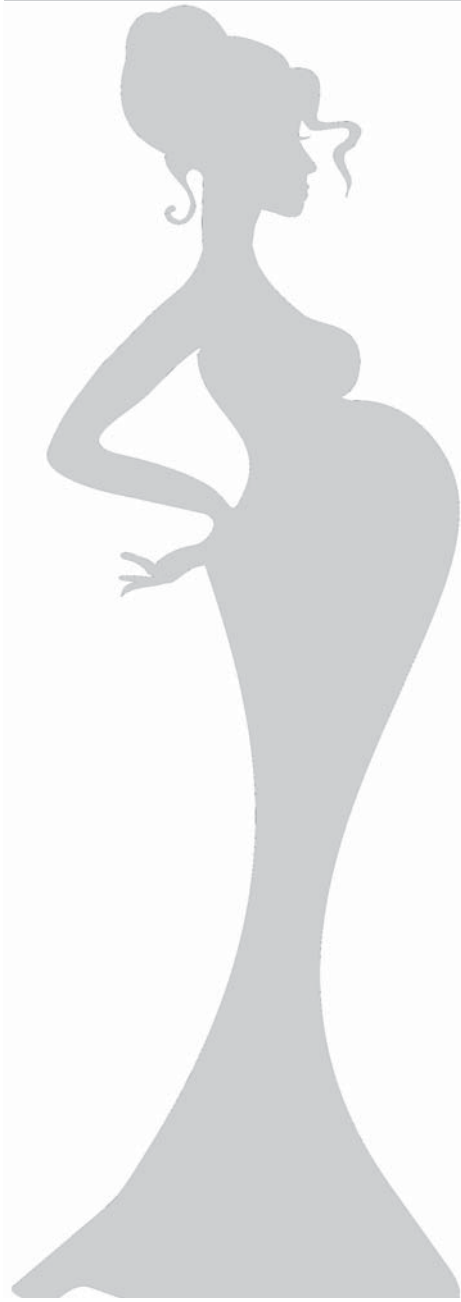
Chapter 1



Introduction and aims of this thesis

Maternal infections in pregnancy can lead to adverse pregnancy outcomes or subsequent neonatal disease, such as spontaneous abortion, prematurity, stillbirth, congenital anomalies, and mental and physical retardation (1). In the Netherlands screening all pregnant women for HIV, hepatitis B and syphilis is cost-effective and part of the prenatal screening program. Pregnant women are screened for these diseases according to the 'opting out' method. This screening program is effective in identifying pregnant women with HIV, hepatitis B and syphilis, and in preventing transmission of these infections from the mother to the child (2). There are also numerous other infectious diseases that can and should be avoided in pregnancy, including infections with *Toxoplasma gondii*, *Listeria monocytogenes* and cytomegalovirus (CMV). Furthermore, there are infectious diseases for which the screening strategy in pregnancy is based on risk assessment, including *Chlamydia trachomatis* infection (3).

In the Netherlands, as in many other countries, pregnant women are not regularly screened for toxoplasmosis, listeriosis or CMV, as screening for these infectious diseases is not cost-effective. Instead, health education and promotion of preventive behaviour is the main preventive strategy for these infections. In the Netherlands most pregnant women start prenatal care in primary midwifery care (4). As pregnant women are likely to change their behaviour based on advice from a health care professional, primary care midwives have an important role as an advisor and educator for pregnant women or women who are planning to get pregnant (5-7). Health education about methods to prevent infections is verbally provided during the intake consultation and additional written materials can be provided to the pregnant women. In addition, despite international recommendations for universal screening for chlamydia in pregnant women, in the Netherlands screening is based on risk assessment. Therefore, midwives should be able to identify women who are at an increased risk for having an infection.

This thesis consists of two parts; the first part deals with knowledge and prevention behaviour of pregnant women and knowledge and health education habits of primary care midwives in the Netherlands concerning toxoplasmosis, listeriosis and cytomegalovirus; the second part deals with knowledge and attitudes towards screening among pregnant women and their partners, and with the knowledge and test practices among primary care midwives in the Netherlands regarding chlamydia infections.

PART I: Toxoplasmosis, Listeriosis & Cytomegalovirus

Toxoplasma gondii, *Listeria monocytogenes* and CMV can all negatively affect pregnancy outcomes, but can be prevented by lifestyle and behaviour habits of the pregnant woman (6, 8-11). Informing pregnant women about these infections and how to prevent them can support women to change their lifestyle and behavioural habits in order to prevent themselves from getting infected and transmitting the infection to their foetus (5, 12).

Toxoplasmosis

Toxoplasmosis is a disease that is caused by the protozoan parasite *Toxoplasma gondii* (13). Toxoplasmosis is mainly transmitted to humans through three routes: 1) ingestion of tissue cysts in raw or undercooked contaminated meat; 2) ingestion of *Toxoplasma gondii* oocysts that have been shed in the environment through cat litter, soil or contaminated water; and 3) congenital in which maternal infection is passed through the placenta (14, 15). Maternal infections with toxoplasmosis are often mild and may result in fever, fatigue, malaise and lymphadenopathy (15).

Seroprevalence rates of toxoplasmosis have decreased during the past decade in developed countries. In the Netherlands, the seroprevalence rate of toxoplasmosis is approximately 26%, and in women of reproductive age approximately 18% (14). This means that many women are at risk for acquiring a primary infection with toxoplasmosis during pregnancy. Annually in the Netherlands, two children per 1,000 live births are infected with congenital toxoplasmosis (16). This is, for example, ten times higher than in Denmark, and twenty times higher than in Ireland (17).

Primary infection with *Toxoplasma gondii* in pregnancy can lead to spontaneous abortion or stillbirth. An unborn child infected with *Toxoplasma gondii* may develop congenital toxoplasmosis with serious consequences, such as chorioretinitis, intracranial calcifications, and hydrocephalus (14, 15, 18). The risk of congenital diseases is lowest (10-25%) when the infection is acquired in the first trimester of pregnancy, and highest (60-90%) when the infection is acquired in the third trimester of pregnancy. However, the severity of congenital toxoplasmosis is worse if the infection is acquired in the first trimester (15). Most congenital infected infants do not have obvious signs and symptoms of the disease at birth, but up to 80% develop learning and visual disabilities later in life (14).

Risk behaviour for acquiring toxoplasmosis includes: cleaning the cat litter box, eating raw or undercooked meat (e.g. pork, mutton, lamb, beef, or mince meat

products), eating raw or unwashed fruits or vegetables, gardening involving contact with soil, having poor hand hygiene, washing kitchen knives infrequently and travel outside Europe, the United States, or Canada (15). A study in six European countries showed that eating undercooked meat, contact with soil and travel outside Europe, the United States or Canada were the risk behaviours most strongly associated with toxoplasmosis in pregnant women (19). The consumption of raw or undercooked meat contributed to 30-63% of the infections, and contact with soil contributed to 6-17% of toxoplasmosis cases (19). Owning a cat is not an independent risk factor for acquiring toxoplasmosis, but rather from being exposed to cat faeces from a cat that sheds oocysts, which is only a few weeks during their entire lives (15, 19).

Antibiotic treatment is advised when a pregnant woman is diagnosed with primary *Toxoplasmosis gondii* infection, however no consensus on the exact treatment exists. In addition, maternal treatment does not decrease the chance for neonatal signs and symptoms of the disease and there is currently weak evidence that treatment reduces the risk for maternal-foetal transmission. Therefore, primary prevention strategies remain important to prevent congenital toxoplasmosis (20).

Studies from the United States showed that pregnant women had low levels of knowledge about methods to prevent toxoplasmosis, as less than half of the respondents had heard, read or seen information about the infection (21, 22). Of the respondents who had read or seen information about toxoplasmosis, the majority had read about it in books or magazines about childbirth, or had heard about the infection from health care professionals, or from family and friends (21, 22). Both studies showed that pregnant women had knowledge about the association between cats and toxoplasmosis, but showed to have very little knowledge about avoiding raw or uncooked meat. Knowledge levels about toxoplasmosis increased with age, higher educational levels and among certain ethnic groups (21, 22). In addition, a study among health care professionals in the United States showed that health care professionals did inform pregnant women about not changing the cat litter, but they needed to provide more information about avoiding raw or undercooked meat, gardening with gloves and washing fruits and vegetables (12).

Listeriosis

Listeriosis is a food-borne infection caused by the bacteria *Listeria monocytogenes*. Listeriosis is mainly transmitted through contaminated food. Pregnant women are seventeen to twenty times more at risk for acquiring an infection with listeriosis than the general population, due to impaired immune functions, which are associated with

specific hormonal changes in pregnancy (7, 13, 23-26). Maternal listeriosis is often asymptomatic or presents itself with mild flu-like illness (23).

The estimated incidence rate of pregnancy-related listeriosis in the Netherlands is between 1.3 and 2.4 cases per 100,000 pregnancies over 24 weeks of gestation (27). In addition, 10% of all patients with listeriosis in the Netherlands in 2011 were pregnant, which is higher than in previous years (27, 28). Even though listeriosis is a rare disease, it can have serious consequences (27, 29). Listeriosis occurs mainly in the third trimester, although cases have been observed at lower gestational ages. However, the incidence rate at lower gestational ages may be underestimated due to missing cultures from foetal tissue from spontaneous abortions (23). Pregnancy outcomes for infections acquired in the first trimester are worse than those acquired at a later gestational age (29). In total, 10-20% of the pregnancies complicated by listeriosis end in spontaneous abortion, 50% results in preterm birth, and in approximately 11% of the cases intrauterine foetal death occurs (23, 29, 30). In addition, two-thirds of surviving infants develop clinical neonatal listeriosis (27, 29). Neonatal listeriosis is one of the most common causes of neonatal meningitis and the mortality rate is 20-60% (23). Antibiotic treatment of listeriosis in pregnancy is directed towards improving neonatal outcome. In addition, treatment of maternal listeriosis and delay of delivery can result in the birth of a healthy new-born at term (23).

Possible risk behaviours for acquiring an infection with *Listeria monocytogenes*, is the consumption of contaminated food. In addition, *Listeria monocytogenes* can survive refrigerator temperatures, and therefore, ready-to-eat foods served without further cooking are associated with listeriosis (31). Outbreaks of listeriosis have been attributed to unpasteurized dairy products, soft cheeses, ready-to-eat foods, raw vegetables or salads, cooked or smoked ham, smoked seafood, and eating in a restaurant (27, 31).

Studies among pregnant women from the United States and Australia showed that there was a general lack of knowledge regarding listeriosis, as only a minority of the respondents had heard, read or seen information about the infection (7, 31, 32). On the contrary, a study among mothers who recently gave birth in Western Australia showed that the majority of respondents had heard of listeriosis (11). Those who had not heard of listeriosis were more likely to be young, single mothers, to live in rural areas, to speak a foreign language at home, or to have less formal education (11). Most respondents received information about listeriosis from their health care providers, from magazines and books about childbirth, or from family and friends. In addition, respondents were most likely to follow up health advice if it

was provided by a health care professional (7, 31). The study from the United States showed that less than 30% of the respondents knew they could prevent listeriosis by avoiding eating soft cheeses, unpasteurized dairy products, and ready-to-eat foods (32). Regarding health care professionals, a study from Canada reported that health care professionals are aware of the infection, although the majority did not know listeriosis is more common in pregnant women compared to the general population (24). The likelihood of being aware of listeriosis was not affected by the numbers of years in practice or the practice location (24). Studies showed low rates of information provision about risk factors for listeriosis in general (24, 33). The main reasons for not informing pregnant women about the risks were lack of knowledge of the risk factors, the perception that listeriosis is a rare disease and thus not an important concern for pregnant women, or that health care professionals did not had enough time or because they just forgot about it (24). Another reason mentioned for not informing pregnant women was that nutritional education had a lower priority than education about other pregnancy related risks (7).

Cytomegalovirus (CMV)

CMV belongs to the family of the herpes viruses, the most common cause of viral infections in pregnancy, and the most common cause of viral congenital infections (13, 34). CMV transmission occurs through direct contact with infected body fluids, such as urine, saliva, breast milk, cervical and vaginal secretions, and semen (1). For women of reproductive age, exposure to urine and saliva of young children seems to be the biggest risk factors for transmission (35-38). Sometimes viral reactivation or re-infection occurs (34). Maternal infection with CMV is usually asymptomatic, and when clinical signs are present, they are often non-specific (39).

In women of reproductive age, CMV seroprevalence rates vary between 40% and 85% in the United States and Western Europe, and may be above 90% in developing countries (34). CMV seroprevalence rates increases with age and vary widely between subgroups based on ethnic and socioeconomic background (34). In the Netherlands, seroprevalence rates vary between 41% and 73% (40, 41). The worldwide birth prevalence of congenital CMV is 0.64% (34), and in the Netherlands this is 0.54%; a prevalence that translates in 1,000 infants infected with congenital CMV infection annually (42) which is equal to that of Down syndrome (43, 44).

Maternal CMV infection in seronegative women (primary infection) is transmitted to the foetus in approximately 32% of the cases, whereas maternal CMV infection in seropositive women (non-primary infection) is transmitted to the foetus in

approximately 1% of the cases (34, 42). Approximately 10-15% of the live-born infants with congenital CMV infection have signs and symptoms at birth (34, 42). These disease manifestations can range from mild non-specific symptoms to multiple organ system involvement. Most common symptoms include petechia, rash, jaundice and hepatosplenomegaly with neurologic abnormalities as microcephaly and ocular or auditory damage (45, 46). Approximately half of the infants born with symptoms are small for gestational age, one-third is born prematurely, and the mortality rate is probably less than 5% (45). An additional 15-20% of infected infants without symptoms at birth will develop neurologic complications throughout their first five years of life, including hearing loss (34, 42).

Because maternal CMV infections are mainly acquired by urine or saliva from young children, the main risk factors for pregnant women for acquiring a CMV infection are having preschool children in the household who attend a day care setting and working in a paediatric setting or in a day care setting (9, 41). Women working in children day care settings have a 5 to 25 fold higher risk for acquiring a primary CMV infection during their pregnancy, especially during the first two years of employment, compared to women not in contact with young children (41).

Currently, there is no effective treatment for primary CMV infection in pregnancy, which indicates the necessity of prevention (43). The most effective prevention method is frequent hand washing, especially after contact with saliva or urine of infants and young children (10, 43, 47-49). And although it is difficult to investigate the exact impact of hygienic interventions on reducing the risk of maternal CMV infection, different studies consistently showed that education on hygienic behaviour can reduce the risk of acquiring maternal CMV infection (9, 10, 48-51).

Studies from the United States showed that less than 22% of women had heard about CMV infection (8, 52, 53). However, a study from France showed that 60% of the pregnant women studied had heard of the infection (54). Differences between women who had heard of CMV infection and women who had not heard about the infection were related to gestational age, gravidity, ethnicity, educational levels, and having ever worked as a health care professional (54). Most women who had heard of CMV infection got their information from their health care professional, and less frequently from family and friends, or from the Internet (8, 53, 54). One study showed that although pregnant women had a low level of accurate knowledge about CMV infection and its symptoms, 57% of the respondents correctly indicated that CMV infection could be prevented by frequent hand washing (53). In addition, the study from France showed that the majority of pregnant women who had heard of the

infection, correctly indicated that frequent hand washing (92%), not sharing cups or utensils with young children (85%) and not kissing a young child on the mouth (89%) were methods to prevent CMV infection (54). Regarding health care professionals, studies from the Netherlands, France and the United States reported a gap between health care professionals' knowledge of CMV infection in pregnancy and the burden of disease (55-57). The study from the United States showed that many of the health care professionals did not have a comprehensive understanding of the modes of transmission and the possible prevention measures (57). Furthermore, fewer than half of the health care professionals informed their clients about CMV infection prevention (57).

Prenatal health education

As described above, some international studies evaluated the awareness and knowledge of pregnant women about toxoplasmosis, listeriosis and CMV infection. Some of these studies showed that there was little awareness about the threat of toxoplasmosis, listeriosis and CMV infection during pregnancy (7, 8, 22, 31, 32, 52, 53, 58), while others showed that there was some level of awareness or knowledge regarding these three infectious diseases (11, 54). Knowledge is an important determinant in establishing changes in lifestyle and behaviour (59). People must have knowledge about a certain disease, which will influence their attitudes, before changes in behaviour can occur (60). However, this hypothesis is poorly supported, and establishing changes in behaviour and lifestyle habits seems to be more complicated (60, 61). The Health Belief Model indicates that the decision of people to exhibit healthy behaviour is determined by the perceived health threat (also known as the perceived risk perception) and the evaluation of the recommended behaviour (62). In addition, a 'trigger' is needed in order to change behavioural or lifestyle habits, which are called 'cues to action'. Information, advice from other people, illness among family and friends, and life-events, such as pregnancy, are a couple of the many 'cues to action' to establish behavioural change (61).

Health education about methods to prevent infectious diseases can encourage pregnant women to change their behaviour and lifestyle habits, thereby reducing the risk of acquiring an infection or transmitting the infection to their foetus or new-born baby (6). In addition, people will tend to follow the advice from their health care professional, and therefore, health education about preventable infectious diseases by prenatal health care providers remains important. When people think that the actual threat of the health problem is big and that whatever they must do

to prevent the disease is effective to reduce the risk of the health problem, they are more likely to change behaviour and lifestyle habits (59). In most studies it was noticed that the majority of pregnant women reported to receive information about infectious diseases most of the times from their health care professional (7, 8, 22, 31, 53, 54, 58). A requisite for adequate health education and risk assessment is that health care professionals are be aware and have knowledge of the epidemiology, transmission, symptoms and risk factors for infectious diseases in pregnant women (6, 8, 12, 56). However, not all health care professionals provide optimal information to their pregnant clients about methods to prevent these infections (7, 12, 24, 31, 57, 58).

PART II: Chlamydia trachomatis infection

Chlamydia trachomatis is a sexually transmitted infection (STI) that may cause adverse pregnancy outcomes or subsequent maternal and neonatal disease (1). In the Netherlands, screening during pregnancy for chlamydia is performed when the patient's history suggests relevant risk exposure. According to the Dutch Health Council these risk factors are young age, Surinam or Antillean ethnic origin, attending clinics for STI's, multiple sexual partners, symptoms of the infection, a chlamydia positive partner, and mothers from chlamydia positive new-borns (3).

In pregnancy, chlamydia infection increases the risk of spontaneous abortion, preterm labour, perinatal mortality, and low birth weight, and contributes to subsequent neonatal morbidity, such as neonatal conjunctivitis and neonatal pneumonia (63-70). The risk for infection in infants born to women with untreated chlamydia infection is 50% to 75% (1). Neonatal conjunctivitis occurs within the first two weeks of life in 20% to 50% of the exposed infants and pneumonia occurs within three to four months in 5% to 20% of the exposed infants (1, 65, 71).

Transmission of chlamydia occurs mainly through sexual contact and many infected men (50%) and most infected women (80%) are asymptomatic or minimally symptomatic (1). If symptoms are present in pregnant women, an infection with chlamydia can result in abnormal vaginal discharge, burning micturition, vaginal blood loss, blood loss after sexual intercourse or lower abdominal pain (72). Because chlamydia is often asymptomatic and often non-specific, the pathogen can sustain in a community (1). In addition, it has been estimated that the single exposure male-to-female transmission rate of chlamydia is only 32% (73). This means that an uninfected pregnant woman might get infected later during her pregnancy if her partner is

infected with chlamydia. Partners of pregnant women may transmit chlamydia during pregnancy. In addition, in asymptomatic couples only half of partners seem infected by testing at one time-point (74). Chlamydia infection is the most prevalent STI in women worldwide. The most recently recorded prevalence rate of chlamydia among women in the Netherlands is 4.4% (75). In pregnant women, international studies in industrialized countries reported prevalence rates of chlamydia infection varying from 3.2% to 5.9% (76-80). A study in Rotterdam, the Netherlands, found an overall prevalence rate of 3.9% among pregnant women (64). Age-specific prevalence in this study was 13.5% in pregnant women aged 20 years or less, 6.7% in women between 21 and 25 years of age and 3.3% in women between 26 and 30 years of age (64). Other studies confirm these high prevalence rates of chlamydia among pregnant teenagers (76-80). Risk factors for a chlamydia infection have been determined in several studies. Young age and urban residence have been among the most consistent risk factors. However, low socio-economic status, single marital status, certain ethnicities, and low educational levels have been associated with an increased risk for chlamydia infection as well. In addition, behavioural factors, such as multiple sexual contacts, a new sexual partner, history of an STI, and late initiation of antenatal care have been associated with chlamydia infection (64, 75, 76, 81-83).

Testing for *Chlamydia trachomatis*

Most chlamydia infections are asymptomatic and therefore, screening is the only means to detect infections. Screening, and - if necessary - treatment, is an effective method to prevent transmission from mother to child during labour or to prevent adverse pregnancy outcomes. Studies suggest that selective screening for chlamydia reduces the prevalence of the infection (76, 82). In addition, prevalence rates of chlamydia have declined in areas where screening and treatment programs have been implemented (1). Sensitive and specific non-invasive tests to detect chlamydia infection are available, using Nucleic Acid Amplification Techniques (NAATs), and the infection can easily be treated during pregnancy, which may improve maternal and neonatal outcomes (71).

International guidelines in industrialized countries recommend universal screening of all pregnant women or only those of 25 years or younger (84-87). However, the Dutch Health Council only recommends screening for chlamydia in women with the following risk factors: young age, Surinam or Antillean ethnic origin, attending clinics for sexually transmitted infections, multiple sexual partners, symptoms of the infection, a *Chlamydia trachomatis* positive partner, mothers from *Chlamydia*

trachomatis positive new-borns. No recommendations specific for pregnant women exist in the Netherlands(3).

For effective management using a risk assessment approach regarding chlamydia testing in pregnancy, it is necessary that healthcare providers have knowledge about the possible symptoms and consequences of the infection, and the risk and behavioural factors associated with infection. Insufficient knowledge can influence test practices. Not many studies evaluated the knowledge of prenatal health care professionals about chlamydia (88, 89). A study from Greece evaluated the awareness and knowledge of Greek midwives and midwifery students and found that, although they claimed they were aware of the transmission, symptoms, diagnosis, treatment and prevention of chlamydia infection, a significant proportion of them had inaccurate knowledge about these topics (88). In addition, they were ignorant about the potential consequences of chlamydia infection (88). In contrast to the Greek study, a study in the United States among nurse practitioners showed that respondents were generally knowledgeable about chlamydia infection, but identified inadequate screening and treatment practices (89). The attitudes of health care providers towards testing for an infection may also influence test practices. One study showed that if health care professionals had a positive attitude towards screening, they were more likely to actually test someone for the infection (90). In addition to knowledge and attitudes, a study showed that health care professionals' characteristics, such as gender, age, work experience, practice location, practice size, and place of graduation, may also influence screening practices (91). Finally, appropriate risk assessment may be hindered by health care providers' discomfort or lack of training in speaking openly with patients about sexual behaviour and sexually transmitted diseases (92, 93).

Another key factor for an effective screening program is that women have some knowledge about the infection and there must be a certain level of public acceptance of screening (94). Previous studies among women attending genitourinary medicine (GUM) clinics or sexual health clinics, abortion clinics and family planning clinics showed contradicting knowledge levels about chlamydia. In addition, age and prior screening for an STI seems to have a positive effect on the level of knowledge (94-96).

Women who are tested positive for a chlamydia infection may have negative feelings, such as guilt, shame or stigmatization (97-99). However, a study focused especially on pregnant women showed that they found it acceptable to screen for chlamydia in antenatal care, because of the benefits and the reduced risks for their foetus or new-born baby (100).

The partner of a pregnant woman is not involved as a patient in the antenatal care and is often mainly seen as a psychosocial support for the pregnant woman. Therefore, the biological health risk of transmitting an STI to the woman and the new-born baby is neglected (101). Little research into partners' attitudes and experiences towards chlamydia testing has been done. Partners may have positive attitudes towards STI testing in pregnancy and it may be possible that testing would make them feel more involved in the pregnancy, as it would protect the health of their unborn baby (101).

Not many studies evaluated the knowledge, screening habits and attitudes towards testing for chlamydia infection among prenatal health care providers. In addition, the attitudes and experiences of pregnant women and their partners about being tested for chlamydia are not often mentioned.

Aims and outline of this thesis

In conclusion, prevention of toxoplasmosis, listeriosis, CMV and chlamydia infection in pregnant women can reduce adverse pregnancy and neonatal outcomes. In the Netherlands, the prevalence rate of congenital toxoplasmosis is high compared to other industrialized countries, and although listeriosis is a rare disease, the incidence rate of pregnancy related listeriosis increased over the past few years. In addition, the prevalence rate of congenital CMV is relatively high and the burden of disease may be high. Education about preventive behaviour by health care professionals seems effective. However, even though healthcare providers seem to have some knowledge about toxoplasmosis and listeriosis, they often do not inform pregnant women about the methods to prevent these infections. Regarding CMV infection, health care providers seem to lack awareness and knowledge and provide inadequate hygienic prevention information to their clients. Less is known about how well pregnant women adopt certain behaviour to prevent these infections during their pregnancy. As a consequence, it seems that pregnant women do not have a comprehensive understanding about these infections or how they can prevent them. Furthermore, in the Netherlands, testing for chlamydia infection in antenatal care is based on risk assessment. However, not much is known about how well midwives perform risk assessment, nor about whether pregnant women and their partners find it acceptable to be tested for chlamydia infection.

In summary, midwives should have knowledge about toxoplasmosis, listeriosis, CMV infection and chlamydia in order to provide effective health education. Regarding chlamydia, midwives' knowledge and attitudes towards testing for chlamydia may

influence the implementation of the recommendations for testing pregnant women at an increased risk for the infection.

For midwifery care practice in the Netherlands it is relevant to systematically assess these topics, in order to improve prevention of these infectious diseases and its sequel, which may result in lower infection rates and subsequent disease in the mother as well as the foetus or new-born.

Aim

The overall aim of this thesis was to gain insight into the role of clients, midwives and health policy in preventing infectious diseases during pregnancy. The first aim of this thesis was to assess the knowledge of and risk behaviour related to toxoplasmosis, listeriosis and CMV infection among pregnant women. The second aim was to assess the knowledge of pregnant women and their partners about chlamydia infection, and their attitudes and experiences towards testing. The third aim was to assess the knowledge and the actual amount of health education provision of toxoplasmosis, listeriosis and CMV, and the test practices and attitudes towards testing for chlamydia among primary care midwives in the Netherlands.

Outline of this thesis

Part I of this thesis is about toxoplasmosis, listeriosis and CMV infection prevention in general. A cross-sectional study was carried out to assess knowledge of and risk behaviour related to toxoplasmosis, listeriosis and CMV infection prevention in pregnant women who are cared for by a primary care midwife in the Netherlands. The data were used to determine which demographic characteristics are related to risk behaviour; i.e. not adopting preventive strategies for toxoplasmosis, listeriosis and CMV infection (**chapter 2**). Video-taped intake consultations were used to assess the information provided by midwives about strategies to prevent toxoplasmosis, listeriosis and CMV, and whether the amount of provided information varied according to clients' and midwives' characteristics (**chapter 3**). The knowledge of Dutch primary care midwives about CMV transmission and maternal symptoms and the information provided about CMV infection prevention and the reasons for not providing information on CMV infection prevention to pregnant women are described in **chapter 4**.

Part II of this thesis is about *Chlamydia trachomatis* infection. **Chapter 5** describes a cross-sectional study to assess the knowledge of pregnant women and their partners regarding chlamydia. In addition, their attitudes towards testing pregnant

women and their partners in pregnancy were determined as well as their experiences of being offered a chlamydia test by their primary care midwife. These data were also used to determine if demographic characteristics of pregnant women and their partners are related to knowledge of chlamydia. **Chapter 6** describes midwives' knowledge in terms of symptomatology and pregnancy outcomes, test practices, risk assessment behaviour, and attitudes regarding chlamydia testing. These data were obtained in a national cross-sectional study. The data were also used to evaluate the association between midwives' demographic and professional characteristics and their knowledge of chlamydia infection in terms of symptomatology and pregnancy outcomes.

Finally, in **chapter 7** (**part III**) the results of this thesis are summarized, discussed, and put into broader and future perspectives. **Chapter 7** also includes recommendations for pregnant women and midwives for preventing infectious diseases, and for future research.

References

1. Remmington JS, Klein JO, Wilson CB, Baker CJ. Infectious diseases of the fetus and newborn infant. 6th ed. Philadelphia, United States: Elsevier Ltd.; 2006.
2. Op de Coul EL, Hahne S, van Weert YW, Oomen P, Smit C, van der Ploeg KP, Notermans DW, Boer K, van der Sande MA. Antenatal screening for HIV, hepatitis B and syphilis in the Netherlands is effective. *BMC Infect Dis.* 2011; 11: 185.
3. Health Council of the Netherlands. Screening for chlamydia, nr 2004/07. *the Hague.* 2004.
4. Wiegers TA. The quality of maternity care services as experienced by women in the Netherlands. *BMC Pregnancy Childbirth.* 2009; 9: 18.
5. Ross DS, Rasmussen SA, Cannon MJ, Anderson B, Kilker K, Tumpey A, Schulkin J, Jones JL. Obstetrician/gynecologists' knowledge, attitudes, and practices regarding prevention of infections in pregnancy. *J Womens Health (Larchmt).* 2009; 18(8): 1187-93.
6. Gollub EL, Leroy V, Gilbert R, Chene G, Wallon M, European Toxoprevention Study Group (EUROTOXO). Effectiveness of health education on toxoplasma-related knowledge, behaviour, and risk of seroconversion in pregnancy. *Eur J Obstet Gynecol Reprod Biol.* 2008; 136(2): 137-45.
7. Bondarianzadeh D, Yeatman H, Condon-Paoloni D. Listeria education in pregnancy: Lost opportunity for health professionals. *Aust N Z J Public Health.* 2007; 31(5): 468-74.
8. Ross DS, Victor M, Sumartojo E, Cannon MJ. Women's knowledge of congenital cytomegalovirus: Results from the 2005 HealthStyles survey. *J Womens Health (Larchmt).* 2008; 17(5): 849-58.
9. Harvey J, Dennis CL. Hygiene interventions for prevention of cytomegalovirus infection among childbearing women: Systematic review. *J Adv Nurs.* 2008 Sep; 63(5): 440-50.
10. Adler SP, Finney JW, Manganello AM, Best AM. Prevention of child-to-mother transmission of cytomegalovirus among pregnant women. *J Pediatr.* 2004 Oct; 145(4): 485-491.
11. Torvaldsen S, Kurinczuk JJ, Bower C, Parsons DE, Roberts CL. Listeria awareness among new mothers in Western Australia. *Aust N Z J Public Health.* 1999; 23(4): 362-7.
12. Kravetz JD, Federman DG. Prevention of toxoplasmosis in pregnancy: Knowledge of risk factors. *Infect Dis Obstet Gynecol.* 2005; 13(3): 161-5.
13. Coonrod DV, Jack BW, Stubblefield PG, Hollier LM, Boggess KA, Cefalo R, Cox SN, Dunlop AL, Hunter KD, Prasad MR, Lu MC, Conry JA, Gibbs RS, Hogan VK. The clinical content of preconception care: Infectious diseases in preconception care. *Am J Obstet Gynecol.* 2008; 199(6 Suppl 2): S296-309.
14. Hofhuis A, van Pelt W, van Duynhoven YT, Nijhuis CD, Mollema L, van der Klis FR, Havelaar AH, Kortbeek LM. Decreased prevalence and age-specific risk factors for toxoplasma gondii IgG antibodies in the Netherlands between 1995/1996 and 2006/2007. *Epidemiol Infect.* 2011; 139(4): 530-8.
15. Jones JL, Lopez A, Wilson M, Schulkin J, Gibbs R. Congenital toxoplasmosis: A review. *Obstet Gynecol Surv.* 2001; 56(5): 296-305.
16. Kortbeek LM, Hofhuis A, Nijhuis CD, Havelaar AH. Congenital toxoplasmosis and DALYs in the Netherlands. *Mem Inst Oswaldo Cruz.* 2009; 104(2): 370-3.
17. Schmidt DR, Hogh B, Andersen O, Fuchs J, Fledelius H, Petersen E. The national neonatal screening programme for congenital toxoplasmosis in Denmark: Results from the initial four years, 1999-2002. *Arch Dis Child.* 2006; 91(8): 661-665.
18. Lopez A, Dietz VJ, Wilson M, Navin TR, Jones JL. Preventing congenital toxoplasmosis. *MMWR Recomm Rep.* 2000; 49(RR-2): 59-68.

19. Cook AJ, Gilbert RE, Buffolano W, Zufferey J, Petersen E, Jenum PA, Foulon W, Semprini AE, Dunn DT. Sources of toxoplasma infection in pregnant women: European multicentre case-control study. European Research Network on congenital toxoplasmosis. *BMJ.* 2000; 321(7254): 142-7.

20. SYROCOT (Systematic Review on Congenital Toxoplasmosis) study group, Thiebaut R, Leproust S, Chene G, Gilbert R. Effectiveness of prenatal treatment for congenital toxoplasmosis: A meta-analysis of individual patients' data. *Lancet.* 2007; 369(9556): 115-22.

21. Jones JL, Ogunmodede F, Scheftel J, Kirkland E, Lopez A, Schulkin J, Lynfield R. Toxoplasmosis-related knowledge and practices among pregnant women in the United States. *Infect Dis Obstet Gynecol.* 2003; 11(3): 139-45.

22. Ogunmodede F, Scheftel J, Jones JL, Lynfield R. Toxoplasmosis prevention knowledge among pregnant women in Minnesota. *Minn Med.* 2005; 88(2): 32-4.

23. Lamont RF, Sobel J, Mazaki-Tovi S, Kusanovic JP, Vaisbuch E, Kim SK, Uldbjerg N, Romero R. Listeriosis in human pregnancy: A systematic review. *J Perinat Med.* 2011; 39(3): 227-36.

24. Kirkham C, Berkowitz J. Listeriosis in pregnancy: Survey of British Columbia practitioners' knowledge of risk factors, counseling practices, and learning needs. *Can Fam Physician.* 2010; 56(4): e158-66.

25. Morris JG, Potter M. Emergence of new pathogens as a function of changes in host susceptibility. *Emerg Infect Dis.* 1997; 3(4): 435-41.

26. Farber JM, Peterkin PI. Listeria monocytogenes, a food-borne pathogen. *Microbiol Rev.* 1991; 55(3): 476-511.

27. Doorduyn Y, de Jager CM, van der Zwaluw WK, Wannet WJ, van der Ende A, Spanjaard L, van Duynhoven YT. Invasive listeria monocytogenes infections in the Netherlands, 1995-2003. *Eur J Clin Microbiol Infect Dis.* 2006; 25(7): 433-42.

28. Friesema IHM, van der Zwaluw WK, Notermans DW, Biesta-Peters EG, van der Ende A, Spanjaard L, van Pelt W. Surveillance van listeria monocytogenes in Nederland, 2011. *Infectieziekten Bulletin.* 2013; 24(3): 84-8.

29. Mylonakis E, Paliou M, Hohmann EL, Calderwood SB, Wing EJ. Listeriosis during pregnancy: A case series and review of 222 cases. *Medicine (Baltimore).* 2002; 81(4): 260-9.

30. McLauchlin J. Human listeriosis in Britain, 1967-85, a summary of 722 cases. 1. listeriosis during pregnancy and in the newborn. *Epidemiol Infect.* 1990; 104(2): 181-9.

31. Athearn PN, Kendall PA, Hillers VV, Schroeder M, Bergmann V, Chen G, Medeiros LC. Awareness and acceptance of current food safety recommendations during pregnancy. *Matern Child Health J.* 2004; 8(3): 149-62.

32. Ogunmodede F, Jones JL, Scheftel J, Kirkland E, Schulkin J, Lynfield R. Listeriosis prevention knowledge among pregnant women in the USA. *Infect Dis Obstet Gynecol.* 2005; 13(1): 11-5.

33. Morales S, Kendall PA, Medeiros LC, Hillers V, Schroeder M. Health care providers' attitudes toward current food safety recommendations for pregnant women. *Appl Nurs Res.* 2004; 17(3): 178-86.

34. Kenneson A, Cannon MJ. Review and meta-analysis of the epidemiology of congenital cytomegalovirus (CMV) infection. *Rev Med Virol.* 2007; 17(4): 253-76.

35. Cannon MJ, Hyde TB, Schmid DS. Review of cytomegalovirus shedding in bodily fluids and relevance to congenital cytomegalovirus infection. *Rev Med Virol.* 2011; 21(4): 240-55.

36. Hyde TB, Schmid DS, Cannon MJ. Cytomegalovirus seroconversion rates and risk factors: Implications for congenital CMV. *Rev Med Virol.* 2010; 20(5): 311-26.

37. Revello MG, Campanini G, Piralla A, Furione M, Percivalle E, Zavattoni M, Gerna G. Molecular epidemiology of primary human cytomegalovirus infection in pregnant women and their families. *J Med Virol.* 2008; 80(8): 1415-25.

38. Staras SA, Flanders WD, Dollard SC, Pass RF, McGowan JE,Jr, Cannon MJ. Cytomegalovirus seroprevalence and childhood sources of infection: A population-based study among pre-adolescents in the United States. *J Clin Virol.* 2008; 43(3): 266-71.

39. McCarthy FP, Giles ML, Rowlands S, Purcell KJ, Jones CA. Antenatal interventions for preventing the transmission of cytomegalovirus (CMV) from the mother to fetus during pregnancy and adverse outcomes in the congenitally infected infant. *Cochrane Database Syst Rev.* 2011; 16;(3).

40. Gaytant MA, Galama JM, Semmekrot BA, Melchers WJ, Sporken JM, Oosterbaan HP, van Dop PA, Huisman A, Merkus HM, Steegers EA. The incidence of congenital cytomegalovirus infections in the Netherlands. *J Med Virol.* 2005; 76(1): 71-5.

41. Stelma FF, Smismans A, Goossens VJ, Bruggeman CA, Hoebe CJ. Occupational risk of human cytomegalovirus and parvovirus B19 infection in female day care personnel in the Netherlands; a study based on seroprevalence. *Eur J Clin Microbiol Infect Dis.* 2009; 28(4): 393-7.

42. de Vries JJ, Korver AM, Verkerk PH, Rusman L, Claas EC, Loeber JG, Kroes AC, Vossen AC. Congenital cytomegalovirus infection in the Netherlands: Birth prevalence and risk factors. *J Med Virol.* 2011; 83(10): 1777-82.

43. Cannon MJ, Davis KF. Washing our hands of the congenital cytomegalovirus disease epidemic. *BMC Public Health.* 2005; 5: 70.

44. van Gameren-Oosterom HB, Buitendijk SE, Bilardo CM, van der Pal-de Bruin KM, Van Wouwe JP, Mohangoo AD. Unchanged prevalence of down syndrome in the Netherlands: Results from an 11-year nationwide birth cohort. *Prenat Diagn.* 2012; 32(11): 1035-40.

45. Boppana SB, Ross SA, Fowler KB. Congenital cytomegalovirus infection: Clinical outcome. *Clin Infect Dis.* 2013; 57 Suppl 4: S178-81.

46. Fowler KB, Stagno S, Pass RF, Britt WJ, Boll TJ, Alford CA. The outcome of congenital cytomegalovirus infection in relation to maternal antibody status. *N Engl J Med.* 1992; 326(10): 663-7.

47. Ross DS, Jones JL, Lynch MF. Toxoplasmosis, cytomegalovirus, listeriosis, and preconception care. *Matern Child Health J.* 2006; 10(5 Suppl): S187-91.

48. Adler SP, Finney JW, Manganello AM, Best AM. Prevention of child-to-mother transmission of cytomegalovirus by changing behaviors: A randomized controlled trial. *Pediatr Infect Dis J.* 1996; 15(3): 240-6.

49. Finney JW, Miller KM, Adler SP. Changing protective and risky behaviors to prevent child-to-parent transmission of cytomegalovirus. *J Appl Behav Anal.* 1993; 26(4): 471-2.

50. Picone O, Vauloup-Fellous C, Cordier AG, Parent Du Chatelet I, Senat MV, Frydman R, Grangeot-Keros L. A 2-year study on cytomegalovirus infection during pregnancy in a French hospital. *BJOG.* 2009; 116(6): 818-23.

51. Vauloup-Fellous C, Picone O, Cordier AG, Parent-du-Chatelet I, Senat MV, Frydman R, Grangeot-Keros L. Does hygiene counseling have an impact on the rate of CMV primary infection during pregnancy? results of a 3-year prospective study in a French hospital. *J Clin Virol.* 2009; 46 Suppl 4: S49-53.

52. Cannon MJ, Westbrook K, Levis D, Schleiss MR, Thackeray R, Pass RF. Awareness of and behaviors related to child-to-mother transmission of cytomegalovirus. *Prev Med.* 2012; 54(5): 351-7.

53. Jeon J, Victor M, Adler SP, Arwady A, Demmler G, Fowler K, Goldfarb J, Keyserling H, Massoudi M, Richards K, Staras SA, Cannon MJ. Knowledge and awareness of congenital cytomegalovirus among women. *Infect Dis Obstet Gynecol.* 2006; 2006.

54. Cordier AG, Guitton S, Vauloup-Fellous C, Grangeot-Keros L, Ayoubi JM, Benachi A, Picone O. Awareness of cytomegalovirus infection among pregnant women in France. *J Clin Virol.* 2012; 53(4): 332-7.

55. Cordier AG, Guitton S, Vauloup-Fellous C, Grangeot-Keros L, Benachi A, Picone O. Awareness and knowledge of congenital cytomegalovirus infection among health care providers in France. *J Clin Virol.* 2012; 55(2): 158-63.

56. Korver AM, de Vries JJ, de Jong JW, Dekker FW, Vossen AC, Oudesluys-Murphy AM. Awareness of congenital cytomegalovirus among doctors in the Netherlands. *J Clin Virol.* 2009; 46 Suppl 4: S11-5.

57. Centers for Disease Control and Prevention (CDC). Knowledge and practices of obstetricians and gynecologists regarding cytomegalovirus infection during pregnancy--United States, 2007. *MMWR Morb Mortal Wkly Rep.* 2008; 57(3): 65-8.

58. Jones JL, Krueger A, Schulkin J, Schantz PM. Toxoplasmosis prevention and testing in pregnancy, survey of obstetrician-gynaecologists. *Zoonoses Public Health.* 2010; 57(1): 27-33.

59. Brug J, van Assema P, Lechner L. Gezondheidsvoorlichting en gedragsverandering: Een planmatige aanpak. 6th ed. Assen, the Netherlands: van Gorcum & Comp. B.V.; 2008.

60. Shirreffs JH. Expanded response-ability: A prescription for health promotion. *Health Education.* 1990; 21(3): 29-35.

61. Meillier LK, Lund AB, Kok G. Cues to action in the process of changing lifestyle. *Patient Educ Couns.* 1997; 30(1): 37-51.

62. Janz NK, Becker MH. The health belief model: A decade later. *Health Educ Q.* 1984 Spring; 11(1): 1-47.

63. Silva M, Florencio GLD, Gabiatti JRE, do Amaral RL, Eleuterio J, Goncalves AKD. Perinatal morbidity and mortality associated with chlamydial infection: A meta-analysis study. *Brazilian Journal of Infectious Diseases.* 2011; 15(N6): 533-9.

64. Rours GI, Duijts L, Moll HA, Arends LR, de Groot R, Jaddoe VW, Hofman A, Steegers EA, Mackenbach JP, Ott A, Willemse HF, van der Zwaan EA, Verkooijen RP, Verbrugh HA. *Chlamydia trachomatis* infection during pregnancy associated with preterm delivery: A population-based prospective cohort study. *Eur J Epidemiol.* 2011; 26(6): 493-502.

65. Rours GI, Hammerschlag MR, Van Doornum GJ, Hop WC, de Groot R, Willemse HF, Verbrugh HA, Verkooyen RP. *Chlamydia trachomatis* respiratory infection in Dutch infants. *Arch Dis Child.* 2009; 94(9): 705-7.

66. Rours IG, Hammerschlag MR, Ott A, De Faber TJ, Verbrugh HA, de Groot R, Verkooyen RP. *Chlamydia trachomatis* as a cause of neonatal conjunctivitis in Dutch infants. *Pediatrics.* 2008; 121(2): e321-6.

67. Blas MM, Canchihuaman FA, Alva IE, Hawes SE. Pregnancy outcomes in women infected with *Chlamydia trachomatis*: A population-based cohort study in Washington State. *Sex Transm Infect.* 2007; 83(4): 314-8.

68. Kovacs L, Nagy E, Berbik I, Meszaros G, Deak J, Nyari T. The frequency and the role of *Chlamydia trachomatis* infection in premature labor. *Int J Gynaecol Obstet.* 1998; 62(1): 47-54.

69. Gravett MG, Hummel D, Eschenbach DA, Holmes KK. Preterm labor associated with subclinical amniotic fluid infection and with bacterial vaginosis. *Obstet Gynecol.* 1986; 67(2): 229-37.

70. Martin DH, Koutsky L, Eschenbach DA, Daling JR, Alexander ER, Benedetti JK, Holmes KK. Prematurity and perinatal mortality in pregnancies complicated by maternal *Chlamydia trachomatis* infections. *JAMA.* 1982; 247(11): 1585-8.