Viral infections in young infants : epidemiologic and diagnostic aspects of ToRCH, enterovirus and human parechovirus

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HOW TO USE... NEONATAL TORCH TESTING

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ABSTRACT

Toxoplasma gondii, rubella, cytomegalovirus and herpes simplex virus have in common that they can cause congenital (ToRCH) infection, leading to fetal and neonatal morbidity and mortality. During the last decades, ToRCH screening, which is generally considered to be single serum testing, has been increasingly used inappropriately and questions have been raised concerning the indications and cost-effectiveness of ToRCH testing. The problems of ToRCH screening lie in requesting the screening for the wrong indications, wrong interpretation of the single serum results and in case there is a good indication for diagnosis of congenital infection, sending in the wrong materials. This review provides an overview of the pathogenesis, epidemiology and clinical consequences of congenital ToRCH infections and discusses the indications for, and interpretation of, ToRCH screens.

INTRODUCTION

Toxoplasma gondii, rubella, cytomegalovirus (CMV) and herpes simplex virus (HSV) have in common that they can cause congenital infection, leading to foetal and neonatal morbidity and mortality. The acronym ToRCH, which originally grouped these 4 pathogens, was first proposed by Nahmias et al. in 1971 [1] to simplify diagnostic procedures in severely ill neonates and to impose clearer structure in the large differential diagnosis of congenital infections. Since then the acronym has been expanded, with the addition of syphilis (ToRCHe**S**), and parvovirus B19, enterovirus, hepatitis B and HIV as 'others' (ToRCH) [2].

During the last decades, ToRCH screening, which is generally considered to be single serum-testing, has been increasingly used inappropriately and questions have been raised concerning the indications and cost-effectiveness of ToRCH testing [3-7]. The problems of ToRCH screening lie in requesting the screening for the wrong indications, wrong interpretation of the single serum results and in case there is a good indication for diagnosis of congenital infection, sending in the wrong materials.

The start of good laboratory practice for congenital infections is good clinical practice. The long list of pathogens capable of congenital infection should be considered in view of clinical symptoms of the neonate, epidemiology, maternal vaccination status, standard early pregnancy screening and risk factors, such as travelling to endemic areas or sexual behaviour. Good laboratory practice starts with an appropriate set of materials at the right time and the use of sensitive and specific assays.

This review provides an overview of the pathogenesis, epidemiology and clinical consequences of congenital ToRCH infections and discusses the indications for, and interpretation of, ToRCH screens.

PHYSIOLOGICAL BACKGROUND

Toxoplasmosis

The protozoan parasite *Toxoplasma gondii* can cause infection when its oocysts or tissuecysts are ingested [8 9]. Primary infection in pregnancy has been associated with spontaneous abortion and stillbirth [10-12]. The epidemiology of *Toxoplasma gondii* infection varies worldwide. Table 4.1 shows the seroprevalence of IgG of women of childbearing age [13]. Although we present data per continent, large variation in regional seroprevalence within one continent may exist due to differences in climate, cultural differences in amount of raw meat consumed, and increased consumption of meat from animals farmed outdoors and frozen meat [9].

Vertical transmission only occurs if the mother becomes infected for the first time during her pregnancy. The highest risk of giving birth to a child with symptomatic congenital toxoplasmosis (about 10%) is when seroconversion occurs at 24–30 weeks' gestation [12 14 15]. Clinical signs and symptoms of congenital toxoplasmosis, if present, are often not recognized at birth, as sequelae usually develop later in life [16]. Most children develop normally, but about 20% develop sequelae [17]. Congenital toxoplasmosis may result in retinochoroiditis and retinal scarring in 12% of children and neurological abnormalities such as cerebral calcifications and hydrocephalus in 12–16% of cases [12 18-22].

Rubella

The exact pathogenesis of rubella infection is not fully understood, though it is clear that structural damage to the foetus is caused by defective organogenesis. The virus has been isolated from all organs following congenital infection in the first trimester of pregnancy [23].

Most countries have now integrated rubella vaccination in their national vaccination program. However, routine rubella vaccination currently is not in use in large parts of Africa and some countries in South-East Asia [24].

With the decrease of (maternal) rubella infection, incidence of congenital rubella syndrome (CRS) has also declined, although isolated unvaccinated populations may still be at risk [16]. Table 4.1 shows differences in seroprevalence of IgG antibodies between geographic regions.

When primary maternal infection occurs during the first trimester, the virus will cross the placenta and cause foetal infection in about 80% of cases. The risk for foetal infection declines thereafter, as does the risk for congenital defects [25].

The features of congenital rubella syndrome (CRS) were originally described as the triad of cataracts, heart defects and sensorineural hearing loss [26]. Since then almost every foetal organ has been described to be infected by rubella and the clinical spectrum ranges from miscarriage or stillbirth to severe multiple birth defects to no apparent defect at birth. Late onset manifestations (after the second year of life) of congenital rubella syndrome are caused by progressive disease due to persistent viral infection and defects in immune response. This can cause a progression (or late onset) of eye, hearing and developmental defects [27].

Cytomegalovirus

Humans are the only known reservoir of CMV and viral transmission occurs by close contact with infected secretions, including urine, saliva, cervical and vaginal secretions, semen and breast milk.

After mucosal infection and local replication, the virus spreads to lymphoid tissue and spreads to visceral organs, preferably liver and spleen, after which viral load increases and the infection spreads to distal organs and sites of persistence [16].

In Table 4.1 seroprevalence rates are shown for women of childbearing age. In industrialised countries, the birth prevalence of congenital CMV is about 0.6–0.7%, whereas it can be as high as 2% in developing countries [28 29].

The risk of in utero transmission of CMV is highest (approximately 32%) following primary maternal infection. But, in contrast to congenital rubella and toxoplasmosis, the relative immunocompromised state of pregnancy can result in maternal reinfection (with a different strain) or reactivation which can also lead to congenital infection [16 30 31].

About 10–15% of congenitally infected newborns have symptoms of disease at birth, including low birth weight, central nervous system (CNS) damage, liver involvement and ocular or auditory damage (sensorineural hearing loss) [20 28 32]. Another symptom of congenital CMV, indicating extramedullary haematopoiesis, is blueberry muffin spots. Approximately half of children who are symptomatic at birth eventually have CNS involvement [20]. Though almost 90% of the congenitally infected children are asymptomatic at birth, of these an estimated 13.5% will develop long term neurologic sequelae, predominantly sensorineural hearing loss.

Herpes simplex virus

This pathogen is 'the odd one out' in the ToRCH acronym because although HSV can be vertically transmitted during pregnancy, this is extremely rare. Neonatal disease is the result of perinatal transmission (usually during birth).

Prevalence of HSV antibodies differ by HSV type. HSV-I can be acquired during childhood and antibodies rise from young childhood to the beginning of the second decade of life to approximately 70–95% in individuals from lower socioeconomic populations, and to 30–40% in higher socioeconomic populations [33-35]. HSV-II is usually acquired through sexual contact, seroprevalence varies greatly and is associated with geographic region, sex, age, race, and high-risk behaviours [35]. In Table 4.1 continental differences of seroprevalence for both HSV-I and HSV-II are shown.

Of all children born with neonatal HSV infection 60–80% of mothers are asymptomatic for the disease and they and their partner have no history of genital herpes [16 36]. True primary infection (a first infection with HSV in the individual) has the highest risk for transmission, about 50% [36]. This is probably due to the high viral load and longer period

Table 4.1: IgG seroprevalence of women of childbearing age for ToRCH

	Toxoplasmosis	Rubella	Cytomegalovirus	Herpes simplex virus
Europe	19.4–43.8% [72-74]	* 96.5–97.7% [75-77]	41–69.4% [78 79]	**HSV-I:** 68.7–79.4% **HSV-II:** 5.7–21.2% [33 80 81]
Asia	8% [82]	73.1–80.2% [83]	100% [84]	**HSV-I:** 90.3% **HSV-II:** 7.8–12.5% [85 86]
USA	11% [8]	* 91.5% [87]	70–90% [88]	**HSV-I:** 56% **HSV-II:** 17% [35 89]
Latin America	53% [90]	* 62% [91]	100% [92]	**HSV-I:** 80.7–75.8% **HSV-II:** 4–33.3% [93 94]
Africa	72.5–88.8% [10]	64.8–72.2% [95 96]	72.2–100% [95 97]	**HSV-I:** 92% [98] **HSV-II:** 33.2–35% [99 100]

* Indicates reference from a country/continent with national vaccination programme for rubella.

of viral shedding in the mother. Infants born to mothers with a new, but non-primary (infection with another HSV type or strain) infections have a somewhat lower risk that was estimated to be about 30%. Reactivation of a latent infection has the lowest risk for maternal-foetal transmission (2%). If active infection with genital lesions is present, delivery by caesarean section has a protective effect on acquiring HSV infection for the newborn [36 37]. The incidence of herpes neonatorum varies between 31 in 100,000 live births in the USA, 3.2 per 100,000 live births in the Netherlands [38] and 1.65 per 100,000 live births in the UK [39]. Regardless of maternal signs of herpes simplex infection, a paediatrician should consider the diagnosis if a child has symptoms that fit the diagnosis. Neonatal infection with HSV is symptomatic in almost all cases and is divided into localized, CNS disease and disseminated disease. Localized congenital HSV infection is limited to the skin, eye or mouth, whereas CNS disease results in encephalitis and disseminated disease leads to multiple organ involvement [16].

TECHNOLOGICAL BACKGROUND

General considerations

Interpretation of serology for congenital infections should be done with care. Knowledge on foetal and neonatal serology is required. IgM is foetally derived and a positive IgM is indicative of foetal infection, however, negative IgM results cannot exclude foetal infection. IgG, in contrast, can cross the placenta and is maternal in origin. Therefore, in the absence of foetal infection neonatal IgG titres will fall after birth.

Table 4.2: Diagnostic options for newborn samples

Pathogen	Material	Method	Sensitivity	Specificity
Toxoplasmosis	Serum (single sample)	IgM/IgA	61–68% [42 101]	77–100% [42 102 103]
	Repeated serum	IgM/IgA	No data	No data
	Serum	IgG	65–73% [42]	96–100% [42]
	Serum	IgM/IgA mother infant pair	88-96% [42]	77–100% [42]
	Amniotic fluid	PCR	71% [104]	98% [104]
Rubella	Serum (Obtained before 3 months of age)	IgM	85–100% [105]	No data
	Urine / saliva (Obtained before 3 months of age)	PCR	89–90% [105]	No data
Cytomegalovirus	Serum (Obtained before 3 weeks of age)	IgM	20–70.7% [52 106 107]	100% [106]
	Dried blood spot	PCR	71–100% [49 50]	99.3–100% [49 50]
		Viral culture (regarding PCR as reference)	89.3% [107]	No data
	Urine / saliva	PCR	> 97% [47 108]	99.9% [47 108]
Herpes simples virus	Blood, nasopharyngeal swab, conjunctivae swab, CSF	Viral culture	99% [109]	100% [109]
	Blood, nasopharyngeal swab, conjunctivae swab, CSF	PCR	> 95% [54]	100% [54]

Table 4.2 shows an overview of diagnostic tests with their sensitivities and specificities for the different types of congenital infection.

Toxoplasmosis

Postnatal diagnosis of congenital toxoplasmosis relies on a series of serologic tests. The diagnosis congenital toxoplasmosis can be rejected if neonatal IgM and IgG are both negative. This is most reliable if maternal infection occurred more than two weeks before, otherwise she could infect the foetus whilst not yet possessing antibodies herself. Congenital

toxoplasmosis is confirmed if neonatal IgM is positive, and persists after 1 month of age, or if specific IgG-antibodies persist after 1 year [40]. When IgM and IgA results are negative, but a positive IgG is found, use of IgG western blots of mother-infant pairs can prove useful [41 42]. Recently Sterkers et al. (2011) described molecular diagnosis by PCR on peripheral blood as a sensitive and highly specific test for congenital toxoplasmosis, establishing the diagnosis in 5/6 cases correctly, and earlier than serological testing [43].

Rubella

To confirm suspected congenital rubella, both maternal and neonatal specimens should be investigated. Congenital rubella infection is diagnosed when the newborn possesses rubella specific IgM antibodies [16]. Congenital rubella syndrome is defined as combination of a positive rubella specific IgM and clinically confirmed CRS [24]. The highest sensitivity and specificity of IgM testing can be achieved by using a μ-capture ELISA and by testing a sample within 3 months after birth. In addition monitoring of rubella specific IgG may be helpful, as persistence of rubella specific IgG after 4–6 months of age is highly indicative of congenital infection [27]. Although this method is useful, if the rubella virus is circulating in the general population (for example in countries without a national rubella vaccination programme), physicians should be aware of not mistaking congenital infection for postnatal acquired rubella [16]. If available, detection of viral RNA on urine and throat swab by PCR offers fast and reliable diagnosis [44-46].

Cytomegalovirus

The gold standard for diagnosis of congenital CMV is viral PCR or culture of neonatal urine and/or saliva in the first 2–3 weeks of life. In addition, the detection of CMV specific IgM antibodies in this period of life may confirm congenital CMV, but is only present in about 20–70% of newborns [29 47 48]. After this period diagnosis of congenital CMV can be made by performing PCR on the dried blood spots (DBS), retrieved in the first week of life. The sensitivity of this PCR varies between 71–100% depending on the population studied and on the DNA extraction methods used [49]. A recent study reported a sensitivity of only 34% in the setting of neonatal screening [50]. The viral load in neonatal blood and DBS has been shown to be associated with clinical outcome [49 51]. Therefore, if DBS-testing is used in a clinical setting for diagnosis of congenital CMV in a symptomatic child the sensitivity, if technical performance is of high quality, is expected to be acceptable [52 53].

Herpes simplex virus

For the diagnosis of neonatal HSV infection viral detection remains the gold standard for diagnosis and should be performed on blood, vesicles, nasopharyngeal swab, conjunctivae and CSF samples. PCR is nowadays becoming more readily available in most hospitals and is gradually replacing viral culture. To detect encephalitis or disseminated infection, PCR on cerebrospinal fluid is the most rapid method, showing similar results as CSF viral culture [54 55].

CLINICAL QUESTIONS

Should we perform a ToRCH screen in all small for gestational age (SGA) newborns?

There is no clear answer to this question due inconclusive evidence from a small number of studies which often had severe methodological flaws. Neonatal birth weight below the 10th percentile for its gestational age is defined as SGA [56]. SGA can occur because of a wide variety of disorders [57 58]. Since congenital infections are one of the possible underlying pathologic processes linked to SGA, some authors have suggested that ToRCH screening should be part of the routine diagnostic work-up in SGA newborns [58 59]. However, the association of congenital infections and SGA is merely speculative and based on limited data [4 59]. In the last two decades several studies have assessed the association between SGA and ToRCH infections. None showed cost-effectiveness for a complete 'ToRCH-screening' for isolated SGA without any further clinical signs of congenital infection. ToRCH screening should thus, at the most, be limited to CMV testing, which is supported by some evidence [4 60 61]. For example, one study showed that CMV infection was associated with low birth weight with a prevalence ratio of 3.4 (CI 1.4–8.5) [60]. Another study showed that CMV urine culture was positive in 2% of cases of SGA newborns, whereas no other infectious causes were found [4].

Neurological indication for ToRCH screening

Congenital infections have a certain predilection to infect neurons and can cause different types of CNS disorders including cerebral lesions, meningoencephalitis, and hearing loss, which are discussed further below.

a. Should we investigate cerebral lesions detected with cerebral imaging with a ToRCH screen?

A classic example of the association between cerebral imaging abnormalities and congenital infection is that of the association of intracranial calcifications with congenital toxoplasmosis, which has been known for several decades [19 62 63]. Several types of cerebral lesions detected with cranial ultrasound or magnetic resonance imaging have been

associated with congenital infections including hydrocephalus, migratory disorders and white matter lesions, which may be investigated by ToRCH screening are outlined in Table 4.3. Of note, recommendations for ToRCH testing in cerebral abnormalities are based on small cases series and level of evidence is mainly based on expert opinion.

b. Should every case of neonatal meningoencephalitis be investigated with a ToRCH screen?

HSV infection may involve the CNS and lead to meningoencephalitis, which is fatal if left untreated. Therefore, it is common practice that all cases of neonatal meningoencephalitis should be investigated for HSV infection by means of PCR of CSF, nasopharyngeal swab and serum. As early diagnosis and prompt treatment with acyclovir is essential, there must be a high level of awareness of the serious nature of neonatal HSV infection [64-67].

Table 4.3: CNS imaging abnormalities and recommended test

Intracranial abnormalities	Described in	Type of evidence (literature reference)	Recommended test
Hydrocephalus or Ventriculomegaly	Toxoplasmosis, CMV	- Case series [20]	Urine CMV Toxoplasma serology
Calcifications	Toxoplasmosis, CMV	- Case report; n = 1 toxoplasmosis [19] - Case series; 18/33 toxoplasmosis [63] - Case series; 1/16 CMV [110]	Urine CMV Toxoplasma serology
Lenticulostriate vasculopathy	Toxoplasmosis, CMV	- Case series; 0/58 had positive torch screening [3] - Case series, 1/70 toxoplasmosis and 1/70 CMV [111]	Urine CMV Toxoplasma serology
Subependymal (pseudo-) cysts	Rubella, CMV, *rarely toxoplasmosis*	- Case series; 1/59 CMV [5] - Case series; 1/16 CMV [110] - Case series, 1/13 rubella and 2/13 CMV [112] - Meta-analysis; 1/120 toxoplasmosis, 9/120 CMV, 4/120 rubella [113] - Case series, 1/24 CMV [114]	Urine CMV Rubella serology *Toxoplasma only on indication (maternal risk factors)*
Microcephaly	Rubella, CMV	- Case report, n = 1 rubella [115] - Case series, 1/9 rubella [116] - Cohort study, 2/56 CMV [117]	Urine CMV Rubella serology
Meningoencephalitis	Herpes simplex virus	Incidence of herpes simplex virus induced meningoencephalitis varies per geographic region (Table 4.1). Early recognition and treatment of HSV meningoencephalitis reduces mortality and morbidity [66 118 119].	Herpes PCR on neonatal serum, CSF, nasopharynx and/or skin-vesicle

c. Should we use ToRCH-screening in every case of hearing impairment?

CMV is an overlooked cause of permanent hearing impairment in children. About 8% of children with sensorineural hearing loss (SNHL) have had congenital CMV. In children with profound and/or bilateral SNHL CMV is an even more frequent cause (23%). Children with hearing loss due to CMV would usually have had passed the neonatal hearing screen as the damage to the inner ear does not manifest itself until early childhood. CMV DNA can then be detected in dried blood spots collected at birth as described by Barbi et al with a maximum sensitivity of 100% and specificity of 99% when a viral load of 4–5 log(10) copies/L are present [49 68-70].

Congenital rubella infection (in light of local epidemiology and maternal vaccination status) can also cause early onset or delayed onset SNHL [71] and should be investigated if SNHL is detected, especially in countries where rubella vaccination is not part of the vaccination program.

FUTURE RESEARCH

The guidelines we provide in this review are mostly based on small sample sized and retrospective studies. Although the currently available evidence shows no indications for full ToRCH screening should be performed in cases of isolated SGA or minor cerebral lesions, large prospective, possibly international, studies are necessary to produce a higher level of evidence.

Furthermore studies are needed to investigate the consequences of ToRCH screening. It would be interesting to know whether a positive ToRCH screen leads to adjustment of treatment and subsequently better outcome.

Also studies regarding follow-up of children after a positive ToRCH screening are necessary. Long term neurodevelopmental outcome of children with SGA or minor cerebral abnormalities with and without positive ToRCH screening could be compared.

CONCLUSIONS

During the last decade, several studies have investigated when testing for toxoplasmosis, rubella, CMV and herpes simplex is indicated. ToRCH testing should not be regarded as one single serum-testing. International consensus to determine which clinical condition in a newborn is a good indication for ToRCH testing is not available. To indicate pre-test risks for infection with one of these pathogens, geographic region, first-trimester maternal antibody

status and clinical signs and symptoms must be taken into account before deciding which laboratory test is useful to discriminate.

This review provides insight in these variables and contains guidelines for appropriate diagnostic testing. Although complicated due to the low incidence of congenital infections, structured follow-up studies are necessary to obtain insight in the use and consequences of 'ToRCH' testing.

CLINICAL BOTTOM LINE

- There is no high level evidence showing that ToRCH screening should routinely be performed in all SGA newborns.
- There is no high level evidence showing that ToRCH screening should routinely be performed in newborns with minor cerebral abnormalities (such as LSV and SEC).
- CMV screening should be performed in infants with hearing impairment to exclude congenital CMV.
- In infants with suspected herpes neonatorum, early diagnosis (with complete HSV screening using PCR-tests) and prompt treatment is essential.

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REFERENCES

1. Nahmias AJ, K.W. W, J.A. S. The ToRCH complex-perinatal infections associated with toxoplasma and rubella, cytomegalo- and herpes simplex viruses. Pediatr Res 1971;5:405-06.
2. Tolan RWJ. Passing the "TORCH". Infectious Diseases in Clinical Practice 2008;16(1):4-5 10.1097/IPC.0b013e3181373d27.
3. de Jong EP, Lopriore E, Vossen AC, et al. Is routine TORCH screening warranted in neonates with lenticulostriate vasculopathy? Neonatology 2010;97(3):274-8. doi: 10.1159/000255166
4. van der Weiden S, de Jong EP, Te Pas AB, et al. Is routine TORCH screening and urine CMV culture warranted in small for gestational age neonates? Early Hum Dev 2011;87(2):103-7. doi: 10.1016/j.earlhumdev.2010.11.005
5. van der Weiden S, Steggerda SJ, Te Pas AB, et al. Routine TORCH screening is not warranted in neonates with subependymal cysts. Early Human Development 2010;86(4):203-07. doi: 10.1016/j.earlhumdev.2010.02.009
6. Abdel-Fattah SA, Bhat A, Illanes S, et al. TORCH test for fetal medicine indications: only CMV is necessary in the United Kingdom. Prenatal Diagnosis 2005;25(11):1028-31. doi: 10.1002/pd.1242
7. Khan NA, Kazzi SN. Yield and costs of screening growth-retarded infants for torch infections. Am J Perinatol 2000;17(3):131-5. doi: 10.1055/s-2000-9288 [published Online First: 2000/09/30]
8. Jones JL, Dargelas V, Roberts J, et al. Risk factors for Toxoplasma gondii infection in the United States. Clin Infect Dis 2009;49(6):878-84. doi: 10.1086/605433 [published Online First: 2009/08/12]
9. Cook AJ, Gilbert RE, Buffolano W, et al. Sources of toxoplasma infection in pregnant women: European multicentre case-control study. European Research Network on Congenital Toxoplasmosis. BMJ 2000;321(7254):142-7. [published Online First: 2000/07/14]
10. Onadeko MO, Joynson DH, Payne RA, et al. The prevalence of toxoplasma antibodies in pregnant Nigerian women and the occurrence of stillbirth and congenital malformation. Afr J Med Med Sci 1996;25(4):331-4. [published Online First: 1996/12/01]
11. Goldenberg RL, Thompson C. The infectious origins of stillbirth. Am J Obstet Gynecol 2003;189(3):861-73. doi: S0002937803004708 [pii] [published Online First: 2003/10/04]
12. Foulon W, Villena I, Stray-Pedersen B, et al. Treatment of toxoplasmosis during pregnancy: a multicenter study of impact on fetal transmission and children's sequelae at age 1 year. Am J Obstet Gynecol 1999;180(2 Pt 1):410-5. doi: S0002937899001325 [pii] [published Online First: 1999/02/13]
13. Benard A, Petersen E, Salamon R, et al. Survey of European programmes for the epidemiological surveillance of congenital toxoplasmosis. Euro Surveill 2008;13(15) doi: 18834 [pii] [published Online First: 2008/05/01]
14. Dunn D, Wallon M, Peyron F, et al. Mother-to-child transmission of toxoplasmosis: risk estimates for clinical counselling. Lancet 1999;353(9167):1829-33. doi: S0140-6736(98)08220-8 [pii] 10.1016/S0140-6736(98)08220-8 [published Online First: 1999/06/08]
15. Villena I, Ancelle T, Delmas C, et al. Congenital toxoplasmosis in France in 2007: first results from a national surveillance system. Euro Surveill 2010;15(25) doi: 19600 [pii] [published Online First: 2010/07/01]
16. Remington JS, Klein JO, Wilson CB, et al. Infectious Diseases of the Fetus and Newborn. 7th edition ed: Elsevier Saunders 2007.
17. Freeman K, Salt A, Prusa A, et al. Association between congenital toxoplasmosis and parent-reported developmental outcomes, concerns, and impairments, in 3 year old children. BMC Pediatr 2005;5:23. doi: 1471-2431-5-23 [pii] 10.1186/1471-2431-5-23 [published Online First: 2005/07/15]

18. Gras L, Wallon M, Pollak A, et al. Association between prenatal treatment and clinical manifestations of congenital toxoplasmosis in infancy: a cohort study in 13 European centres. Acta Paediatr 2005;94(12):1721-31. doi: P1938576GU58296G [pii] 10.1080/08035250500251999 [published Online First: 2006/01/20]
19. Hoekstra F, Buzing C, Sporken JM, et al. [Congenital toxoplasmosis: severe ocular and neurological complications]. Ned Tijdschr Geneeskd 2011;155(18):A2853. [published Online First: 2011/05/12]
20. de Vries LS, Verboon-Maciolek MA, Cowan FM, et al. The role of cranial ultrasound and magnetic resonance imaging in the diagnosis of infections of the central nervous system. Early Hum Dev 2006;82(12):819-25. doi: S0378-3782(06)00229-5 [pii] 10.1016/j.earlhumdev.2006.09.006 [published Online First: 2006/10/25]
21. Tan HK, Schmidt D, Stanford M, et al. Risk of visual impairment in children with congenital toxoplasmic retinochoroiditis. Am J Ophthalmol 2007;144(5):648-53. doi: S0002-9394(07)00635-6 [pii] 10.1016/j.ajo.2007.07.013 [published Online First: 2007/09/15]
22. Cortina-Borja M, Tan HK, Wallon M, et al. Prenatal treatment for serious neurological sequelae of congenital toxoplasmosis: an observational prospective cohort study. PLoS Med 2010;7(10) doi: e1000351 [pii] 10.1371/journal.pmed.1000351 [published Online First: 2010/10/23]
23. Lee JY, Bowden DS. Rubella virus replication and links to teratogenicity. Clin Microbiol Rev 2000;13(4):571-87. [published Online First: 2000/10/12]
24. http://www.who.int/immunization_monitoring/diseases/rubella/en/index.html 01-02-2012 [2011-02-01]. Available from: http://www.who.int/immunization_monitoring/diseases/rubella/en/index.html
25. Miller E, Cradock-Watson JE, Pollock TM. Consequences of confirmed maternal rubella at successive stages of pregnancy. Lancet 1982;2(8302):781-4. [published Online First: 1982/10/09]
26. Gregg NM. Congenital cataract following German measles in the mother. Trans Ophthalmol Soc Aust 1941;3:35.
27. Best JM. Rubella. Semin Fetal Neonatal Med 2007;12(3):182-92. doi: S1744-165X(07)00018-2 [pii] 10.1016/j.siny.2007.01.017 [published Online First: 2007/03/06]
28. Dollard SC, Grosse SD, Ross DS. New estimates of the prevalence of neurological and sensory sequelae and mortality associated with congenital cytomegalovirus infection. Rev Med Virol 2007;17(5):355-63. doi: 10.1002/rmv.544 [published Online First: 2007/06/02]
29. Kenneson A, Cannon MJ. Review and meta-analysis of the epidemiology of congenital cytomegalovirus (CMV) infection. Rev Med Virol 2007;17(4):253-76. doi: 10.1002/rmv.535 [published Online First: 2007/06/21]
30. Tian C, Ali SA, Weitkamp J. Congenital Infections, Part 1: Cytomegalovirus, Toxoplasma, Rubella and Herpes Simplex. NeoReviews 2010;11(8):e436-e46.
31. Boppana SB, Rivera LB, Fowler KB, et al. Intrauterine transmission of cytomegalovirus to infants of women with preconceptional immunity. N Engl J Med 2001;344(18):1366-71. doi: 10.1056/nejm200105033441804 [published Online First: 2001/05/03]
32. Malm G, Engman ML. Congenital cytomegalovirus infections. Semin Fetal Neonatal Med 2007;12(3):154-9. doi: S1744-165X(07)00013-3 [pii] 10.1016/j.siny.2007.01.012 [published Online First: 2007/03/06]
33. Sauerbrei A, Schmitt S, Scheper T, et al. Seroprevalence of herpes simplex virus type 1 and type 2 in Thuringia, Germany, 1999 to 2006. Euro Surveill 2011;16(44). doi: 20005 [pii] [published Online First: 2011/11/17]
34. Wentworth BB, Alexander ER. Seroepidemiology of infectious due to members of the herpesvirus group. Am J Epidemiol 1971;94(5):496-507. [published Online First: 1971/11/01]
35. Smith JS, Robinson NJ. Age-specific prevalence of infection with herpes simplex virus types 2 and 1: a global review. J Infect Dis 2002;186 Suppl 1:S3-28. doi: JID020147 [pii] 10.1086/343739 [published Online First: 2002/09/28]

36. Prober CG, Sullender WM, Yasukawa LL, et al. Low risk of herpes simplex virus infections in neonates exposed to the virus at the time of vaginal delivery to mothers with recurrent genital herpes simplex virus infections. N Engl J Med 1987;316(5):240-4. doi: 10.1056/nejm198701293160503 [published Online First: 1987/01/29]
37. Brown ZA, Wald A, Morrow RA, et al. Effect of serologic status and cesarean delivery on transmission rates of herpes simplex virus from mother to infant. JAMA 2003;289(2):203-9. doi: joc20645 [pii] [published Online First: 2003/01/09]
38. Poeran J, Wildschut H, Gaytant M, et al. The incidence of neonatal herpes in The Netherlands. J Clin Virol 2008;42(4):321-5. doi: S1386-6532(08)00063-2 [pii] 10.1016/j.jcv.2008.02.004 [published Online First: 2008/03/25]
39. Tookey P, Peckham CS. Neonatal herpes simplex virus infection in the British Isles. Paediatr Perinat Epidemiol 1996;10(4):432-42. [published Online First: 1996/10/01]
40. Hartup C, Johnson JD, Holliman RE. Toxoplasma and pregnancy. Lancet 1991;338(8762):317-8. doi: 0140-6736(91)90459-3 [pii] [published Online First: 1991/08/03]
41. Montoya JG, Liesenfeld O. Toxoplasmosis. Lancet 2004;363(9425):1965-76. doi: 10.1016/S0140-6736(04)16412-X S014067360416412X [pii] [published Online First: 2004/06/15]
42. Pinon JM, Dumon H, Chemla C, et al. Strategy for diagnosis of congenital toxoplasmosis: evaluation of methods comparing mothers and newborns and standard methods for postnatal detection of immunoglobulin G, M, and A antibodies. J Clin Microbiol 2001;39(6):2267-71. doi: 10.1128/jcm.39.6.2267-2271.2001 [published Online First: 2001/05/29]
43. Sterkers Y, Ribot J, Albaba S, et al. Diagnosis of congenital toxoplasmosis by polymerase chain reaction on neonatal peripheral blood. Diagn Microbiol Infect Dis 2011;71(2):174-6. doi: S0732-8893(11)00225-2 [pii] 10.1016/j.diagmicrobio.2011.06.006 [published Online First: 2011/08/23]
44. Revello MG, Baldanti F, Sarasini A, et al. Prenatal diagnosis of rubella virus infection by direct detection and semiquantitation of viral RNA in clinical samples by reverse transcription-PCR. J Clin Microbiol 1997;35(3):708-13. [published Online First: 1997/03/01]
45. Okamoto K, Fujii K, Komase K. Development of a novel TaqMan real-time PCR assay for detecting rubella virus RNA. J Virol Methods 2010;168(1-2):267-71. doi: S0166-0934(10)00199-0 [pii] 10.1016/j.jviromet.2010.05.016 [published Online First: 2010/06/29]
46. Abernathy E, Cabezas C, Sun H, et al. Confirmation of rubella within 4 days of rash onset: comparison of rubella virus RNA detection in oral fluid with immunoglobulin M detection in serum or oral fluid. J Clin Microbiol 2009;47(1):182-8. doi: JCM.01231-08 [pii] 10.1128/JCM.01231-08 [published Online First: 2008/11/14]
47. Schlesinger Y, Halle D, Eidelman AI, et al. Urine polymerase chain reaction as a screening tool for the detection of congenital cytomegalovirus infection. Arch Dis Child Fetal Neonatal Ed 2003;88(5):F371-4. [published Online First: 2003/08/26]
48. Stagno S, Tinker MK, Elrod C, et al. Immunoglobulin M antibodies detected by enzyme-linked immunosorbent assay and radioimmunoassay in the diagnosis of cytomegalovirus infections in pregnant women and newborn infants. J Clin Microbiol 1985;21(6):930-5. [published Online First: 1985/06/01]
49. de Vries JJ, Claas EC, Kroes AC, et al. Evaluation of DNA extraction methods for dried blood spots in the diagnosis of congenital cytomegalovirus infection. J Clin Virol 2009;46 Suppl 4:S37-42. doi: S1386-6532(09)00415-6 [pii] 10.1016/j.jcv.2009.09.001 [published Online First: 2009/09/29]
50. Boppana SB, Ross SA, Novak Z, et al. Dried blood spot real-time polymerase chain reaction assays to screen newborns for congenital cytomegalovirus infection. JAMA 2010;303(14):1375-82. doi: 303/14/1375 [pii] 10.1001/jama.2010.423 [published Online First: 2010/04/15]
51. de Vries JJ, Wessels E, Korver AM, et al. Rapid genotyping of cytomegalovirus in dried blood spots by multiplex real-time PCR assays targeting the envelope glycoprotein gB and gH genes. J Clin Microbiol 2012;50(2):232-7. doi: JCM.05253-11 [pii] 10.1128/JCM.05253-11 [published Online First: 2011/11/26]

52. de Vries JJ, Vossen AC, Kroes AC. Screening newborns for congenital cytomegalovirus infection. JAMA 2010;304(4):407; author reply 08. doi: 304/4/407 [pii] 10.1001/jama.2010.1023 [published Online First: 2010/07/29]
53. Lazzarotto T, Guerra B, Lanari M, et al. New advances in the diagnosis of congenital cytomegalovirus infection. J Clin Virol 2008;41(3):192-7. doi: S1386-6532(07)00377-0 [pii] 10.1016/j.jcv.2007.10.015 [published Online First: 2007/12/07]
54. Whitley RJ, Lakeman F. Herpes simplex virus infections of the central nervous system: therapeutic and diagnostic considerations. Clin Infect Dis 1995;20(2):414-20. [published Online First: 1995/02/01]
55. Kimura H, Futamura M, Kito H, et al. Detection of viral DNA in neonatal herpes simplex virus infections: frequent and prolonged presence in serum and cerebrospinal fluid. J Infect Dis 1991;164(2):289-93. [published Online First: 1991/08/01]
56. Battaglia FC, Lubchenco LO. A practical classification of newborn infants by weight and gestational age. J Pediatr 1967;71(2):159-63. [published Online First: 1967/08/01]
57. Gardosi J, Chang A, Kalyan B, et al. Customised antenatal growth charts. Lancet 1992; 339(8788):283-7. doi: 0140-6736(92)91342-6 [pii] [published Online First: 1992/02/01]
58. Vandenbosche RC, Kirchner JT. Intrauterine growth retardation. Am Fam Physician 1998;58(6):1384-90, 93-4. [published Online First: 1998/11/06]
59. Primhak RA, Simpson RM. Screening small for gestational age babies for congenital infection. Clin Pediatr (Phila) 1982;21(7):417-20. [published Online First: 1982/07/01]
60. Al-Hareth Z, Monem F, Abdel Megiud N. Is low birth weight a risk indicator for congenital cytomegalovirus infection? J Infect Dev Ctries 2010;4(1):44-7. [published Online First: 2010/02/05]
61. Freeman K, Oakley L, Pollak A, et al. Association between congenital toxoplasmosis and preterm birth, low birthweight and small for gestational age birth. BJOG 2005;112(1):31-7. doi: BJO00299 [pii] 10.1111/j.1471-0528.2004.00299.x [published Online First: 2005/01/25]
62. Couvreur J, Desmonts G. Congenital and maternal toxoplasmosis. A review of 300 congenital cases. Dev Med Child Neurol 1962;4:519-30. [published Online First: 1962/10/01]
63. Lago EG, Baldisserotto M, Hoefel Filho JR, et al. Agreement between ultrasonography and computed tomography in detecting intracranial calcifications in congenital toxoplasmosis. Clin Radiol 2007;62(10):1004-11. doi: S0009-9260(07)00197-3 [pii] 10.1016/j.crad.2007.05.001 [published Online First: 2007/09/04]
64. Kimberlin DW. Herpes simplex virus infections of the newborn. Semin Perinatol 2007;31(1):19-25. doi: S0146-0005(07)00004-3 [pii] 10.1053/j.semperi.2007.01.003 [published Online First: 2007/02/24]
65. Caviness AC, Demmler GJ, Selwyn BJ. Clinical and laboratory features of neonatal herpes simplex virus infection: a case-control study. Pediatr Infect Dis J 2008;27(5):425-30. doi: 10.1097/INF.0b013e3181646d95 [published Online First: 2008/03/25]
66. Kimberlin DW, Lin CY, Jacobs RF, et al. Safety and efficacy of high-dose intravenous acyclovir in the management of neonatal herpes simplex virus infections. Pediatrics 2001;108(2):230-8. [published Online First: 2001/08/03]
67. Wolfert SI, de Jong EP, Vossen AC, et al. Diagnostic and therapeutic management for suspected neonatal herpes simplex virus infection. J Clin Virol 2011;51(1):8-11. doi: S1386-6532(11)00076-X [pii] 10.1016/j.jcv.2011.02.008 [published Online First: 2011/03/11]
68. Korver AM, de Vries JJ, Konings S, et al. DECIBEL study: Congenital cytomegalovirus infection in young children with permanent bilateral hearing impairment in the Netherlands. J Clin Virol 2009;46 Suppl 4:S27-31. doi: S1386-6532(09)00423-5 [pii] 10.1016/j.jcv.2009.09.007 [published Online First: 2009/10/20]
69. Grosse SD, Ross DS, Dollard SC. Congenital cytomegalovirus (CMV) infection as a cause of permanent bilateral hearing loss: a quantitative assessment. J Clin Virol 2008;41(2):57-62. doi: S1386-6532(07)00336-8 [pii] 10.1016/j.jcv.2007.09.004 [published Online First: 2007/10/26]

70. Barbi M, Binda S, Primache V, et al. Cytomegalovirus DNA detection in Guthrie cards: a powerful tool for diagnosing congenital infection. . J Clin Virol 2000;17(3):159-65.
71. Wild NJ, Sheppard S, Smithells RW, et al. Onset and severity of hearing loss due to congenital rubella infection. Arch Dis Child 1989;64(9):1280-3. [published Online First: 1989/09/01]
72. Edelhofer R, Prossinger H. Infection with Toxoplasma gondii during pregnancy: seroepidemiological studies in Austria. Zoonoses Public Health 2010;57(1):18-26. doi: JVB1279 [pii] 10.1111/j.1863-2378.2009.01279.x [published Online First: 2009/09/12]
73. Berger F, Goulet V, Le Strat Y, et al. Toxoplasmosis among pregnant women in France: risk factors and change of prevalence between 1995 and 2003. Rev Epidemiol Sante Publique 2009;57(4): 241-8. doi: S0398-7620(09)00293-4 [pii] 10.1016/j.respe.2009.03.006 [published Online First: 2009/07/07]
74. Pinto B, Castagna B, Mattei R, et al. Seroprevalence for toxoplasmosis in individuals living in North West Tuscany: access to Toxo-test in central Italy. Eur J Clin Microbiol Infect Dis 2011 doi: 10.1007/s10096-011-1422-8 [published Online First: 2011/10/04]
75. Ramos JM, Milla A, Rodriguez JC, et al. Rubella immune status among immigrant and nonimmigrant women in Spain. J Med Virol 2012;84(3):548-50. doi: 10.1002/jmv.23195 [published Online First: 2012/01/17]
76. Byrne L, Brant L, Reynolds C, et al. Seroprevalence of low rubella IgG antibody levels among antenatal women in England tested by NHS Blood and Transplant: 2004-2009. Is rubella susceptibility increasing? Vaccine 2012;30(2):161-7. doi: S0264-410X(11)01830-5 [pii] 10.1016/j.vaccine.2011.11.045 [published Online First: 2011/11/29]
77. Kurugol Z, Midyat L, Turkoglu E, et al. Rubella seroprevalence among healthy individuals in Izmir, Turkey. Hum Vaccin 2011;7(9):972-5. doi: 16370 [pii] 10.4161/hv.7.9.16370 [published Online First: 2011/08/24]
78. Gaytant MA, Galama JMD, Semmekrot BA, et al. The incidence of congenital cytomegalovirus infections in The Netherlands. Journal of Medical Virology 2005;76(1):71-75. doi: 10.1002/jmv.20325
79. de Ory F, Ramirez R, Garcia Comas L, et al. Is there a change in cytomegalovirus seroepidemiology in Spain? Eur J Epidemiol 2004;19(1):85-9. [published Online First: 2004/03/12]
80. Kucera P, Gerber S, Marques-Vidal P, et al. Seroepidemiology of herpes simplex virus type 1 and 2 in pregnant women in Switzerland: an obstetric clinic based study. Eur J Obstet Gynecol Reprod Biol 2012;160(1):13-7. doi: S0301-2115(11)00545-8 [pii] 10.1016/j.ejogrb.2011.09.030 [published Online First: 2011/10/11]
81. Vilibic-Cavlek T, Kolaric B, Ljubin-Sternak S, et al. Herpes simplex virus infection in the Croatian population. Scand J Infect Dis 2011;43(11-12):918-22. doi: 10.3109/00365548.2011.588611 [published Online First: 2011/06/24]
82. Zhou P, Chen Z, Li HL, et al. Toxoplasma gondii infection in humans in China. Parasit Vectors 2011;4:165. doi: 1756-3305-4-165 [pii] 10.1186/1756-3305-4-165 [published Online First: 2011/08/26]
83. Sharma HJ, Padbidri VS, Kapre SV, et al. Seroprevalence of rubella and immunogenicity following rubella vaccination in adolescent girls in India. J Infect Dev Ctries 2011;5(12):874-81. [published Online First: 2011/12/16]
84. Dar L, Pati SK, Patro AR, et al. Congenital cytomegalovirus infection in a highly seropositive semi-urban population in India. Pediatr Infect Dis J 2008;27(9):841-3. doi: 10.1097/INF.0b013e3181723d55 [published Online First: 2008/07/23]
85. Biswas D, Borkakoty B, Mahanta J, et al. Seroprevalence and risk factors of herpes simplex virus type-2 infection among pregnant women in Northeast India. BMC Infect Dis 2011;11:325. doi: 1471-2334-11-325 [pii] 10.1186/1471-2334-11-325 [published Online First: 2011/11/25]
86. Lin H, He N, Su M, et al. Herpes simplex virus infections among rural residents in eastern China. BMC Infect Dis 2011;11:69. doi: 1471-2334-11-69 [pii] 10.1186/1471-2334-11-69 [published Online First: 2011/03/19]

87. Hyde TB, Kruszon-Moran D, McQuillan GM, et al. Rubella immunity levels in the United States population: has the threshold of viral elimination been reached? Clin Infect Dis 2006;43 Suppl 3:S146-50. doi: CID39407 [pii] 10.1086/505947 [published Online First: 2006/09/26]
88. Cannon MJ, Schmid DS, Hyde TB. Review of cytomegalovirus seroprevalence and demographic characteristics associated with infection. Rev Med Virol 2010;20(4):202-13. doi: 10.1002/rmv.655 [published Online First: 2010/06/22]
89. Xu F, Sternberg MR, Kottiri BJ, et al. Trends in herpes simplex virus type 1 and type 2 seroprevalence in the United States. JAMA 2006;296(8):964-73. doi: 296/8/964 [pii] 10.1001/jama.296.8.964 [published Online First: 2006/08/24]
90. Vaz RS, Thomaz-Soccol V, Sumikawa E, et al. Serological prevalence of Toxoplasma gondii antibodies in pregnant women from Southern Brazil. Parasitol Res 2010;106(3):661-5. doi: 10.1007/s00436-009-1716-2 [published Online First: 2010/01/20]
91. Goncalves MA, Matos Cde C, Spegiorin LC, et al. Seropositivity rates for toxoplasmosis, rubella, syphilis, cytomegalovirus, hepatitis and HIV among pregnant women receiving care at a public health service, Sao Paulo state, Brazil. Braz J Infect Dis 2010;14(6):601-5. doi: S1413-86702010000600009 [pii] [published Online First: 2011/02/23]
92. Mussi-Pinhata MM, Yamamoto AY, Moura Brito RM, et al. Birth prevalence and natural history of congenital cytomegalovirus infection in a highly seroimmune population. Clin Infect Dis 2009;49(4):522-8. doi: 10.1086/600882 [published Online First: 2009/07/09]
93. Uribe-Salas F, Palma-Coca O, Sanchez-Aleman MA, et al. Population-based prevalence of antibodies against herpes simplex virus type 2 and socio-demographic characteristics in Mexico. Trans R Soc Trop Med Hyg 2009;103(2):151-8. doi: S0035-9203(08)00468-9 [pii] 10.1016/j.trstmh.2008.10.033 [published Online First: 2008/12/17]
94. Clemens SA, Farhat CK. Seroprevalence of herpes simplex 1-2 antibodies in Brazil. Rev Saude Publica 2010;44(4):726-34. doi: S0034-89102010000400017 [pii] [published Online First: 2010/08/03]
95. Hamdan HZ, Abdelbagi IE, Nasser NM, et al. Seroprevalence of cytomegalovirus and rubella among pregnant women in western Sudan. Virol J 2011;8:217. doi: 1743-422X-8-217 [pii] 10.1186/1743-422X-8-217 [published Online First: 2011/05/17]
96. Bamgboye AE, Afolabi KA, Esumeh FI, et al. Prevalence of rubella antibody in pregnant women in Ibadan, Nigeria. West Afr J Med 2004;23(3):245-8. [published Online First: 2004/12/14]
97. Schopfer K, Lauber E, Krech U. Congenital cytomegalovirus infection in newborn infants of mothers infected before pregnancy. Arch Dis Child 1978;53(7):536-9. [published Online First: 1978/07/01]
98. Kasubi MJ, Nilsen A, Marsden HS, et al. Prevalence of antibodies against herpes simplex virus types 1 and 2 in children and young people in an urban region in Tanzania. J Clin Microbiol 2006;44(8):2801-7. doi: 44/8/2801 [pii] 10.1128/JCM.00180-06 [published Online First: 2006/08/08]
99. Mmbaga EJ, Leyna GH, Stray-Pedersen B, et al. Herpes simplex virus type-2 and human immunodeficiency virus infections in a rural population in Kilimanjaro Tanzania. East Afr J Public Health 2011;8(1):28-32. [published Online First: 2011/11/10]
100. Mugo N, Dadabhai SS, Bunnell R, et al. Prevalence of herpes simplex virus type 2 infection, human immunodeficiency virus/herpes simplex virus type 2 coinfection, and associated risk factors in a national, population-based survey in Kenya. Sex Transm Dis 2011;38(11):1059-66. doi: 10.1097/OLQ.0b013e31822e60b6 00007435-201111000-00014 [pii] [published Online First: 2011/10/14]
101. Wallon M, Dunn D, Slimani D, et al. Diagnosis of congenital toxoplasmosis at birth: what is the value of testing for IgM and IgA? Eur J Pediatr 1999;158(8):645-9. [published Online First: 1999/08/13]

102. Rabilloud M, Wallon M, Peyron F. In utero and at birth diagnosis of congenital toxoplasmosis: use of likelihood ratios for clinical management. Pediatr Infect Dis J 2010;29(5):421-5. doi: 10.1097/INF.0b013e3181c80493 [published Online First: 2009/12/03]
103. Gilbert RE, Thalib L, Tan HK, et al. Screening for congenital toxoplasmosis: accuracy of immunoglobulin M and immunoglobulin A tests after birth. J Med Screen 2007;14(1):8-13. doi: 10.1258/096914107780154440 [published Online First: 2007/03/17]
104. Thalib L, Gras L, Romand S, et al. Prediction of congenital toxoplasmosis by polymerase chain reaction analysis of amniotic fluid. BJOG 2005;112(5):567-74. doi: BJO00486 [pii] 10.1111/j.1471-0528.2005.00486.x [published Online First: 2005/04/22]
105. Banatvala JE, Brown DW. Rubella. Lancet 2004;363(9415):1127-37. doi: 10.1016/S0140-6736(04)15897-2 S0140673604158972 [pii] [published Online First: 2004/04/06]
106. Revello MG, Zavattoni M, Baldanti F, et al. Diagnostic and prognostic value of human cytomegalovirus load and IgM antibody in blood of congenitally infected newborns. J Clin Virol 1999;14(1):57-66. doi: S1386-6532(99)00016-5 [pii] [published Online First: 1999/11/05]
107. de Vries JJ, van der Eijk AA, Wolthers KC, et al. Real-time PCR versus viral culture on urine as a gold standard in the diagnosis of congenital cytomegalovirus infection. J Clin Virol 2012;53(2):167-70. doi: S1386-6532(11)00468-9 [pii] 10.1016/j.jcv.2011.11.006 [published Online First: 2011/12/20]
108. Boppana SB, Ross SA, Shimamura M, et al. Saliva polymerase-chain-reaction assay for cytomegalovirus screening in newborns. N Engl J Med 2011;364(22):2111-8. doi: 10.1056/NEJMoa1006561 [published Online First: 2011/06/03]
109. Nahmias AJ, Whitley RJ, Visintine AN, et al. Herpes simplex virus encephalitis: laboratory evaluations and their diagnostic significance. J Infect Dis 1982;145(6):829-36. [published Online First: 1982/06/01]
110. Ramenghi LA, Domizio S, Quartulli L, et al. Prenatal pseudocysts of the germinal matrix in preterm infants. J Clin Ultrasound 1997;25(4):169-73. doi: 10.1002/(SICI)1097-0096(199705)25:4<169::AID-JCU3>3.0.CO;2-C [pii] [published Online First: 1997/05/01]
111. El Ayoubi M, de Bethmann O, Monset-Couchard M. Lenticulostriate echogenic vessels: clinical and sonographic study of 70 neonatal cases. Pediatr Radiol 2003;33(10):697-703. doi: 10.1007/s00247-003-0948-z [published Online First: 2003/08/09]
112. Herini E, Tsuneishi S, Takada S, et al. Clinical features of infants with subependymal germinolysis and choroid plexus cysts. Pediatr Int 2003;45(6):692-6. doi: 1814 [pii] [published Online First: 2003/12/04]
113. Makhoul IR, Zmora O, Tamir A, et al. Congenital subependymal pseudocysts: own data and meta-analysis of the literature. Isr Med Assoc J 2001;3(3):178-83. [published Online First: 2001/04/17]
114. Rademaker KJ, De Vries LS, Barth PG. Subependymal pseudocysts: ultrasound diagnosis and findings at follow-up. Acta Paediatr 1993;82(4):394-9. [published Online First: 1993/04/01]
115. Tran DN, Vu MP, Ha MT, et al. Viral molecular characterization of the first congenital rubella syndrome case in Vietnam. Clin Lab 2011;57(5-6):397-401. [published Online First: 2011/07/16]
116. Yoshimura M, Tohyama J, Maegaki Y, et al. [Computed tomography and magnetic resonance imaging of the brain in congenital rubella syndrome]. No To Hattatsu 1996;28(5):385-90. [published Online First: 1996/09/01]
117. Ahlfors K, Ivarsson SA, Bjerre I. Microcephaly and congenital cytomegalovirus infection: a combined prospective and retrospective study of a Swedish infant population. Pediatrics 1986;78(6):1058-63. [published Online First: 1986/12/01]
118. Kimberlin DW. Neonatal herpes simplex infection. Clin Microbiol Rev 2004;17(1):1-13. [published Online First: 2004/01/17]
119. Kimberlin DW. Advances in the treatment of neonatal herpes simplex infections. Rev Med Virol 2001;11(3):157-63. doi: 10.1002/rmv.313 [pii] [published Online First: 2001/05/29]