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Review

Waning of measles maternal antibody in infants in measles elimination settings – A systematic literature review

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ABSTRACT

Introduction: Most infants are born with immunity to measles through maternal antibodies transferred in pregnancy, which decay over time. However, in measles elimination settings, where measles does not circulate endemically and most immunity is from immunization rather than infection, maternal antibody levels are lower. This results in infant immunity that wanes earlier, and a wider susceptibility gap between maternal antibody decay and infant immunization than in non-eliminated settings. We aimed to systematically quantify the extent and duration of protection from measles in infants in settings that have sustained measles elimination.

Methods: We conducted a systematic review of studies of measles maternal antibody waning in infants in measles elimination settings. We searched MEDLINE, Embase, CINAHL, Scopus, BIOSIS Previews, and Global Health databases for relevant studies. Studies were included if they were set in countries that had eliminated measles for ≥3 years, and if the study cohort included healthy, full-term, unvaccinated infants ≤12 months, born to healthy mothers, and reported a relevant measure of measles maternal antibody in infants. We assessed study quality using the MetaQAT tool.

Results: We identified 4692 unique citations, eight of which met inclusion criteria. One study reported anti-measles antibody in cord blood, six reported antibody in infant sera, and one reported both. Two studies reported that 80 and 100% of infants were protected from measles at birth. One study reported no protection amongst 3–7 month old infants, and another reported limited protection in infants >4 months. The remaining studies reported the proportion of infants with detected antibody, but not the proportion immune.

Conclusion: Although limited, these data suggest that in settings that have sustained measles elimination, some infants are susceptible to measles well before the age of routine measles immunization. Setting-specific seroprevalence and vaccine effectiveness studies are required to evaluate this in different jurisdictions.

Abbreviations: MCV1, first dose of measles-containing vaccine; WHO, World Health Organization; PICOS, participants, interventions, comparisons, outcomes, study design; RVC, Regional Verification Commission; PRNT, plaque reduction neutralization test; GMT, geometric mean titers; MetaQAT, Meta Quality Appraisal Tool; ELISA, enzyme-linked immunosorbent assay; MMR, measles-mumps-rubella.

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Contents

1. Introduction

Despite the existence of a highly effective vaccine, measles continues to be a significant source of morbidity and mortality, with approximately 89,780 estimated deaths from measles globally in 2016, mostly in children under 5 years of age [1,2]. Disease in susceptible infants is of particular concern, as this age-group has a high incidence of infection, hospitalization, and death [3,4]. Most infants are born immune to measles through maternal antibodies transferred during pregnancy, which decay over the first year of life. The quantity of antibody transferred and therefore the duration of protection is determined by several maternal and infant factors [5,6]. Vaccinated mothers have lower antibody titres than those who were previously infected with measles, and therefore transfer fewer antibodies to their infant [7–9]. Since humoral immunity in vaccinated individuals can wane over time, especially in settings where measles does not circulate and there is no immune boosting, in vaccinated mothers maternal age is inversely correlated to the amount of antibody transferred [5,6]. Gestational age of the infant directly correlates to the amount of antibody transferred transplacentally, with premature infants receiving lower titres of maternal antibodies [10,11].

The timing of the first dose of measles-containing vaccine (MCV1) balances the risk of infection with the assumptions that the vaccine is less effective in early infancy due to interference from maternal antibodies [12] and an immature immune system [13], and that infants are protected from measles for most of the first year of life through a combination of passive immunity and herd immunity. However, recent evidence shows that in low-incidence settings or jurisdictions where measles has been eliminated, defined by the World Health Organization (WHO) as jurisdictions where endemic transmission of the virus has been interrupted for ≥12 months [14], maternal antibody levels wane more rapidly [15–17]. This occurs in elimination settings because maternal immunity is derived mostly from immunization rather than infection, and also because with less virus circulating, women do not receive the benefit of immune boosting from exposure to circulating virus [6,18]. As a result, lower titres of maternal antibody are transferred to infants, resulting in a wider susceptibility gap between waning of maternal antibody and infant immunization [15–17], which is recommended at 12 months in elimination or near elimination settings [1].

Understanding the infant susceptibility gap in measles-eliminated jurisdictions is particularly urgent because despite there being no endemic transmission of virus, sporadic imported/import-related cases still occur, putting infants at risk. In many measles-eliminated jurisdictions, immunization policies - including the optimal age for MCV1 and the management of exposed infants - are still largely based on evidence from pre-elimination settings. We have conducted a systematic review to quantify the level and/or proportion of infants with protective or detectable levels of anti-measles antibody between birth and 12 months of age. We focused on settings that have sustained measles elimination in order to provide updated evidence to inform the public health management of measles in post-elimination settings.

2. Methods

2.1. Literature search strategy

We used a participants, interventions, comparisons, outcomes, study design (PICOS) approach to identify appropriate key words to formulate a sensitive search strategy (Appendix 1). Search terms included "measles", "infant$", "neonat$", "maternal", "maternal antibod$", "women vaccinated", "vaccinated women", "placental antibody", "placental transfer", "transplacental", "passive transmission", "antibod$", "seroepidemiology", "serosurvey", "breast milk." We applied the search strategy on November 6, 2015 to MEDLINE, Embase, CINAHL, Scopus, BIOSIS Previews, and Global Health, and ran updates on May 6, 2016 and September 21, 2017. We restricted the search to human studies only. No restrictions were placed on study design, publication year, language of publication, or geographic setting. Although the results presented here are focused on settings that have achieved measles elimination, the literature search included settings with any level of measles burden. Non-research articles including commentaries, letters and errata, as well as conference abstracts, book chapters and grey literature were included in the search. We removed duplicate results prior to screening the literature.

2.2. Screening strategy

We applied two levels of screening to identify studies with relevant data. In level 1 screening, one reviewer screened titles and

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