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**Author:** Mourad-Baars, Petronella Elisabeth Cornelia  
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CHAPTER 9
Summary
Samenvatting
In this thesis the prevalence, diagnosis and treatment of *Helicobacter pylori* (*Hp*) infection in children are discussed.

Chapter 1 is a general introduction to the subject: it describes the history, clinical features such as transmission and virulence factors, gastrointestinal and extra-intestinal symptoms, as well as the diagnosis, epidemiology, reinfection and spontaneous clearance of the infection. Some aspects of current guidelines for diagnosis and treatment are discussed as well as the increasing prevalence of resistance to antibiotics.

Section A: Reviews

In Chapter 2 the developments on *Helicobacter pylori* in children are discussed for the time frame April 2005 until March 2006. The Canadian Helicobacter Study Group Consensus Conference published their evidence-based evaluation of the approach to *Helicobacter pylori* infection in children and adolescents that was later adopted by the Pediatric Task Force in the USA. Various diagnostic tools for *Helicobacter pylori* infection in children were compared, such as the urea breath test, stool tests, monoclonal and polyclonal tests, as well as newly introduced rapid tests, urine test and serology. Increasing resistance of *Hp* in children led to the introduction of novel therapeutic schemes, for example sequential therapy (omeprazole plus amoxicillin, followed by omeprazole plus clarithromycin and tinidazole) instead of conventional triple therapy. At the time, extra-digestive manifestations of *Hp* in children were not yet documented sufficiently. During the period of the review the Nobel Prize was awarded for the discovery of *Helicobacter pylori*, and its role in gastritis and peptic ulcer disease and this led to a renewed interest in the field.

Chapter 3 provides a review of the advances in pediatric *Helicobacter pylori* infections from April 2009 - March 2010. Studies on genetic variability between adult and childhood *Hp*-isolates did not establish a correlation between CagA, VacA and the histopathology in children. There was no association of *Hp* and some extra-intestinal manifestations as recurrent abdominal pain, gastroesophageal reflux disease and growth retardation. However, the guidelines on *Hp* screening in children with those symptoms were contradictory.

The emergence of *Hp*-negative duodenal and gastric ulcers in children was noted and led to the European multicenter pilot study on ulcers/and erosions, described in chapter 5. The number of publications on drug resistance had increased enor-
mously up to 2010 and this increase has continued since. We concluded that the results of studies on sequential therapy were too variable to adopt this new first-line eradication regimen for children. No benefits were found for probiotic administration on *Hp* eradication in children. Vaccination studies were performed dealing with the way of administration of the vaccine, the efficacy and the cost-benefit and the translation of studies from mice to humans.

**Section B: Prevalence**

**Chapter 4.** In view of the generally early acquisition of *Hp* infection, we studied the prevalence of *Hp* infection in young children living in the Netherlands. Prevalences were very low (1.2%), with a significant difference between the children with parents who are both Dutch (0.5%) and children with at least one non-Dutch parent (2.6%). The frequency of *Hp* in children with parents from the three largest immigrants groups in the Netherlands (originating from Suriname, Morocco and Turkey) was 5.3%. Therefore, children belonging to the aforementioned groups are at a relatively high risk and would benefit most from early diagnosis and treatment.

**Chapter 5** describes the results of a prospective European multicenter study on the frequency and risks of gastric and duodenal ulcers or erosions in children. The study showed a frequency of 8.1% of ulcers and/or erosions, mainly appearing during teenage years. It appeared that an *Hp* infection was implicated less frequently as a cause of this pathology than expected.

**Chapter 6** reports a follow-up study on the prevalence of *Helicobacter pylori* infection in young children living in Bandung, Indonesia. The prevalence of *Hp* in the age-group 3-9 months was 8%, indicative of a very early acquisition of the infection. However, two years later all children tested negative. This chapter also discusses the limitations of the diagnostic test, the role of breastfeeding in prevention and (spontaneous) clearance of the infection.

**Section C: Diagnosis**

**Chapter 7** deals with *Hp* resistance related issues. The antimicrobial resistance of *Hp* was determined in a 10-year’s retrospective database study at Leiden University Medical Center, the Netherlands. Resistance to clarithromycin was detected in 8.5-9.4% of the *Hp* isolates of adults and in 6.5-7.2% of the children, respectively. Resistance to metronidazole was detected in 20.7-22.9% of the adults and 10.4-11.7% of the children, respectively. These resistance rates are low in comparison to rates

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**Summary**

in other countries and are compatible with a test-and-treat regimen for both adults and children in the Netherlands.

**Chapter 8** comprises the general discussion and conclusions of this thesis. It also provides an outlook for future research on *Hp* infection in children.