Respiratory syncytial virus
Part II: Epidemiology of infantile respiratory infections

Author: Gordana Mlinaric-Galinovic, MD, PhD

Department of Microbiology University Medical School of Zagreb and Department of Virology, Croatian National Institute of Public Health and, Rockefellerova 12, 10000 Zagreb, Croatia

2.1. Viral acute respiratory tract infections

Respiratory syncytial virus (RSV) is a major cause of acute lower respiratory tract infections (LRTI) in infants and young children in both developed and developing countries (1-6). RSV accounts for 25% of hospital admissions of infants and young children for pneumonia, and for up to 43% of cases of bronchiolitis in this age group (5). In the USA, RSV was estimated to cause 73,400-126,300 hospitalizations annually for bronchiolitis and pneumonia among children younger than 1 year (7). RSV infection was detected in 23.3% of infants and children hospitalized for any acute respiratory tract infection (ARTI) (8-10). It has been estimated that more than half of infants who are at risk will become infected during an RSV epidemic (1). The attack rates among susceptible infants and children are extraordinarily high, approaching 100% in settings such as day-care centers where large numbers of susceptible infants are present (11). In our 11 consecutive years (1994-2005) of studying RSV infections in children in Croatia, it was discovered that RSV caused the greatest number of overall ARTIs (32.3%), followed by adenoviral infections in 3.9% cases, parainfluenza viral infections in 3.7% instances and influenza virus infections in 2.9% cases (10). Almost the same percentage (33.6) of RSV infections among ARTIs was found in an earlier season (1986/87) (12). When infections caused by human metapneumovirus (HMPV) were further explored, this virus ranked third, after adenovirus and RSV among children with ARTI (13), which is more or less in agreement with the second-only position of HMPV in the finding of Williams JV at al (14).While the incidence of RSV infections declined with age (from 42% to 16% from birth to 5 years of age), the incidence of infections due to other viruses remained within the range of 6 to 15% in the same age range (10).

2.2. Sex, race and age

Infection rates are unrelated to either race or sex, although illness is more severe in male infants (15-17). However, in our study, RSV showed the highest prevalence (75%) among Caucasian children in Texas, USA (18). Also, higher hospitalization rates were associated with RSV infections at a younger age (<1 year) in black and Hispanic ethnicity, and with the presence of chronic underlying illness (17). In the USA, the estimated number of RSV hospitalizations per 1,000 children was 388 for those with bronchopulmonary dysplasia and 92 for those with congenital heart disease (19).
RSV infections manifest themselves as mild upper respiratory tract infections (URTIs) or LRTIs: bronchitis, bronchiolitis, and pneumonia (9,20-22). In our study among RSV-positive inpatients, aged 0-10 years, for the period 2009-2010, the virus proved to cause bronchiolitis in 30.19% and pneumonia in 13.49% cases (22) (Figure 1).

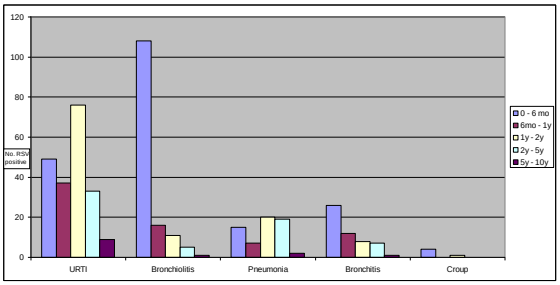

Figure 1. Distribution of clinical syndromes caused by respiratory syncytial virus by age groups and clinical syndromes in Zagreb and Zagreb County during 2009 and 2010

Rates of illness are highest among infants 1 to 6 months of age, peaking between 2 and 3 months of age. The prevalence of RSV infections drops with age. The results of this

study showed that in Croatia 63.8% of all RSV infections occurred in the first 6 months of life, 18.6% in the second 6 months of life, 12.4% in the second year of life, and only 4% in children 2 to 5 years old (20). Said values, however, do oscillate depending on the season (9,23,24). In newborn infants LRTIs are sparing during the first 6 weeks of life, while RSV-positive newborn infants usually produce URTI (25-27.). However, Bruckova et al. reported 60% of LRTIs at the premature children's' ward (28). Our study showed that LRTIs were less common (bronchitis 20%, bronchiolitis 10%, pneumonia 20%) in neonates than in other infants and small children (12,20,29) (Figure 2).

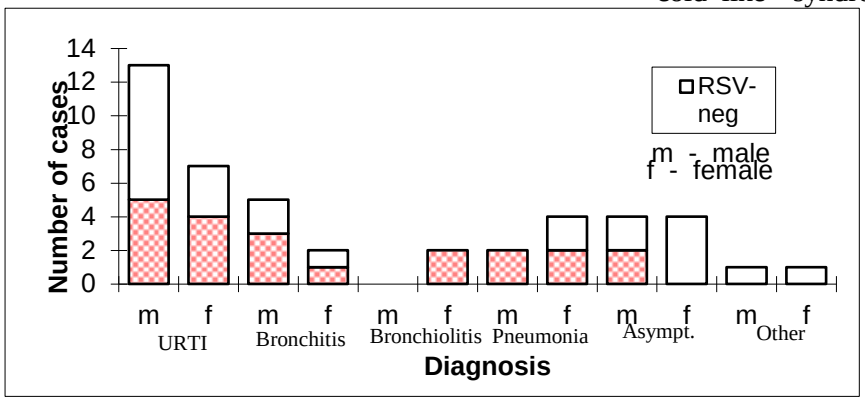

Figure 2. Finding of respiratory syncytial virus in 44 neonates with respect to syndrome and sex, Zagreb, Croatia (1986-1987)

Out of 20 RSV-positive neonates, 10 were premature, and no significant statistical difference in susceptibility to the infection was noticed among premature children (Chi-square=0.0, $p > 0.05$) (29). In the USA, the estimated number of RSV hospitalizations per 1,000 children was 70 for children born at <28 weeks' gestation, 66 for those born at 29-33 weeks, 57 for those born at 33-36 weeks, and 30 for children born at term with no underlying medical condition (19).

2.3. Reinfection

Primary infection is often associated with significant morbidity, particularly in infants younger than six months of age or with underlying cardiopulmonary disease, as well as in infants from lower socioeconomic groups in both industrial and developing countries (30,31). By age 2, virtually all children will have been infected with RSV (32).

Reinfection with RSV is common, and older children and adults are not immune (33,34). In older children and adults, reinfection with RSV is frequent, but the disease is milder than in infancy. Children previously infected with a virus of one type appear to be somewhat less susceptible to repeated infections with a virus of the same type, perhaps due to residual antibodies specific to the G protein (35). Asymptomatic forms of disease are rare even in reinfections (15, 36,37).

RSV infections in adults and the elderly represent reinfections in which the hosts have had many prior episodes (38,39). A common cold–like syndrome is the illness most commonly associated with RSV infection in adults (8). Severe lower respiratory tract disease with pneumonitis can occur in elderly (often institutionalized) adults and in patients with immunocompromising disorders or treatment, including recipients of bone-marrow and solid-organ transplants (40,41)

2.4. Transmission

The virus is transmitted either directly or indirectly through large droplets via fomites and direct contact with secretion (42). RSV is transmitted primarily by close contact with contaminated fingers or fomites and by self-inoculation of the conjunctiva or anterior nares. Virus may also be spread by coarse aerosols produced by coughing or sneezing, but it is inefficiently spread by fine-particle aerosols. Target cells for the virus are ciliary epithelium cells in the respiratory tract (43).

The attack rate in household contacts of infected children is about 40% (44). The spread of virus within a family is efficient: up to 40% of siblings may become infected when RSV is introduced into the family setting (44). RSV is also an important nosocomial pathogen (45,46). During an outbreak, it can infect pediatric patients and up to 25 to 50% of the staff in pediatric wards (47). Ward

personnel probably has a central role in introducing and spreading the virus.
Incubation period for RSV disease is 3-5 days (16). LRTI symptoms usually appear 1-3 days after the onset of rhinorrhea by spreading via respiratory epithelium or through aspirated secretion (8). The virus shedding phase is shorter in adults than in children (1.6 vs. 3.9 days) (44). Virus shedding may last for ≥2 weeks in children and for shorter periods in adults. In immunosuppressed patients, shedding can be prolonged by several weeks.

2.4. Outbreaks

2.4.1. Climate zones

Infection with RSV is seen throughout the world in regular, predictable intervals that in temperate climate occur in late fall, winter, or spring and last up to 5 months (9,15,16,20). RSV seasons vary in different parts of the world. In Rochester, New York, USA, RSV outbreaks usually start in October and end in April, generally peaking in January (3). In Galveston, Tx, RSV outbreak usually starts in October or November, peaking in December and January, and ends in March (18,48). The virus is rarely encountered during the summer (Figure 3).

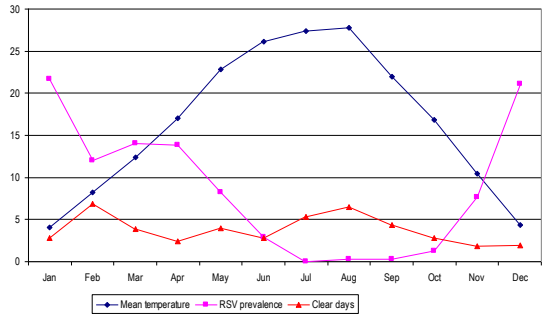

Figure 3. The prevalence of respiratory syncytial virus infections, mean monthly temperature, and number of clear days during the period 1994-2005 in Croatia

In months with an average temperature over 25ºC there are virtually no RSV infections, whereas the latter appear most often in months with an average temperature under 5ºC (Analysis of variance, p> 0,001)/ (49). In tropical or subtropical areas, outbreaks usually occur during the rainy season (50). In northern tropical area in Asia, RSV season is associated with a decrease in temperatures and increase in rainfall (51). In northern tropical areas of South America, RSV is present year round, with some increase in months with dry weather (52). In southern tropical areas in South America, RSV occurs in the dry cool season (53).

2.4.2. Circulation pattern

Monophasic and annual RSV epidemics were found in Great Britain (54), Belgium (55), the USA (56,57), South America (58,59), Japan (60) and China (61).
The biennial pattern of RSV outbreaks was noted in Germany, Switzerland, Austria, Finland and Sweden (62-67), and Croatia. It was established that RSV outbreaks in Croatia have been occurring in two-year cycles for at least the past 15 years (49,68,69). Thus, RSV epidemics in Croatia peaked in December/January of years 1994/95, 1996/97, 1998/99, 2000/01, 2002/03, and 2004/05 (“large seasons”), and March/April of years 1996, 1998, 2000, 2002, and 2004 (”small seasons”) (49)
The role of climate (the effects of air temperature and humidity) in causing this epidemic pattern was studied in northwest Croatia. Climate conditions correlated only with those RSV seasons when outbreaks peaked in December/January, and not with those outbreaks which occurred in the spring (March/April) (49). In large seasons, the number of RSV cases was inversely related to the average maximum daily temperature (Pearson correlation coefficient; $r = -0.7$; $p<0.001$) (Figure 4) and directly linked to average maximum air humidity (Pearson correlation coefficient; $r = 0.6$; $p<0.001$) (Figure 5).

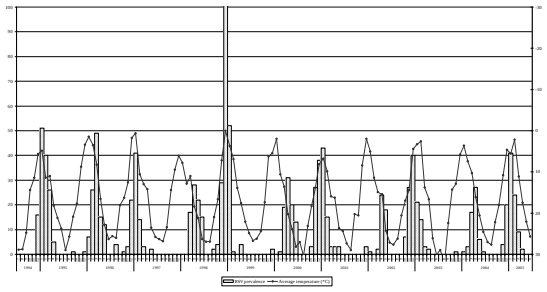

Figure 4. Seasonal occurrence of respiratory syncytial virus infections and average maximum temperature (1994-2005) in Croatia

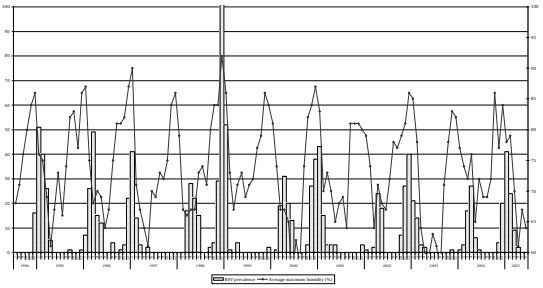

Figure 5. Seasonal occurrence of respiratory syncytial virus infections and average maximum air humidity (1994-2005) in Croatia

In small seasons, however, the number of RSV cases was not significantly correlated with temperature ($r = 0.06$; $p=0.64$) and was inversely associated to relative humidity ($r = -0.3$; $p<0.01$).

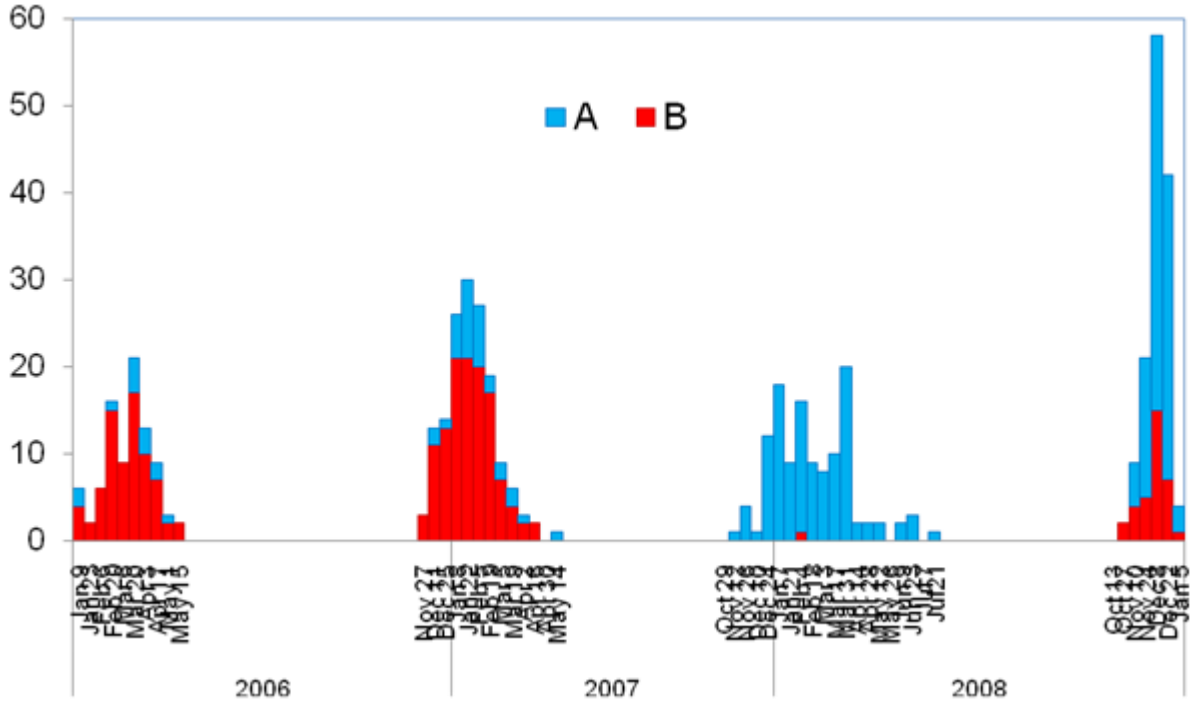

Figure 6. Respiratory syncytial virus infection occurrence (stacked area showing contribution of subtype A above subtype B) by calendar week in the epidemic waves during 2006-2008 for children aged 0-5 years in Zagreb area

Since the two-year periodicity of RSV infections in Croatia could not be related to climatic factors, we examined whether this epidemiological characteristic of RSV infections in Croatia could be associated with a regular exchange of the two viral subtypes (70,71). However, biennial virus cycles were found to be persistent, although the predominant RSV subtype in the first two epidemic waves was subtype B, while in the second two subtype A. Consequently, according to current findings, it may be concluded that neither of the predominant RSV types and genotypes has an effect on the periodicity of RSV infections in Croatia (70,71, 72) (Figure 6).

Many earlier studies have attempted to explain the epidemic pattern of RSV activity, but an explanation for this epidemic variation has not been identified. The possibility of one extensive epidemic partially immunizing infants, thereby postponing the next epidemic and reducing it in size, has been considered. The result of RSV type circulation for the 0-5 age group matches the result for the 0-1 age group, which does not argue in favor of the above hypothesis (71).

Recent studies have investigated the genotypic pattern of RSV strains during epidemics. In a 2-year virus cycle there was a 64% reduction in the incidence of infection by a homologous strain compared to a 16% reduction against a heterologous strain (73). A possible correlation between newly emerging genotypes and higher chances for reinfection eventually lead to large outbreaks (55,60).

References:

1. Parrott RH, Kim HW, Arrobio JO, Hodes DS, Murphy BR, Brandt CD, Camargo E, Chanock RM.

Epidemiology of respiratory syncytial virus infection in Washington, D.C. II Infection and disease with respect to age, immunologic status, race and sex. Am J Epidemiol 1973; 98:289-300.
2. Selwyn B. The epidemiology of acute respiratory tract infection in young children: comparison of findings from several developing countries. *Reviews in Infectious Disease* 1990, 12: 870-888.
3. Hall CB: Respiratory syncytial virus. In: Feigin RD, Cherry JB (ed): Textbook of pediatric infectious disease. W.B. Saunders, Philadelphia, 1981, p. 1247-1267.
4. Belshe RB, Bernstein JM, Dansby KN: Respiratory syncytial virus. In: Belshe RB, ed. Textbook of Human Virology. Littleton, PSG Publishing Company, 1984, p. 361-383.
5. Kim HW, Arrobio JO, Brandt CD, Jeffries BC, Pyles G, Reid JL, Chanock RM, Parrott RH: Epidemiology of respiratory syncytial virus in Washington, D.C. I. Importance of the virus in different respiratory tract disease syndromes and temporal distribution of infection. Am J Epidemiol 1973; 98:215-225.
6. Martin AJ, Gardner PS, McQuillin J: Epidemiology of respiratory viral infection among pediatric inpatients over a six year period in northeast England. Lancet 1978; 2:1035-1038.
7. Shay DK, Holman RC, Roosvelt GE, Clarke MJ, Anderson LJ. Bronchiolitis-associated mortality and estimates of respiratory syncytial virus-associated deaths among U.S. children, 1979-1997. J Infect Dis 2001; 183:16-22.
8. Collins PL, Crowe JEJr. Respiratory syncytial virus and metapneumovirus. In: Knipe DM, Howley PM, eds. Fields Virology. 5th ed. Philadelphia: Lippincott Williams & Wilkins, 2007:1601-1646.
9. Mlinaric-Galinovic G, Ugrcic I, Bozikov J: Respiratory syncytial virus infections in SR Croatia, Yugoslavia. Pediatr Pulmonol /Philadelphia/1987, 3:304-308.
10. Mlinaric-Galinovic G, Vilibic-Cavlek T; Ljubin-Sternak S; Drazenovic V; Galinovic I; Tomic V; Welliver RC: Eleven consecutive years of respiratory syncytial virus outbreaks in Croatia. Pediatrics International 2009; 51 (2):237-40.
11. Henderson FW, Collier AM, Clyde WAJr, Denny FW. Respiratory syncytial-virus infections, reinfections and immunity. A prospective, longitudinal study in young children. N Engl J Med 1979; 300: 530-534.
12. Mlinaric-Galinovic B, Ugrcic I, Detic D, Bozikov J. Epidemiological picture of respiratory viral infections in Croatia. Acta Med Iug 1991;45:203-11.
13. Ljubin-Sternak S, Santak M, Cepin-Bogovic J, Bace A, Vojnovic G, Mlinaric-Galinovic G, Forcic D, Drazenovic V, Falsey AR. Detection of genetic lineages of human metapneumovirus in Croatia during the winter season 2005/2006. J Med Virol 2008; 80(7):1282-1287.
14. Williams JV, Harris PA, Tollefson S, JHalburnt-Rush LL, Pingsterhaus JM, Edwards KM, Wright PF, Crowe JE Jr. Human metapneumovirus and lower respiratory tract disease in otherwise healthy infants and children. N Engl J Med 200; 350:443-450.
15. Brandt CD, Kim HW, Arrobio JO, Jeffries BC, Wood SC, Chanock RM, Parrott RH: Epidemiology of respiratory syncytial virus infection in Washington, D.C. III. Composite analysis of eleven consecutive yearly epidemics. American Journal of Epidemiology 1973, 98: 355-364.
16. Jackson GG, Muldoon RL: Viruses causing common respiratory infection in man. University of Chicago Press, Chicago, 1975, p. 116-131.
17. Iwane MK, Edwards KM, Szilagyi PG, Walker FJ, Griffin MR, Weinberg GA, Coulen C, Poehling KA, Shone LP, Balter S, Hall CB, Erdman DD, Wooten K, Schwartz B; New Vaccine Surveillance Network.. Population-based surveillance for hospitalizations associated with respiratory syncytial virus, influenza virus, and parainfluenza viruses among young children. Pediatrics 2004; 113:1758-1764.
18. Mlinaric-Galinovic G, Chonmaitree T, Cane PA, Pringle CR, Ogra PL: Antigenic diversity of respiratory syncytial virus subgroup B strains circulating during a community outbreak of infection. J Med Virol 1994, 42:380-384.
19. Boyce TG, Mellen BG, Mitchel EFJr, Wright PF, Griffin MR. Rates of hospitalization for respiratory syncytial virus infection among children in Medicaid. J Pediatr 2000; 137:865-970.
20. Mlinaric-Galinovic G, Ugrcic I, Detic D, Bozikov J: Characteristics of outbreak of respiratory syncytial virus in Croatia in the 1986/1987 winter season. Cro Med J 1992, 33(4):225-229.
21. Collins PL, Crowe JEJr. Respiratory syncytial virus and metapneumovirus. In: Knipe DM, Howley PM, eds. *Fields Virology*. 5th ed. Philadelphia: Lippincott Williams & Wilkins, 2007:1601-1646.
22. Mlinarić-Galinović G, Jović M, Knezović I, Tešović G, Čepin-Bogović J, Ivković-Jureković I, Sim R. Epidemiološke osobine infekcija respiratornim sincicijskim virusom tijekom 2009 i 2010 godine u Zagrebu i zagrebačkoj županiji, Medicina fluminensis 2012, 48(1):79-84..
23. Mlinaric-Galinovic G, Ugrcic I, Cvetkovic M, Pende B, Ivankovic D: Rapid detection of respiratory syncytial virus in clinical specimens. Acta virol 1987, 31:410-416.
24. Mlinaric-Galinovic G, Bace A, Cepin-Bogovic J, Ivkovic-Jurekovic I, Sim R, Cosic M: Znacajke epidemije respiratornim sincicijskim virusom u sezoni 2006./2007. u zagrebackoj zupaniji: potvrda predvidivosti periodiciteta epidemija. Paediatria Croatica 2009, 53 (2): 49-52.
25. Parrott RH, Kim HW, Arrobio JO, Hodes DS, Murphy BR, Brandt CD, Camargo E, Chanock RM. Epidemiology of respiratory syncytial virus infection in Washington,D.C. II Infection and disease with respect to age, immunologic status, race and sex. Am J Epidemiol 1973:98:289-300.
26. Neligan GA, Steiner H, Gardner PS, McQuillin J. Respiratory syncytial virus infection of the newborn. Br Med J 1970:3:146-7.
27. Hall CB, Kopelman AE, Douglas RG, Geiman JM, Meagher MP. Neonatal respiratory syncytial virus infection. N Engl J Med 1979:300:393-6.
28. Bruckova M, Kunzova L, Jezkova Z, Vocel J. Incidence of RS Virus infections in premature children's ward. J Hyg Epidemiol Microbiol Immunol 1979:23:389-96.
29. Mlinaric-Galinovic G, Polak-Babic J, Plese M, Koprcina B, Ugrcic I, Bozikov J, Begovic I: Respiratory syncytial virus infection in neonatal units. Cro Med J 1994, 35(3): 168-171.
30. Chanock RM, Kim HW, Brandt CD, Parrott RH: Respiratory syncytial virus. In: Evans AS (ed): Viral

infections of humans. Plenum, New York, 1982, p. 471-489.
31. Clarke SKR, Gardner PS, Poole PM, Simpson H, Tobin JOH: Respiratory syncytial virus infection: admissions to hospital in industrial urban, and rural areas: report to the Medical Research Council subcommittee on respiratory syncytial virus vaccines. British Medical Journal 1978, ii: 796-798.
32. Glazen WP, Taber LH, Frank AL, Kasel JA. Risk of primary infection and reinfection with respiratory syncytial virus. Am J Dis Child 1986; 140:543-546.
33. Ditchburn RK, McQuillin J, Gardner PS, Court SDM: Respiratory syncytial virus in hospital cross-infection. British Medical Journal 1971, 3: 671-673.
34. Johnson KM, Chanock RM, Rifkind D, Kravetz HM, Knight V: Respiratory syncytial virus: IV. Correlation of virus shedding, serological response, and illness in adult volunteers. Journal of American Medical Association 1961, 176: 663-677.
35. Mufson MA, Belshe RB, Orvell C, Norrby E: Subgroup characteristics of respiratory syncytial virus strains recovered from children with two consecutive infections. Journal of Clinical Microbiology 1987, 25: 1536-1539.
36. Chanock RM, Kim HW, Vargosko AJ, Deleva A, Johnson KM, Cumming C, Parrott RH: Respiratory syncytial virus: I Virus recovery and other observations during 1960 outbreak of diseases in children. JAMA 1961,176:663-77.
37. Jacobs JW, Peacock DB. Corner BD, Caul ED, Clarke SKR: Respiratory syncytial virus and other viruses associated with respiratory disease in infants. Lancet 1971, 1:871-6.
38. Agius G, Dindinaud G, Biggar RJ, Peyre R, Vaillant V, Ranger S, Poupet JY, Cisse MF, Castets M: An epidemic of respiratory syncytial virus in elderly people: Clinical and serological findings. J Med Virol 1990, 30: 117-127.
39. Mlinaric-Galinovic G, Falsey AR, Walsh EE: Respiratory syncytial virus infection in the elderly. Eur J Clin Microbiol Infect Dis 1996, 15: 777-781.
40. Harrington RD, Hooton TM, Hackman RC, Storch GA, Osborne B, Gleaves CA, Benson A, Meyers JD: An outbreak of respiratory syncytial virus in a bone marrow transplant center. Journal of Infectious Diseases 1992, 165: 987-983.
41. Khanna N, Hirsch HH. Respiratory Syncytial Virus Infection in Immunocompromised Patients Revisited. Clin Infect Dis 2008; 46 (12):1934-1935.42. Hall CB, Douglas RG. Modes of transmission of respiratory syncytial virus. J Pediatr 1981; 99:100-103.
42. Hall CB, Douglas RG Jr, Geiman JM Possible transmission by fomites of respiratory syncytial virus.J Infect Dis. 1980; 141(1):98-102.
43. Gardner PS, McQuillin J. Rapid virus diagnosis. Application of immunofluorescence. London, Butterworth's, 1974.
44. Hall CB, Geiman JM, Biggar R, Kotok DI, Hogan PM, Douglas RG: Respiratory syncytial virus infections within families. New England Journal of Medicine 1976, 294: 414-419.
45. Mlinaric-Galinovic G, Varda-Brkic D. Nosocomial respiratory syncytial virus infections in children's wards. Diagn Microbiol Infect Dis 2000; 37:237-246.
46. Mlinaric-Galinovic G. Nosocomial respiratory syncytial virus infections in Zagreb hospitals. Paediatr Croat 2000; 44:136-140.
47. Hall CB, Douglas RG Jr, Geiman JM, Messner MK. Nosocomial respiratory syncytial virus infections. N Engl J med 1975; 293:1343-1346.
48. Chonmaitree T, Truant AL: What's new in the diagnosis of viral respiratory infections in children. Part 1. Texas Medicine 1985; 81:39-42.
49. Mlinaric-Galinovic G, Welliver RC, Vilibic-Cavlek T, Ljubin-Sternak S, Drazenovic V, Galinovic I, Tomic V. The biennial cycle of respiratory syncytial virus outbreaks in Croatia. Virol J 2008; 5(1):18-22.
50. Hillis WD, Cooper MR, Bang FB, Dey AK, Shah KV. Respiratory syncytial virus infection in children in West Bengal. Indian J Med Res 1971; 59:1354-1364.
51. Doraisingham S, Goh KT, Ling AE. Epidemiology of virus infection in Singapore. Ann Acad Med Singapore 1987; 16:243-249.
52. Borrero I, Fajardo L, Bedoya A, Zea A, Carmona F, Borrero MF. Acute respiratory tract infections among a birth cohort of children from Cali, Colombia, who were studied through 17 months of age. Rev Infect Dis 1990; 12:S950-S956.
53. Carballal G, Videla C, Sequeira MD, Mistchenko A, Requeijo PV, Arbiza J. Respiratory syncytial virus: changes in prevalence of subgroups A and B among Argentinean children, 1990-1996. J Med Virol 2000; 61:275-279.
54. Goddard NL, Cooke MC, Gupta RK, Nguyen-Van-Tam JS. Timing of monoclonal antibody for seasonal RSV prophylaxis in the United Kingdom. Epidemiol Infect 2007; 135:159-162.
55. Zlateva KT, Vijgen L, Dekeersmaeker N, Naranjo C, Van Ranst M. Subgroup prevalence and genotype circulation patterns of human respiratory syncytial virus in Belgium during ten successive epidemic seasons. J. Clin. Microbiol 2007; 45:3022-3030.
56. Peret TCT, Hall CB, Schnabel KC, Golub JA, Anderson LJ. Circulation pattern of genetically distinct group A and B strains of human respiratory syncytial virus in a community. J Gen Virol 1998; 79: 2221-2229.
57. Hall CB, Weinberg GA, Iwane MK, Blumkin AK, Edwards KM, Staat MA, Auinger P, Griffin MR, Poehling KA, Erdman D, Grijalva CG, Zhu Y, Szilagyi P. The burden of respiratory syncytial virus infection in young children. N Engl J Med 2009; 360:588-598.
58. Oliveira TFM, Freitas GRO, Ribeiro LZG, Yokosawa J, Siqueira MM, Portes SAR, Silveira HL, Calegari T, Costa LF, Mantese OC, Queiroz DAO. Prevalence and clinical aspects of respiratory syncytial virus A and B groups in children seen at Hospital de Clinicas of Uberlandia, MG, Brazil. Memórias do Instituto Oswaldo Cruz 2008; 103(5): 417-422.
59. Galiano MC, Palomo C, Videla CM, Arbiza J, Melero JA, Carballal G. Genetic and antigenic variability of human respiratory syncytial virus (groups A and B) isolated over seven consecutive seasons in Argentina (1995 to 2001). J Clin Microbiol 2005; 43(5): 2266-2273.
60. Shobugawa Y, Saito R, Sano Y, Zaraket H, Suzuki Y, Kumaki A, Dapat I, Oguma T, Yamaguchi M, Suzuki H. Emerging genotypes of human respiratory syncytial virus subgroup A among patients in Japan. J. Clin. Microbiol 2009; 47:2475-2482.
61. Zhang ZY, Du LN, Chen X, Zhao Y, Liu EM, Yang XQ, Zhao XD. Genetic variability of respiratory syncytial viruses (RSV) prevalent in Southwestern China from 2006 to 2009: emergence of subgroup B and A RSV as dominant strains. J Clin Microbiol 2010; 48(4):1201-7.

62. Terletskaia-Ladwig E, Enders G, Schalasta G, Enders M. Defining the timing of respiratory syncytial virus (RSV) outbreaks: an epidemiological study. BMC Infect Dis 2005; 5:20-27.
63. Berner R, Schwoerer F, Schumacher RF, Meder M, Forster J. Community and nosocomially acquired respiratory syncytial virus infection in German paediatric hospital from 1988 to 1999. Eur J Pediatr 2001; 160: 541-547.
64. Duppenthaler A, Gorgievski-Hrisoho M, Frey U, Aebi C. Two-year periodicity of respiratory syncytial virus epidemics in Switzerland. Infection 2003; 31 (2): 75-80.
65. Aberle SW, Aberle JH, Sandhofer MJ, Pracher E, Popow-Kraupp T. Biennial spring activity of human metapneumovirus in Austria, Pediatr Infect Dis J 2008; 27: 1065.
66. Waris M. Pattern of respiratory syncytial virus epidemics in Finland: two-year cycles with alternating prevalence of group A and B. J Infect Dis 1991, 163:464-469.
67. Reyes M, Eriksson M, Bennet R, Hedlund KO, Ehrnst A. Regular pattern of respiratory syncytial virus and rotavirus infections and relation to weather in Stockholm, 1984-1993. Clin Microbiol Infect 1997; 3: 640-646.
68. Mlinaric-Galinovic G, Sim R, Skenderovic I. Infekcije respiratornim sincicijskim virusom u zimskoj sezoni 2005/2006. Hrvatski casopis za javno zdravstvo 2008; 3:1-6.
69. Mlinaric-Galinovic G, Bace A, Cepin-Bogovic J, Ivkovic-Jurekovic I, Sim R, Cosic M. Znacajke javljanja epidemije respiratornim sincicijskim virusom u sezoni 2006/7 u zagrebackoj zupaniji: potvrda predvidivosti periodiciteta epidemija. Paediatr Croat 2009; 53:49-52.
70. Mlinaric-Galinovic G, Vojnovic G, Bogovic-Cepin J, Bace A, Bozikov J, Welliver RC, Wahn U, Cebalo L. Does the viral subtype influence the biennial cycle of respiratory syncytial virus?, Virol J 2009; 6 (1):133.
71. Mlinaric-Galinovic G, Tabain I; Vojnovic G; Kukovec T; Bozikov J; Cepin-Bogovic J, Ivkovic-Jurekovic I; Knezovic I; Tešović G; Welliver RC: Analysis of biennial outbreak pattern of respiratory syncytial virus according to subtype (A and B) in the Zagreb region, Pediatrics International 2012, 54 (3): 331-335).
72. Mlinaric-Galinovic G, Forcic D, Ivancic-Jelecki J, Vojnovic G, Bozikov J, Welliver RC. Do circulating RSV-genotypes affect established biennial epidemic periodicity in Zagreb region? Open Journal of Respiratory Diseases 2012: 2, 91-94.
73. White LJ, Waris M, Cane PA, Nokes DJ, Medley GF. The transmission dynamics of group A and B human respiratory syncytial virus (hRSV) in England and Wales and Finland: seasonality and cross protection. Epidemiol Infect 2005; 133:279-289.