These bacteria differentiate into "persister cells." Persister cells are a subgroup of temporarily.1 antibiotic-tolerant bacterial cells. They often have a slow or arrested growth and can continue growing after severe stress. They are associated with recurrent persistent bacterial infections. They are linked to an increased risk of AMR [43]. It has been found that children can be exceptional hosts of biofilms. They receive medical devices. The devices range from central venous catheters to complex heart defect patches. They also include ventriculoperitoneal shunts. These devices can be a formidable breeding ground for biofilms and bacteria. Antibiotics can't reach them. These may predispose to long-term infections. Sometimes, the only definitive treatment is removing and replacing the device. Generally, many infections in children are linked to biofilms. This happens even when no medical devices are present. Biofilms have also been found in the nasopharynx of children affected with repeated upper airways and middle ear infections. This may explain the frequent lack of efficacy of antibiotic therapy in these cases [44]. In particular, biofilms have been recognized as responsible for recurrent acute otitis media. They also cause otitis media with effusion. This finding may be explained by evidence that otitis media with effusion often has a negative culture. However, molecular research for pathogens is often positive. It is often unresponsive to antibiotics and highly recurrent. Moreover, children with chronic rhinosinusitis are more likely to have biofilms. This is more common than in children without an underlying condition. It's also more common than in children with acute rhinosinusitis. Researchers found mature biofilms in 95% of adenoids removed from children with chronic rhinosinusitis (45). Chronic conditions, like cystic fibrosis (CF), cause serious illness and early death. This happens because people with these conditions frequently get long-lasting infections. These infections may result from the disease's precise cause. They may also result from frequent and prolonged hospital stays. The chronic use of multiple antibiotics raises the chance of MDR. In particular, pediatric CF patients seem to harbor different opportunistic infections compared to adults. This is because different bacteria use type VI secretion systems to compete with each other [46]. This also impacts antibiotic treatment in young and adult CF patients. It may explain the emergence of AMR. 3. Emerging Threats The WHO recently published a list of bacteria for which new antimicrobials are urgently needed [47]. This comes from observing a progressive decrease in the R&D pipeline of new antibiotics. This is in dire contrast with the concerning rise of resistant infections. Pediatric antibiotics research and development needs oral formulations for community-acquired infections with high morbidity. We need oral antibiotics for drug-resistant ESBL-producing Enterobacteriaeceae, Neisseria gonorrhoeae, and Salmonella typhi. 3.1. Resistant Staphylococcus Aureus Strains of MRSA were first identified as a threat in adult patients in the 1960s. MRSA infections were uncommon in children until the 1990s. Infections in adults and children, with no prior risk factors or healthcare contact, began to show resistant strains [48]. Thus, healthcare-acquired MRSA (HA-MRSA) began circulating together with community-acquired MRSA (CA-MRSA). [49]. Trimethoprim-sulfamethoxazole and clindamycin are often used in the treatment of CA-MRSA. Resistance to trimethoprim/sulfamethoxazole is relatively uncommon. However, clindamycin resistance has increased in the past decade [49]. Doctors often apply mupirocin ointment to the anterior nares. They often also use chlorhexidine baths. This helps to eradicate MRSA carriage and limit its spread. Since these practices started, resistance to mupirocin and chlorhexidine have emerged [50].

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Vancomycin has long been considered the last resort for treating MRSA infections. However, in 1997, the first strain of vancomycin-intermediate susceptible Staphylococcus aureus (VISA) was isolated from a surgical wound of a Japanese child. The child's infection did not respond well to long-term vancomycin therapy [51]. Since then, vancomycin resistance has cast a dark shadow on anti-MRSA antibiotic treatment. This is especially true for children. Their therapeutic options remain few, including daptomycin and linezolid. Nonetheless, daptomycin is of no use in treating lung infections. It binds surfactant, which inactivates it [52]. Interestingly, ceftaroline is often overlooked. It is effective against MRSA. It maintains cephalosporin's safety. It has a wide range of uses, whether on or off label [53]. It has been approved for children older than two months of age. No widespread resistance has been identified so far. 3.2. ESBL-Producing Enterobacteriaceae (ESBL-Ent) and Carbapenem-Resistant Enterobacteriaceae (CRE) In the U.S.A., there has been a significant increase of ESBL-Ent infections in children. This increase is correlated with the spread of MDR ST131 CTX-M-producing E. coli strains [54]. The acquisition of ESBL-Ent varies greatly. It depends on country, age, healthcare exposure, organism, and ESBL genotype. International studies in hospitals show an increase in ESBL-Ent colonization. For this population, risk factors include younger gestational age, low birth weight, antibiotic use, and prolonged mechanical ventilation [55]. Outside the neonatal age, risk factors for ESBL-Ent infections are similar to those of adults. These factors include antibiotic use, chronic clinical conditions, healthcare access, and recurrent infections [56]. Neurological diseases might be a predisposing risk for the pediatric population [57]. Therapeutic options for ESBL-Ent include piperacillin-tazobactam, ceftazidime-avibactam, cefepime, fluoroquinolones, aminoglycosides, tigecycline, fosfomycin, and carbapenems. However, safety profiles and dosage guidelines often limit these options for children. Consider carbapenem-sparing strategies first to combat their overuse. When possible, use a step-down strategy after empirical therapy. There might be decreased sensitivity to carbapenems. This might be because of carbapenemases, which are ?-lactamases. They break down penicillins (cephalosporins, carbapenems, and monobactams). It might also be because of the production of ESBL or downregulated porins. Resistance to carbapenems in pediatric populations has dramatically increased in recent decades. The 2013 CDC report described this as an urgent threat. It highlighted a 50% mortality rate in hospitalized patients with bloodstream CRE infection [16]. A significant increase in CRE frequency was noted in some pediatric populations, especially for the Enterobacter species. The frequency increased from 0% in 2000 to 4.5% in 2012, particularly in ICU settings [58]. Therapeutic options for CRE are few. Pediatric options are further limited. The use of tigecycline is carefully weighed for people

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