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Antibiotic Resistance Crisis

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Annotation: Irrational Antibiotic Therapy: A Global Concern and Widespread Scourge. Prescribing antibiotics "just in case" for acute respiratory viral infections and viral diarrhea, inappropriate dosages, unsuitable medications, incorrect treatment durations, and unwarranted antibiotic combinations—these issues are compounded by low patient adherence: "took it once, forgot it twice." Rational use of any medication is a fundamental principle of clinical practice. Violating this principle leads to reduced quality of care, increased treatment costs, and a higher risk of side effects. When it comes to antibiotics, in addition to all the aforementioned consequences, improper use can exacerbate a severe global issue: the rise of antibiotic resistance in pathogenic microorganisms.

Keywords: crisis, infection, antibiotics, anti-bacterial agents, antibiotic resistance, children.

A typical clinical situation that arises almost daily. A child, 11 months old, was examined on the fourth day of illness. The child had no previous health issues, no underlying pathology, was vaccinated according to the schedule, and had no contact with infectious patients. The temperature has been 39°C since the first day, and on the third day, a watery stool with a mushy consistency appeared, without mucus or blood, three times. When the temperature decreases, the child is active, plays, and eats well. The child urinates enough. On examination, the skin is pink and warm. There is slight hyperemia of the palatal arches. That's all!

What do we expect from this child, dear colleagues? A high temperature for three days, good general condition, slightly reddened throat, and mild diarrhea (which can accompany almost any childhood infection). These are non-specific symptoms. In such cases, the most likely diagnosis is sudden exanthem — infantile roseola — a common viral disease that tends to resolve spontaneously. Alternatively, a febrile form of enteroviral infection could be considered. The differential diagnosis can be broad, but serious illnesses are unlikely to be at the top of the list — after all, it's the third day of illness, with no rash or signs of meningismus (so, it's not

meningococcal), and no signs of respiratory tract involvement (so, it's not pneumonia). There's also tick-borne encephalitis through the alimentary route, but this is rare, and the mother denies feeding raw milk or dairy products from "farmer's" sources. There is occult bacteremia (fever without a visible infection focus, often caused by pneumococci), but this usually presents much more severely, with signs of infectious toxicosis. Even in cases of suspicion, hospitalization would be required. Urinary tract infections can also occur, but this pathology presents with more pronounced intoxication syndrome and additional symptoms. If a urinary tract infection is suspected, a urine test is necessary.

So, what do we have in conclusion? A febrile pediatric patient, with more evidence pointing towards a viral infection. What type of medical help does the child need? First and foremost, dynamic observation. Who will observe? The local pediatrician is often so overloaded that there is no time for even basic monitoring — let alone detailed observation. However, the mother seems responsible and can be instructed on how to monitor the child's condition. There is also a nurse who can make a daily phone call to the mother and report the results to the doctor. Does the child need further examination? Probably not. What treatment does the child need? Almost none: plenty of fluids and antipyretic medications (if necessary).

On the second day of illness, the child was examined by the local pediatrician. Dynamic observation was not organized, and no laboratory tests were ordered. The child was prescribed an antibiotic, amoxicillin-clavulanate, and this led to diarrhea, as expected (clavulanate affects the motility of the small intestine)! Despite the antibiotic, the child continued to have a fever for another two days, after which the temperature normalized and a rash appeared — roseola infantum, which was the diagnosis all along! And two days of unnecessary antibiotic therapy…

"UNNECESSARY" ANTIBIOTICS

Excessive use of antibiotics by outpatient doctors is often justified within the medical community ("doctors are busy, they don't have time to observe patients"), which is evident from reading medical forums. But this problem is not limited to local pediatricians and not only to Russia. Unwarranted antibiotic prescriptions are widespread in economically developed and developing countries, in outpatient clinics and hospitals, both in pediatric and other departments. For example, according to a study by K. Fleming-Dutra and colleagues, in the United States, about 30% of outpatient antibiotic prescriptions are unnecessary. The study authors noted that antibiotics were prescribed for conditions where such therapy was not indicated: bronchitis (except for chronic bronchitis, emphysema, or chronic obstructive pulmonary disease), bronchiolitis, viral upper respiratory infections, asthma, influenza, viral pneumonia, and otitis media. The rate of unnecessary antibiotic prescriptions is highest among children under two years old.

Does this sound familiar to us? Excessive, irrational use of antibiotics in outpatient pediatric care can reach alarmingly high levels. E. Alili-Idrizi and colleagues reported that in a pediatric clinic in Tetovo (Albania), antibiotic therapy was unnecessary in 92% of cases it was prescribed — for laryngitis, viral tonsillopharyngitis, acute otitis media, and bronchitis. Irregular antibiotic prescriptions in intensive care units (incorrect choices, inappropriate dosages, or unnecessary administration) have been reported in 30-60% of cases.

Key Situations of Unjustified Antibiotic Prescriptions

Research from multiple countries, along with the author's own experience, shows that the most common situations where antibiotics are unnecessarily prescribed in outpatient pediatrics are fever, persistent cough, and tonsillitis. For patients in infectious disease departments, these three situations are supplemented by a fourth — diarrhea.

Fever. Elevated body temperature is a symptom of a wide range of diseases, both infectious and non-infectious. The most common cause of fever in children is viral infections. Fever caused by viruses can last for varying lengths of time: up to 5 days for infantile roseola, up to 7 days for enteroviral infections, and up to 14 days or more for infectious mononucleosis. Antibiotics

prescribed for viral infections do not affect the course of the illness, do not shorten the fever period, and do not reduce the risk of complications. These facts call into question the validity of the popular unwritten "rule of three days": "Three days of high temperature — antibiotics should be given." When fever is present, efforts should focus on determining the nature of the temperature response and identifying the affected organ or system. Empirical antibiotic therapy should be avoided in mild cases; it should be limited to severe cases where the patient's condition warrants not waiting for test results, and there are strong suspicions of bacterial infection — signs of septic shock, severe hyperthermia, significant neutrophilic leukocytosis, or symptoms of systemic infection in immunocompromised patients.

Persistent Cough. This is another reason for unnecessary antibiotic prescriptions. Cough is a symptom that can deeply concern parents, sometimes even more than the child themselves.

The result of this anxiety is repeated visits to the doctor ("the child is still coughing, something must be done!"), and consequently, the prescription of antibiotics by the doctor under the pressure of parents. However, the main causes of a prolonged cough do not require antibacterial therapy but rather diagnostic investigations. A persistent cough can be associated with post-nasal drip, gastroesophageal reflux, or asthma. Post-infectious cough, caused by damage to the airway epithelium and an increased sensitivity threshold of cough receptors, can last for weeks. Perhaps the only cause of a persistent cough in children without chronic bronchopulmonary diseases that requires antibiotic therapy is whooping cough. In the late stage of whooping cough, the use of macrolides is prophylactic: prescribed during the paroxysmal cough stage, they do not affect the duration of the disease or the severity of symptoms, but they reduce the period of contagion of the infection source.

Tonsil inflammation. Tonsillitis, tonsillopharyngitis (or, using the traditional Russian medical term, sore throat) can be caused by various pathogens, and the need for antibiotic therapy arises mainly in cases of infection with group A beta-hemolytic *Streptococcus pyogenes* (GAS). This accounts for only 15-30% of patients with acute tonsillitis. GAS tonsillitis is very rare in children under 5 years of age and almost never occurs in the first two years of life. Symptoms of tonsillitis can be caused by a variety of viruses, including adenoviruses, respiratory syncytial viruses, coronaviruses, the influenza virus, and Epstein–Barr virus. The presence of exudates (films) on the tonsils is not pathognomonic for streptococcal tonsillitis; this symptom can also be observed in viral infections. For clinical diagnosis of streptococcal infections and deciding on antibiotic therapy, special assessment scales (MacIsaac scale) and rapid tests for GAS in the oral cavity are successfully used: they help reduce unnecessary antibiotic prescriptions.

Diarrhea. This is another clinical situation where antibiotics are prescribed excessively, not according to indications. Although diarrheal infections are caused by a wide variety of pathogens, most cases are self-limiting and only require adequate rehydration. Antibiotics are not indicated in watery diarrhea, regardless of its severity (except in cases where cholera is suspected). Indications for antibiotic therapy include invasive diarrhea of severe, or in high-risk groups, moderate severity (shigellosis, typhoid fever, dysentery-like forms of non-typhoidal salmonellosis and campylobacteriosis, intestinal amebiasis, and symptomatic giardiasis). In the absence of extra-intestinal infection sources, antibiotics are recommended in oral form.

Why do doctors prescribe unnecessary antibiotics? There are many different reasons why doctors prescribe antibiotics when patients appear to have symptoms indicating a viral infection. Any person who has graduated from a medical university knows that antibiotics do not act on viruses and is aware of the problem of antibiotic resistance. However, doctors often believe that their individual prescription is unlikely to contribute to this problem and are confident that the negative consequences of this one incorrect prescription will be minimal (if there are any at all).

The following reasons are considered for prescribing antibiotics without indications or irrational antibiotic selection.

Pressure from patients. It is not necessarily a direct request for an antibiotic, though this is not uncommon. How many pediatricians have not heard the phrase: "We need something stronger, so the child can recover quickly"? Even when parents don't say this, the doctor does not want to be accused of inadequate treatment if the illness does not go smoothly. Sometimes, it may be thought that this pressure only exists in the doctor's mind, who believes that the prescription of antibiotics is expected. However, a study by M. Ashworth and colleagues shows that limiting antibiotic prescriptions leads to a decrease in patient satisfactione, more patient education is needed!

Lack of time. In outpatient settings, doctors have limited time for each patient. It's much quicker to prescribe a medication than to spend time explaining the nature of the illness and the lack of need for certain medicines. The less time the doctor spends listening to and informing the patient (or their parents), the more likely they are to prescribe antibiotics. Conversely, spending more time talking to the patient allows for the avoidance of unnecessary prescriptions without reducing patient satisfaction .

Doct There is a psychological phenomenon called decision fatigue. It means that the quality of decisions decreases as many decisions are made over a long period of time. This fully applies to the work of a doctor, as each patient requires a diagnostic-therapeutic decision. Studies have shown that the quality of decisions made by doctors decreases by the end of the workday: the number of antibiotics prescribed for acute upper respiratory infections significantly increases at the end of the shift .

Pressure from cal companies. In some countries, pressure from pharmaceutical companies on doctors through their medical representatives is cited as a reason for the overprescription of antibiotics. In an effort to increase sales, companies mislead doctors about indications for antibiotic prescriptions, while downplaying side effects. Additionally, inaccurate information about competitor products is often provided. This not only encourages doctors to prescribe antibiotics when they are unnecessary but also makes it harder to choose the appropriate medication. For fairness, it should be noted that the "commercial itch" of some of our colleagues, associate professors, and professors who give "commissioned lectures" that mislead doctors still exists.

Objective challenges. Rational antibiotic selection, its dosage, and the optimal duration of therapy are based on several variables — the affected organ, the presumed pathogen, the bioavailability of the drug, the characteristics of the host’s body, and regional data on antibiotic sensitivity. Reliable etiological diagnostic methods are often unavailable in real practice: diagnoses are made based on clinical manifestations. Clinicians diagnose and treat infectious syndromes, not knowing for sure but only assuming the likely causative agent. Regional data on the sensitivity of pathogens to antibiotics are also often unavailable.

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