



REVIEW

The potential role of microbiota for controlling the spread of extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBL-PE) in neonatal population [version 1; peer review: 2 approved]

Thibaud Delerue¹, Loic de Pontual², Etienne Carbonnelle^{1,3}, Jean-Ralph Zahar ^{1,3}

¹Département de Microbiologie Clinique et Unité de Contrôle et de Prévention du risque Infectieux, Groupe Hospitalier Paris Seine Saint-Denis, AP-HP, 125 rue de Stalingrad, 9300 Bobigny, France

²Service de pédiatrie, hôpital Jean-Verdier, Groupe Hospitalier Paris Seine Saint-Denis, Université Paris 13, AP-HP, 93140 Bondy, France

³IAME, UMR 1137, Université Paris 13, Sorbonne Paris Cité, France

V1 First published: 25 Jul 2017, 6(F1000 Faculty Rev):1217
<https://doi.org/10.12688/f1000research.10713.1>

Latest published: 25 Jul 2017, 6(F1000 Faculty Rev):1217
<https://doi.org/10.12688/f1000research.10713.1>

Abstract

The spread of extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBL-PE) in the hospital and also the community is worrisome. Neonates particularly are exposed to the risk of ESBL-PE acquisition and, owing to the immaturity of their immune system, to a higher secondary risk of ESBL-PE-related infection. Reducing the risk of acquisition in the hospital is usually based on a bundle of measures, including screening policies at admission, improving hand hygiene compliance, and decreasing antibiotic consumption. However, recent scientific data suggest new prevention opportunities based on microbiota modifications.

Keywords

Extended Spectrum Beta-lactamase – Producing Enterobacteriaceae, ESBL-PE, neonatal infections,

Open Peer Review

Approval Status  

| | 1 | 2 |
|---------------------------------|---|---|
| version 1 25 Jul 2017 |  |  |

Faculty Reviews are review articles written by the prestigious Members of **Faculty Opinions**. The articles are commissioned and peer reviewed before publication to ensure that the final, published version is comprehensive and accessible. The reviewers who approved the final version are listed with their names and affiliations.

1. **Gyula Tálosi**, Department of Pediatrics, University of Szeged, Szeged, Hungary
2. **Colum P Dunne**, University of Limerick, Limerick, Ireland

Any comments on the article can be found at the end of the article.

Corresponding author: Jean-Ralph Zahar (jrzahar@gmail.com)

Competing interests: The authors declare that they have no competing interests.

Grant information: The author(s) declared that no grants were involved in supporting this work.

Copyright: © 2017 Delerue T *et al.* This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Delerue T, de Pontual L, Carbonnelle E and Zahar JR. **The potential role of microbiota for controlling the spread of extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBL-PE) in neonatal population [version 1; peer review: 2 approved]** F1000Research 2017, **6**(F1000 Faculty Rev):1217 <https://doi.org/10.12688/f1000research.10713.1>

First published: 25 Jul 2017, **6**(F1000 Faculty Rev):1217 <https://doi.org/10.12688/f1000research.10713.1>

Introduction

One of the most worrisome challenges of the last few years is the spread of multidrug-resistant organisms (MDROs) in the community and the hospital. The rise of MDROs most frequently concerns Enterobacteriaceae isolates and is driven by the spread of extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBL-PE)^{1,2}. The unfortunate spread of ESBL-producing bacteria can occur either by emerging clones or by horizontal transfer of ESBL plasmids between bacteria of the same or different species. This family of enzymes hydrolyzes the beta-lactam ring, rendering most beta-lactam antibiotics ineffective³. As options for treatment are limited and due to the high risk of mortality related to inadequate antibiotic therapy, the clinical impact of ESBL-PE spreading is important. Neonates, specifically those hospitalized in neonatal intensive care units (NICUs), are at high risk of ESBL-PE acquisition and are highly susceptible to ESBL-PE infection due to the immaturity of their immune systems^{4,5}. Indeed, ESBL colonization rates in pediatric intensive care units (PICUs) range up to 12% for *Escherichia coli* and 39% for *Klebsiella* spp.⁶. ESBL rates as high as 60% for *Klebsiella* spp. and 75% for *E. coli* have been reported from blood cultures from infected infants in some NICUs⁷. Also, as Enterobacteriaceae are recognized as serious pathogens in the NICU and rates of *E. coli* early-onset sepsis have increased along with infection in infants with very low birth weight, the spread of ESBL-PE presents major challenges in managing neonatal sepsis. According to the literature, two main factors seem to be associated with the risk of acquisition/transmission: antibiotic consumption and compliance to hand hygiene⁸.

Bacterial acquisition and route of transmission

Unlike adults, the newborn is exposed at birth and during the first weeks of life to multiple possible sources of MDRO acquisition. Recent studies^{9,10} suggested that bacterial acquisition may commence *in utero* long before delivery but that bacterial acquisition will continue during labor and within the first weeks of life. At birth, the intestinal tract becomes progressively colonized with potentially pathogenic isolates¹¹. Outside the hospital, sources of microbial colonization for newborns are parents and even other relatives^{12,13}. In NICUs, MDRO acquisition will occur from health-care workers (as reservoirs or vectors) but also from parents and visitors.

Determining the route of MDRO acquisition in and outside the hospital seems to be very important to understand the best way to limit and control the risk of outbreaks. During NICU stay, infants are exposed to specific and non-specific factors that increase the risk of MDRO acquisition, including invasive procedures and the frequent use of broad-spectrum antimicrobial drugs⁷. Also, transmission of ESBL-PE (and other MDRO isolates) may occur in the NICU via either medical staff or equipment; however, other sources of MDRO bacterial acquisition in infants could be the mother, and specific practices such as skin-to-skin care that, despite positive effects in the care of premature babies¹⁴, could expose infants to a higher risk of acquisition¹³.

How to control the risk of transmission

Until now, most of the data have not allowed us to identify the modes of acquisition and to consider the best control policies. Indeed, the most frequent published reports regarding the risk factors of infection or colonization by ESBL-PE bacteria were from NICUs^{9,15-19}, and little is known about factors associated with spreading in the community. Most reports often describe single-unit outbreaks^{16,17,20} and health care-related risk factors. Several risk factors have been identified, such as younger gestational age, low birth weight, length of hospital stay, invasive devices, antibiotic use, and hand hygiene compliance²¹⁻²⁴. However, these different studies did not take into account several other risk factors.

Indeed, one of the most important risk factors neglected in several studies is related to colonization pressure. Nowadays, ESBL-PE colonization is considered an endemic situation, and investigators estimate that 5% to 70% of inhabitants of different countries are colonized²⁵. Analyzing risk factors of ESBL-PE acquisition in neonates without taking into account mother or family carriage (or both) may be the cause of major bias. Several studies suggested that the main route of transmission was the maternal-neonatal one^{11,26-29}. In a multivariate analysis in a first study conducted at the Charité - Universitätsmedizin Berlin hospital, Denk and colleagues¹¹ identified ESBL-PE-positive mothers as the main risk factor of ESBL-PE acquisition in newborns, suggesting maternal-neonatal as the main source of acquisition²⁷. In a recent prospective study conducted in Israel²⁸ aiming to determine whether the route of ESBL-PE transmission to hospitalized newborns was from the mother, the authors found that mothers of 13 out of 14 positive newborns were colonized by ESBL-producing *E. coli*. However, in a cross-sectional study conducted in Tanzania²⁹, the prevalence of carriage of ESBL-PE was 25.4% in neonates, and the authors suggested that neonates acquire these strains from sources other than post-delivery women, such as transmission from the environment or relatives.

Several studies conducted in adult and pediatric populations have identified the measures needed to control the spread of ESBL-PE into the hospital during outbreaks^{30,31}. Controlling the spread during outbreaks needs screening policies, decreasing antibiotic consumption, and improving hand hygiene. Indeed, surveillance may help to identify sources of infection and can be a powerful tool in the elimination of ESBL bacteria from the NICU, and the surveillance of maternal ESBL carriage can help in the prevention of neonatal colonization^{32,33}. Moreover, prevention can occur through implementation of strict infection control guidelines, effective hand washing, minimization and safety in the use of invasive devices, and judicious use of antimicrobials such as third-generation cephalosporins^{34,35}.

Also, little is known about how to control the spread in the community setting. Antibiotic courses seem to be a major risk factor related to the spread and acquisition in community onset³⁶.

The role of microbiota in the acquisition of multidrug-resistant organisms

Recent clinical data has highlighted the protective role of the human microbiome in MDRO and specifically ESBL-PE acquisition. As is well known, the human microbiome plays an important role in protecting the host from *de novo* colonization with exogenous pathogenic bacteria³⁷. This colonization resistance is disrupted by exposure to antimicrobials and is one of the major risks for MDRO acquisition³⁸. In a prospective study conducted in a tertiary care center in Boston³⁹, the authors compared the fecal microbiota of healthy and hospitalized subjects and made special reference to those who acquired MDROs during their hospital stay. The fecal microbiota of the hospitalized patients had abnormal community composition, and *Lactobacillus* spp. was associated with lack of MDRO acquisition, consistent with a protective role. In a study that addressed the role of certain changes in the composition of the microbiota as a risk factor of ESBL-PE colonization, Gosalbes and colleagues highlighted a similar richness of taxa but a significant difference in species of four genera between carriers and non-carriers⁴⁰.

These two recent reports suggest the role of microbiome as a risk factor associated with a higher risk of MDRO acquisition. As is well known, the intestinal microbiome during infancy plays a major role in human health. Several factors influence the establishment of the microbiome in neonates, such as mode of delivery, antibiotic administration during pregnancy or after birth, and also type of feeding. For example, breast milk seems to influence initial bacterial colonization and can reduce the risk of intestinal inflammation⁴¹ and has a major role in the prevention of colonization and late-onset sepsis^{42,43}. Indeed, recent studies demonstrate the presence of a necrotizing enterocolitis-associated

gut microbiome and the presence of *Clostridium perfringens* in the meconium⁴⁴.

These data make it possible to revive the protective role of certain bacterial species. Indeed, recent data suggested that *Lactobacillus plantarum* had antagonistic properties against both *Acinetobacter baumannii* and *Pseudomonas aeruginosa* strains⁴⁵; also, *Bifidobacterium breve* seems to have antimicrobial activity against several enteropathogenic strains⁴⁶. Moreover, oral administration of a mix of probiotics for 1 week to children on broad-spectrum antibiotics in a PICU decreased intestinal colonization by *Candida* and led to a 50% reduction in candiduria⁴⁷. However, further studies are needed to address the optimal probiotic organisms, dosing, timing, and duration⁴⁸.

In conclusion, several factors are associated with acquisition and transmission of ESBL-PE in infants, and our understanding of risk factors needs new studies, including the protective role of the microbiome, the impact of antibiotic consumption, and the role of maternal-neonatal transmission. The recently published studies suggesting a protective role of the microbiome for MDRO acquisition open a large field of investigation and could help us to better understand this phenomenon and to adapt our infection control measures.




Competing interests

The authors declare that they have no competing interests.

Grant information

The author(s) declared that no grants were involved in supporting this work.

References

1.  Flokas ME, Detsis M, Alevizakos M, *et al.*: **Prevalence of ESBL-producing Enterobacteriaceae in paediatric urinary tract infections: A systematic review and meta-analysis.** *J Infect.* 2016; **73**(6): 547–57.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
2. Toubiana J, Timsit S, Ferroni A, *et al.*: **Community-Onset Extended-Spectrum β -Lactamase-Producing Enterobacteriaceae Invasive Infections in Children in a University Hospital in France.** *Medicine (Baltimore).* 2016; **95**(12): e3163.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
3. Brolund A, Sandegren L: **Characterization of ESBL disseminating plasmids.** *Infect Dis (Lond).* 2016; **48**(1): 18–25.
[PubMed Abstract](#) | [Publisher Full Text](#)
4. Lukac PJ, Bonomo RA, Logan LK: **Extended-spectrum β -lactamase-producing Enterobacteriaceae in children: old foe, emerging threat.** *Clin Infect Dis.* 2015; **60**(9): 1389–97.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
5.  Giuffrè M, Geraci DM, Bonura C, *et al.*: **The Increasing Challenge of Multidrug-Resistant Gram-Negative Bacilli: Results of a 5-Year Active Surveillance Program in a Neonatal Intensive Care Unit.** *Medicine (Baltimore).* 2016; **95**(10): e3016.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
6. Badal RE, Bouchillon SK, Lob SH, *et al.*: **Etiology, extended-spectrum β -lactamase rates and antimicrobial susceptibility of gram-negative bacilli causing intra-abdominal infections in patients in general pediatric and pediatric intensive care units—global data from the Study for Monitoring Antimicrobial Resistance Trends 2008 to 2010.** *Pediatr Infect Dis J.* 2013; **32**(6): 636–40.
[PubMed Abstract](#) | [Publisher Full Text](#)
7. Roy S, Gaind R, Chellani H, *et al.*: **Neonatal septicaemia caused by diverse clones of *Klebsiella pneumoniae* & *Escherichia coli* harbouring blaCTX-M-15.** *Indian J Med Res.* 2013; **137**(4): 791–9.
[PubMed Abstract](#) | [Free Full Text](#)
8. Zahar JR, Lesprit P: **Management of multidrug resistant bacterial endemic.** *Med Mal Infect.* 2014; **44**(9): 405–11.
[PubMed Abstract](#) | [Publisher Full Text](#)
9.  Stapleton PJ, Murphy M, McCallion N, *et al.*: **Outbreaks of extended spectrum beta-lactamase-producing Enterobacteriaceae in neonatal intensive care units: a systematic review.** *Arch Dis Child Fetal Neonatal Ed.* 2016; **101**(1): F72–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
10. Stinson LF, Payne MS, Keelan JA: **Planting the seed: Origins, composition, and postnatal health significance of the fetal gastrointestinal microbiota.** *Crit Rev Microbiol.* 2017; **43**(3): 352–69.
[PubMed Abstract](#) | [Publisher Full Text](#)
11.  Denkel LA, Schwab F, Kola A, *et al.*: **The mother as most important risk factor for colonization of very low birth weight (VLBW) infants with**



- extended-spectrum β -lactamase-producing Enterobacteriaceae (ESBL-E). *J Antimicrob Chemother.* 2014; **69**(8): 2230–7.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
12. Jimenez-Truque N, Tedeschi S, Saye EJ, *et al.*: Relationship between maternal and neonatal *Staphylococcus aureus* colonization. *Pediatrics.* 2012; **129**(5): e1252–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 13. O'Connor C, Philip RK, Kelleher J, *et al.*: The first occurrence of a CTX-M ESBL-producing *Escherichia coli* outbreak mediated by mother to neonate transmission in an Irish neonatal intensive care unit. *BMC Infect Dis.* 2017; **17**(1): 16.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 14. Conde-Agudelo A, Díaz-Rossello JL: Kangaroo mother care to reduce morbidity and mortality in low birthweight infants. *Cochrane Database Syst Rev.* 2014; (4): CD002771.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 15. Loyola S, Gutierrez LR, Horna G, *et al.*: Extended-spectrum β -lactamase-producing Enterobacteriaceae in cell phones of health care workers from Peruvian pediatric and neonatal intensive care units. *Am J Infect Control.* 2016; **44**(8): 910–6.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 16. Nakamura K, Kaneko M, Abe Y, *et al.*: Outbreak of extended-spectrum β -lactamase-producing *Escherichia coli* transmitted through breast milk sharing in a neonatal intensive care unit. *J Hosp Infect.* 2016; **92**(1): 42–6.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 17. Haller S, Eller C, Hermes J, *et al.*: What caused the outbreak of ESBL-producing *Klebsiella pneumoniae* in a neonatal intensive care unit, Germany 2009 to 2012? Reconstructing transmission with epidemiological analysis and whole-genome sequencing. *BMJ Open.* 2015; **5**(5): e007397.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 18. Nordberg V, Quizpe Peralta A, Galindo T, *et al.*: High proportion of intestinal colonization with successful epidemic clones of ESBL-producing Enterobacteriaceae in a neonatal intensive care unit in Ecuador. *PLoS One.* 2013; **8**(10): e76597.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 19. Sumer S, Turk Dagi H, Findik D, *et al.*: Two outbreaks of ESBL-producing *Klebsiella pneumoniae* in a neonatal intensive care unit. *Pediatr Int.* 2014; **56**(2): 222–6.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 20. Naas T, Cuzon G, Robinson AL, *et al.*: Neonatal infections with multidrug-resistant ESBL-producing *E. cloacae* and *K. pneumoniae* in Neonatal Units of two different Hospitals in Antananarivo, Madagascar. *BMC Infect Dis.* 2016; **16**: 275.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 21. Tsai MH, Chu SM, Hsu JF, *et al.*: Risk factors and outcomes for multidrug-resistant Gram-negative bacteremia in the NICU. *Pediatrics.* 2014; **133**(2): e322–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 22. Crivaro V, Bagattini M, Salza MF, *et al.*: Risk factors for extended-spectrum beta-lactamase-producing *Serratia marcescens* and *Klebsiella pneumoniae* acquisition in a neonatal intensive care unit. *J Hosp Infect.* 2007; **67**(2): 135–41.
[PubMed Abstract](#) | [Publisher Full Text](#)
 23. Pessoa-Silva CL, Meurer Moreira B, Câmara Almeida V, *et al.*: Extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* in a neonatal intensive care unit: risk factors for infection and colonization. *J Hosp Infect.* 2003; **53**(3): 198–206.
[PubMed Abstract](#) | [Publisher Full Text](#)
 24. Mammina C, Di Carlo P, Cipolla D, *et al.*: Surveillance of multidrug-resistant gram-negative bacilli in a neonatal intensive care unit: prominent role of cross transmission. *Am J Infect Control.* 2007; **35**(4): 222–30.
[PubMed Abstract](#) | [Publisher Full Text](#)
 25. Singh N, Patel KM, Léger M, *et al.*: Risk of resistant infections with Enterobacteriaceae in hospitalized neonates. *Pediatr Infect Dis J.* 2002; **21**(11): 1029–33.
[PubMed Abstract](#)
 26. Woerther PL, Burdet C, Chachaty E, *et al.*: Trends in human fecal carriage of extended-spectrum β -lactamases in the community: toward the globalization of CTX-M. *Clin Microbiol Rev.* 2013; **26**(4): 744–58.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 27. Rettedal S, Løhr IH, Bernhoff E, *et al.*: Extended-spectrum β -lactamase-producing Enterobacteriaceae among pregnant women in Norway: prevalence and maternal-neonatal transmission. *J Perinatol.* 2015; **35**(11): 907–12.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 28. Peretz A, Skuratovsky A, Khabra E, *et al.*: Peripartum maternal transmission of extended-spectrum β -lactamase organism to newborn infants. *Diagn Microbiol Infect Dis.* 2017; **87**(2): 168–71.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 29. Nelson E, Kayega J, Seni J, *et al.*: Evaluation of existence and transmission of extended spectrum beta lactamase producing bacteria from post-delivery women to neonates at Bugando Medical Center, Mwanza-Tanzania. *BMC Res Notes.* 2014; **7**: 279.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 30. Pelat C, Kardaş-Sloma L, Birgand G, *et al.*: Hand Hygiene, Cohorting, or Antibiotic Restriction to Control Outbreaks of Multidrug-Resistant Enterobacteriaceae. *Infect Control Hosp Epidemiol.* 2016; **37**(3): 272–80.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 31. Derde LP, Cooper BS, Goossens H, *et al.*: Interventions to reduce colonisation and transmission of antimicrobial-resistant bacteria in intensive care units: an interrupted time series study and cluster randomised trial. *Lancet Infect Dis.* 2014; **14**(1): 31–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 32. Széi B, Reiger Z, Urbán E, *et al.*: Successful elimination of extended-spectrum beta-lactamase (ESBL)-producing nosocomial bacteria at a neonatal intensive care unit. *World J Pediatr.* 2017; **13**(3): 210–6.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 33. Patyi M, Tóth Z, Kelemen E, *et al.*: [Examination of maternal extended spectrum beta-lactamase bacterial colonization and follow-up of newborns requiring Neonatal Intensive Care Unit admission]. *Orv Hetil.* 2016; **157**(34): 1353–6.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 34. Cipolla D, Giuffrè M, Mammina C, *et al.*: Prevention of nosocomial infections and surveillance of emerging resistances in NICU. *J Matern Fetal Neonatal Med.* 2011; **24**(Suppl 1): 23–6.
[PubMed Abstract](#) | [Publisher Full Text](#)
 35. Legeay C, Bourigault C, Lepelletier D, *et al.*: Prevention of healthcare-associated infections in neonates: room for improvement. *J Hosp Infect.* 2015; **89**(4): 319–23.
[PubMed Abstract](#) | [Publisher Full Text](#)
 36. Tosh PK, McDonald LC: Infection control in the multidrug-resistant era: tending the human microbiome. *Clin Infect Dis.* 2012; **54**(5): 707–13.
[PubMed Abstract](#) | [Publisher Full Text](#)
 37. Buffie CG, Pamer EG: Microbiota-mediated colonization resistance against intestinal pathogens. *Nat Rev Immunol.* 2013; **13**(11): 790–801.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 38. Dethlefsen L, Relman DA: Incomplete recovery and individualized responses of the human distal gut microbiota to repeated antibiotic perturbation. *Proc Natl Acad Sci U S A.* 2011; **108**(Suppl 1): 4554–61.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 39. Araos R, Tai AK, Snyder GM, *et al.*: Predominance of *Lactobacillus* spp. Among Patients Who Do Not Acquire Multidrug-Resistant Organisms. *Clin Infect Dis.* 2016; **63**(7): 937–43.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 40. Gosalbes MJ, Vázquez-Castellanos JF, Angebault C, *et al.*: Carriage of Enterobacteria Producing Extended-Spectrum β -Lactamases and Composition of the Gut Microbiota in an Amerindian Community. *Antimicrob Agents Chemother.* 2015; **60**(1): 507–14.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 41. Gregory KE, Samuel BS, Houghteling P, *et al.*: Influence of maternal breast milk ingestion on acquisition of the intestinal microbiome in preterm infants. *Microbiome.* 2016; **4**(1): 68.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 42. Mahon J, Claxton L, Wood H: Modelling the cost-effectiveness of human milk and breastfeeding in preterm infants in the United Kingdom. *Health Econ Rev.* 2016; **6**(1): 54.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 43. Lee J, Kim HS, Jung YH, *et al.*: Oropharyngeal colostrum administration in extremely premature infants: an RCT. *Pediatrics.* 2015; **135**(2): e357–66.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 44. Heida FH, van Zoonen AGJF, Hulscher JBF, *et al.*: A Necrotizing Enterocolitis-Associated Gut Microbiota Is Present in the Meconium: Results of a Prospective Study. *Clin Infect Dis.* 2016; **62**(7): 863–70.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 45. Soltan Dallal MM, Davoodabadi A, Abdi M, *et al.*: Inhibitory effect of *Lactobacillus plantarum* and *Lb. fermentum* isolated from the faeces of healthy infants against nonfermentative bacteria causing nosocomial infections. *New Microbes New Infect.* 2017; **15**: 9–13.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 46. Delcaru C, Alexandru I, Podgoreanu P, *et al.*: Antagonistic activities of some *Bifidobacterium* sp. strains isolated from resident infant gastrointestinal microbiota on Gram-negative enteric pathogens. *Anaerobe.* 2016; **39**: 39–44.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 47. Singhi SC, Kumar S: Probiotics in critically ill children [version 1; referees: 2 approved]. *F1000Res.* 2016; **5**: pii: F1000 Faculty Rev-407.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 48. Zhang GQ, Hu HJ, Liu CY, *et al.*: Probiotics for Preventing Late-Onset Sepsis in Preterm Neonates: A PRISMA-Compliant Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Medicine (Baltimore).* 2016; **95**(8): e2581.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)

Open Peer Review

Current Peer Review Status:  

Editorial Note on the Review Process

Faculty Reviews are review articles written by the prestigious Members of **Faculty Opinions**. The articles are commissioned and peer reviewed before publication to ensure that the final, published version is comprehensive and accessible. The reviewers who approved the final version are listed with their names and affiliations.

The reviewers who approved this article are:

Version 1

1. **Colum P Dunne**

University of Limerick, Limerick, Ireland

Competing Interests: No competing interests were disclosed.

2. **Gyula Tálosi**

Department of Pediatrics, University of Szeged, Szeged, Hungary

Competing Interests: No competing interests were disclosed.

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com

F1000Research