International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319 – 6505, Impact Factor: SJIF: 5.995
Available Online at www.journalijcar.org
Volume 6; Issue 10; October 2017; Page No. 6381-6386
DOI: http://dx.doi.org/10.24327/ijcar.2017.6386.0931

Research Article

IMMUNOLOGY OF INFECTIONS AT THE PRESENT STAGE, MICROBIOTA AND MICROBIOTA DISEASES

Zemskov A.M[1].,. Zemskov V.M[2]*., Zemskova V.A[1]., Morozov A.N[1] and Mamchik N.P[1]

[1]Voronezh State Medical University, Voronezh, Russia
[2]Vishnevsky Institute of Surgery, Moscow, Russia

ARTICLE INFO

Article History:

Received 15th July, 2017
Received in revised form 19th August, 2017 Accepted 25th September, 2017
Published online 28th October, 2017

Key words:

Microbiota, microflora, dysbacteriosis.

ABSTRACT

The data on the microbiota, its biotopes, the qualitative composition, the role in the regulation of immunity and other functions of the body, disorders types and mechanisms, diagnostics, medical correction, complications are given.

INTRODUCTION

Microbiota

Man is an inhabitant of the Earth's biosphere inhabited by a huge number of microorganisms. On the one hand, he himself is the source of a multitude of microbes entering the environment; on the other hand, he represents a symbiotic community of numerous eu- and prokaryotic cells (bacteria, archaea, viruses, fungi, protozoa), the optimal ratio and interaction of which to a large extent determine the quality of life and health [1].

The five most important biotopes of the human body - the oral cavity, the intestines, the respiratory tract, the skin, the genito-urinary system - are inhabited by various types of microbial cells, which number is ten times higher than the number of cells of the body itself. All other organs and tissues (lungs, uterus, etc.), body fluids should normally be sterile[2, 3].

Biotopes vary considerably in pH level, in the gas composition of the medium, in the spectrum of enzymes, in immune factors, which results in the ambiguity of their microflora quantitative and qualitative composition. Each biotope, together with the microbes inhabiting it, constitutes a small ecosystem - microbiocenosis. The natural microflora of the body is a single natural complex consisting of a set of heterogeneous microbiocenoses in various parts of the human body.

Corresponding author:* **Zemskov V.M
Vishnevsky Institute of Surgery, Moscow, Russia

The symbiotic automicroflora includes more than 500 species; it has about 10^{14}cells [4].

To study the qualitative and quantitative parameters of the microbiota, cultivation methods and molecular technologies are used - sequencing of nucleic acids, mass spectrometry with subsequent bioinformation analysis, etc.

According to dr. L.I. Kafarskaya and others, the main domain of adult microbiota is represented by 6 main types of microorganisms: Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, Verrucomicrobia and Fusobacteria. The representation of the domains Archaea (mainly methanogenic microorganisms such as Metanobrevibacterium smithia) and Eukarya (yeast-like fungi of the genus Candida) does not exceed 1% of the total microbial community. Absolutely dominant representatives of human microbiota are bacteria of the types Bacteroidetes and Firmicutes (up to 90% in total). Normal microflora is divided into permanent (resident) microflora which consists of saprophytic and opportunistic microorganisms (M/o), accidental (transitory) microflora consisting of saprophytes, opportunistic and pathogenic M/o, obligatory microflora and facultative microflora which determines, appropriately, fermentation or putrefaction processes [5].

Microflora of the Oral Cavity

In the first months of life in the oral cavity of a child, aerobes and facultative anaerobes such as Streptococcus Salivarius, Streptococcus Mutans, Streptococcus Mitis, Lactobacteria and Neisseria predominate. An insignificant amount of anaerobic

bacteria may vegetate in the mucosal folds. Teeth eruption contributes to the appearance of Veillonella and Fusobacteria. Spirochetes and Bacteroides appear in the oral cavity at about 14 years old, which is associated with a change in the hormonal background of the organism.

Microflora of the Intestines

It is known that the esophagus and stomach microflora is variable; it depends on the nature of food.In the esophagus, it corresponds to the oral cavity microbial landscape, and in the stomach,it is poor because of the gastric juice acidity.In the duodenum, Lactobacteria, Streptococci (fecal) and Veillonella are predominant; in the ileum - E.Coli, anaerobic bacteria. With the distance from the stomach, the amount of M/o in the small intestine increases. The large intestine microflora is most abundant and diverse.The large intestine mucosa is densely populated with associations of anaerobic and facultative anaerobic bacteria. Apart from parietal microflora, there is luminal microflora with a total of 10^9 - 10^{12}colony forming units (CFU) weighing 1.5-2 kg.There are Bacteroides(10^9-10^{12}CFU), Bifidumbacteria(10^8-10^{12}CFU), Clostridia(10^3-10^5 CFU). Aerobes and facultative anaerobes account for 3-5% consisting of Enterobacteria (10^4-10^8CFU), Enterococci (10^5-10^8CFU), Lactobacteria (10^6-10^9CFU), Staphylococci (10^5-10^7 CFU), Fungi (up to 10^5CFU).

Microflora of the RespiratoryTract

Most M/o of inhaled air linger in the nasal cavity where they die. The normal microflora of the nose consists of Staphylococci, Streptococci, Diphtheriodes, *Haemophilus influenzae*, Staphylococcus aureus. In the nasopharynx and tonsils, along with the above microorganisms, there are also Bacteroides, Neisseria, Meningococci, Fusobacteria, Vibrios and Spirilla. The bronchi and lungs are normally sterile. Only when the activity of the bronchi epithelium is disturbed, M/o can penetrate into the depth of the bronchial tree.

Microflora of the Skin

In this area, both aerobic and anaerobic M/o are found in the concentration and species diversity of which depend on the medium pH, the content of sebum, humidity, age, etc. On the surface of the skin, the obligate microflora comprising of cocci - Micrococci, Staphylococci (including Staphylococcus aureus, about 5%), Diphtheriodes, Propionibacteria–vegetates. Non-pathogenic Staphylococci and Diphtheriodes exhibit maximal antagonistic activity towards accidental opportunistic M/o. A healthy, non-elderly person should not have signs of yeast-like fungi of the genus Candida, Enterobacteria and Bacteroides.

Microflora of the Genitourinary System

Kidneys, ureters and urine should be sterile in a healthy person. The urethral medium is weakly alkaline, so there are Peptococci, Streptococci, Corynebacteria, Mycobacteria, Bacteroides. The microflora of the vagina is hormone-dependent. Estrogens saturate epithelial cells with glycogen. As a result of its fermentation with acidophilic lactobacteria, a lot of lactic acid is formed; the medium pH becomes acidic, which prevents colonization by other M/o. An insignificant amount of nonpathogenic Corynebacteria, Bifidobacteria, Cocci (Staphylococci, Streptococci) can be present. This kind of microflora appears in girls in the first months of life (due to mother's estrogens) and remains stable from puberty until menopause. Approximately within 10 years (from 2 to 12) glycogen disappears because of a lack of estrogens, the amount of lactobacteria decreases sharply and the medium pH changes to weakly alkaline. As a result, Cocci dominate and their antagonistic properties are low compared to lactobacteria. Therefore, girls under the age of 12 are at risk of domestic contamination with sexually transmitted infections. Pregnancy accompanied by an estrogen "explosion" facilitates the development of lactobacteria and the birth canal purification from adverse M/o. Pregnancy termination gives the opposite effect, which can lead to the development of purulent-inflammatory processes of the endogenous nature. However, the uterusis normally sterile.

Microbiota Functions

In fact, [6] the human microbiota is an "extracorporeal" organ that performs the following functions:

1. Colonization resistance of the skin and mucous organs open to the external environment. This function is provided not only by competition for food and territory but also by inter-microbial antagonism of variants of different species with the help of colicins, lantibiotics, short-chain fatty acids, etc.
2. Stimulation of natural anti-infectious resistance and the immune system function in newborns and adults including specific protective reactions with the help of mimicry antigens of opportunistic and virulent M/o.
3. Formation of short-chain fatty acids which are sources of energy for colonocytes and histone deacetylase inhibitors, anti-inflammatory effect inducers, T-regulatory cells suppression, neutrophil chemotaxis stimulation, and delayed maturation of dendritic cells.
4. Regulation of the motor-evacuation function of the intestine. So, Bac. Fragilis produce γ-Aminobutyric acid and glutamate which inhibit or stimulate intestinal peristalsis.
5. Inactivation of toxic products of the exo- and endogenous nature by means of biodegradation and biotransformation mechanisms. For example, E. coli, Proteus, etc. are capable of destroying toxin proteins to intermediate and final products, synthesizing necessary amino acids from ammonia and other poisons.
6. Realization of the genetic function by transfer of genetic information from micro- to macroorganism through phagocytosis.
7. Maintenance of carcinolytic properties of blood through antimutagenic and antiviral action, for example, bifidobacteria.
8. Digestion of food;calcium ions, vitamin D and iron absorption intensification; regulation of water-salt metabolism and intestinal gas composition; exchange of amino acids, proteins, carbohydrates, fatty and nucleic acids, cholesterol, vitamins; recirculation of steroid hormones, bile salts.
9. Morphokinetic action in the development of tissues and organs, inflammation, epithelial changes, etc.

Microbiota diseases

Dysbacteriosis

It is necessary to note that dysbiosis and dysmicrobiocenosis is a stable qualitative and quantitative change in the composition of normal microflora towards an increase in pathological microflora and a sharp decrease in normal microflora, which may be accompanied by a typical clinical picture or vice versa, this condition arises from any pathological process. In fact, dysbiosis is a premorbid state in which it does not seem possible to detect a causative agent. At the same time, in a specific epitope there are: *(1)* a sharp decrease in the total number of microorganisms, *(2)* a decrease or complete disappearance of some typical pathogens, *(3)* the accumulation of microbes with atypical enzymatic and other characteristics, *(4)* their associations with fungi, i.e. a microbial landscape diversity. These secondary pathological processes are experienced by more than 90% of the world's population[7, 8].

Classification

Dysbacteriosis is differentiated according to the area of localization - nose, mouth, pharynx, intestine and its various parts (large, small), vagina, skin, etc.[3].

Degrees of Severity of Intestinal Dysmicrobiocenosis in Children

First degree

In which anaerobic flora prevails over anaerobic one; bifidobacteria are found in a dilution of 10^{-8} – 10^{-7} CFU. Opportunistic bacteria are determined in a 10^{-4} – 10^{-2}CFU dilution.

Second degree

In which anaerobic flora is suppressed;its amount is equal to that of aerobic flora. Opportunistic pathogens are found in associations with a dilution rate of 10^{-6} -10^{-7}.

Third degree

In which aerobic flora prevails over anaerobic one; bifido- and lactobacteria are absent or their quantity is reduced. The content of opportunistic bacteria is increased; the formation of their associations is possible.

Associative Forms of Dysbacteriosis

They have a number of features:

1. Greater aggressiveness and low compliance to therapeutic measures.
2. Microorganisms associations have significantly more energy to multiply.
3. Associative forms of dysbacteriosis are much more often accompanied by destructive processes in tissues, up to necrosis and bleeding in the parenchymal organs, greater changes in mucous membranes, for example, in the intestine.

Clinical Classification of Dysbacteriosis

In this aspect they are divided into:

1. Latent or compensated form of dysbacteriosis in which there are no clinical manifestations. Diagnosis is carried in the course of special laboratory studies.
2. Local or subcompensated form which is characterized by local or less common changes, for example, in certain areas of the intestine (duodenitis, enteritis, colitis) with unexpressed clinical symptoms.
3. Decompensated form in which an endogenous infection is formed as a result of violation of antibacterial barriers and immune homeostasis, intoxication, organ system insufficiency or inflammation. There is a certain uniformity of the intestinal "tube" microflora reaction to various pathological agents.

Stages of Change in Normal Microflora in Dysbacteriosis

First stage

It is characterized by a significant increase in the number of normal symbionts in their natural habitats, which, however, is combined with a decrease in the amount of anaerobic and aerobic lactobacilli - bifidobacteria and acidophilus bacteria.

Second stage

It is characterized by the appearance of microorganisms which are very rare in norm. Besides, there is an increase in the content of E. coli with altered enzymatic and other properties.

Third stage

In this case, microbes are accumulated in places where they are not usually found. A large number of associations of hemolytic and other microorganisms are observed.

Fourth stage

In this stage, the above disorders are accompanied by the phenomena of increased toxigenicity and virulence of some representatives of autoflora or their associations, the factors that cause dysbacteriosis which are numerous and diverse.

Factors Provoking Dysbacteriosis

They include

1. Pathological processes and diseases: prematurity, intestinal infections, allergies, which form dysbacteriosis in 9-100% of cases; diseases of the urinary and hepatobiliary systems, ENT organs (ear, nose, throat) - in 80-87%. The same can be said with regard to the cardiovascular and bronchopulmonary systems, the digestive tract and endocrine organs when pathological processes develop in 68-74%. 2. Dyskinesia of the gastrointestinal tract, dyspepsia, malabsorption, non-infectious inflammatory disorders of the large intestine (nonspecific ulcerative colitis, Crohn's disease), stress, irradiation, surgical interventions, etc.
2. Antibacterial agents.
3. Narcotic drugs and local anesthetics.
4. Emetic, absorbing, enveloping, cathartic, expectorant, choleretic drugs.
5. Medications that inhibit the intestinal motility.
6. Antihistamines, psychotropic and hormonal agents.
7. Heavy metal salts, dyes, nitrates, nitrites.
8. Complicated chronic course of various diseases of the bronchopulmonary, intestinal, genitourinary and other systems.
9. Long-termpresence of a person in confined spaces (submarines, spacecrafts).
10. Nutritional disorders (starvation, overeating, vitamin deficiency, different diets).

11. Immunodeficiency conditions, allergization, induction of autoagressive reactions.
12. Occupational hazard (microbiological, textile, chemical and other industries).
13. Seasonal factors. In April-May, the symptoms of dysbacteriosis (changes in the composition, the presence of hemolytic microbes, spore-forming bacteria) are less pronounced than during the winter months - in January-February. In July, the number of microbes that characterize dysbacteriosis is significantly increased.
14. Acute dysbacteriosis develops when adapting to a new living environment under the influence of extreme climatic and social factors. Thus, 30% of army conscripts experience dysbacteriosis immediately after their arrival at military units in winter. In summer, this index is 50%. The maximum changes in the microflora composition were detected during the second month in conscripts of spring and autumn appeals. Later, 85-90% of soldiers experienced the self-elimination of dysmicrobiocenosis.

In general, the formation of dysbacteriosis is a factor aggravating the clinical state of patients. It causes a long, chronic, relapsing course of diseases, sensitization. Abnormally multiplying microorganisms produce indole, skatole, ammonia, hydrogen sulphide and other toxic substances, which increases the load on the body's detoxification systems, blood formation, etc.

Principles of Diagnosis of Dysbacteriosis

Dysbacteriosis is diagnosed by a comprehensive assessment of the microflora state, its metabolic activity by spectra and levels of metabolites (volatile fatty acids in feces and saliva), the formation of phenol, indole, and other compounds. It is also diagnosed by using a microbiological method - repeated (with an interval of 5-7 days) bacteriological examination with the use of the methods of quantitative isolation of species and variants of microorganisms that make up the microbiocenosis. The results of the studies are compared with the data on the normal composition of the microbiocenosis of the biotope.

Criteria for Dysbacteriosis Assessment

1. A sharp (by several orders of magnitude) decrease in the number of species and variants of microorganisms common for a given biotope;
2. A sharp (by several orders of magnitude) increase in the population of species that are found in small numbers in the normal biocenosis;
3. Appearance of a large population of microbial species in the biotope that they do not usually inhabit;
4. appearance of a large number of microorganisms with altered properties (multiple resistance to antibiotics, disinfectants, high toxicity, etc.). According to the latest data, the normal intestinal microflora representatives are 90% anaerobic and therefore do not grow on traditional nutrient media. In other words, so called dysbacteriosis is 10% of actual changes.

Treatment of Dysbacteriosis

In connection with the involvement of microbiota, primarily of the intestine alone, in the development of a variety of diseases, various approaches are being created for its correction [1, 4].

The main means of treatment are the following:

1. Functional nutrition– *the use of food products* with food fibers, wheat bran, seeds; *the enrichment* of yogurts, biscuits, ice cream, juices, butter, cheese, chewing gums with live bifidobacteria; *the use of fermented milk products* –anti-acid bifilact, acidoflora, biofructolact, bifidokefir, enriched biolact, milk bifilact, acidophilic fungi.
2. *Probiotics* - various preparations of normal human microflora, *eubiotics* and their products with absent pathogenicity; *prebiotics* (stimulants for the growth of their own microflora) and *synbiotics* - combinations of pro- and prebiotics. The medicines, which are used as probiotics, include: Lactobacillus acidophilus, L.plantarum, L.casei, L.bulgaricus, Bifidobacterium longum, B. bifidum, B. breve, Enterococcus faecium, etc. The proposed mode of action of probioticsis associated with the abilities of microorganisms that compose them:*(1)*to survive in acidic environments, *(2)*to attach effectively to the epithelial cells of the intestinal mucosa and colonize it, *(3)*to produce antimicrobial substances, *(4)*to cause stimulation of the immune system, *(5)*to prevent excessive growth and reproduction of pathogenic M/o and to restore the normal intestinal microflora.
3. The method of fecal microbiota transplantation– the introduction of a suspension of microorganisms from a healthy donor by enema, through a colonoscope, or through a nasogastric or nasoduodenal tube into the intestine. This methodological approach is devoid of them a in disadvantage of probiotic drugs and makes it possible to transfer an entire microbial community including non-culturable and hard-to-cultivate microorganisms to the recipient.
4. Nevertheless, the best prebiotic nowadays is considered to be the stymbifide, which includes fructooligosaccharides (raftilin) and fructopolysaccharides (raftilose P-950), the action of which is enhanced by a complex of vitamins. Stymbifide and raftilin are produced in Belgium. They create favorable conditions for increasing the number of beneficial bifidobacteria. Mineral-vitamin complex developed in Switzerland. In its composition - *antioxidants - vitamins E and C, minerals of zinc and selenium, the most important vitamins of group B (B1, B3, B5, biotin, B12*. Vitamin C is a powerful antioxidant, neutralizes the effect of many allergens, increases immunity, reduces the risk of thrombus formation.Vitamin E (tocopherol) improves the supply of O_2 organs and tissues, prevents new thrombosis and dissolves the existing thrombi. Protects against oxidation a number of useful materials. **Indication:** *restoration of normal intestinal microflora, creation of conditions for reproduction of bifidobacteria, growth of pathogenic microflora and its displacement from the body*.(1) intestinal dysbiosis. (2) chronic and acute

intestinal infections, prevention of infections.(3) immunodeficiency, allergy. (4) nonspecific chronic colitis, impaired bowel function. (5) after treatment with antibiotics, with chemotherapy. (6) increased resistance of mucous membranes to inflammatory factors. (7) normalization of lipid metabolism and weight. (8) improvement of calcium absorption, prevention of osteoporosis.

Auxiliary Methods of Treatment of Dysbacteriosis

1. Selective stimulation of growth and reproduction of the native indigenous flora –*HylakForte, Normase, Enterol.*
2. Selective decontamination of pathogenic flora with specific bacteriophages (staphylococcal, Klebsiella, coliprotein, Pseudomonas aeruginosa); lysozyme, antagonists of opportunistic bacteria –*Bactisubtil, Biosporin, Flonivin, etc.*
3. In take of enzyme preparations for optimal functioning of the parietal flora – *Festal, Panzinorm, Mezym Forte, Pancreatin, Pepsin, Abomin, Orazum, Solizym, Panurmen, Digestal, Cotazym Forte*.
4. Use of membrane-stabilizing agents – *Essentiale*, Karsil, *Lipostabil.*
5. Prescription of enteric sorbents – *Smecta,MicroSorb II, Enterocat, Enterosorbentum SKII, Rheaban, Polyphepan, Lignosorb, Polyphan, Carbolenum, Enterodes.*
6. Pathogenic microflora decontamination requires antibacterial agents – *Nitrophuran, Mexaform, Chlorophyllipt, Amoxigal, Lysozyme, Biseptol, semi-synthetic penicillins, Polymyxin.*
7. In dysbacteriosis, there is a decrease in the formation of immune serum globulin A, lysozyme, the number of the main population and subpopulations of lymphocytes as well as the inhibition of phagocytosis, which requires the stimulation of the main components of the immune system with *complex immunoglobulin protein, Myelopid, Sodium Nucleinate, Lactoglobulin, thymic and polysaccharide preparations.*
8. *Hypoxen, Cigapan, Wobenzym, Viusid, Milife, Preventan, Polystyme* are used to correct metabolic changes.

Dysbacteriosis Therapy Algorithms in Children

1.Degree Compensated Dysbacteriosis

Moderately active multicomponent probiotics – **bifidobacterial** (*Sorbed Bifidumbacterin Forte,Bifiform*) or **lactobacterial**(*Biobactone,Linex*) – are used. Biologically active additives and/or probiotic products (*Bifidox, kefirs, yoghurts, Imunele*) as well as vitamin preparations are prescribed afterwards. Immuno correctors are prescribed only after two-three courses of background treatment in case of its insufficient efficiency.

II -III Degree Subcompensated Dysbacteriosis

First stage

In this form of dysbacteriosis, highly active (sorbed, combined) probiotics from normal microflora (*Probiophore, Bifilysis, Acipol, Acylact*) are used. They are taken concurrently with the opportunistic microflora «elimination course»: for candidiasis (accumulation of yeast-like fungi in the intestine) – probiotics from saccharomycetes and bacteria (*Enterol, Sporobacterin*), antimycotics (*Fluconazole (Diflucan), Nystatin*); for excessive growth of staphylococcus – *Chlorophyllipt*; for sensitivity – *specific bacteriophages*. Immune drugs (*Complex Immunoglobulin Protein, Hepon, Lysozyme*) can be used from the beginning of treatment. The duration of the elimination course is 5-7 to 10 days; a one time dose is enough with Diflucan, a 7-10 days courseis required with Nystatin.

Second stage

Are covery course is used with the prescription of sorbed probiotics (*Florin Forte, Bifidumbacterin Forte*), multicomponent and combination drugs (*Bifilysis*), biologically active additives (*Normoflorin*) which are prescribed for 3 weeks; on medical grounds, lactose-containing preparations (*Acylact, Acipol*) should preferably be used with Bifidumbacterin, Bifidumbacterin Forte, Bifiform. In total, 1-3 courses of probiotic correction are required for treatment with the inclusion of metabolic probiotics (*Hylak Forte*), prebiotics, biologically active additives, vitamins and probiotic products during the second or third course of treatment. The immunotherapy with *Complex Immunoglobulin Protein, Lysozyme, Hepon, Licopid, Sodium Nucleinate* should be long-term and reasonable; it should also be carried out in accordance with the patient's immune clinical status.

III (II in rare cases) Degree Decompensated Dysbacteriosis

First stage

In this stage, the treatment is similar to that for subcompensated dysbacteriosis but more comprehensive and prolonged with a 7-10-day elimination course. In addition, intestinal antiseptics (*Ercefuryl, Macmiror, Enterofuryl*) are prescribed; immune preparations (*Hepon, Complex Immunoglobulin Protein, Sodium Nucleinate*) are recommended to be taken from the beginning of therapy. Phage therapy should be used in addition to immunotropic and antiseptic drugs.

Second stage

Here, restorative treatment corresponds to the therapy of subcompensated dysbacteriosis. A total of 2-4 courses of probiotic correction with an interval of 1-2 weeks are normally given.

Decompensated dysbacteriosis in its different phases requires the use of immune preparations –*Hepon* (5-7 days), *Complex Immunoglobulin Protein*(orally - 5 days), *Kipferon* (in suppositories - 5 days), *Lysozyme*(7-14 days), *interferons, Licopid, Polyoxidonium* (according to the schemes), *Sodium Nucleinate*(2-3 weeks). Vitamins, probiotic biologically active additives and products enriched with them are indicated at all stages of treatment of intestinal dysbacteriosis.

Symptomatic and other additional medicines in the intestinal microflora disorders treatment are prescribed, as in case of the elimination course, in addition to reconstructive probiotic correction with the use of enteric sorbents, antispasmodic drugs, simethicone, enzyme preparations, sometimes – antacids, prokinetics, etc.

Complications in the Treatment of Dysbacteriosis

They emerge in the event of:

1. The administration of probiotics to children with severe immunodeficiency; for example, the development of fulminant sepsis becomes possible as a result of chemotherapy for malignant neoplasms (for example, in case that 5 live-culture yoghurts are taken).
2. The concurrent prescription of antibacterial agents and probiotics to patients with dysbacteriosis; there is a risk of rapid induction of the microflora interspecific antibiotic resistance.

References

1. Vorobyev A.A., Krivoshein Y.S., ShirobokovV.P. Medical and Sanitary Microbiology. Manual. 4thedition. Moscow. PublishingCenter: Academy. 2010. - 464 p.
2. Vorobyev A.A. (Ed.) Medical Microbiology, Virology and Immunology. Moscow. Publishing House: Medical Information Agency. 2008. - 720 p.
3. Pokrovsky V.I., Pak S.G., Briko N.I. Infectious Diseases and Epidemiology. Textbook. 3rd edition, revised and enlarged. Moscow. Publishing House: GEOTAR-Media.2013. - 1008 p.
4. Zemskov A.M., Zemskov V.M., Chereshnev V.A. (Ed.). Encyclopedia of Immunology in 5 volumes. Moscow. Publishing House: Triada-X. 2013. - 1962 p.
5. Tsarev V.N. (Ed.). Microbiology, Virology and Immunology.Textbook for High Schools. Moscow. Publishing House: GEOTAR-Media. 2010. - 5436 p.
6. Zemskov A.M., Zemskov V.M., Karaulov A.V. Clinical Immunology. Textbook for Students of Medical Schools. Moscow. PublishingHouse: GEOTAR-Media. 2008. - 426 p.
7. Zemskov A.M., Zemskov V.M., Zemskov V.A., Zoloedov V.I. Handbook of a Clinical Immunologist "Theoretical, Practical and Applied Aspects of Clinical Immunology at the Present Stage." Moscow. Publishing House: Triada-X. 2015. -704 p.
8. Labinskaya A.S., Volina E.G. (Ed.). Manual of Medical Microbiology. General and Sanitary Microbiology. Book 1. Moscow. Publishing House: BINOM. 2008. - 1077 p.

How to cite this article:

Zemskov A.M *et al* (2017) 'Immunology of Infections at the Present Stage, Microbiota and Microbiota diseases ', *International Journal of Current Advanced Research*, 06(10), pp. 6381-6386.
DOI: http://dx.doi.org/10.24327/ijcar.2017.6386.0931

****