AMERICAN ACADEMIC PUBLISHER

INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

ISSN NUMBER: 2692 - 5206 Volume 5. No 11. November ,2025

INFANT RESPIRATORY TRACT MICROBIOME

Karimdjanov I.A.

Tashkent State Medical University

Contact: Prof. Karimdjanov I.A., Head of the Department of Pediatrics in Family Medicine,

dr.ilhomjon@mail.ru

Abstract: Over the past two thousand years, the microbial community of the human body has been recognized as a key factor determining the physiology and pathology of the organism. This review critically analyzes the results of studying the microbiome of the upper respiratory tract in pediatric practice.

The current data from foreign and domestic literature on microbiocenosis in newborns and young children are reflected. The stages of the formation of the microbiota of the respiratory tract at different periods of childhood are considered. Particular attention is paid to the set of genes of microorganisms that are resistant to antimicrobial drugs. Thus, today one of the most promising research areas in medicine is the study of the set of genes responsible for the formation of the microbiota of various localizations. The study of the microbiome in newborns implements the principles of prevention, personification, predicativity as the main directions of modern high-tech medicine in this group of patients.

Keywords: microbiome, resistance, newborns, infants, premature infants, delivery method, antibiotic resistance.

Introduction. The work on genome sequencing has been a milestone in science and medicine. New discoveries have made it possible to understand that a person is not only the result of his genes. To fully understand the genetic basis of human activity, it is important to sequence the genomes of human bacteria - from the upper and lower respiratory tract, as well as the skin. At the beginning of the 21st century, the method of sequencing the 16S ribosomal RNA (16S rRNA) gene was first used to study the intestinal microbial population (12,16). The gene encoding 16S rRNA has become an ideal marker for identifying microorganisms. This gene is present in the genome of all bacteria, but is absent in eukaryotes and viruses, and has conserved regions that are the same in all prokaryotes and are species-specific. The 16s RNA nucleotide sequences of all known bacteria are currently publicly available and are reflected in the GenBank (https://www.ncbi.nlm.nih.gov/genbank/) [1, 2, 5, 6].

Objectives

Based on the analysis of this literature, to assess the characteristics of the upper respiratory tract microbiome in pediatric practice and to identify patterns of formation.

Materials and methods

The database search was carried out among materials published until 20.05.2023. Initially, a standard search strategy was used to select articles from the Cochrane Neonatal Central Controlled Trials Register, PubMed, EMBASE and SSTARD, MEDLINE databases. In addition, a search was carried out in the reference lists found through searches of clinical trial databases, conference proceedings and articles from randomized controlled trials.

Results and Discussion

The Human Microbiome Project (HMP) is a research program initiative of the US National Institutes of Health, whose main goal is to improve our understanding of the characteristics of the microbiota associated with human health and disease. The first phase of the program, launched in 2008, was a 5-year project that allowed us to determine the size and key characteristics of the human microbiota. The second phase, known as the Integrated Human Microbiome Project, was launched in 2014 with the aim of pooling resources to determine the role of microbes in maintaining human health and developing diseases. The microbiota is assessed using non-culture methods, in particular metagenomics, as well as the study of the 16S rRNA gene sequencing of microbiota bacteria [6, 12].

Terminology

The main terms used in modern scientific studies of the human microbiome are listed in the table.

Key terminology in the study of the human microbiome [12]

Term	Definition
Microbiota	A collection of microorganisms of a specific location
Microbiome	A collection of microorganisms, their genes, and environmental factors determined by a local location
Metatranscriptomics	The process of identifying and characterizing microbial genes expressed by the microbiota
Microbiome density	The total number of bacteria in a biological sample
16s rRNA gene study	Analysis of the 16S ribosomal RNA gene sequence in total DNA extracts; the data are used to develop microbial community composition profiles

Characteristics of the upper respiratory tract microbiome in premature infants

The development of non-culture methods for identifying microorganisms and the reduction in the cost of sequencing platforms have allowed us to intensify research in this area, obtain conclusions that are applicable in clinical practice, and expand our understanding of human diseases [12, 13].

By 2010, the "microbes – respiratory system" paradigm had changed due to the widespread introduction of non-culture methods for studying microorganisms. The dogma of healthy lungs was a thing of the past. Currently, the main postulates of the respiratory microbiome are:

1) healthy lower respiratory tracts contain bacteria that are different from bacteria in the upper respiratory tract;

2) the respiratory tracts of patients with respiratory diseases contain microbial communities that differ from those of healthy newborns.

In a recent publication, researchers have shown the potential impact of microbial colonization of the fetus from the embryonic period [14], as well as the increase in microbial colonization immediately after birth, mainly by maternal bacteria, with representatives of the vaginal and intestinal microbiota dominating. Furthermore, we have previously noted that this colonization process differs markedly between infants born naturally and those delivered by cesarean section [15, 16]. The composition of the lung microbiome is determined by the balance of three factors: microbial immigration into the airways, microbial clearance from the airways, and the local growth state of the microbial community, which is determined by local conditions.

The nasal cavity is inhabited by a relatively simple set of bacteria, the composition of which differs little between children and adults. Representatives of Corynebacterium,

Propionibacterium, Staphylococcus spp. they are the main colonizers of the nasal cavity and retain their dominance until adulthood,

the Moraxella species are added. The nasal microbiota profiles in children vary greatly depending on the season, often in autumn / winter Proteobacteria and Fusobacteria predominate.

The nasopharyngeal microbiome is a very dynamic ecosystem that undergoes changes and differentiation during the maturation process, which can last up to 2 years, which is strikingly different from the adult microbiome. The nasopharynx is initially populated by representatives of the Corynebacterium and Staphylococcus spp. and is subsequently replenished by gram-positive bacteria of the genus Dolosigranulum (especially characteristic

for breast-fed children), the genera Alloiococcus and Moraxella. The oropharynx is the anatomical barrier between the respiratory tract and the gastrointestinal tract, which leads to the existence of the most variable bacterial ecosystem in it. The upper respiratory tract is an ecological niche for protobionts: S. pneumoniae, H. influenzae, and S. aureus. Up to 93% of children under 2 years of age are colonized by one of the upper respiratory tract protobionts, even when assessed by classical culture methods. What defines them as classical is that they are resident members of the upper respiratory tract microbiome. The dual role of protobionts in the development of respiratory diseases in newborns is that on the one hand, colonization of the upper respiratory tract by protobionts is a risk factor for infection, on the other hand, it is a factor of voluntary infection and even resistance to the acquisition of new pathogenic strains.

In patients with pneumonia, a higher density of bacteria and less diversity in the lower respiratory tract were found, with a homogenous distribution of species. Typically, one taxon with the highest dominant frequency of Streptococcus spp., Haemophilus spp., Moraxella spp. Patients with high levels of butyrate-producing bacteria (Inhibitor short-chain fatty acid) in their gut microbiome have a reduced risk of developing lower respiratory tract viral infections. Streptococcus viridans. Streptococcus viridans. During the first day of life, the newborn infant changes its microbial landscape from a variable combined microbiome to a profile dominated by Streptococcus viridans. The composition of the nasopharynx in children differs in the early neonatal period. Predominant in the beginning

Staphylococcus aureus, followed by water Sigranulum pigrum, Socntebacterium pseudodiphteriticum/propinquum,

Streptococcus pneumoniae, Moraxella catarrhalis/nonliquefacieens or Haemophilus influenzae. Infants born by cesarean section lag behind in the development of the respiratory microbiota profile, which is reflected in the reduction of Corynebacterium and Dolosigranulum. According to M. Hilti's studies, the lungs are sterile, and bacterial DNA is found only in respiratory tract samples [9]. At the same time, it was found that the child's stay on artificial ventilation leads to the formation of bacterial biofilms due to contamination of the intubation tube with pathogenic or opportunistic microflora [4].

The composition of the biocenosis of the mucous membranes of the pharynx (a mixture of the microflora of the oral cavity and the respiratory tract) is recognized as the most diverse: Neisseriaceae, Streptococcus spp., non-hemolytic (green) streptococci, Eteokosossaseae, Mollicutes, Staphylococcus epidermidis, Moraxellaceae, Bacteroidaceae, Borrelia, Tgeropema, Actinobacterideae. The main place in terms of quantitative composition in the upper respiratory tract is occupied by Neisseriance and Streptococcus spp., less often Staphylococcus epidermidis, Borrelia, Haemophilus influenzae, Streptococcus pneumoniae, Bacteroideceae[7, 8, 10, 11]. Contamination of the oropharyngeal mucosa of the newborn occurs during the passage of the fetus through the birth canal. By the middle of the first day after birth, Streptococcus ruodepes [3] joins the oral microflora.

Karaulov A. V., Afanasyev S. S. considered the "colonization resistance" of open body cavities as a protection of the ecosystem of microflora and macroorganism mucous membranes from pathogenic microorganisms. The authors showed that biocidal and biostatic products of secretions, microbial adhesion inhibitors, mechanical factors (the integrity of the ciliated epithelium, skin and mucous membranes), local factors of innate and adaptive immunity determine the colonization resistance of microorganisms. Microbiology introduced the concept of "colonization resistance phenomenon" into the terminology, which defines the essence of the influence of open mucosal microbiocenoses on cavities and mucosal immunity as an integral structural and functional system of the body [3, 8, 9].

The role of the microbiome in immune maturation and immune system calibration.

As with the gut and skin microbiota, early colonization of the infant's upper respiratory tract by microbes plays an important role in immune system maturation and immune response calibration, as demonstrated in studies that observed high levels of airway eosinophilia in sterile mice and the accumulation of invariant NK cells (natural killer cells) that were not seen in microbially colonized mice [17-19].

It should be noted that invariant natural killer cells, also known as classical NKT cells or type I NKT, are a population of T lymphocytes that express the invariant αβ T-cell receptor and specific molecules that are common to NK cells. Although monocytes are rare in peripheral blood, accounting for only 0.001–1% of mononuclear blood cells, they are important immune regulatory elements that produce a large number of cytokines, which in turn affect all other cells of the immune system.

Microbiome-based approaches to overcome molecular mechanisms of antibiotic resistance in premature infants

Antibiotic-resistant bacteria are a major threat to global medicine today. This is especially true because antibiotic resistance genes are not only widespread among infectious pathogens, but also among the human population of commensal bacteria of the microbiome. One of the first studies showed that a significant part of the anaerobe community in the microbiome of healthy people is resistant to one or more antibiotics, and the proportion of such bacteria increases significantly after antibiotic treatment [20]. The use of antibiotics leads to the accumulation of antibiotic resistance genes.

Surprisingly, antibiotic resistance genes have been identified in the microbiome of mummies from the 11th century, in frozen sediments from 30,000 years ago, and in a cave in New Mexico that has been isolated for millions of years [21-23]. Furthermore, both the DNA sequence and structural organization of gene operons identified in these ancient bacteria have been shown to be very similar to those carried by resistant microbes today. Thus, the resistome is the collection of all antibiotic resistance genes in the microbiome. The resistome is determined by the 2nd month of life of a child [24].

Interesting fact: horizontal gene transfer mechanisms are used by bacteria in response to antibiotic treatment (conjugation, transduction, and transformation) [25, 26].

The wide distribution of both phenomena: on the one hand, the ability of individual microorganisms to synthesize antibiotics, and on the other hand, the possession of resistance to them molecules that regulate gene transcription, is associated with the fact that antibiotics play the role of intracellular signals at concentrations found in natural ecosystems. A change in the response of the bacterial communicative community to a given signal as a result of an increase or, conversely, a loss of antibiotic resistance leads to the emergence of new ecotopes. In the evolution of antibiotic resistance, plasmids and conjugative transposons act as genetic platforms for the collection and sorting of antibiotic resistance genes inserted into transposons, integrons, gene cassettes, and insertion cryptic sequences.

The formation of antibiotic-resistant biofilms is the main strategy for combating gram-positive bacteria, including streptomycetes. Resistance to any antibiotic leads to a change in the response of the bacterium to a given signal. Antibiotic-resistant mutants of bacteria, as well as initially sensitive strains, respond to this antibiotic. But their transcriptome is different from the original strains. The spontaneous emergence of resistance to some antibiotics contributes to the formation of other bacterial ecotypes.

The antiquity of the genetic mechanisms of antibiotic biosynthesis suggests the existence of equally ancient genetic mechanisms of protection against them. The spread of antibiotic resistance genes between bacteria occurs due to the activity of mobile genetic elements. There are two types of them: genetic elements that can move independently between bacteria (conjugative plasmids and conjugative transposons); and genetic elements that move within the bacterial cell (along the chromosome, from the chromosome to the plasmid and vice versa: transposons, gene cassettes, integrons, etc.). Plasmids and conjugative transposons are a kind of platform on which the assembly and selection of antibiotic resistance genes occurs by various recombination systems of the bacterial cell.

Mobile genetic elements were involved in the transfer of antibiotic resistance genes between bacteria even before the introduction of antibiotics into clinical practice. An E. coli strain isolated as early as 1937, containing a plasmid (R-factor) that confers resistance to tetracycline and streptomycin, was described.

Conclusion

The composition of the respiratory microbial community in early childhood is associated with the consequences of the development of respiratory pathology in older children. Understanding the processes leading to disruption of the respiratory microbiome and, as a result, the susceptibility and severity of respiratory diseases will help develop new methods for diagnosing, predicting and treating this pathology.

We should not forget about the problem of antibiotic resistance among clinically important microorganisms, which is based on complex ecological and evolutionary relationships between microorganisms themselves, which were formed long before the emergence of humans as a biological species. A huge potential for antibiotic resistance genes is accumulated in superintegrons that do not participate in genetic exchange between microorganisms found in the clinic. Interpreting the widespread spread of antibiotic-resistant bacterial strains in the clinic as a phenomenon caused solely by the use of antibiotics greatly simplifies the understanding of this problem and creates the illusion of the possibility of achieving its solutions by limiting the use of antibiotics in clinical practice.

It is advisable to expand the scope of the problems being studied in the clinic related to the spread of antibiotic-resistant pathogenic microorganisms to include the processes of accumulation and exchange of antibiotic-resistant genes among bacteria.

References:

1. Ankirskaya A., Prilepskaya V., Bayramova G., Muravyeva V. Bacterial vaginosis: clinical course features, diagnosis and treatment. Breast cancer.
1998;5:276–282. (in Russian)
2. Astafyeva N., Kobzev D., Gamova I., Perfilova I., Udovichenko E., Skuchaeva L., Mikhailova I. The role of the microbiome of the respiratory tract in
respiratory health. The attending physician. 2019;5:88. (in Russian)
3. Zakharova I., Kuchina A. Microbiota of breast milk (presentation, sources, role of bacteria for the child and mother). Medical advice. 2022;16(1).
(in Russian)
4. Nikolaeva I., Tsaregorodtsev A., Shaikhieva G. Formation of the intestinal microbiota of a child and factors influencing this process. Russian

Bulletin of Perinatology and Pediatrics. 2018;63(3):13–18. (in Russian)
5. Pustotina O., Seliverstov A. The influence of the microbiome of breast milk on the health of the mother and newborn. Medical advice. 2019;13:36–40.
(in Russian)
6. Sidorova I. Microbiocenosis of the genital tract of women of reproductive age. Obstetrics and gynecology. 2005;2:7–9.
7. Jost T., Lacroix C., Braegger C., Chassard C. Assessment of bacterial diversity in breast milk using culture-dependent and culture-independent
approaches. British Journal of Nutrition. 2013;110(7):1253–1262.
8. Karaulov A., Afanasyev S., Aleshkin V. Microflora, colonization mucosal resistanceand mucosal immunity. Immunologia. 2015;36(5):290–295.
(in Russian)
9. Karaulov A., Aleshkin V., Voropaeva E. Colonization resistance indicators of oropharynx mucous membraneas objective criteriaof mucosal
immunity at bronchitis in children. Immunologia. 2012;33(5):255–259. (in Russian)
10. Karimdzhanov I.A., Yusupova G.A., Iskanova G.Kh., Israilova N.A. Dysbiosis of the Intestine in the Genesis of the Immune Failure in Children with Recurrent Bronchitis. Eurasian Medical Research Periodical. 2023;v.18(3):49-54

11. Zverev V., Boichenko M. (eds.) Medical microbiology, virology and immunology: a textbook. Volume 1. Moscow: GEOTAR-Media. 2010;448.
(in Russian)
12. Stoma I. Microbiome in medicine: a guide for doctors. Moscow: GEOTAR-Media, 2020;320.
13. Karimdjanov I.A., Zakirova U.I. Recurrent bronchitis in children. Proceedings of International Conference on Modern Science and Scientific Studies. 2023; 2(5): 70–87.
14. Stensballe L.G. Use of antibiotics during pregnancy increases the risk of asthma in early childhood. J.Pediatr. 2013;162(4):832–838.e3
15. Dominguez-Bello M.G. Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns.
Proc. Natl Acad.Sci. USA. 2010;107(26):11971–11975.
16. Dominguez-Bello M.G. Partial restoration of the microbiota of cesareanborn infants via vaginal microbial transfer. Nat. Med. 2016;22(3):250–253.
17. Guyatt G.H. Users’ guides to the medical literature. A method for grading health care recommendations. Evidense-Based Medicine Working
Group. JAMA. 1995;274(22):1800–1804.
18. Murad M.H. New evidence pyramid. BMJ Evid. Based Med. 2016;21(4):125–127.
19. Rondatelli M. Review on microbiota and effectiveness of probiotics use in older. World J.Clin.Cases. 2015;3(2):156–162.
20. Levy S.B. High frequency of antimicrobial resistance in human fecal flora. Antimicrob. Agents Chemother. 1988;32(12):1801–1806.
21. D’Costa V.M. Antibiotic resistance is ancient. Nature. 2011;477(7365):457–461.
22. Santiago-Rodriguez T.M. Gut microbiome of an 11 th century A.D. pre-Columbian Andean mummy. PLoS One. 2015;10(9).
23. Bhullar K. Antibiotic resistance is prevalent in an isolated cave microbiome. PLoS One. 2012;7(4).
24. Moore A.M. Gut resistome development in healthy twin pairs in the first year of life.

Microbiome. 2015;3(27).
25. Beaber J.W., Hochhut B., Waldor M.K. SOS response promotes horizontal dissemination of antibiotic resistance genes. Nature. 2004;427(6969):72–74.
26. Modi S.R. Antibiotic treatment expands the resistance reservoir and ecological network of the phage metagenome. Nature. 2013;499(7457):219–222.