7. Cleft Palate. 3,068 hyperemetic women, no association between hyperemesis gravidarum and cleft lip or palate was found. (29)
8. An increase in central nervous system abnormalities was observed in the offspring of hyperemetic women. Hyperemesis 6/413; no vomiting 3/833. Abnormalities in hyperemetic offspring: two anencephalics, one microcephaly, one craniosynostosis, one separation of cranial sutures and one cranial suture separation with hydrocephaly. (22)
9. Most women who reported vomiting were mothers of longitudinal limb defects (98 cases) (e.g. absence of radius and thumb where longitudinal bands of limb tissue were missing). These were infants born alive with these defects within New South Wales and the Australian capital territory between 1970 and 1981 inclusive.
The estimate of risk association with vomiting in the first trimester for women of the longitudinal group and their controls were significant. RR = 2.3 (CL 1.3, 4.0). (97)

35c. SPECIFIC FETAL ABNORMALITY LESS LIKELY TO OCCUR WITH HYPEREMESIS GRAVIDARUM. CONGENITAL HEART DISEASE

1. Cardiac defects. 3,068 hyperemetic women. There were 24 cardiac defects, close to the expected number of 22. (29)
2. 6,376 pregnancies. 894 took anti-emetic drugs. Only two of 35 women who had infants with congenital heart disease took anti-emetic drugs. (16)
3. The most severe nausea during pregnancy was associated with a lower risk for congenital heart defect (CHD) in the child compared to no nausea (or 0.81, 95% confidence interval (CI) 0.67-0.99). The lower risk tended to disappear with less severe levels of nausea and the trend was statistically significant.
998 cases mothers. 3,029 control mothers. (67)
A possible reason for the lower risk of CHD among children with mothers who took anti-nauseant medication may be that they had more severe nausea of pregnancy which could not be measured by our scale. Alternatively, maternal use of high doses of Vit B6 (contained in Bendectin) may have had a protective effect on the embryonic heart development. (67)

35d. **NO INCREASED FETAL ABNORMALITY ASSOCIATED WITH HYPEREMESIS GRAVIDARUM (Total Ten References)**

1. 246 hyperemesis patients, only 2% incidence of deformity - no greater than average incidence for the population as a whole. 1968. (10)
2. In a study of maternal states in relation to congenital malformations, in a survey of 14,813 pregnancies, found no relationship between hyperemesis gravidarum and congenital malformation. 1950. 15 patients with hyperemesis gravidarum. (84)
3. 30 patients with hyperemesis gravidarum showed no fetal deformity. 1990. (36)
4. There was no statistical difference in congenital abnormalities in babies born to women who had hyperemesis gravidarum. Hyperemesis gravidarum 1/164, controls 2/209 1%. 1995. (64)
5. The foetuses of gravidas admitted with hyperemesis gravidarum are not at increased risk of congenital abnormalities. 138 patients with hyperemesis gravidarum. 1996. (62)
6. The pregnancy outcome between hyperemesis gravidarum (193 patients) and the general population (13,053 pregnant women in the study) was similar for the incidence of fetal abnormalities. 1996. (61)
7. Major malformations, 3 (1.9%) in 162 patients treated for HG over three years. This number is comparable to our normal population. (82)
8. 20 patients with hyper emesis gravidarum, none showed any signs of congenital abnormalities. (125)
9. No congenital malformations have occurred in 130 pregnancies complicated by hyperemesis gravidarum. (150)
10. In a review of over 33,000 pregnancies complicated by nausea and vomiting there was no evidence that vomiting or a diagnosis of hyperemesis gravidarum was associated with an increased or decreased incidence of malformations. (147)

Pooled population 936 pregnancies with HG in 9 references.

35e. **NO INCREASED FETAL ABNORMALITY ASSOCIATED WITH NVP (Five References)**

1. Vomiting during pregnancy does not increase the risk of having a malformed infant. 9,255 women vomited, 7,143 did not vomit. 1986. (20)
2. No statistically significant association observed between nausea and vomiting of pregnancy and fetal abnormality, 873 women in study population. 1989. (44)
3. Our observations indicate that nausea and vomiting of pregnancy does not imply an excess risk of malformations. 309 singleton pregnancies in study. (13)
4. There was no general increase in the risk for a congenital malformation but sooner the opposite an apparently protective effect. 16,536 women used meclozine in the first 12 weeks of pregnancy mainly for NVP. Compared to 540,660 births whose mothers did not use meclozine. 2003. (133)
5. In a review of over 33,000 pregnancies complicated by nausea and vomiting there was no evidence that vomiting or a diagnosis of hyperemesis gravidarum was associated with an increased or decreased incidence of malformations. (147)

Pooled population of 67,115 pregnancies in 5 references.

35f. **FREEDOM FROM NVP NOT RELATED TO FETAL ABNORMALITY**

1. No significant association for freedom of nausea with fetal abnormality. 7,767 pregnancies, 2,253 no nausea. (51)
2. Here were no major malformations among the offspring of 130 women not experiencing nausea and vomiting. There were two major malformations among 246 women experiencing vomiting (0.81%). (123)

Summary of results in Review item 35

a.	<u>Fetal abnormality associated with hyperemesis gravidarum.</u> (10) (plus 3 references from 10) (29)	Five References	No specific abnormalities named in these references
b.	<u>Specific fetal abnormality associated with hyperemesis gravidarum.</u> Congenital dislocation of the hip 1 positive reference (16) Hip Dysplasia 1 positive reference (29) Undescended testicles 1 positive, 1 negative reference each (28) (20) Down's Syndrome 1 positive reference (29) Cleft palate 1 positive, 1 negative reference (10) (29) Central nervous system 1 positive reference (22) Skeletal malformations 1 positive reference (97)	One Reference One Reference Two References One Reference Two References One Reference One Reference	Apply to seven different abnormalities
	Total: Nine References		
c.	<u>Specific fetal abnormalities less likely to occur with hyperemesis gravidarum.</u> Congenital hernia 1 reference (20) Cardiac defects 3 references (29) (16) (67)	One Reference Three References Total: Four References	
d.	<u>No increased fetal abnormality associated with hyperemesis gravidarum.</u> (10) (36) (61) (62) (64) (82) (84) (125)	Ten References	968 women with HG 2805 controls
e.	<u>No increased risk of fetal abnormality associated with pregnancy nausea and vomiting.</u> (13) (20) (44) (133) (147)	Five References	
f.	<u>No significant association with freedom from nausea and fetal abnormality.</u> (51) (123)	Two References	

Conclusion

The spread of evidence in these papers suggest there is no positive correlation between NVP or HG and congenital abnormalities.

35g. **INCIDENCE OF MAJOR CONGENITAL DEFECTS IN THE GENERAL POPULATION**

Major malformations defined as the presence of any congenital anomaly that has an adverse effect on either the function or social acceptability of the individual. (135)

1. Major congenital defects occur in 1-3% of the general population at birth. Careful follow up increases the number detected to up to 5% later in life. (130)
2. In summary it is probably not far wrong to say that 2 to 3 percent of all live born infants show one or more significant congenital malformations and that at the end of one year this figure is doubled by the discovery of malformations not manifest at birth. (131)
3. In the cohort of women (n=187) exposed to ginger during pregnancy all of whom used it during the first trimester the results do not suggest that there is a higher risk of major malformations above the base-line rate of 1-3%. (135)
4. In all pregnancies there is a base-line risk of 1-3% of having a baby with a major congenital abnormality. (136)
5. Percentage of all congenital malformations to total births in Northern Ireland.

1966	3.3%	
1976	3.2%	(137)
6. The rate of congenital disorders diagnosed at birth among infants exposed to Bendectin (14 of 1000) is identical to that among infants who were not exposed (14 of 1000). (138)
7. The 2-3% risk that any pregnancy has just by chance for serious malformation. (139)
8. Of 291 women in study a total of 9 babies (3%) were born with a major or minor congenital abnormality. In the year 2000 there were 770 (4.3%) birth defects in South Australia, this included minor and major malformations. (140)

Summary

In all pregnancies there is a base-line risk of 1-3% of the baby having a major congenital abnormality at birth. Eight References

36. **STILLBIRTHS AND PERINATAL MORTALITY IN RELATION TO NAUSEA AND VOMITING OF CURRENT PREGNANCY**

1. Hyperemesis patients did not have any increased risk of stillbirth or neonatal death. (10)
2. Women with hyperemesis (419) had a significantly reduced risk of stillbirth >20 weeks compared to 836 women who did not vomit. $6/419 = 1.43\%$, $25/836 = 3\%$. (22)
3. No excess of perinatal death rate in hyperemesis gravidarum. 3,068 women with hyperemesis gravidarum. (29)
4. No statistically significant association was observed between nausea and vomiting of pregnancy and perinatal mortality. 873 women in study, 69% had NVP. (44)
5. Pregnancy outcome between hyperemesis patients (193) and the general population (13,053 women in study) was similar for perinatal mortality. (61)
6. There was no statistical difference in perinatal mortality between women with hyperemesis gravidarum and the control group. Hyperemesis gravidarum 1.9%, 3/164. Control 1.9%, 4/209. (64)
7. There were no stillbirths or neonatal deaths in 64 women with HG. (42)
8. The evidence from reanalysis and meta-analysis indicates that the decreased mortality risk associated with NVP was restricted to the first 20 weeks gestation, and was not detected during the last 20 weeks or in the neonatal period. (30)
9. No significant association of freedom from nausea with stillbirth. 7,767 pregnancies in study, 29%, i.e. 2,252 pregnancies had no nausea. (51)
10. An association between higher neonatal and perinatal mortality rates and the absence of nausea and vomiting during the first trimester is demonstrated. 7,027 women in study. (5)

Summary

1. No increased risk of stillbirth or perinatal mortality with NVP or HG.
(10) (29) (42) (44) (61) (64) (30) Seven References
Pooled population 2908 HG pregnancies 602 NVP pregnancies
2. Significant reduced risk of stillbirth in women with hyperemesis gravidarum.
(22) One Reference
3. No significant association of freedom from nausea and stillbirth. (51)
One Reference
4. Higher neonatal and perinatal mortality rates and the absence of nausea and vomiting are demonstrated. (5) One Reference

D. **OTHER SIGNIFICANT INFORMATION RELATING TO NVP AND HG**

37. **FOOD CRAVINGS RELATED TO NVP**

1. Women with food cravings had significantly more nausea and vomiting during pregnancy. 36 (30%) of those with no symptoms of NVP experienced cravings compared with 158 (42%) of those with NVP who had cravings. (27) 500 women in study
2. 420 out of 983 (42.7%) developed food cravings in early pregnancy. The development of cravings was associated with a higher incidence of nausea. (40)
3. The proportion of women who reported pronounced cravings ranged from 67% with urban blacks (412 women) to 84% with whites, 256 women. Cravings were more intense in the first trimester. (41)
4. Cravings appear to increase during pregnancy. Women with moderate to severe vomiting report more cravings before and during pregnancy. Nausea severity showed no association to cravings, either prior to or during pregnancy. (77) 129 women in study
5. Most of the changes in diet, cravings and aversions occurred between the last menstrual period and the 12th week of pregnancy. (21)

Summary

Development of an increased number or more pronounced food cravings associated with increased NVP. (27) (40) (77) Total: Three References
Pooled population 1612 women in 3 references.

Food craving increased in first trimester of pregnancy. (41) (21) Total: Two References

37a. **FOOD AVERSIONS RELATED TO NVP**

1. Food aversions appeared to increase during pregnancy, and women who experienced more severe episodes of vomiting reported more food aversions. 129 women in study. (77)
Fewer foods were reported as aversive by pregnant women than as being craved. No association between pregnancy nausea severity and reported aversions was seen. (77)
2. The majority of women 65 ± 15% experienced at least one aversion during pregnancy. (86)
Many pregnant women have aversions to alcoholic and non-alcoholic caffeinated beverages (which include coffee, tea and soda), and strong tasting vegetables, especially during the first trimester. However, the greatest aversions are to meats, fish, poultry and eggs. (86)
Usually the foods were reported aversive because they provoked nausea. 5,432 women experienced food aversions in the study group. (86)
3. Most of the changes in diet, cravings and aversions occurred between the last menstrual period and the 12th week of pregnancy. (21)
4. 15% of women's NVP was made worse after drinking tea or coffee. 363 women in study (Gadsby 1993 not published).
5. Women reporting aversive stimuli (n = 162) had significantly more NVP than those (n = 122) who did not. (141)

Summary

Food aversions associated with NVP. (77) (86) (21) (Gadsby) (141)

Five References

Pooled population 5763 women in 4 references

38. EFFECT OF CAFFEINE ON NAUSEA AND VOMITING OF PREGNANCY

1. The presence of nausea was associated with a tendency to decrease caffeine consumption. 59% of the nauseated controls decreased their consumption compared with 52% of non-nauseated controls. Similarly, 44% of the nauseated cases (women who had a spontaneous abortion) decreased their caffeine intake, compared to 36% of the non-nauseated cases. 607 women who had a miscarriage and 1,284 controls in study. (43)
2. 15% of women's symptoms of NVP were worse after drinking tea or coffee. 363 women. (Gadsby - not published)
3. Among those affected with aversions in pregnancy, there were dislike or a much reduced consumption of tea or coffee. 1,771 women in study. (41)
4. Smell of coffee pots made NVP worse. (70)
5. The second most aversive food category in pregnant women, particularly in the first trimester, was non-alcoholic beverages which included coffee and tea. (86)
6. 49 women, 28.8% of the 250 women in the study, decreased their intake of coffee in the first half of the pregnancy. About half of all women diminishing coffee consumption specifically cited a response to or provocation of nausea as an explanation. (71)
7. Effective self care actions to reduce NVP cutting down on drinks of cola, tea, coffee, stated by 24% of 37 women. (102)
8. Some women reported they were unable to tolerate coffee because it provoked their symptoms of NVP. 124 women returned completed clinical diaries. (108)
9. Higher caffeine intake was only associated with lower risk of nausea and of nausea and vomiting in pregnancy. It is not possible to deduce from our data the casual nature of this association, whether women who drink caffeine do so because they have less nausea, or the higher caffeine intake itself reduces the risk of nausea. ($P < 0.001$). 1,513 women. (45)
10. Avoidance of high caffeine sources is common among pregnant women although this is not necessarily associated with NVP. (96)
11. Of 162 respondents, 26% ($n = 41$) stated a drink made NVP worse, of these 75.6% ($n = 31$), stated the drink was coffee. (141)

Summary

Increased caffeine consumption makes NVP worse.

(43) Gadsby (41) (70) (86) (71) (102) (108) (141)

Total: Nine References

Increased caffeine consumption associated with reduced NVP. (45) [▲]

Total: One Reference

Caffeine consumption not necessarily related to NVP. (96) Total: One Reference

[▲] P value recorded.

39. **NATURAL FACTORS WHICH IMPROVE SYMPTOMS OF NVP**

1. Lying down early during an episode of NVP. Stated by 28/44, 63% of women. (23) Eating crackers. 23/44, 52% of women. 78 women in study. (23)
2. From 147 women:
Eating. 52.8% (every two hours, bland carbohydrate foods, rice cakes, crackers, toast, baked potatoes, macaroni).
Recumbent rest. 25%
Nothing. 9.7%
Vomiting. 5.6% (54)
3. 51% of 363 women stated in their prospective diaries that eating improved their symptoms. (Gadsby - not published).
4. 52% of 1,000 women who were nauseated reported that eating improved their symptoms while 33% of these women who vomited said that eating improved their symptoms (40)
5. When they are hungry they want to eat right now! 30 minutes can make the difference between a patient's eating and becoming nauseated.
Minimising odours is key to controlling NVP.
Reassure patients they are not unique or strange.
Food - let women have their cravings. Potato crisps settle the stomach and drive a thirst. Patients often want cold, tart or sweet drinks, e.g. lemonade. After crisps women can eat a better meal. (70)
6. As soon as they are hungry they should be encouraged to eat frequent small amounts of whichever food appeals to them. Emphasis on intake rather than content. (92)
7. Suggestions of foods which appeal to pregnant women because of taste and texture:
Salty - crisps and pretzel
Tart/sour - pickles, lemonade
Earthy - brown rice, mushroom soup
Bland - mashed potatoes
Soft - bread, noodles
Sweet - cake, sugary cereal
Fruity - juices, fruity popsicles
Wet - juice seltzer
Dry - crackers
Crunchy - celery sticks, apples. (72)
8. No attempt should be made to eat according to normal mealtimes. Rather the patient should be encouraged to take whatever food seems acceptable as the desire arises. (74)

Item 39, continued....

9. The majority of women, 571 (94%), had tried one or more comfort measures/medication to try to relieve their symptoms. Women used a change of dietary behaviours, most frequently (63%) - this involved experimenting with and making changes to diet, changes included small frequent meals, eating less fried and fatty meals, minimising time spent in the kitchen, eating bland foods, avoiding odours that trigger nausea and eating a dry biscuit before rising in the morning. Sucking sweets.

Other measures taken to relieve NVP

- | | |
|----------------------------------------------------|----------|
| Ginger, relaxation, naturopath | 42% |
| Resting | 39% |
| Vitamin B6 | 23% |
| Use of anti-emetics (Maxolon the most widely used) | 26% (81) |
10. Rest, preferably recumbent position, especially after meals. Fresh air. Bland food, water. Silence. Some women reported they were unable to tolerate prenatal vitamin preparations or coffee. Several participants notes nothing helps. 124 women returned clinical diaries. (108)
11. Eating. 62% reported relief of nausea with eating.
Resting. Lying or sitting down.
Eating crackers or toast.
Small frequent meals.
38% of the time “nothing worked”. (109)
19 women in study. Each kept record of nausea for seven days.
12. Effective self-care actions to reduce morning sickness. Number of subjects reporting “used, helped” (n=37):
- | | |
|-------------------------------------------------------------------------|----------|
| Getting more rest | 27 = 73% |
| Eating several small meals per day | 24 = 69% |
| Avoid bad smells | 21 = 57% |
| Avoiding greasy or fried foods | 21 = 57% |
| Avoiding cooking | 19 = 51% |
| Receiving extra attention from partner | 19 = 51% |
| Eating when feeling nauseous | 16 = 43% |
| Keeping myself busy | 16 = 43% |
| Sharing experiences with another mother | 13 = 35% |
| Eating bland foods, e.g. baked potato, hot cereal | 13 = 35% |
| Eating dry toast or crackers before getting up in the morning | 11 = 30% |
| Cutting down on drinks of caffeine (Cola, tea, coffee) | 9 = 24% |
| Having someone tell me that morning sickness is normal and will go away | 7 = 19% |

55 women in study, 37 experienced NVP. (102)

Item 39, continued....

13. Interventions used by women to alleviate NVP.
Most of the five hundred in the study assessed themselves as having moderate to severe NVP. The three most important features for alleviation of symptoms were rest, getting fresh air and taking frequent small snacks. Emotional support from partner, family, friends etc.... and eating food were in the top five items to afford some relief. Only 30% of women took medication, but when taken medication, was the second most helpful item to relieve symptoms. (114)
14. 'I like to get outside to breathe the fresh air'
'I sat on the front door step to get the fresh air'
(personal communications to Barnie-Adshead).
15. Of 162 respondents n=55 (34%) stated nothing helpful.
A total of 110 (39%) did mention a coping strategy.
- | | |
|------------------------------------------------------------|------------|
| Eating small meals | n 66 (60%) |
| Eating certain food | n 66 (60%) |
| Dry biscuits | n 16 (14%) |
| Sweets - mints | n 13 (12%) |
| Ginger biscuits | n 11 (10%) |
| Drinks | n 31 (28%) |
| Water | n 12 (11%) |
| Fizzy drinks | n 7 (6%) |
| Other strategies; | |
| Rest, sleep, relaxation | n 21 (19%) |
| Fresh air, drugs, Gaviscon acupressure (combined category) | n 9 (8%) |

Women reported a variety of strategies to assist NVP relief but those appear to be individualistic in nature. (141)

Item 39, continued....

Summary

1. Eating as soon as nausea stops or when feeling hungry or when feeling nauseous.
(23) (54) Gadsby (40) (70) (92) (74) (109) (102) (114) (141)
Eleven References
2. Nausea improved after eating. 8 references containing 2254 with NVP
(23) (54) Gadsby (40) (81) (109) (102) (141) 1248 nausea better after food = 55%
3. Frequent small meals. (23) (54) (92) (81) (109) (102) (114) (141)
Eight References
4. Nausea improved after eating small frequent meals in 61% of women with NVP.
962 women with NVP, 582 women NVP improved
(23) (54) (81) (102) (109) (141) Six References
5. Getting more rest. (23) (54) (81) (102) (108) (109) (114) (141)
Eight References
6. Lying down positional changes avoided especially after meals or during an episode of nausea.
(23) (54) (81) (108) (109) Five References
7. Getting fresh air. (23) (108) (114) (Barnie-Adshead) (141) Five References
8. Minimise odours. (70) (81) (108) (102) Four References
9. Nothing helps. (54) (108) (109) (141) Four References
10. Let them have their cravings, intake rather than content. (70) (92) (74)
Three References
11. Medication. (81) (141) Two References
12. Ginger. (81) (141) Two References
13. Reassure them they are not unique or strange. (70) One Reference

40. NATURAL FACTORS MAKING NVP WORSE

1. Fatty smells, cooking smells and smoke precipitate NVP. 78 women in study.(23)
2. The following items women stated made their symptoms worse. Smell of food, cooking, smell of fatty foods, tea, coffee, being hungry. 363 women in study. (Gadsby - not published).
3. From 147 women, the following made NVP worse:
 - Ingesting particular foods and beverages, 34.3%.
 - Not eating (being hungry), 20.3%.
 - Physical position or position changes, 16.8%.
 - Sensory stimulation
 - Olfactory, 16.1%
 - Mental or auditory, 5.6%.
 - Visual, 2.8%. (54)
4. Among those affected with aversions in pregnancy, there were dislikes or much reduced consumption of tea, coffee, meat, fish, fatty or oily foods. 1,771 women in study. (41)
5. Passive smoking is associated with more than a two-fold increased risk of severe vomiting. 201 women with severe vomiting in study. (65)
6. Foods' appearance, texture and smell. - Smells, especially food and cooking smells make NVP worse. Also, the smell of coffee pots or perfume. Swallowing saliva can precipitate NVP. (70)
7. Increased sensitivity to odours. Aromas of cooking food as well as aromas in the workplace may initiate nausea, e.g. perfume, smoke. (92)
8. Hyperolfactory and sensitivity to motion are seen in many patients with hyperemesis. Some women are able to tolerate a meal in bed in the morning but not after rising or moving around. (74)
9. Travel sickness is aggravated during pregnancy in emetic women. 92 patients in study. (19)
10. Many pregnant women have aversions to alcoholic and non-alcoholic (coffee and tea) beverages and strong tasting vegetables, especially during the first trimester. However, the greatest aversions are to meat, fish, poultry and eggs. 20 study summaries included information from 5,432 women who had food aversions. Usually the foods were reported aversions because they provoked nausea. (86)
11. NVP often co-existed with hunger, 43% and fatigue, 63%. Women described a sudden onset of intense hunger requiring them to eat immediately. This was followed by nausea and often vomiting. (103) 27 women in study
12. Stimuli for NVP;
 - Positional changes, e.g. walking.
 - Odours which are usually inoffensive, e.g. perfumes, deodorants.
 - Any noxious odours - everything smells funny.
 - Spicy food.
 - Sight of food.
 - Loud noises.
 - Diaries. Detailed daily diaries can highlight problems to be avoided or be used beneficially. (108) 124 women in study

Item 40, continued....

13. Factors contributing to nausea;
Fatigue, 45%.
Eating, 18%.
Hunger, 10%.
Odours, 6.9%.
19 women in study, each kept record of nausea for seven days during the first trimester. (109)
14. Major factors which interfere with the ability to use relief measures for NVP.
Work.
Insomnia.
Travel (particularly to work).
Child responsibilities.
Shopping.
Decreased appetite. (109)
19 women in study kept diaries of NVP for seven days in the first trimester.
15. I can smell odours in a room nobody else can smell, with resultant increased NVP.
(personal communication to Bernie-Adshead)
16. I have said to my husband that room smells unpleasant. He replies "I cannot detect any problem".
(personal communication to Bernie-Adshead)
17. 50% of respondents to a questionnaire containing the nausea and vomiting instrument (NVPI) and open ended questions relating to perceived aversive and helpful stimuli, could identify something that made nausea worse, stated that olfaction appears to be the primary mechanism involved. (141)

Women with more severe NVP were more likely to state food or cooking odour as adverse stimuli. (141)

Aversive stimuli - a total of 72% of respondents stated a food; 26% a drink and 31% non-food. Of the food category n = 45 (28%) reported fat/fried food; n = 20 (12%) reported oriental, spicy, garlic; 17% fish, meat, eggs and poultry (combined strategy). Drinks included coffee, 19%; tea 11%; non foods included cigarettes 9%; perfumes 7% and cleaning products 5%. (141)

Item 40, continued....

Summary

Increased olfactory sensation. (54) (74) (92) (108) (Barnie-Adshead - twice) (141)	Seven References
Examples:-	
Fatty or cooking smells (23) (Gadsby) (54) (41) (70) (92) (74) (108) (109) (141)	Ten References
Beverages, especially tea, coffee - taste or smell of (Gadsby) (54) (41) (70) (86) (141)	Six References
Cigarette smoke (23) (65) (92) (141)	Four References
Perfume (smell of) (70) (92) (108) (141)	Four References
Other Factors:-	
Being hungry (Gadsby) (54) (103) (109)	Four References
Positional change (54) (74) (19) (109)	Five References
Fatigue or tiredness (109) (103)	Two References
Various foods, e.g. meat, fish (41) (86) (141)	Three References
Oriental, spicy, garlic (141)	One Reference
Swallowing saliva (70)	One Reference
<u>Factors preventing women from resting</u> e.g. avoid loud noises (108)	One Reference
Work	}
Travel, particularly to work	}
Child responsibilities	}
Shopping	} Please see Review Indices 41 and 42
Cooking	}
Cleaning	}

41. **EMPLOYMENT IN RELATION TO NVP. TIME LOST FROM WORK**

1. Of 206 working pregnant women, 65% lost no time from work due to NVP. The remaining 73 (35%) lost 4,528 hours of work. The average loss of time per working woman who required time from work in the study was 62 hours. The average loss of time from work for all working women was 22 hours. Assuming 57% of women work during pregnancy then approximately 8.6 million hours per year of paid employment in England and Wales are lost through pregnancy sickness symptoms. (50) 363 women in study.
2. Employment outside the home made no statistical difference to the amount of nausea and vomiting, neither did the type of work carried out. Manual, non-manual or student groups were compared. 75% of 243 employed, complained of NVP. One in four actually needed to take time off work. (27) 243 women in study.
3. In 12% of 948 cases, emesis was so pronounced and/or of such duration that it rendered ordinary work impossible. (6) 948 women in study.
4. All 147 women admitted to one Obstetrician or two nurse-midwifery practices for pre-natal care in the U.S.A were asked whether or not nausea and vomiting during pregnancy affected their ability to perform daily activities. 120 (83%) replied in the affirmative. 41 (34%) said that symptoms were sufficiently severe that they were obliged to alter their daily schedules in some way.
Four out of five in group one with the severest symptoms stated that they would not plan or welcome another pregnancy. Five out of five in group one were unable to perform their normal house-keeping duties. Three out of five in group one worked outside home. All stopped work for 3/12. (54) 147 women in study.
5. Women employed outside the home, manual or service workers experienced more severe nausea symptoms than did clerical or secretarial workers. 100 women in study. (48)
6. In a study of 611 American women who exhibited the more severe symptomatology of NVP, two thirds worked outside the home and lost a mean of 206 hours of paid employment. (88)
7. Over half of women in employment took time off sick from work, with an estimated 808 working days lost among women prior to interview. In these early weeks 14 women (4%) resigned from work, 95 women (28%) made changes in their work schedule, coming in later or leaving earlier, and 221 women (65%) thought they were less attentive at work. 593 women with nausea and/or vomiting in study. (81) 593 women in study
8. 78% of women in the study population lost some time from outside employment. Study population, 260 women who contacted the health-line in Canada presented with more severe NVP than the average in the population. (91) 260 women in study.
9. We suggest that an appropriate role for care givers is to encourage frequent periods of rest. It may be important to assist in educating employers of the need for some women to take leaves from work or modify their work schedule while they are experiencing NVP. (108) 124 women in study.

Item 41, continued....

10. Because fatigue seems to exacerbate NVP, women should be encouraged to increase their rest, especially when they are symptomatic. It would seem appropriate for health care providers to adopt a liberal attitude toward providing leaves-of-absence from work. Such policy should ultimately shorten the number of days lost from work. (115)
11. Among women who have worked, 494 (14%) reported that they had stayed away from work because of NVP. The length of leave was stated by 437 women. The average length of leave was 13 days but the mean was 5 days and two thirds (289) had less than 10 days leave. The total number of days sick leave because of NVP was 5583 days. NVP caused some 28% of all sick leave during pregnancy before week 28. (132) 3675 women in study.

Summary

Time lost from work due to NVP was significant.
(50) (27) (6) (54) (81) (88) (91) (108) (115) (132)
Pooled population 7064 women in 10 studies

Total: Ten References

Approximately 30% of working pregnant women need to take time off work due to NVP.
(50) (27) (6) (54) (81)
Pooled population 2294

Total: Five References

42. **ADVERSE EFFECTS OF SEVERE NVP ON QUALITY OF PREGNANT WOMEN'S LIVES**

1. If you heard that a woman might be left to suffer from nausea and vomiting for at least a couple of months, without any nursing or medical attention, you would be rather perturbed. At the same time if a condition that caused 8.5 million working hours to be lost each year in England and Wales was not addressed, you would be surprised. But this is exactly what happens when women suffer from morning sickness. (87)
2. A study of 611 American women calling a health line for women with current nausea and vomiting of pregnancy (NVP) in Canada between February 1996 and August 1998 at approximately 8 weeks of gestation, and followed up at 20 weeks of gestation, naturally included women who exhibited more severe symptomatology of NVP compared to figures from population-based studies. These women reported due to NVP, 39% felt depressed always or most of the time, 40% said that NVP adversely affected the relationship with their partner and 14% stated they would be less likely to consider having more children due to their experience with NVP. Two thirds of these women worked outside the home and lost a mean of 206 hours of paid employment. These data suggest that lack of an approved treatment can cause women unwarranted and preventable suffering. (88)
3. This report focuses on 3,201 telephone callers to the NVP health-line in Canada who reported having nausea and vomiting of pregnancy (NVP) in a previous pregnancy. Half reported on pregnancies that had occurred over 4 years prior to contact with the NVP health-line. A high prevalence of reported psychosocial problems were attributed by these women to NVP. All of the following were reported more commonly among women with more severe nausea and vomiting. Feelings of depression always, to most of the time 52%; consideration of termination of pregnancy 18%; an adverse effect on their relationship with their partner 50%; an adverse effect on their partner's daily life 61%; the fear of the likelihood that NVP would harm their fetus 61%. The prevalence (n =108;3.4%) of elective termination of pregnancy due to NVP was relevant despite the fact that 75% of pregnancies were said to be planned. No information was obtained on previous history of depression or the quality of the relationship with women's partners. It is therefore not clear which came first, the NVP or the psychosocial factors. However, even if the psychosocial factors reported predated pregnancy, the fact that they were independently related to use of anti-emetic medication suggests that they should be taken into consideration when managing women with NVP. (89)
There was another notable finding: there was a clinically important prevalence of psychosocial problems even among women with mild nausea and vomiting, for example 21-23% of women reported feeling depressed (due to nausea or vomiting respectively) always or most of the time, and 43% reported an adverse effect on their partner's everyday life. (89)

Item 42, continued....

- In deciding whether or not to initiate anti-emetic therapy consideration should be given to the impact that NVP is having on a woman's life. Treatment may be appropriate for less severe nausea and vomiting that does not necessarily cause dehydration and/or malnutrition. (89)
4. In England and Wales from 1979 to 1992 a range of 25-59 legal abortions were performed annually for ICD code 643 'excessive vomiting of pregnancy' (personal communication, Abortion Statistics IPSC London UK, November 1995). This corresponds to 6.0 such abortions (median 3.7-9.5) per 100,000 pregnancies and 97% (range 60-100%) of all terminations for maternal indications. (100)
 5. Over the study period, February 1996 - March 1997, pregnancies complicated by NVP were retrospectively reported to the NVP health line in Canada, 108 terminations of pregnancy due to NVP, 413 cases in which termination due to NVP had only been considered, and 2,609 pregnancies in which no termination due to NVP had been considered were reported. Women who terminated pregnancy were significantly younger and more likely to have reported NVP in an unplanned pregnancy and to be multiparous. Nausea was usually severe in all groups and worse in the group of women who terminated than in those women who never considered termination ($P < 0.0001$) with a similar finding for vomiting. The following factors were independently associated with actual termination of pregnancy attributed to NVP: unplanned pregnancy ($P = 0.0001$); multiparity ($P = 0.03$) and feelings of depression ($P = 0.001$). However, adverse effects of NVP on women's relationship with their partner and on their partner's daily lives were also significantly related to consideration of termination of pregnancy. The assessment of women with NVP should include an evaluation of both physical and psychosocial health. (90)
 6. From February to August 1997, 260 women formed the study population of women suffering from nausea and vomiting of pregnancy who telephoned a health-line in Canada when they were less than 20 weeks pregnant. Women who contact the health line presented with more severe nausea and vomiting than the average population. (91)
60% of these women reported some degree of depression because of NVP and 50% were concerned that their NVP would impact negatively on the health of their child. Moreover, 12% of patients considered termination of pregnancy because of the severity of their NVP. This possibility reflects the severe nature of the disease in this population. In terms of lifestyle changes, 78% reported some time lost from outside employment. Almost half of the women felt that NVP adversely affected the relationship with their partner and over half of the women felt that NVP had an adverse effect of their partner's day to day life. (91)
A large educational effort based on evidence-based management is needed among health professionals and patients to optimise management and eradicate misinformation about NVP. (91)

Item 42, continued....

7. Each year, a significant number of women are admitted to hospital for hyperemesis gravidarum and many require such interventions as total parental nutrition. 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, dietary and lifestyle advice as well as pharmaceutical and alternative forms of therapeutic interventions. (92)
Conclusion. Nausea and vomiting are frequent symptoms in pregnant women which can affect their quality of life significantly. It is recommended that all health practitioners should question women early in their pregnancies about the presence of these symptoms and offer intervention with advice about diet, lifestyle adjustment and medical treatment. (92)
8. Twenty-seven women who were experiencing different degrees of nausea and vomiting were selected from 147 pregnant women and asked to participate in semi-structured telephone interviews. All participants reported changes in family, social or occupational functioning as a result of these symptoms. Nausea and vomiting can impose substantial lifestyle limitations on pregnant women that can have short and long-term consequences for them and their families. (54)
9. Another cost of severe nausea and vomiting of pregnancy is the effect on the quality of life of the pregnant woman and her family. Quality of life may be considered to have the following dimensions: i) physical functioning, e.g. work, household activities; ii) social functioning e.g. disruption of normal social activities; iii) psychological functioning, e.g. anxiety and depression; iv) disease and treatment related symptoms, here severe nausea. All of these are drastically affected by nausea of the severity that leads of hospitalisation. (93)
10. 593 women with nausea and/or vomiting presented at a mean gestational age of 8.5 weeks. The majority of these women reported that nausea and vomiting affected their ability to carry out day to day activities, with the greatest interference reported to household activities, 89%. Cooking, shopping, washing and cleaning activities were also restricted. 483 women, 81% took longer to get things done in general and 389 women, 65%, carried out the bare minimum of activities during the early weeks of pregnancy. Amongst 269 women, 70% thought they were less effective parents. Women interacted less well with their children, made greater use of crèches and placed greater reliance on existing childcare arrangements, with close relatives assisting. (81)
Women's sense of loss of well-being and health status during these early months was considerable and emphasises the misery many experience. There is a need for health professionals to disseminate information on effective treatment measures and for employers, family and friends to provide emotional and practical help to ease the burden of NVP many experience during the early weeks of pregnancy. (81)
11. The majority of women still suffer some form of nausea or vomiting in early pregnancy and although not a life threatening condition, it often remains a cause of much discomfort and concern to the pregnant patient and her family. Numerous treatments have been tried. Even if considered safe, they may be rejected by informed women who are aware of catastrophes caused by drugs in pregnancy. (27)

Item 42, continued....

12. NVP produced additional worries about the effect on the baby. Women asked, how does this effect the baby? or, does this mean there is anything wrong with the baby? and expressed concern that some harm would come from the violent vomiting and perceived lack of adequate nutrition. 27 women in study. (103)
13. Whether or not neurosis may be the cause of vomiting (in Hyperemesis Gravidarum) we are convinced that the health and even the life of the patient depends upon one's ability to control the symptoms. (Written in 1938). (14)
14. A review of stressors identified by women with nausea and vomiting of pregnancy reinforces the challenges imposed by the pressure of severe nausea and vomiting at a time that should be filled with anticipation and assumption of the mother-to-be role. These stressors seen in their entirety illustrate why these women are so in need of nursing care:-
 - Lack of understanding and support from others.
 - Inability to take vitamins or eat healthily.
 - Taking medications perceived risky.
 - Missing out on the fun of being pregnant.
 - Loss of "normal" pregnancy.
 - Loss of work days or quitting work.
 - Putting life "on hold".
 - Longing to eat and drink normally.
 - Money expended on care and support.
 - Lack of energy, fatigue.
 - Irritability and lack of enjoyment of life.
 - Memory loss or inability to think clearly.
 - Burden of care and time on others.
 - Lack of socialisation and isolation.
 - Inability to prepare for birth and arrival of baby.
 - Inability to care for family and home.
 - Fear of painful treatments.
 - Wanting pregnancy over or to end the misery.
 - Others' perception that hyperemesis is only in her mind.
 - Reluctance of doctors to treat because of cost of liability.
 - Weight loss or inadequate weight gain for gestational age of baby.
 - Fluctuating emotions due to hormones and illness.
 - Sense of inadequacy and failure at being unable to cope and function.
 - Fear of pain or difficult birth.
 - Fear of morbidity or death.
 - Difficulty bonding with infant.
 - Lack of energy and socialisation with other children.
 - Lack of excitement about infant's arrival.(From www.hyperemesis.org). (143)

Item 42, continued....

15. Department of health official abortion statistics 1992-2006 excessive vomiting in pregnancy relating to abortion.

YEAR	TOTAL	YEAR	TOTAL
1992 =	25	1999 =	25
1993 =	28	2000 =	15
1994 =	24	2001 =	16
1995 =	37	2002 =	<10
1996 =	23	2003 =	<10
1997 =	15	2004 =	<10
1998 =	31	2005 =	<10

Totals under 10 are suppressed for reasons of confidentiality in line with Office for National Statistics Guidance 2005. (144)

16. Women who actually terminated were more likely to report a negative attitude from their care giver. At least a third reported no help from their care giver. It is not surprising that most of them (87%) expressed the reason for their termination “no hope of relief” (145).
 In a target group of women with an history of hyperemesis gravidarum n=808, 15% (121) reported terminating at least one pregnancy because of this condition. Among those who did or did not terminate 19% reported a fear of the pregnancy and 37% either decided or deliberated to forgo future pregnancies after their HG experience. 191 (23.6%) wanted to limit family size, 224 (27%) wanted no more pregnancies and 38 (4%) were sterilised. (145)
17. In addition to increased hospital admissions some women experience significant psychosocial morbidity caused by nausea and vomiting of pregnancy resulting in pregnancy termination. (124)

Summary

Adverse effects of severe NVP on quality of pregnant women’s lives.

(14) (87) (88) (89) (100) (90) (91) (92) (54) (93) (27) (81) (103) (124) (143) (145)

(Department of Health Official Abortion Statistics)

Total: Seventeen References

Pooled population 5647 women with severe NVP

Areas of women’s lives effected

- Felt depressed most of the time. (88) = 39%; (89) = 52%; (91) = 60%
- Adversely effected the relationship with their partner.
(88) = 40%; (89) = 50%; (91) = 45%
- Had an adverse effect on their partner’s daily life. (89) = 61%; (91) = 55%
- Less effective parent. (81) = 70%
- Worried that NVP would impact negatively on the health of their child.
(91) = 50%
- Women less likely to have more children. (88) = 14% (145) = 27%
- Consideration of termination of pregnancy due to NVP. (89) = 18%; (91) = 12%
- Elective termination of pregnancy due to excessive vomiting in pregnancy.
(89) = 3.4%; (90) = 25-59 terminations annually 1979-92.
1992 - 2001 = 15-37 terminations annually (90)
2002 - 2006 = <10 terminations annually due to excessive vomiting in pregnancy in England.
(144)

- In a large group of women with a history of hyperemesis gravidarum n=805, n121 = 15% reported terminating at least one pregnancy because of this condition. (145)

Even mild NVP's effect on pregnant women's quality of life

- Feeling depressed most of the time. (89) = 21-23%
- Adverse effect on partner's everyday life. (89) = 43%

42a. **DOES NVP REQUIRE TREATMENT?**
PREFERABLY EARLY TREATMENT OF NVP ADVISABLE

1. 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 in study. (17)
2. This report focused on 3,201 telephone callers to the NVP helpline in Canada who reported having nausea and vomiting in a previous pregnancy. There was a clinically important prevalence of psychosocial problems even among women with mild nausea and vomiting, for example 21-23% of women reported feeling depressed (due to nausea or vomiting respectively) always or most of the time, and 43% reported an adverse effect on their partner's everyday life. In deciding whether or not to initiate anti-emetic treatment therapy, consideration should be given to the impact that NVP is having on a woman's life. Treatment may be appropriate for less severe nausea and vomiting that does not necessarily cause dehydration and/or malnutrition. (89)
3. All know that effectively treating symptoms of NVP in early pregnancy can make a woman less sick and decrease the time it takes to recover. (Key Speech by T Goodwin. Hyperemesis.org.uk. Updated March 2006).
4. The value of drug treatment, if any, is at the stage of intractable vomiting when any of the stated anti-emetics, e.g. anti-histamines 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. Nausea and vomiting are frequent symptoms in pregnant women, which can effect their quality of life significantly. It is recommended that all health practitioners should question women early in their pregnancies about the presence of these symptoms and offer intervention with advice about diet, lifestyle adjustment and medical treatment. (92)
6. 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)
7. Benefits and 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 systems, 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)
8. It is important to recognise and treat those patients early who suffer from the extreme form of hyperemesis gravidarum to avoid adverse outcomes in both mother and baby. (126)

Item 42a, continued....

9. On June 9th, 1983, Bendectin tablets widely used throughout the world to treat nausea and vomiting during pregnancy, were 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 came 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 anti-histamine with anti-nauseant properties) and Pyridoxine (Vit B6), has been available in Canada since 1983 with gradually increasing sales. Sales reached about 23% of the previous annual sales of Bendectin in Canada and USA by 1989. Bendectin was shown to be effective 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)
10. We are convinced that the health and even the life of the patient suffering from hyperemesis gravidarum depend upon one's ability to control the symptoms. (Written in 1938). (14)
11. A study of 611 American women who exhibited the more severe symptomatology of nausea and vomiting of pregnancy reported that due to NVP, 39% felt depressed always or most of the time, 40% said that NVP adversely affected the relationship with their partner, and 14% stated that they would be less likely to consider having more children due to their experience with NVP. Two thirds of these women worked outside the home and lost a mean of 206 hours of paid employment. These data suggest that lack of an approved treatment can cause women unwanted and preventable suffering. (88)
12. If you heard that a woman might be left to suffer from nausea and vomiting for at least a couple of months, without any nursing or medical attention, you would be rather perturbed. At the same time if a condition that caused 8.5 million working hours to be lost in England and Wales each year was not addressed, you would be surprised. But this is exactly what happens when women suffer from morning sickness. (87)
13. There is no reason to believe that alleviating the symptoms of normal NVP (e.g. excluding hyperemesis gravidarum) will improve the outcome of the pregnancy. Indeed doing so could have the opposite effect if it interferes with the expulsion of potentially dangerous foods, or with learning to avoid them. (86)
14. Once symptoms of nausea and vomiting progress, treatment can become more difficult; treatment in the early stages may prevent more serious complications including hospitalisation. (124)

Summary

NVP needs treatment. (14) (17) (75) (87) (88) (89) (92) (93) (101) (115) (124) (126) (Goodwin)
Total: Thirteen References

Preferably early treatment of NVP advisable.
(17) (75) (89) (92) (101) (115) (124) (126) (Goodwin) Total: Nine References

NVP should not be treated. (86) Total: One Reference

43. **SUMMARY OF RESULTS FROM REFERENCES**

Index No.	Subject	Number of references Stating same result
1.	Incidence of NVP. 73.4% of births	Twenty Six References
2a.	Percentage of women with nausea only, 32.0%.	Ten References
2b.	Episodic nature of NVP.	Five References
2b.	85% of pregnant women have two episodes of NVP per day.	One Reference
2b.	70% of episodes lasted 1-4 hours.	Two References
2c.	Regular daily pattern of episodes.	Four References
2d.	NVP lasts for a mean of approximately 6.5 weeks.	Five References
2e.	Nausea most distressing symptom of NVP.	Seven References
2f.	HG develops from NVP	Six References
2g.	NVP is unusual compared to nausea associated with other conditions.	Four References
3.	<u>Incidence of vomiting 47.1% of births.</u> Increased nausea statistically correlated with increased vomiting.	Thirteen References Three References
4.	<u>Analysis of early and late onset of symptoms.</u>	
4a.	Mean day of onset NVP 39 from LMP.	Five References
4b.	13.2% of women start NVP before day 28 from LMP.	Five References
4c.	90% of women start NVP before day 56 from LMP.	Seven References
	Maximum time for NVP weeks 7-13 from LMP.	Six References
4f.	<u>Peak of NVP symptoms between weeks 7-9 from LMP, median week 9 after rising sharply from week 6.</u>	One Reference
5.	<u>Mean week of cessation of NVP variation considerable.</u> 60% end of week 12 from LMP. 50% by week 14 from LMP. Range 91% ceased by end of week 16 from LMP. 90% resolved by 22 nd week from LMP.	One Reference One Reference Two References
6.	25% of women who deliver a singleton normal infant had no NVP.	Sixteen References

7a.	<u>Percentage of women with NVP in morning only 13.6%.</u>	Six References
7b.	NVP most commonly occurs before and after midday.	Thirteen References
7c.	<u>Correct name pregnancy nausea and vomiting, not morning sickness.</u>	Eight References
7d.	Vomiting occurred in 42.6% of women before midday.	Two References
8a.	<u>NVP and HG can vary from pregnancy to pregnancy in the same woman.</u>	Five References
8b.	NVP can recur similarly from one pregnancy to the next in the same woman.	Six References
8c.	There is 50-66% chance that symptoms will be similar from one pregnancy to the next in the same woman.	Four References
8d.	Recurrence rate for HG in succeeding pregnancies 70-80%.	Seven References
9a.	<u>Incidence of hyperemesis gravidarum (HG).</u> Range 0.14-1.3% (definitions of HG vary).	Eighteen References
9b.	<u>HG - Peak time of admission to hospital.</u> 9-11 weeks from LMP.	Twelve References
9c.	Average length of stay in hospital for HG between 3-4 days.	Eleven References
9d.	Re-admission to hospital due to recurrence of HG about 25%. Re-admissions reduced by oral steroid treatment.	Thirteen References Two References
9e.	Prompt recovery from NVP after termination, or delivery following HG or NVP	Six References
9f.	Importance of HG in early pregnancy.	Nine References
10.	<u>Animals and NVP.</u> Animals do not suffer from vomiting due to pregnancy.	Five References
11.	<u>Marital status.</u> No relation between marital status and NVP.	Six References
12.	<u>Wanted or unwanted pregnancies and NVP.</u>	
12a.	Wanted pregnancies more NVP.	Five References
12b.	Unwanted pregnancies more NVP.	Two References
12c.	No difference in NVP for wanted or unwanted pregnancy.	One Reference

13.	<p><u>Ethnic origin and NVP.</u> No difference in incidence of NVP with ethnic origin. NVP more common in Negros. Low incidence of NVP in Eskimos and native African tribes. White ethnicity associated with increased vomiting. Stable diet of maize associated with no NVP.</p>	<p>Six References Three References One Reference One Reference One Reference</p>
14.	<p><u>Genetic factors in relation to NVP.</u> Women whose mothers suffered from NVP more likely to have NVP themselves. Maternal factor responsible for NVP. Mothers' NVP not related to study subjects' experience of NVP. Women whose sisters had NVP more likely to have NVP. Paternal contribution does not affect NVP.</p>	<p>Three References Three References One Reference One Reference One Reference</p>
15.	<p><u>Pre-pregnancy motion sickness in relation to NVP.</u> Women who regularly suffered from travel sickness get more NVP. No difference in emesis rate, for those who did or did not have pre-pregnancy travel sickness. Travel sickness worse during pregnancy.</p>	<p>Two References Two References Two References</p>
16.	<p><u>Smoking and NVP in the current pregnancy.</u> NVP including HG more common in non-smokers. Smoking not associated with nausea or vomiting.</p>	<p>Fourteen References One Reference</p>
17.	<p><u>Alcohol intake and NVP.</u> Alcohol consumption not related to NVP. Women who consume alcohol prior to conception were at decreased risk of NVP.</p>	<p>Three References Two References</p>
18.	<p><u>Age in relation to NVP.</u> Women of younger age, up to 26 years, likely to have increased NVP and HG. Six refer to HG. Women of older age less likely to have NVP or HG Women's age not related to NVP.</p>	<p>Thirteen References Three References Eleven References</p>

19.	<u>Parity and NVP.</u> HG more common in primipara (nullipara). The greater the gravida the less likely to have HG. Primipara no marked increase in vomiting. Primigravida (Parity 0) decreased risk of NVP. Multipara more NVP than primipara. No relationship between NVP and parity.	Seven References Two References One Reference One Reference Five References Eight References
20.	<u>Women's initial weight and NVP.</u> NVP more common in heavier women. No relation between NVP and mother's body weight. Initial low body weight associated with HG	Three References Four References Three References
21.	<u>NVP in relation to nausea when previously taking an oral contraceptive.</u> Women who had nausea with an oral contraceptive more likely to have NVP. Four statistically significant at the P<0.05 level. A history of nausea when taking an oral contraceptive was unrelated to NVP.	Five References One Reference
22.	<u>Pre-pregnancy diabetes in relation to NVP.</u> No increase in NVP in diabetic women.	Four References
23.	<u>HG as a cause of Maternal Mortality.</u> 1925-1936 - 369 cases of HG, 15 maternal deaths. 1955-1959 - no maternal deaths.	One Reference Four Similar References
24.	<u>HG more common with Hydatidiform Moles than normal pregnancy.</u> Excessive vomiting doesn't occur in trophoblastic diseases.	Eight References One Reference
25.	<u>NVP and previous unsuccessful pregnancy. Abortion, stillbirth and neonatal death.</u> Increased NVP Not related to NVP	Four Refs, 3 Refer to HG Four References
26.	<u>NVP in relation to miscarriage.</u> There is a lower incidence or severity of NVP in pregnancies resulting in a spontaneous miscarriage.	Eighteen References

27.	<u>Reduced maternal weight gain related to NVP and HG.</u> NVP not related to maternal weight gain. HG associated with reduced weight gain.	Two References Five References
28.	<u>Pre-eclamptic Toxaemia (P.E.T) in the current pregnancy and NVP or HG.</u> NVP not increased in women who later develop P.E.T. High incidence of HG in eclamptic patients. Modest association between severe vomiting and P.E.T.	Eight References One Reference One Reference
29.	<u>Intra-Uterine Growth Retardation and NVP or HG.</u> <u>Severe</u> HG associated with intra-uterine growth retardation. HG not associated with intra-uterine growth retardation. No association between freedom from NVP and intra-uterine growth retardation.	Four References Two References One Reference
30.	<u>Length of pregnancy (< 37 weeks) and NVP.</u> Women with HG and NVP not likely to experience delivery before 37 weeks. Moderate increase in somewhat short pregnancies in HG. HG and low pregnancy weight gain delivered before 37 weeks	Sixteen References One Reference One reference
31.	<u>Sex of baby and NVP.</u> No association between NVP and sex of baby. In Hyperemesis Gravidarum more female infants.	Six References Seven References
32.	<u>Birth weight of baby and NVP.</u> Birth weight not related to NVP. Hyperemesis associated with low birth weight babies HG associated with average birth weight babies. Severe HG associated with low birth weight babies. Absence of NVP is associated with low birth weight babies.	Nine References One Reference Seven References Five References Three References
33.	<u>Twins and Hyperemesis Gravidarum.</u> Increased incidence of HG in twin pregnancies. Increased incidence of NVP with twin pregnancies.	Four References Four References
34.	<u>Placental weight and NVP.</u> NVP not associated with placental weight. There was a positive correlation for heavier placental weight and increased total hours of nausea.	Three References Two References

35.	<u>Fetal abnormality and Hyperemesis Gravidarum or NVP.</u>	
35a.	Fetal abnormalities associated with HG. No specific abnormalities mentioned.	Five References
35b.	Specific fetal abnormalities associated with HG. One different abnormality from each of the seven references used.	Seven References
35c.	Specific fetal abnormalities <u>less</u> likely to be associated with HG. (Only cardiac defect significant)	Four References
35d.	No increased incidence of fetal abnormality for mothers who have HG.	Ten References
35e.	No increased incidence of fetal abnormality and NVP.	Five References
35f.	No significant association with freedom from nausea with fetal abnormality. <u>Conclusion:- 35 a-f</u> The spread of evidence in these papers suggests there is no positive correlation between NVP or HG and specific congenital abnormalities.	Two References
35g.	In all pregnancies there is a base line risk of 1-3% of the baby having a major congenital abnormality at birth.	Eight References
36.	<u>Stillbirth, Perinatal Mortality and NVP in current pregnancy.</u> No increased risk of stillbirth or perinatal mortality with NVP or HG. Significantly <u>reduced</u> risk of stillbirth with HG. No significant association for <u>freedom from nausea</u> and stillbirth. Higher neonatal and perinatal mortality rates in the absence of nausea and vomiting.	Seven References One Reference One Reference One Reference
37.	Development of an increased number of or more pronounced food cravings associated with NVP.	Five References
37a.	Food aversion in pregnancy associated with increased NVP.	Five References
38.	<u>Effects of taking caffeine and NVP.</u> Increased caffeine intake increased NVP. Increased caffeine intake, associated with lower risk of NVP.	Nine References One Reference

39.	<p><u>Factors which improve symptoms of NVP.</u> Eating (before nausea starts and when one feels hungry, even when nauseous). Nausea improved after eating in 55% of women with NVP Frequent small meals. Nausea improved after eating small frequent meals in 61% of women with NVP Getting more rest. Lying down. Positional changes avoided. Minimise odours. Getting fresh air. Let them have their cravings. Nothing helps. Ginger. Medication.</p>	<p>Eleven References Eight References Eight References Six References Eight References Five References Four References Five References Three References Four References Two References Two References</p>
40.	<p><u>Factors which make NVP worse.</u> <u>Increased or altered olfactory sensation.</u> <u>Examples:</u> Fatty or Cooking smells. Drinking or the smell of tea or coffee. Cigarette smoke. Perfume. <u>Other Factors:</u> Positional changes. Being hungry. Fatigue. Various foods, e.g. meat, fish, fatty or oily foods.</p>	<p>Seven References Ten References Six References Four References Four References Five References Four References Two References Three References</p>
41.	<p><u>Time lost from work due to NVP</u> very significant. Approximately 30% of women need to take time off work.</p>	<p>Ten References Five References</p>
42.	<p><u>Adverse effects of severe NVP on quality of pregnant women's lives.</u></p>	<p>Seventeen References</p>
42a.	<p><u>NVP assessed for treatment.</u> NVP needs treatment. Preferably early treatment of NVP advisable. NVP does not need treatment.</p>	<p>Thirteen References Nine References One Reference</p>

44. **FACTORS RELATED SIGNIFICANTLY TO NAUSEA AND VOMITING OF PREGNANCY (NVP) OR HYPEREMESIS GRAVIDARUM (HG) WITH A BALANCE OF AT LEAST FOUR REFERENCES GIVING A POSITIVE OR ADVERSE RELATION TO NVP OR HG**

Index No.	Total Number of References
1. Incidence of NVP, 73.4% of births.	26
2a. Incidence of nausea only: 32.0% of women with NVP.	10
2b. Episodic nature of nausea in NVP.	5
2c. Regular daily pattern of NVP.	4
2d. NVP last for a mean of approximately 6.5 weeks.	5
2e. Nausea the most distressing symptom of NVP.	7
2f. HG develops from NVP.	6
2g. Nausea of NVP unusual compared to nausea with other conditions	4
3. Incidence of vomiting 47.1% of births.	13
4. Mean day of onset of NVP 39 from LMP.	5
13.2% of women start NVP before day 28 from LMP.	5
90% of women start NVP before day 56 from LMP.	5
5. Mean weeks of cessation of NVP. Weeks 12-14 from LMP	4
Later weeks variation considerable, range 91% ceased by end of week 16 or 90% ceased by week 22.	6
6. 25.6% of women who delivered a singleton normal infant had no NVP	16
7a. Percentage of women with NVP in the morning only: 13.6%.	6
7b. NVP most commonly occurs before and after midday.	13
7c. <u>Correct name pregnancy nausea and vomiting not morning sickness.</u>	8
8a. NVP can vary from pregnancy to pregnancy in the same woman.	5
8b. NVP can recur similarly from one pregnancy to the next in the same woman.	6
8c. 50-66% chance that NVP will be similar from one pregnancy to the next in the same woman.	4
8d. Recurrence rate of HG for succeeding pregnancies between 70-80%	7
9a. Incidence of HG, range 0.14%-1.3% of pregnant women.	18
9b. HG peak time of admission to hospital 9-11 weeks from LMP.	12
9c. Length of stay in hospital 3 to 4 days.	11
9d. Re-admission to hospital 25%.	13
9e. Prompt recovery from NVP or HG after termination or delivery.	6
9f. Importance of HG in early pregnancies, incidence, cost.	9
10. <u>Animals</u> do not suffer vomiting due to pregnancy.	5
11. <u>Marital status</u> not related to NVP.	6
13. No difference in incidence of NVP with <u>ethnic origin</u> .	6
14. Material genotype influences NVP and HG	4
16. NVP more common in <u>non-smokers</u> .	14
21. Nausea when previously taking an <u>oral contraceptive</u> positively related to NVP.	5

Item 44, continued....

Index	Total Number
No.	of References
22. No increase in NVP in <u>diabetic women</u> compared to non-diabetic women.	5
24. HG more common with <u>Hydatidiform Moles</u> than in normal pregnancy.	8
26. <u>Lower occurrence or lower severity of NVP in pregnancies resulting in a spontaneous miscarriage.</u>	18
27. Hyperemesis associated with reduced maternal weight gain.	5
28. NVP not <u>increased</u> in women who later develop <u>pre-eclamptic toxoemia</u> .	8
30. Women with HG or NVP <u>not likely</u> to experience delivery <u>before 37 weeks</u> .	16
31. Sex of baby. HG associated with more girls.	7
32a. NVP not related to birth weight of baby.	10
32b. HG associated with average birth weight babies.	7
<u>32c. Severe HG</u> associated with low birth weight babies.	5
33. Increased incidence of HG or NVP in <u>twin pregnancy</u> .	8
35. No specific reported foetal abnormality associated with HG or NVP	15
35g. In all pregnancies there is a base line risk of 1-3% of the baby having a major congenital abnormality at birth.	8
36. <u>No increased risk of Stillbirth or Perinatal Mortality</u> associated with NVP or HG of the current pregnancy.	7
37. Development of <u>pronounced food</u> cravings associated with NVP.	5
37a. Food aversions associated with increased NVP.	5
38. Caffeine consumption makes NVP worse.	9
39. Factors which <u>improve NVP</u> .	
Eating as soon as nausea starts and when hungry.	11
Nausea improved after eating 55% of women with NVP	8
Nausea improved eating frequent small meals	6
Nausea improved after eating small frequent meals 61% of women with NVP	8
Getting more rest.	8
Lying down positional changes avoided.	5
Getting fresh air.	5
Minimise odours.	4
Nothing helps.	4
40. Factors which make <u>NVP worse</u> . <u>Increased olfactory sensation</u>	7
Fatty or cooking smells.	10
Drinking or smell of tea or coffee.	6
Cigarette smoke.	4
Perfume.	4
<u>Other factors</u>	
Positional changes.	5
Being hungry.	4
Which prevent women from resting	7
41. <u>Time lost</u> from work due to NVP significant.	10
42. Adverse effects of severe NVP on <u>quality of pregnant women's lives</u> .	17
42a. NVP needs <u>treatment</u> .	13
Early treatment of NVP advisable.	9

45. **FACTORS IN WHICH THERE IS NOT A BALANCE OF FOUR REFERENCES STATING A POSITIVE OR NEGATIVE RELATION TO NVP OR HG**

Index No.	subject	Total number of references on each			
		Total	Positive	Negative	Equivocal For NVP
12.	Wanted or unwanted pregnancy.	8	5	2	1
15.	Women who have had more pre-pregnancy motion sickness get NVP.	6	4	0	2
17.	Alcohol consumption unrelated to the occurrence of NVP.	5	3	2	0
18.	Maternal age. Younger age (up to 26 yrs) more likely to have increased symptoms of NVP	27	13	3	11
19.	NVP or HG more common in nullipara (primigravida)	22	9	5	8
20.	Women's initial weight NVP more in heavier women	10	3	3	5
25.	Previous unsuccessful pregnancy. (miscarriage, stillbirth, neo-natal death) increased NVP or HG. Four positive papers for HG	8	4	4	0
29.	Intra-uterine growth retardation associated with hyperemesis.	6	4	2	0
34.	Placental weight increased NVP associated with heavier placenta.	5	2	3	0

ACKNOWLEDGEMENTS

We thank **Dr I.B. Shine** for constant advice with the manuscript, **The George Eliot Hospital Trust Library Staff** for obtaining documents and **Mrs L Brunton** for efficient and patient word processing, Mr. **Terry Salter** for preparing the information for the website and **Wilkinson Printers** for printing this review.

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