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Review of cytomegalovirus shedding in bodily fluids and relevance to congenital cytomegalovirus infection

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SUMMARY

Congenital cytomegalovirus (CMV) infections are a leading cause of sensorineural hearing loss (SNHL) and neurological impairment. Congenital transmission of CMV can occur with maternal primary infection, reactivation, or reinfection during pregnancy. We reviewed studies of CMV shedding in bodily fluids (defined as CMV detected by culture or CMV DNA detected by polymerase chain reaction). Following diagnosis at birth, children with congenital CMV infection exhibited the highest prevalences of CMV shedding (median = 80%, number of sample population prevalences [N] = 6) and duration of shedding, with a steep decline by age five. Healthy children attending day care shed more frequently (median = 23%, N = 24) than healthy children not attending day care (median = 12%, N = 11). Peak shedding prevalences in children occurred at 1–2 years of age, confirming that young children are the key transmission risk for pregnant women. CMV shedding among children was more prevalent in urine specimens than in oral secretions (median prevalence difference = 11.5%, N = 12). Adults with risk factors such as STD clinic attendance had higher shedding prevalences (median = 22%, N = 20) than adults without risk factors (median = 7%, N = 44). In adults with risk factors, CMV was shed more frequently in urine; in adults without risk factors genital shedding was most common. The prevalence of CMV shedding in nine sample populations of pregnant women increased with advancing gestation. In seven sample populations of children with congenital CMV infection, higher viral load at birth was consistently associated with an elevated risk of SNHL. Higher CMV viral load at birth also consistently correlated with the presence of symptoms of congenital CMV at birth. Published 2011. This article is a US Government work and is in the public domain in the USA.

INTRODUCTION

Adults can become infected with cytomegalovirus (CMV) through a variety of transmission routes, including contact with bodily fluids of children or adults who are shedding the virus,

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CONFLICT OF INTEREST

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Supporting information may be found in the online version of this article.

sexual activity, blood transfusion, and organ transplantation [1]. In most cases, CMV infection in immunocompetent adults does not lead to symptomatic disease [1]; however, active CMV infection during pregnancy can result in transmission to the fetus [2] that can in turn result in permanent damage, including SNHL, intellectual disability and, rarely, death [3,4]. The risk of permanent damage appears to be highest among children whose mother experienced primary CMV infection during gestation [5,6]. It has been estimated that more than half a million women of child-bearing age in the United States of America will experience primary CMV infection each year [7].

As with all human herpesviruses, CMV establishes a life-long latent infection during primary infection, and the virus may reactivate at any time with shedding of infectious CMV in saliva, urine and other bodily secretions [1]. Reinfection with a different CMV strain is also associated with shedding [5]. CMV infection and shedding are generally asymptomatic [8], so that individuals are unlikely to know that they have been infected or are shedding the virus. Infants and young children often acquire CMV infection through breastfeeding [9,10] or through contact with other children who are actively shedding virus [11]. Infants and young children may continue shedding virus for a year or more, and probably serve as the leading source for primary infection in women of reproductive age [12–16].

In order to better understand exposures that place women at risk for CMV primary infection or reinfection during pregnancy, we reviewed the available literature on the frequency, magnitude, and risk factors for CMV shedding in various populations.

METHODS

Definition of terms

In this review, we define CMV ‘shedding’ as the presence of CMV detected by culture techniques (e.g. traditional or rapid shell vial) or CMV DNA detected by polymerase chain reaction (PCR; e.g. nested or non-nested)[17]. The testing method is specified in the Tables.

For simplicity and to facilitate comparisons, specimens from the oral cavity, including throat swabs and mouth rinses, were categorized as ‘oral secretions’; cervical and vaginal swabs and lavages were categorized as ‘genital secretions’; and white blood cells, peripheral blood mononuclear cells, and peripheral mononuclear lymphocytes were categorized as ‘blood’.

We grouped adults according to whether or not they had factors that may be associated with CMV infection or shedding. These CMV risk factors included being sexually transmitted disease (STD) clinic attendees, men who have sex with men (MSM), and women with congenitally infected children.

Because of its relatively frequent occurrence in the literature, we created one category for analysis called ‘children with medical conditions’. These children came from studies of children hospitalized for various reasons (other than congenital CMV infection) or children who were institutionalized because of disabilities.

Many studies measured more than one CMV shedding prevalence. This could be because they studied more than one population (e.g. adults and children), more than one specimen

type (e.g. urine and oral secretions), or more than one time point (e.g. all three pregnancy trimesters). We used the term ‘sample population prevalence’ to specify each of these shedding prevalences. Thus, some of the figures have more than one data point from a single study. These multiple sample population prevalences are each listed in the Tables.

Study selection and presentation

We identified studies of CMV shedding published from 1965 through 2009 by carrying out Medline searches using key words such as ‘cytomegalovirus’ or ‘CMV’ and ‘shedding’, ‘culture’, ‘PCR’, ‘epidemiology’, or ‘prevalence’. Additional studies were identified through the reference lists in the articles we retrieved. Because there are numerous studies on CMV shedding, we limited the scope of the review by excluding studies that primarily focused on congenital CMV birth prevalence, breast feeding, shedding in amniotic fluid, HIV-infected individuals, organ transplant recipients, or assay validation. In general, we also excluded studies of fewer than 25 participants. However, we included all studies regardless of sample size that examined CMV viral load, duration of shedding, or frequency of sequelae in children with congenital CMV, because few studies addressed these topics.

Because of space constraints, tables (numbered A1–A5) whose data are displayed in figures are placed in the online appendix in order of appearance. Tables whose data are not displayed in figures are shown in the main text and numbered 1–3 in order of appearance. Study categories used in the various tables included congenitally infected children, healthy children enrolled in day care, healthy children not enrolled in day care, children with medical conditions, seroconverters, adolescents who were shedding CMV, adults with CMV risk factors, and adults without CMV risk factors. For congenitally infected children, diagnostic results were excluded because, by definition, the shedding prevalence at diagnosis is 100%.

RESULTS

From 56 studies, we identified 112 sample population prevalences measured in a single specimen type (e.g. urine, oral secretions) at a single point in time (Figure 1, Tables A1 and A2). From these prevalences, we found that following their diagnosis at birth, congenitally infected children had the highest prevalences of shedding (median = 80%, $N = 6$). Among other children, shedding was more common among those in day care centers (median = 23%, $N = 24$) than among those not in day care centers (median = 12%, $N = 11$) or those with medical conditions (median = 9%, $N = 7$). Adults with CMV risk factors had prevalences of shedding similar to children in day care centers (median = 22%, $N = 20$), whereas adults without risk factors had the lowest prevalences of shedding (median = 7%, $N = 44$).

From 26 studies, we identified 34 sample population prevalences measured in a single specimen type across multiple ages (Figure 2, Table A3). Among children born with congenital CMV infection (by definition 100% were shedding at birth), shedding prevalences steadily declined during the first 5 years of life (Figure 2, panel A), although it remained quite high in a few of the studies. Among children who were not congenitally infected, shedding prevalences generally peaked at 1–2 years of age and subsequently

declined by the age of five (Figure 2, panels B–E), although this age pattern was less pronounced in healthy children not in day care centers (Figure 2, panel D). Results from the two studies reporting age and shedding among adolescents and adults (Table A3) [18,19] suggest that prevalence may decrease with age [18].

We identified 23 studies with 28 sets of sample population prevalences (Table A1) where CMV shedding was compared in more than one specimen type. Among children, CMV shedding was most commonly detected in urine specimens (Figure 3) but was also prevalent in oral secretions (median prevalence difference = 11.5%, $N = 12$). In adults without risk factors for CMV shedding ($N = 10$), genital shedding was most common (although oral secretions were often not tested) (Figure 3). Adults with risk factors for CMV infection ($N = 6$) most often shed virus in urine, although in two studies [20,21] shedding in other specimen types was more frequent (Figure 3). Studies comparing shedding in multiple specimen types did not include certain specimens, such as semen, blood, and rectal secretions, frequently enough to provide insights into their relative shedding frequencies. In general, however, shedding prevalences in blood were lower than prevalences in other specimen types.

Figure 4 displays the shedding data from 18 studies and 20 sets of sample population prevalences that measured shedding in multiple specimen types and/or multiple study visits. These data demonstrate, unsurprisingly, that if shedding is assessed in multiple specimen types at multiple times it is usually more likely to be found.

From five studies, we identified nine sets of sample population prevalences measured in a single specimen type at different times during pregnancy (Table A4). Two of these sets came from the same women followed longitudinally throughout pregnancy [22]. The other sets came from cross-sectional samples of women at different times during pregnancy. The prevalence of CMV shedding in pregnant women increased generally with advancing gestation, reaching peak prevalences in the second and third trimesters (Figure 5). Two of the studies had non-pregnant control groups. In one of them [18], shedding was less frequent in the first and second trimesters but equally frequent in the third trimester for the pregnant women compared with the non-pregnant controls. In the other study [22], shedding was more frequent in every trimester for the pregnant women compared with the non-pregnant controls.

We identified four studies (Table 1) outside of the newborn period that assessed differences in CMV viral load by specimen type. No clear differences in viral load were present for the specimen types examined. Because of differences in how viral loads were measured, it was impossible to assess whether viral loads differed according to specimen type. Studies which compared different specimen types in the newborn period (excluded from this review) have found higher viral loads in urine than in blood [23,24].

In general, the risk for developing SNHL among congenitally infected newborns was strongly and consistently associated with higher viral load measured at birth (Figure 6, Table A5). The six studies used different methods to determine viral load and set variable cut-offs for categorizing viral load. As such, direct comparisons of these studies may be difficult. Nevertheless, the risk for SNHL was not zero among newborns with low viral loads in most

of the studies. Higher CMV viral load at birth also correlated with symptoms of congenital CMV at birth (Table 2). Although differences in mean viral load tended to be no more than 1–2 logs, they were consistent across all five studies.

Studies of the duration of CMV shedding were carried out in limited situations with highly variable follow-up frequency and duration (Table 3). Consequently, it is not surprising that results varied widely. In general, congenitally infected infants and healthy children often shed for months or years. Among adult seroconverters, shedding typically continued for several months but had usually ceased within half a year. In several studies, shedding was intermittent among children and adults.

DISCUSSION

Studies of CMV shedding in various populations have provided valuable insights into the risk of acquiring CMV infection among women of reproductive age. This comprehensive analysis of CMV shedding among a variety of age groups, demographics and social settings, supports other findings that suggest that exposure to young children, especially those ages 1–2 years, poses a great risk for CMV infection [25–27]. Among young children shedding prevalences were lowest among infants less than 1-year-old. Prevalence of CMV shedding was uniformly high among 1- and 2-year-old children, whether they were enrolled in day care centers with large numbers of children or in home care. Thereafter, the prevalence of shedding declined markedly, although still continuing at relatively high levels among 3–4-year-olds. In the several studies that examined children older than five [11,19,28–32], shedding prevalences were similar to those observed in adults (5–10%). Children in day care studied at the University of Alabama at Birmingham had higher prevalences of shedding overall than children in day care studied elsewhere (Figure 1, panels B and C), which may reflect differences in the underlying study populations such as race, socioeconomic status, or mother's serostatus. One notable difference in shedding patterns occurred among children with serious medical conditions, where in several studies the prevalence of shedding stayed at low levels throughout childhood (Figure 2, panel E), perhaps reflecting fewer opportunities for exposure.

Children ages 1–2 years may be a key transmission risk not only because of their high shedding prevalences, but because they are more mobile than younger children and are more likely than older children to spread urine or oral secretions to others because they are not yet toilet trained (e.g. still in diapers) and are more likely to drool (e.g. because of teething). Thus, caregivers who are pregnant or planning a pregnancy should make extra efforts to follow hygienic precautions with 1–2-year-olds [33,34]. Furthermore, providers in day care centers may have lower risk when caring for infants or for older children.

Among children, CMV shedding occurs most frequently in urine but is also commonly found in oral secretions. These studies support the existing consensus that pregnant women should avoid getting urine or saliva in their eyes, nose, or mouth [35–38]. Based on these data, sensible prevention activities for pregnant women would include hand washing after diaper changes or wiping a child's nose or face and avoiding saliva when kissing young children and not sharing food, drink, utensils, or towels.

Adults typically shed CMV less frequently than children, but their prevalence of shedding is rarely zero. Furthermore, contrary to what is sometimes stated in the literature, seroconverting adults shed for many months rather than weeks. Among adults, genital secretions are a common fluid for CMV shedding, consistent with other studies that identified sexual risk factors for CMV seropositivity or seroconversion [25,39–43]. However, adults also shed CMV in oral secretions, suggesting that CMV transmission among adults can occur through kissing or oral sex. Unfortunately, it may be difficult if not impossible to assess the relative risk of these frequently co-occurring intimate behaviors. This presents a challenge for advising women on precautions to take with intimate partners during pregnancy. At a minimum, it would be prudent to limit new sex partners during pregnancy and to use a condom with new partners, even though these practices would not eliminate the risk for oral transmission. In many cases, the risk from regular partners may be less because they typically share the same CMV serostatus—for example, in one very large study in Belgium only 20% of seronegative women had a seropositive partner [26].

Among the different risk groups, children born with congenital CMV infection displayed the highest prevalences of subsequent CMV shedding (Figures 1 and 2). However, a substantial proportion of healthy children also shed CMV, reinforcing the notion that children with congenital CMV do not pose a special risk in day care or classroom settings and should not be excluded or treated differently.

Although the risk of CMV exposure for women of reproductive age may be elevated when their child attends day care, the risk is by no means eliminated for women who care for their children at home. About 20% of children in day care centers are shedding CMV, but about 10% of children not in day care centers are also shedding (Figure 2). As such, pregnant women should follow hygienic precautions whether or not their young children attend day care centers.

Studies that only measure CMV shedding in one specimen type at one point in time invariably underestimate the number of individuals who are shedders. This is because CMV shedding is frequently intermittent [44] and because CMV is shed in some specimen types more frequently than others. Thus, the shedding prevalences in the different risk groups (Figure 1) should be treated as minimum estimates of the prevalence of individuals shedding in bodily fluids. Furthermore, care must be taken when comparing shedding prevalences across studies, because some may present results from a single specimen and time point whereas others combine results from multiple specimens or time points.

Viral shedding was more common among pregnant women as gestation progressed for all five studies that have examined this phenomenon (Table A4). It is not clear why this phenomenon occurs, but because there is no apparent reason why exposure risk should increase with advancing gestation, it may be that this trend is related to a possible altered state of immunity during pregnancy [45,46], which could increase the likelihood of CMV primary infection, reactivation, or reinfection, as well as the duration of viral shedding [47–49].

Approximately from 10% to 15% of congenitally infected children who have asymptomatic infections at birth will develop disabilities within 2 years, most often SNHL [4,50]. It does not appear that CMV shedding or viral load measured after the newborn period is a strong predictor of SNHL [44,51]. In contrast, the observation that the highest viral loads at birth are consistently associated with the greatest risk for developing hearing impairments should be useful for clinical prognoses. However, the positive predictive value of high viral load for SNHL is probably only 30%–80% whereas the negative predictive value of low viral load probably ranges from 50% to 100% depending on the chosen assay cut-off (Figure 6). Nevertheless, all congenitally infected children would probably benefit from regular follow-up audiological testing, but such follow up would be especially important for children with high viral loads at birth.

The findings from CMV shedding studies tended to be consistent with serologic studies that addressed risk factors for CMV transmission [25,52]. Nonetheless, the studies we reviewed had significant differences in study design, population demographics, number of participants studied, and other factors that limited the conclusions we could draw. The majority of studies used viral culture to isolate infectious virus. However, for those studies that used PCR, there was no way to know how well the presence of viral DNA correlated with the presence of infectious virus in any given bodily fluid. Additional studies are needed in a household setting where much child- to-mother transmission is likely to occur [15,53]. Finally, studies comparing a broad selection of clinical specimens (urine, saliva, blood in children; urine, saliva, blood, genital secretions, semen in adults) at multiple time points are needed to better understand and prevent CMV transmission to pregnant women.

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Abbreviations used

MSM	men who have sex with men
SES	socioeconomic status
SNHL	sensory neural hearing loss
STD	sexually transmitted disease

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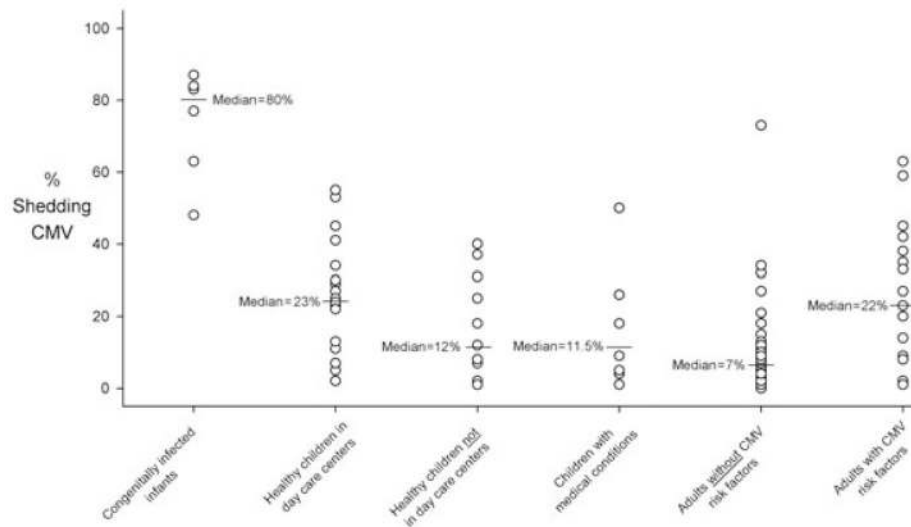


Figure 1. Prevalences of cytomegalovirus (CMV) shedding in various studies that measured a single specimen type (e.g. urine, oral secretions) at a single point in time. Each circle represents the result from an individual study (listed in Tables A2 & A3 [11,14,18–22,27,28,30–32,39,54–78] [79–95]). Studies that measured more than one specimen type have more than one circle plotted above. Prevalences were not stratified by age

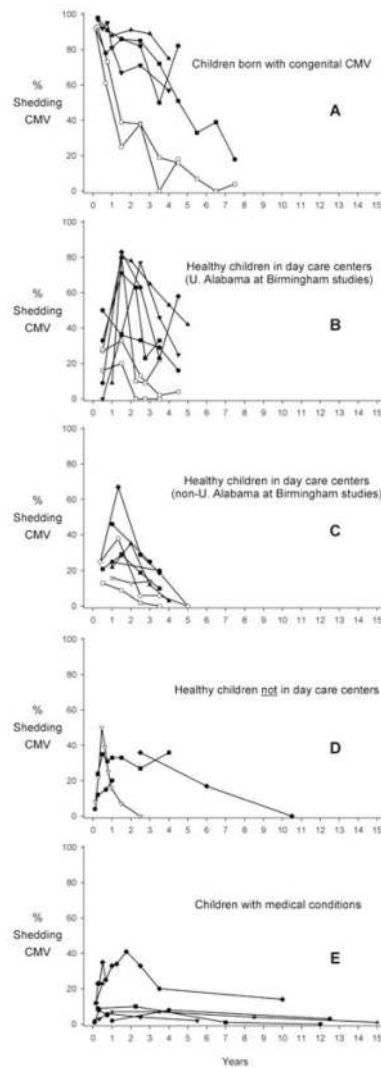


Figure 2. Cytomegalovirus (CMV) shedding as a function of age for different populations of children. Each line represents results from a single study (listed in Table A1 [11,13,14,19,28–32, 55,56,59,62,63,66,69,72,75,78,88–90,96–99]). Black symbols show shedding in urine, white symbols show shedding in oral secretions, and gray symbols show shedding in other specimens. Midpoints were used for ages when an age interval was reported. When age was some value and greater (e.g. ≥ 7 years) the previous age interval was assumed and the midpoint was taken (e.g. if the previous interval was 1 year [6–7 years], then the interval 7–8 years would be assumed, with a midpoint of 7.5 years). Because of the small age-specific sample sizes and very fine time points (i.e. 1-month), Numazaki *et al.*[88] was averaged using 2-month intervals

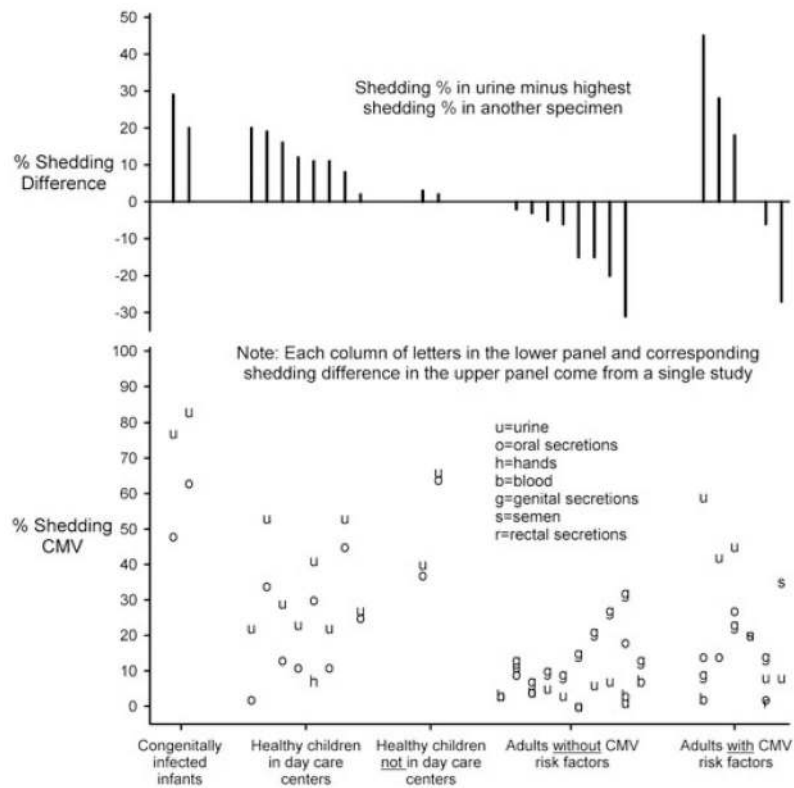


Figure 3. Comparison of cytomegalovirus (CMV) shedding from different bodily fluids and locations according to risk group. Studies were only included if they measured CMV shedding in multiple specimen types. The lower panel compares shedding in different specimens (e.g. urine vs. oral secretions). Each column of letters comes from a single study (listed in Table A2 [14,18,20–22,27,28,54–56,61,63,66,67,71–74,78,84,86,88,100]). Directly above each column of letters, in the top panel, the corresponding difference is shown between shedding percentage in urine and the highest shedding percentage in another specimen

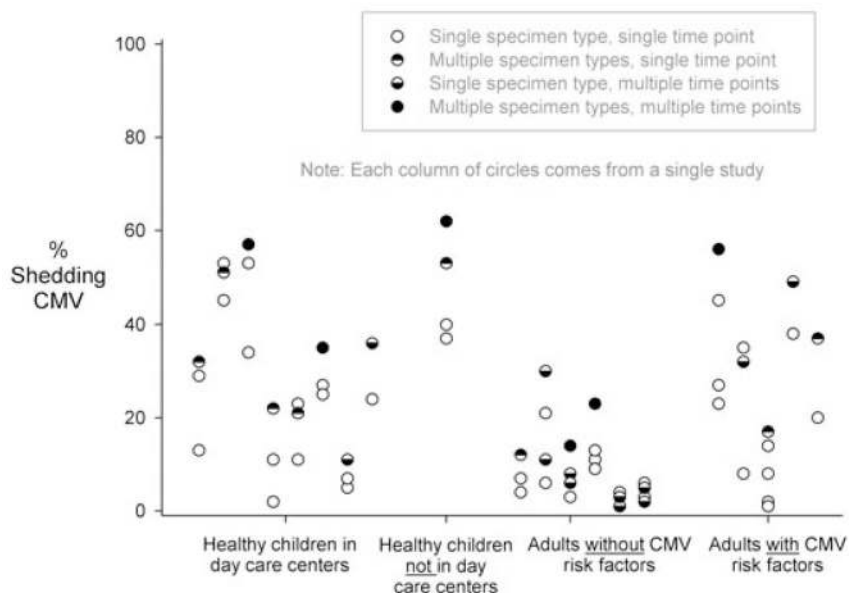


Figure 4. Prevalences of cytomegalovirus (CMV) shedding in various studies that measured not only a single specimen type at a single time point but also multiple specimen types and/or multiple time points. Each column represents results from a single study (listed in Table A3 [14,20,21,39,56,61,63,65–67,71–73,77,86,91,93,100]). Multiple empty circles from a single study occur when CMV shedding was measured separately in more than one specimen type (e.g. one empty circle for shedding in urine, one empty circle for shedding in oral specimens). This figure demonstrates that CMV shedding in individuals is more prevalent if multiple specimen types and/or multiple time points are assessed

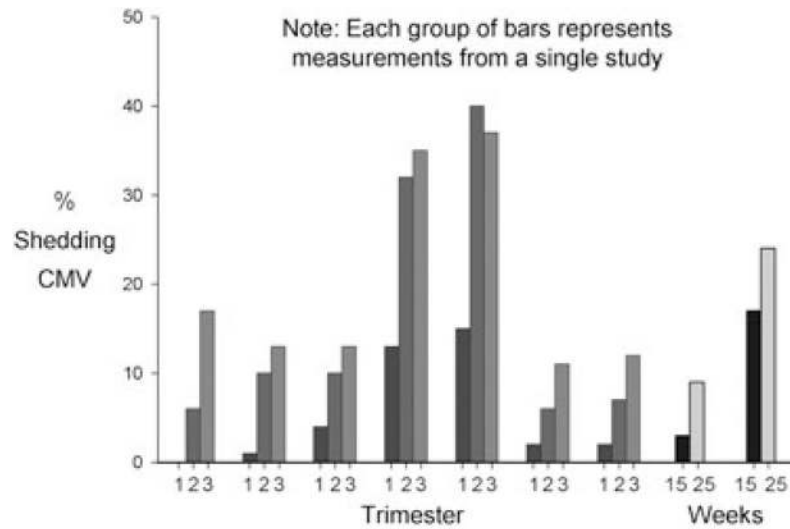


Figure 5. Prevalence of cytomegalovirus (CMV) shedding among pregnant women according to time of gestation. Each group of bars represents results from a single study (listed in Table A4 [18,22,49,71,88,101]). Two studies involved longitudinal specimen collection from the same women, the rest of the studies used cross-sectional specimen collection from women having various times of gestation. Where no bar is apparent, the prevalence is zero

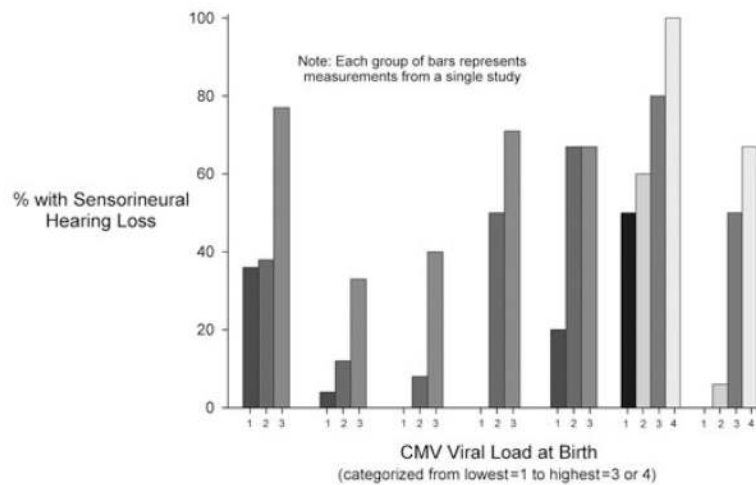


Figure 6. Frequency of sensorineural hearing loss among congenitally infected children according to cytomegalovirus (CMV) viral load at birth. Each group of bars represents measurements from a single study (listed in Table A5 [102–107]). In one study, [104] viral load was measured in urine and blood, so two sets of bars are presented. Viral load categories (i.e. cut-points) varied across different studies and are not necessarily comparable (see Table A5). Those used here correspond to the categorizations chosen by the authors of the different studies. Where no bar is apparent, the prevalence is zero

Table 1

CMV viral load according to risk group and specimen type

Country	Demographics/sampling method	Testing method	Specimen type(s)	Sample size	Viral load
The Gambia [61]	Post-partum women	Culture	Urine	32	3.8 log ₁₀ TCID ₅₀ /mL
			Oral secretions	34	3.2 log ₁₀ TCID ₅₀ /mL
			Breast milk	21	1.4 log ₁₀ TCID ₅₀ /mL
Japan [108]	Infants at 6 months	PCR	Urine	71	3.4 log ₁₀ TCID ₅₀ /mL
			Oral secretions	66	3.7 log ₁₀ TCID ₅₀ /mL
			Urine	14	Median = ~10 ⁷ ge/mL
US-Alabama [104]	Congenitally and postnatally infected newborns	Culture	Dried umbilical cord	30	Median = ~10 ³ ge/μg cellular DNA
			Urine	4	Mean = 1.6 × 10 ⁵ pfu/mL
			Blood	4	Mean = 8.7 × 10 ⁵ ge/mL
			Urine	54	Mean = 2.9 × 10 ⁴ pfu/mL
			Blood	54	Mean = 1.1 × 10 ⁴ ge/mL
			Urine	8	Mean = 4.9 × 10 ² pfu/mL
			Blood	8	Mean = 1.1 × 10 ⁵ ge/mL
			Urine	10	Mean = 3.8 × 10 ⁴ pfu/mL
			Blood	10	Mean = 6.2 × 10 ⁵ ge/mL
			Urine	4	Mean = 1.7 × 10 ³ pfu/mL
US-Iowa [66]	Children in day care centers	Culture	Oral secretions	2	Mean = 2.3 × 10 ⁴ pfu/mL

CMV, cytomegalovirus; PCR, polymerase chain reaction; TCID₅₀, median tissue culture infectious dose; ge, genome equivalents; pfu, plaque forming units; mL, milliliter; μg, micrograms.

Table 2
CMV viral load among congenitally infected newborns according to presence or absence of symptoms

Country	Testing method	Specimen type(s)	Symptoms	Sample size	Viral load
China [109]	PCR	Urine	Asymptomatic	25	Median = 4.50×10^3 ge/mL
Italy [105]	PCR	Blood	Symptomatic	54	Median = 2.95×10^5 ge/mL
			Asymptomatic	22	Log mean = 2.79 ge/ 10^5 PBMC
Italy [110]	Culture	Blood	Symptomatic	17	Log mean = 3.24 ge/ 10^5 PBMC
			Asymptomatic	32	Median = 0 p72 + fibroblasts/ 2×10^5 PBMC
			Symptomatic	9	Median = 1.5 p72 + fibroblasts/ 2×10^5 PBMC
			Asymptomatic	32	Median = 30 ge/ 10^5 PBMC
US-Alabama [104]	Culture	Urine	Symptomatic	9	Median = 3000 ge/ 10^5 PBMC
			Asymptomatic	58	Mean = 3.9×10^4 pfu/mL
			Symptomatic	18	Mean = 2.4×10^5 pfu/mL
			Asymptomatic	58	Mean = 8.2×10^4 ge/mL
			Symptomatic	18	Mean = 4.0×10^5 ge/mL
			Asymptomatic	71	Mean log TCID ₅₀ = 3.82
US-Alabama [28]	Culture	Urine	Symptomatic	33	Mean log TCID ₅₀ = 4.61

CMV, cytomegalovirus; PCR, polymerase chain reaction; TCID₅₀, median tissue culture infectious dose; ge, genome equivalents; pfu, plaque forming units; mL, milliliter; PBMC, peripheral blood mononuclear cells.

Table 3

Duration of CMV shedding

Country	Demographics/sampling method	Testing method	Specimen type(s)	Shedding duration
Category I. Congenitally infected children				
England [62]	25 congenitally infected infants	Culture	Urine, oral secretions	96% were shedding at 30 months of age
Italy [111]	14 congenitally infected infants	PCR	Blood	1–7 days 8–90 days 91–180 days > 180 days 100% 93% 63% 40%
US-New York [112]	20 congenitally infected children	Culture	Urine	100% were still shedding through at least 1 year of age
US-Ohio [113]	15 congenitally infected children	Culture	Urine	73% were still shedding at 4 years of age
Category II. Healthy children enrolled in day care centers				
Sweden [68]	13 children in day care centers who were shedding	Culture	Urine	Virus shedding continued throughout follow-up (6 months–1 year)
US-Iowa [67]	79 children in day care centers	Culture	Urine	Mean duration of shedding = 13 months
			Oral secretions	Mean duration of shedding = 7 months
Category III. Healthy children not enrolled in day care centers				
Finland [31]	39 hospitalized and outpatient children who were shedding	Culture	Urine	29 children always shed during a mean of 10 months follow-up, 10 children shed intermittently
Japan [88]	17 healthy children who were shedding	Culture	Oral secretions	15 stopped shedding within 12 months; most shed for 3–9 months.
Sweden [90]	27 children who were shedding but who were not infected congenitally	Culture	Urine	Up to 2 years of age, 98% of samples were positive
US-California [114]	13 infants in ICU who were shedding	Culture	Oral secretions	Up to 2 years of age, 84% of samples were positive
			Urine	All infants shed weekly for the duration of their hospital stay or the duration of the study (duration of follow-up not shown)
Category IV. Seroconverters				
Austria [115]	48 immunocompetent adult seroconverters	Culture	Serum	Duration of shedding less than approximately 90 days for all (estimated from Figure IC of [115])
Italy [116]	35 IgM + or indeterminate adults, presumed seroconverters	Culture	Blood	Up to 120 days, shedding prevalence > 50%; after 150 days, shedding prevalence = approximately 33% (estimated from Figure 5 of Ref. [116])
Italy [117]	52 immunocompetent seroconverters (including 40 pregnant women)	Culture	Blood	1–30 days 31–60 days 61–90 days 91–180 days >180 days 21% 0 0 0 0
			(by specimen)	
			(by patient)	26% 0 0 0 0
		PCR	(by specimen)	100% 81% 39% 17% 0
			(by patient)	100% 89% 47% 27% 0
Italy [111]	32 seroconverting pregnant women	PCR	Blood	4–30 days 31–60 days 61–90 days 91–180 days >180 days

Country	Demographics/sampling method	Testing method	Specimen type(s)	Shedding duration	Mean ge/10 μ L (estimated from Figure 1 of [118]) for different numbers of days after seroconversion
Italy [118]	74 seroconverting pregnant women 16 seroconverting men and 13 seroconverting non-pregnant women	Culture	Blood	100% 71% 46% 30% 8%	20 days 45 ge 42 ge
US-Alabama [119]	23 seroconverting post-partum women	Culture	Urine, oral secretions, genital secretions	70 days 3 ge 2 ge	150 days 0 ge 0 ge
US-California [21]	22 seroconverting homosexual men	Culture	Urine	Median time from seroconversion to shedding = 2 weeks, range = 0–12 weeks. All shed CMV from at least one site at their subsequent visits, with follow-up as long as 3.5 years	
US-Washington [40]	36 seroconverting women seen at an STD clinic	Culture	Urine, genital secretions	27% shed at some time during follow-up, mean follow-up of 9.3 months	
Category V. Adolescents who were shedding CMV					
US-Alabama [120]	18 adolescent women who were shedding	Culture	Primarily genital secretions	Over 4 years of follow-up, 17% shed at every visit, 67% shed intermittently, and 17% never shed again	
US-Ohio [121]	121 adolescent pregnant women who were shedding	Culture	Urine	In the majority, shedding was intermittent over a period of several months.	

CMV, cytomegalovirus; PCR, polymerase chain reaction; ge, genome equivalents.

Table A1

CMV shedding prevalence according to specimen type^a

Country	Demographics/Sampling Method	Testing Method	Specimen Type(s)	Sample size	Shedding %
Category I. Congenitally infected children					
England [78]	Random selection of specimens from 80 congenitally infected children followed for up to 5 years	Culture	Urine	109	83
US-Alabama [28]	104 congenitally infected children followed for up to 7 years	Culture	Oral secretions Urine Oral secretions	101 772 484	63 77 48
Category II. Healthy children enrolled in day care centers					
US-Alabama [72]	Children in day care centers, maximum of one urine and Oral secretions sample per child	Culture	Urine	231	29
US-Alabama [55]	58 children in day care centers	Culture	Oral secretions Urine Oral secretions	241 54 47	13 41 30
US-Alabama [14]	70 children in day care centers	Culture	Hands Urine	44 68	7 53
US-Alabama [56]	103 children in day care studied at least once (shedding estimated from Figure 2, ref. #117)	Culture	Oral secretions Urine	29 198	45 53
US-California [63]	100 children in day care centers	Culture	Oral secretions	160	34
US-Iowa [66]	63 children in infant development centers	Culture	Urine Oral secretions	90 100	22 11
US-Iowa [67]	48 children in day care centers	Culture	Urine Oral secretions	50 62	22 2
US-Iowa [67]	79 children in day care centers followed for 2.5 years	Culture	Urine Oral secretions	73 80	23 11
The Gambia [61]	178 infants at 6 months	Culture	Urine	79	27
Japan [88]	38 healthy infants between 4-9 months of age	Culture	Oral secretions Urine Oral secretions	178 38 33	37 66 64
Category III. Healthy children not enrolled in day care centers					

Country	Demographics/Sampling Method	Testing Method	Specimen Type(s)	Sample size	Shedding %
Category IV. Adults without CMV risk factors					
Brazil [74]	102 pregnant and non-pregnant women, 98% CMV seropositive	Nested PCR	Genital secretions	102	13
England [19]	402 hospitalized patients, ages 15–60+ years old	Culture	White blood cells Urine	98 402	7 0
The Gambia [61]	178 post-partum women, 88% CMV seropositive	Culture	Oral secretions	402	0
The Gambia [84]	81 post-partum women, all CMV seropositive	PCR	Urine	840	4
Japan [88]	107 pregnant women	Culture	Oral secretions	838	4
Taiwan [71]	350 pregnant women in the 2 nd trimester, all CMV seropositive	PCR	Breast milk	741	3
Taiwan [22]	2219 CMV seropositive pregnant women, including multiple specimens from 207 women	PCR	Genital secretions	178	7
US-Alabama [86]	113 healthy, post-partum women, all CMV seropositive	PCR	Urine	73	1
US-Alabama [73]	81 post-partum women, all CMV seropositive, over an average of 4 visits, with uninfected infants	Culture	Oral secretions	74	18
US-Alabama [18]	659 pregnant women	Culture	Genital secretions	75	32
230 non-pregnant women			Plasma	79	3
			Colostrum	77	38
			Urine	76	0
			Oral secretions	107	0
			Genital secretions	153	15
			Urine	700	6
			Genital secretions	440	21
			Urine	2195	7
			Genital secretions	600	27
			Urine	306	3
			Blood	248	3
			Urine	76	11
			Oral secretions	78	9
			Genital secretions	78	13
			Urine	600	5
			Genital secretions	659	10
			Urine	230	3
			Genital secretions	202	9

Category V. Adults with CMV risk factors

Country	Demographics/Sampling Method	Testing Method	Specimen Type(s)	Sample size	Shedding %
Italy [27]	29 seroconverting pregnant women, 27 husbands, 22 children	Culture	Urine	95	42
US-Alabama [73]	142 post-partum women, all CMV seropositive, over an average of 4 visits, with infected infants	Culture	Oral secretions Urine	36 141	14 45
US-Alabama [54]	6 adolescent seroconverters	Culture	Oral secretions Genital secretions Urine	141 142 54	27 23 59
US-California [21]	52 homosexual men in 1980–81, all CMV seropositive, HIV status unknown	PCR	Oral secretions Genital secretions Blood Blood Plasma	58 45 54 50 50	14 9 2 32 14
US-New York [100]	30 healthy homosexual men	Culture	Urine Semen	52 52	8 35
US-Washington [20]	951 CMV seropositive women presenting with problems at an STD clinic	Culture	Urine Semen Oral secretions Genital secretions Rectal secretions	30 30 890 169 890 432	20 20 8 2 14 1

^aResults from this table are not listed again in Table A2 but, if applicable, are plotted in Figure 3. They are generally single specimen (SS), single time point (ST) sample populations as defined in table A2.

Table A2

CMV shedding prevalence according to risk group, categorized by whether single specimens (SS) or multiple specimens (MS) were used and whether they were collected at a single time point (ST) or multiple time points (MT)^a

Country	Demographics/Sampling Method	Testing Method	Specimen Type(s)	Category	Sample size	Shedding %
		Category I. Congenitally infected children				
Sweden [59]	35 congenitally infected infants, ages 3 months-4 years	Culture	Urine	SS, ST	149	84
US-Alabama [75]	38 congenitally infected infants, ages 1-4 years	Culture	Urine	SS, ST	69	87
		Category II. Healthy children enrolled in day care centers				
England [98]	117 children in day nurseries over a 1-year period, 2-4 specimens per year	Culture	Urine	SS, MT	117	27
France [65]	93 children < 1 year old in day care centers	Culture	Urine	SS, ST	379	24
				SS, MT	93	36
Italy [69]	253 children in day care centers	Culture	Oral secretions	SS, ST	253	13
Japan [64]	54 children in day care centers	PCR	Oral secretions	SS, ST	54	22
Mexico [77]	152 children at day care centers, sampled at 3 visits	Culture	Oral secretions	SS, ST	127	7
				SS, ST	NS	5
				SS, ST	NS	7
				SS, MT	152	11
Sweden [122]	60 children in day care centers followed 12 weeks	Culture	Urine	SS, MT	60	27
Sweden [68]	18 children in day care centers, ages 2-3.5 years, mean follow-up of 35 weeks	Culture	Urine	SS, ST	221	55
US-Alabama [72]	Children in day care centers	Culture	Urine, oral secretions	MS, ST	243	32
US-Alabama [97]	188 children in day care centers	Culture	Urine, oral secretions	MS, ST	188	41
US-Alabama [14]	Children in day care centers	Culture	Urine, oral secretions	MS, ST	71	51
US-Alabama [56]	103 children in day care centers, 1-3 visits each	Culture	Urine, oral secretions	MS, MT	103	57
US-California [63]	100 children in day care centers	Culture	Urine, oral secretions	MS, ST	90	22
US-Iowa [66]	48 children in day care centers	Culture	Urine, oral secretions	MS, ST	80	21
US-Iowa [67]	79 children in day care centers followed for 2.5 years	Culture	Urine, oral secretions	MS, MT	79	35
US-Iowa [13]	219 children in day care centers at entry	Culture	Urine, oral secretions	MS, ST	219	15
				MS, MT	219	28
US-Virginia [11]	219 children in day care centers followed for 2.5-4.5 years	Culture	Urine, oral secretions	MS, MT	66	24
US-Virginia [123]	66 children in day care centers cultured 3 times	Culture	Urine	SS, MT	66	24
				MS, ST	118	44

Country	Demographics/Sampling Method	Testing Method	Specimen Type(s)	Category	Sample size	Shedding %
Category III. Healthy children not enrolled in day care centers						
England [62]	Infants without congenital CMV	Culture	Urine	SS, ST	983	12
The Gambia [61]	178 infants	Culture	Urine, oral secretions	MS, ST	178	53
Japan [64]	61 children not in day care centers	PCR	Oral secretions	MS, MT	150	62
Japan [88]	Infants and children ages 1 month-2 years	Culture	Oral secretions	SS, ST	61	7
Mauritius [58]	121 healthy children	Culture*	Urine	SS, ST	290	25
Sweden [59]	50 children without congenital CMV, ages 3 months-4 years	Culture	Urine	SS, ST	121	2
US-Alabama [57]	87 healthy infants ages 9-15 months	Culture	Oral secretions	SS, ST	225	31
US-Alabama [56]	25 children in home care	Culture	Urine, oral secretions	SS, ST	87	7
US-Iowa [60]	106 children in child care homes	Culture	Urine	MS, ST	25	8
US-New York [32]	200 healthy children	Culture	Urine	SS, ST	106	8
US-New York [30]	38 healthy migrant children	Culture	Urine	SS, ST	200	1
Category IV. Children with medical conditions						
Denmark [89]	262 hospitalized infants, not congenitally infected	Culture	Urine	SS, ST	262	4
England [99]	Hospitalized children	Culture	Urine, oral secretions	MS, ST	1395	3
England [19]	309 hospitalized patients, ages 2 months-14 years	Culture	Urine, oral secretions	MS, ST	309	5
Finland [31]	356 hospitalized and outpatient children > 2 months of age	Culture	Urine	SS, ST	356	26
Mauritius [58]	30 deaf children	Culture	Urine	SS, ST	30	50
Sweden [90]	91 mentally retarded children	Culture	Urine	SS, ST	91	18
US-California [63]	63 children in infant development centers	Culture	Urine	SS, ST	661	9
US-California [114]	93 infants in the intensive care unit, cultured weekly until discharge	Culture	Urine, oral secretions	MS, ST	50	22
US-New York [32]	100 hospitalized children	Culture	Urine	SS, MT	93	14
US-Texas [124]	314 hospitalized children in chronic care	Culture	Urine	SS, ST	100	1
US-Virginia [11]	2729 hospitalized children from newborns up to 18 years old	Culture	Oral secretions, urine, genital secretions	MS, ST	314	9
V. Adults without CMV risk factors						
Egypt [87]	50 women with recurrent abortions	PCR	Serum	SS, ST	2729	5
England [19]	402 hospitalized patients, ages 15-60+ years old	Culture	Urine, oral secretions	MS, ST	50	12
France [91]	231 semen donors	Culture	Semen	SS, ST	402	0
				SS, MT	635	1
				SS, MT	231	1

Country	Demographics/Sampling Method	Testing Method	Specimen Type(s)	Category	Sample size	Shedding %
France [93]	97 semen donors	PCR	Semen	SS, ST	551	4
The Gambia [61]	178 post-partum women, average prevalence in 21 of 3 specimen types over 6 cross-sectional visits		Urine, oral secretions, breast milk	MS, ST	178	12
Greece [92]	113 men at an infertility clinic	Nested PCR	Semen	SS, ST	113	7
Italy [82]	66 women receiving routine gynecological care	PCR	Genital secretions	SS, ST	66	73
Italy [85]	123 patients with fever of unknown origin	PCR	Serum	SS, ST	123	9
Japan [80]	953 blood donors	PCR	Blood	SS, ST	953	3
Japan [81]	993 healthy pregnant women, CMV serostatus undetermined, first trimester	PCR	Genital secretions	SS, ST	993	8
Taiwan [83]	29 post-partum women, CMV serostatus undetermined	PCR	Serum	SS, ST	29	10
Taiwan [71]	350 pregnant women at 2 time points in the 2 nd trimester, all CMV seropositive	PCR	Urine	SS, MT	350	11
Taiwan [22]	105 non-pregnant women from an infertility clinic	PCR	Genital secretions	SS, ST	105	8
Taiwan [95]	Men and women attending infertility clinic	DNA hybridization	Genital secretions	SS, ST	246	34
Turkey [76]	135 pregnant women, CMV serostatus undetermined, first trimester	PCR	Semen	SS, ST	248	34
US-Alabama [86]	113 healthy, post-partum women, all CMV seropositive, mean of 4.9 specimens per woman	PCR	Genital secretions	SS, ST	135	2
US-Alabama [73]	81 post-partum women, all CMV seropositive, over an average of 4 visits, with uninfected infants	PCR	Urine, blood	MS, MT	113	14
US-Massachusetts [94]	241 male infertility clinic attendees	PCR	Urine	SS, MT	113	8
US-New York [70]	181 HIV-negative, CMV-seropositive urban, minority women	Culture	Blood	SS, MT	113	6
US-Ohio [121]	710 CMV seropositive adolescent pregnant women cultured at each antenatal visit	Culture	Urine, Oral secretions, genital secretions	MS, MT	81	23
US-Texas [124]	43 nurses in chronic care	Culture	Semen	SS, ST	241	9
	76 therapists in chronic care	Culture	Genital secretions	SS, ST	181	4
	69 neonatal nurses	Culture	Urine	SS, MT	710	17
		Culture	Oral secretions, urine, genital secretions	MS, ST	43	2
					76	3
					69	3

Country	Demographics/Sampling Method	Testing Method	Specimen Type(s)	Category	Sample size	Shedding %
US-Virginia [12]	239 CMV seropositive day care workers, average of 3.4 culture sets per woman over two years	Culture	Urine, oral secretions	MS, ST	239	7
US-Washington [125]	120 critically ill immunocompetent patients, all CMV seropositive, 1954 samples, 3 samples collected per week, median of 11 samples per patient	PCR	Plasma	MS, MT SS, MT	239 120	11 33
Category VI. Adults with CMV risk factors						
Italy [82]	142 women with abnormal cytology findings	PCR	Genital secretions	SS, ST	142	63
Malawi [126]	19 KS patients and 58 first-degree family members	PCR	Urine, oral secretions	MS, ST	77	53
US-Alabama [73]	142 post-partum women, all CMV seropositive, over an average of 4 visits, with infected infants	Culture	Urine, oral secretions, genital secretions	MS, MT	142	56
US-Alabama [79]	52 women who were attending an STD clinic	PCR	Genital secretions	SS, ST	52	33
US-California [21]	206 CMV seropositive homosexual men, HIV status unknown, followed for a mean of 14.3 months	Culture	Urine	SS, MT	206	32
US-New York [100]	30 healthy homosexual men	Culture	Urine, semen	MS, ST	30	37
US-Washington [39]	191 CMV seropositive women attending an STD clinic, most were symptomatic, mean of 2.7 follow-up visits	Culture	Genital secretions	SS, ST	163	38
US-Washington [20]	951 CMV seropositive women presenting with problems at an STD clinic	Culture	Urine, genital secretions	SS, MT MS, ST	191 951	49 17

^aResults from the category SS, ST were included in Figure 1. When SS, ST results were available for more than one specimen type they were listed in Table A.1 rather than in this table.

Table A3

CMV shedding prevalence according to age^a

Country	Demographics/Sampling Method	Testing Method	Specimen Type (s)	Ages	Samples	Shedding %
England [78]	Congenitally infected children	Culture	Urine	0-3 months	48	92
				4-12 months	18	78
				1-2 years	7	86
				2-3 years	17	82
				3-4 years	8	50
				4-5 years	11	82
				0-3 months	48	92
				4-12 months	18	61
				1-2 years	4	25
				2-3 years	13	38
Sweden [59]	Congenitally infected children	Culture	Urine	3-4 years	7	0
				4-5 years	11	18
				< 1 week	35	100
				3 months	29	97
				6 months	26	92
				9 months	22	95
				12 months	27	81
18 months	21	67				
US-Alabama [28]	Congenitally infected children	Culture	Urine	30 months	17	71
				4 years	7	57
				0-6 months	243	98
				7-12 months	103	91
				13-24 months	101	86
				25-36 months	71	85
				37-48 months	69	72
				49-60 months	53	51
				61-72 months	42	33

Country	Demographics/Sampling Method	Testing Method	Specimen Type (s)	Ages	Samples	Shedding %
				73–84 months	28	39
				≥85 months	62	18
			Oral secretions	0–6 months	131	93
				7–12 months	59	73
				13–24 months	71	39
				25–36 months	50	38
				37–48 months	42	19
				49–60 months	37	16
				61–72 months	27	7
				73–84 months	22	0
				≥85 months	45	4
US-Alabama [96]	Asymptomatic congenitally infected children	Culture	Urine and/or oral secretions	2–3 years	10	90
				4–6 years	8	13
US-Alabama [75]	Asymptomatic congenitally infected children	Culture	Urine	1 year	17	88
				2 years	22	91
				3 years	18	89
				4 years	12	75
Category II. Healthy children enrolled in day care centers						
England [98]	Children in day care centers, shedding at some time during the study	Culture	Urine	< 2 years	26	46
				≥2 years	79	25
Italy [69]	Children in day care centers	Culture	Oral secretions	1 year	59	16
				2 years	126	13
				≥3 years	65	14
US-Alabama [72]	Children in day care centers	Culture	Urine	0–12 months	10	50
				13–24 months	53	36
				25–36 months	52	33
				37–48 months	52	29
				> 48 months	64	16
			Oral secretions	0–12 months	11	27
				13–24 months	54	33
				25–36 months	56	13

Country	Demographics/Sampling Method	Testing Method	Specimen Type (s)	Ages	Samples	Shedding %
US-Alabama [97]	Children in day care centers	Culture	Urine and/or oral secretions	37–48 months	53	2
				> 48 months	67	4
				0–12 months	10	0
				13–24 months	38	37
				25–36 months	35	77
				37–48 months	48	46
				> 48 months	57	25
				< 12 months	9	33
				13–24 months	7	71
				25–30 months	8	63
US-Alabama [55]	Children in day care centers	Culture	Urine	31–36 months	13	23
				37–48 months	18	33
				< 12 months	7	28
				13–24 months	10	80
				25–30 months	10	10
				31–36 months	11	9
				37–48 months	9	22
				< 12 months	6	16
				13–24 months	10	20
				25–30 months	9	0
US-Alabama [14]	Children in day care centers	Culture	Urine and/or oral secretions	31–36 months	11	0
				37–48 months	8	0
				0–12 months	11	9
				13–24 months	18	83
				25–36 months	16	63
				37–48 months	13	23
				49–60 months	12	58
				1 year	29	9
				1.5 years	25	80
				US-Alabama [56]	Children in day care centers	Culture
3 years	46	65				

Country	Demographics/Sampling Method	Testing Method	Specimen Type (s)	Ages	Samples	Shedding %
US-California [63]	Children in day care centers and infant developmental centers	Culture	Urine	4 years	37	53
				5 years	40	42
				0–12 months	33	21
				13–24 months	51	29
				25–36 months	42	19
				≥37 months	10	10
				0–12 months	36	13
				13–24 months	64	9
				25–36 months	50	2
				≥37 months	12	0
US-Iowa [66]	Children in day care centers	Culture	Urine and/or oral secretions	0–9 months	8	25
				10–24 months	13	62
				25–36 months	17	24
				37–48 months	17	18
				49–72 months	25	0
				0–9 months	8	25
				10–24 months	12	67
				25–36 months	14	29
				37–48 months	16	19
				49–72 months	23	0
US-Iowa [13]	Children in day care centers	Culture	Urine and/or oral secretions	0–9 months	8	25
				10–24 months	13	38
				25–36 months	17	6
				37–48 months	17	6
				49–72 months	25	0
US-Virginia [11]	Children in day care centers	Culture	Urine	< 2 years	74	22
				2 years	23	35
				3 years	50	12
				≥4 years	72	3
				0–2 years	31	25
				2–5 years	34	20

Country	Demographics/Sampling Method	Testing Method	Specimen Type (s)	Ages	Samples	Shedding %
Category III. Healthy children not enrolled in day care centers						
England [62]	Infants not congenitally infected	Culture	Urine and/or oral secretions	6 weeks 3 months 8 months 1 year	253 249 247 234	4 12 15 20
Japan [88]	Healthy children	Culture	Oral secretions	1 month 2 months 3 months 4 months 5 months 6 months 7 months 8 months 9 months 10 months 11 months 12 months	34 29 20 21 18 16 19 14 9 7 10 9	6 10 20 24 56 44 42 36 44 0 10 22
Sweden [59]	Children not congenitally infected	Culture	Urine	< 1 week 2 years	50 6	0 0
US-New York [30]	Migrant worker children	Culture	Urine	3 months 6 months 9 months 12 months 18 months 30 months 4 years 1-4 years 4-8 years 8-13 years	42 43 35 36 36 22 11 14 12 12	24 35 31 33 33 27 36 36 17 0

Category IV. Children with medical conditions

Country	Demographics/Sampling Method	Testing Method	Specimen Type (s)	Ages	Samples	Shedding %
Denmark [89]	Hospitalized infants, not congenitally infected	Culture	Urine	< 2 months	105	1
				2–5 months	76	8
				6–12 months	81	5
England [99]	Hospitalized children	Culture	Urine and/or oral secretions	< 3 months	508	2
				3–5 months	220	3
				6–11 months	207	6
				1–4 years	398	4
				> 4 years	62	2
England [19]	Hospitalized patients	Culture	Urine and/or oral secretions	2–5 months	32	9
				6 months - 4 years	104	10
				5–9 years	101	1
				10–14 years	72	0
Finland [31]	Hospitalized and outpatient children	Culture	Urine	2 months	43	12
				3 months	30	23
				4 months	26	23
				5–6 months	34	35
				7–9 months	32	25
				10–12 months	18	33
				13–18 months	35	34
				19–24 months	39	41
				25–36 months	30	33
				37–48 months	20	20
				5–15 years	49	14
Sweden [90]	Hospitalized infants	Culture	Urine	≤4 weeks	394	1
				5–9 weeks	52	12
				2–11 months	215	23
US-New York [32]	Healthy children and children with chronic conditions	Culture	Urine	0–2 years	52	2
				2–6 years	148	8
				6–19 years	145	3
US-Virginia [11, 29]	Hospitalized children	Culture	Urine	Newborns	551	3
				0–2 years	544	7

Country	Demographics/Sampling Method	Testing Method	Specimen Type (s)	Ages	Samples	Shedding %
Category V. Adults without CMV risk factors						
England [19]	Hospitalized patients	Culture	Urine and/or oral secretions	2–5 years	913	7
				5–12 years	476	4
				12–18 years	245	1
				15–24 years	102	0
				25–34 years	100	0
				35–59 years	100	0
				≥60 years	100	0
US-Alabama [18]	Pregnant women	Culture	Urine	≤14 years	38	8
				15–20 years	306	6
				21–25 years	123	4
				26–30 years	44	0
				≥31 years	29	0
			Genital secretions	≤14 years	30	17
				15–20 years	372	11
				21–25 years	111	11
				26–30 years	41	10
				≥31 years	30	0

^a Some of the results from this table are listed in previous tables without stratifying by age.

Table A4

CMV shedding among pregnant women according to time of gestation.

Country	Testing Method	Specimen Type	Time of Gestation	Sample Size	Shedding %
Japan [88]	Culture	Genital secretions	1 st trimester	30	0
			2 nd trimester	62	6
			3 rd trimester	61	17
Taiwan [71]	PCR	Urine	15 weeks	350	3
			25 weeks	350	9
			15 weeks	220	17
			25 weeks	220	24
Taiwan [22]	PCR	Urine (longitudinal collection)	1 st trimester	207	1
			2 nd trimester	207	10
			3 rd trimester	207	13
		Urine (cross-sectional collection)	1 st trimester	906	4
			2 nd trimester	395	10
			3 rd trimester	273	13
			1 st trimester	54	13
			2 nd trimester	54	32
			3 rd trimester	54	35
US-Alabama [18]	Culture	Genital secretions (cross-sectional collection)	1 st trimester	217	15
			2 nd trimester	140	40
			3 rd trimester	81	37
			1 st trimester	183	2
			2 nd trimester	359	6
			3 rd trimester	317	11
US-Pennsylvania [101]	Culture	Genital secretions	1 st trimester	43	2
			2 nd trimester	83	7
			3 rd trimester	49	12

Table A5
 Frequency of sensorineural hearing loss among congenitally infected children according to CMV viral load at birth

Country	Testing Method	Specimen Type(s)	Viral Load	Sample Size	% with Sensorineural Hearing Loss
Belgium [107]	PCR	Urine	< 3 log ge/mL	11	36
			3.0–4.5 log ge/mL	8	38
England [106]	PCR	Dried blood spots	>4.5 log ge/mL	13	77
			Negative	10	50
			2–2.5 log ge/mL	5	60
			2.5–3 log ge/mL	10	80
			>3 log ge/mL	9	100
Italy [105] ^a	PCR	Blood	< 10 ² ge/10 ⁵ PBMCs	4	0
			10 ² –10 ³ ge/10 ⁵ PBMCs	16	6
US-Alabama [104]	Culture	Urine	10 ³ –10 ⁴ ge/10 ⁵ PBMCs	14	50
			> 10 ⁴ ge/10 ⁵ PBMCs	3	67
			< 3500 pfu/mL	26	4
			3500–25000 pfu/mL	26	12
			>25000 pfu/mL	24	33
			< 3500 ge/mL	25	0
US-Alabama [102]	PCR	Blood	3500–25000 ge/mL	25	8
			>25000 ge/mL	25	40
			< 5000 pfu/mL	6	0
US-Alabama, Arkansas, Texas [103]	Culture	Urine	5000–50000 pfu/mL	8	50
			>50000 pfu/mL	7	71
			< 200 ge/mL	5	20 ^b
	PCR	Serum	200–5400 ge/mL	15	67 ^b
			>5400 ge/mL	9	67 ^b

^a All sequelae rather than sensorineural hearing loss only.

^b At 12 months follow-up.

ge, genome equivalents; pfu, plaque forming units; mL, milliliter; PBMC, peripheral blood mononuclear cells.