

# What's New in Pediatric Infections?

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**Source:** Little P, Francis NA, Stuart B, O'Reilly G, Thompson N, Becque T, Hay AD, Wang K, Sharland M, Harnden A, Yao G. Antibiotics for lower respiratory tract infection in children presenting in primary care in England (ARTIC PC): a double-blind, randomised, placebo-controlled trial. *Lancet* 2021. DOI: 10.1016/S0140-6736(21)01431-8

In ARTIC PC, a double-blind, randomized, placebo-controlled trial done at 56 general practices in England, researchers examined the effect of amoxicillin on the duration of moderately bad symptoms in children presenting with uncomplicated (non-pneumonic) lower respiratory tract infections (LRTIs) in primary care, overall and in key clinical subgroups (patients with chest signs, fever, physician rating of unwell, sputum or chest rattle, and short of breath).

- Children aged 6 months to 12 years presenting in primary care with acute uncomplicated LRTI, were randomly assigned to receive amoxicillin 50 mg/kg per day or placebo oral suspension, in three divided doses orally for 7 days.
- The groups had similar median durations of moderately bad or worse symptoms.
- Among children with uncomplicated chest infections, amoxicillin did not seem clinically effective either overall or for key subgroups in whom antibiotics are commonly prescribed.
- Unless pneumonia is suspected, most children presenting with chest infections should be provided safety-netting advice but not antibiotics.

**Source:** Choi GJ, Park JY, Choi JS, Choi SR, Kim D, Lee JH, Woo YJ, Lee J, Kim YJ. Influenza-associated neurologic complications in hospitalized pediatric patients: a multicenter retrospective study in Republic of Korea. *Pediat Infect Dis J* 2021. DOI: 10.1097/INF.0000000000003332

Findings from this retrospective review of hospitalized cases of influenza infection suggest that it is not uncommon that these cases suffer from influenza-associated neurologic complications. Full recovery occurs in most of the cases experiencing the complications. Korean children exhibited the occurrence of influenza-associated neurologic complications at frequency not significantly different from children in Western countries.

- Among a total of 1,988 influenza cases, 161 (8.1%) experienced influenza-associated neurologic complications (8.1%); 113 (70.2%) cases had detection of influenza virus A, 47 (29.2%) cases had influenza virus B and 1 case (0.6%) had detection of both A and B.
- A simple febrile convulsion was the most common diagnosis (44%), followed by complex febrile convulsion (29%), fever-provoked seizure under preexisting neurologic disease or afebrile seizure (14%), encephalopathy/encephalitis (8%) and meningitis (5%).
- Full recovery occurred in 96% of the patients.
- Risk factors of influenza-associated neurologic complications include preexisting neurologic disease, age groups of 6 months to 6 years and 6–12 years.

**Source:** Baguiya A, Bonet M, Cecatti JG, Brizuela V, Curteanu A, Minkauskiene M, Jayaratne K, Ribeiro-do-Valle CC, Budianu MA, Souza JP, Kouanda S. Perinatal outcomes among births to women with infection during pregnancy. *Arch Dis Childhood* 2021;106(10):946–953. DOI: 10.1136/archdischild-2021-321865

One-third of all births had a negative perinatal outcome. The primary risk factors for adverse perinatal outcomes were preexisting maternal medical conditions and severe infection-related maternal outcomes.

- The research was performed in 408 hospitals in 43 LMIC of all the WHO regions in 2017.
- One thousand two hundred nineteen births were analyzed.
- Data reported that 25.9% ( $n = 316$ ) and 10.1% ( $n = 123$ ) were neonatal near-miss (NNM) and perinatal deaths, respectively.
- Maternal preexisting medical condition and maternal infection suspected or diagnosed during labor remained independent risk factors for NNM after adjustment.
- Pre-existing maternal medical condition, infection-related severe maternal outcome, mother's infection suspected or diagnosed within 24 hours after childbirth, and vaginal birth were all independently associated with an elevated risk of perinatal death.

**Source:** Kindgren E, Ludvigsson J. Infections and antibiotics during fetal life and childhood and their relationship to juvenile idiopathic arthritis: a prospective cohort study. *Pedia Rheumat* 2021;19:145. DOI: 10.1186/s12969-021-00611-4

In a large birth cohort from the general population, an association of exposure to antibiotics early in life was observed with an increased risk for juvenile idiopathic arthritis (JIA). A dose dependent relationship was noted between the two. Results thereby support implementation of further, more restrictive, antibiotic policies during the first years of life.

- Data on infections and antibiotic exposure during pregnancy and childhood were retrieved in ABIS (All Babies in Southeast Sweden), a population-based prospective birth cohort of 17,055 children.
- There were 102 children with JIA.

- The odds of developing JIA were 78% higher in those exposed to antibiotics during the first 8 years of life compared with those not exposed (aOR 1.78; 95% CI 1.15–2.73,  $p = 0.009$ ).
- Occurrence of infection during fetal life or childhood showed no significant association with the risk of developing JIA, after confounder adjustment.

**Source: Anderson J, Oeum M, Verkolf E, Licciardi PV, Mulholland K, Nguyen C, Chow K, Waller G, Costa AM, Daley A, Crawford NW. Factors associated with severe respiratory syncytial virus disease in hospitalised children: a retrospective analysis. Arch Dis Childhood 2021. DOI: 10.1136/archdischild-2021-322435**

According to this retrospective cohort study, younger age, prematurity and parainfluenza virus type III (PIV3) co-detection were associated with severe respiratory syncytial virus (RSV) disease in children <2 years of age hospitalized with RSV infection. The link between PIV3 and severe RSV disease is a unique discovery that merits further exploration.

- From January 2017 to December 2019, children <2 years of age hospitalized for RSV lower respiratory tract infection at a single tertiary pediatric hospital over three RSV seasons were analyzed.
- Of the 970 hospitalized children, 386 (40%) were diagnosed as having 'severe' RSV disease, while 584 (60%) were classed as having 'moderate' RSV disease.
- Age <2 months, prematurity and RSV–PIV3 co-detection were all independently related to severe disease in multivariable analysis.

**Source: Glynn JR, Fielding K, Mzembe T, Sichali L, Banda L, McLean E, Kanjala C, Crampin AC, Ponnighaus JM, Warndorff DK, Fine PE. BCG re-vaccination in Malawi: 30-year follow-up of a large, randomised, double-blind, placebo-controlled trial. The Lancet Global Health 2021;9(10):e1451–e1459. DOI: 10.1016/S2214-109X(21)00309-0**

In this rural African population with a high prevalence of HIV, there was no indication that repeated BCG vaccination gives significant protection against overall tuberculosis. Given the many studies performed, subgroup effects should not be over interpreted. The evidence for limited protection against HIV-negative tuberculosis and a delayed benefit in individuals who were vaccinated as children, on the other hand, is consistent with other findings in the literature.

- Between 1986 and 1989, over 47,000 people of all ages living in northern Malawi with a BCG vaccine scar were randomly assigned (1:1) to receive a second BCG or a placebo.
- During the study's follow-up period, 824 people got tuberculosis, including 786 with pulmonary disease, and 383 (63%) of 607 with known HIV status were HIV positive.
- A second BCG dose had no effect on overall or pulmonary tuberculosis, nor on lymph node tuberculosis.
- The OR was lower in individuals with known HIV-negative tuberculosis (0.77; 0.59–1.00), in those vaccinated as children (aged < 5 years, 0.74; 0.41–1.35; aged 5–14 years, 0.77; 0.60–0.99), and in cases occurring at least 20 years following vaccination (0.79; 0.63–1.01).
- There were no changes based on tuberculin status or lineage at the time of vaccination.
- There was no evidence of leprosy protection after 10 years of vaccination (although there have been only nine diagnostically certain cases since 1995).

**Source: Davies P, du Pré P, Lillie J, Kanthimathinathan HK. One-year outcomes of critical care patients post-COVID-19 multisystem inflammatory syndrome in children. JAMA Pediat 2021. DOI: 10.1001/jamapediatrics.2021.2993**

Researchers sought to report medium- to long-term outcomes of the novel pediatric inflammatory multisystem syndrome temporally linked with SARS-CoV-2 (PIMS-TS)1 or multisystem inflammatory syndrome in children (MIS-C).

- A previously published multicenter national critical care cohort admitted to the hospital was assessed for retrieving its follow-up data.
- Collection of data from critical care readmissions and outpatient follow-up clinics was done (1-year post admission).
- Of 76 patients in the initial surviving cohort, 68 (89%) had data available.
- Eighteen of these patients had previously published 6-month outcomes.
- The small numbers, lack of consistent follow-up protocol, and hospital-wide readmission data limited the interpretation, however, it is strengthened by a nationwide data set.
- A significant risk of long-term morbidity was recorded for a group of patients.
- However, the majority of patients had good outcomes with no significant medium- or long-term sequelae which is reassuring.

**Source: Jao J, Balmert LC, Sun S, Qiu Y, Kraus TA, Kirmse B, Sperling RS, Abrams EJ, Myer L, Arpadi S, Geffner ME. Distinct cord blood C-peptide, adipokine, and lipidomic signatures by in utero HIV exposure. Pediat Res 2021;1-9. DOI: 10.1038/s41390-021-01705-1**

The results of this study demonstrate that higher cord insulin and C-peptide in HIV-exposed uninfected (HEU) vs HIV-unexposed uninfected (HUU) newborns, as well as differences in cord metabolites, metabolic-related cytokines, and eicosanoids, may reflect a propensity for fuel storage and an inflammatory milieu suggestive of fetal metabolic changes correlated with *in utero* HIV/ART exposure.

- Researchers enrolled a total of 118 infants, 56 were HEU, ART exposed.
- It has been reported that mean cord insulin ( $\beta = 0.295, p = 0.03$ ) and C-peptide ( $\beta = 0.522, p < 0.01$ ) were significantly higher in HEU vs HUU newborns in adjusted analyses.

- Furthermore, HEU neonates showed primarily positive relationships between complex lipids and C-peptides, indicative of fuel storage, and augmented relationships between cord eicosanoids and cytokines.
- It was shown that HUU neonates indicated negative relationships with lipids and C-peptide indicative of elevated fuel utilization.

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