WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

SJIF Impact Factor: 5.464

ISSN: 2457-0400
Volume: 6.
Issue: 4
Page N. 86-96
Year: 2022

Review Article www.wjahr.com

A REVIEW ON REPORTING PATTERN OF ADVERSE DRUG REACTIONS AND MANAGEMENT OF PEDIATRIC INFECTIONS IN THE COMMUNITY

S. Aishwarya*

Department of Pharmacy Practice, SRM College of Pharmacy, SRM IST, Kattankulathur, Tamil Nadu, India.

Received date: 04 February 2022 **Revised date:** 24 February 2022 **Accepted date:** 14 March 2022

***Corresponding Author: S. Aishwarya**

Department of Pharmacy Practice, SRM College of Pharmacy, SRM IST, Kattankulathur, Tamil Nadu, India.

ABSTRACT

An adverse drug reaction is any undesirable effect of a drug beyond its anticipated therapeutic effects occurring during clinical use. In contrast, an adverse drug event is an untoward occurrence after exposure to a drug that is not necessarily caused by the drug. While there is an impression that children are at a lower risk than adults for ADRs, in fact a number of factors germane to pediatric therapy place certain groups of children at a high risk for adverse events associated with therapy. The drug therapy for children evolves, becomes more complex, and begins to use novel molecules and biologicals there will be an increasing need for pediatric pharmacists to be more involved in clinical care, education, and research specific to drug safety. The pharmacotherapy in children is somewhat unique compared to that in adults in that there is a much less unitary distribution of therapy. The use of prescription medication among children is at first glance much more common than might be associated with ADR. Predictable ADRs are those that can be anticipated predicated on the known pharmacology of the drug. This ADR pattern is the most common type of ADR, and these ADRs tend to be less severe and often self-limited. The unpredictable ADRs are those whose evolution, possibly understood to some degree, is not predictable based on the drug's known pharmacology. Conducting regular training programs in pediatric pharmacy are very well designed to produce the next generation of practitioners as active members of patient care teams. Continuous education is another area in which pediatric pharmacy can play a crucial role in teaching skills germane to patient and drug safety and lowers the occurrence of adverse drug reactions in the clinical practice.

KEYWORDS: Adverse drug reaction, continuous education, pediatric pharmacy, drug safety, patient care.

INTRODUCTION

Adverse drug reactions are defined by the World Health Organization as “a response to a drug which is noxious, and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function”. A systematic review of paediatric ADRs identified 30 studies, detailing incidence rates of ADRs causing hospital admission; the rates ranged from 0.4–10.3%. Internationally, studies have shown that 0.6–16.8% of paediatric inpatients experience an ADR, while prospective data for the UK shows that 17.7% experience at least one ADR. In outpatient and community settings, a similar proportion of ADRs have been reported, ranging from 0.6–11.0%.

The known risk factors for ADRs in children are

- Polypharmacy
- Previous adverse reaction to another drug
- Female sex
- Impaired liver or renal function
- General anaesthetic use
- Off-label and unlicensed drug use
- Genetic polymorphisms

Pharmacists, as medicines experts, should counsel patients on potential ADRs, and also have a role in the identification, management and reporting of ADRs. Opportunities to perform these activities exist in both the inpatient setting (e.g. during ward rounds), and the outpatient setting (e.g. at the point of drug dispensing). Identification of ADRs in children and young people can be particularly challenging.[1-5] This, in part, relates to the

population, as babies and young children have limited communication. One of the challenges of describing ADRs in children is the rapid development that alters their anatomy and physiology. The diseases often experienced by children differ from adults, and manifestations of diseases that occur in both childhood and adulthood may also be different. The most rapid changes in pharmacokinetics occur in the first year of life. By the age of one year, body weight will have tripled and body surface area doubled. The relative proportions of fat, water and protein also change rapidly during infancy. Total body water (TBW) between birth and one year decreases from 80% to 65%. As the proportion of TBW decreases, the percentage of body fat increases, almost tripling by one year of age. In contrast, protein mass does not start to increase significantly until the second year of life, when infants become more ambulatory.

Types of ADRs

The Rawlins and Thompson classification of ADRs include two principal types: type A reactions, which are dose-dependent and predictable (e.g. bleeding and anticoagulants); and type B reactions, which are non-dose-dependent and not predictable (e.g. penicillin hypersensitivity). Over time, this classification system has been extended to include: type C, dose- and time-dependent (chronic) reactions (e.g. corticosteroids and adrenal insufficiency); type D, delayed reactions (e.g. thalidomide and phocomelia); type E, withdrawal reactions (e.g. withdrawal seizures on discontinuation of anticonvulsants) and type F, failure of therapy.[6-8]

Common mechanisms of ADRs include

- Synergistic effects between drug combinations (e.g. use of analgesic combinations post-operatively, specifically the combination of opioids and other analgesics such as non-steroidal anti-inflammatories [NSAIDs] or paracetamol).
- Antagonistic effects between drug combinations (e.g. concurrent use of antiepileptic drugs lamotrigine and carbamazepine can result in reduced levels of lamotrigine).
- Abnormal pharmacokinetics from genetic polymorphisms in drug-metabolizing enzymes (e.g. phase I enzyme cytochrome P450 2D6 [CYP2D6] has 141 different alleles described to date, representing one of the most well understood examples of how pharmacogenetic variation can influence drug metabolism).

The safety of drugs used in patients of an adult age group cannot be extrapolated to a pediatric age group. The pharmacokinetics and pharmacodynamics of many commonly used drugs vary significantly between these two age groups of patients. Further, adverse drug reactions (ADRs) in children can have a relatively more severe effect when compared to adults. Thus, the ADRs can lead to significant morbidity among children. It has been observed that ADRs in children not only result in hospital admissions or prolonged hospitalization but also may lead to permanent disability or even death. The information regarding the frequency, severity and types of drugs most frequently involved in adverse reactions in the pediatric age group is of particular interest, since pre-marketing clinical trials are done mostly in adults. They constitute a reported incidence of 9.5%, including 2.1% of hospital admissions, with 39.3% of them being life-threatening. The safety profile of a drug thus marketed with its testing done on adults can vary significantly when used in children. Studies on ADRs of nonsteroidal anti-inflammatory drugs (NSAIDs) and COX-2 inhibitors in a pediatric population have shown that NSAID exposures were a significant cause of morbidity in children. A cross-reactive hypersensitivity between NSAIDs and paracetamol has been proposed based on an autoimmune mechanism of drug reaction to NSAIDs.

Drug safety in children is major health concern as systematic reviews have shown a high reporting of adverse drug reactions (ADRs) in children. Almost one in ten children in hospital will experience an ADR, 12% of which are serious. Children are more vulnerable than adults as their physiological characteristics are still developing. The pharmacokinetic and pharmacodynamic parameters in children, particularly neonates and infants, change continuously due to physical changes (height and weight) and maturation of renal functions and enzyme systems. Randomized controlled trials (RCTs) are less effective in detecting ADRs and offer limited safety information, as certain vulnerable populations such as pediatric and geriatric patients are often underrepresented in such trials. Normally, only mild, moderate or non-serious ADRs tend to be captured during the development phase of medicines, whereas the serious and latent ones may not be captured. In addition, since RCTs are normally conducted in a controlled environment with predetermined patient criteria, the severity and staging of the disease as well as comorbidities may not reflect those found in routine clinical care, even in the relevant disease. In order to overcome the shortfalls of RCTs, spontaneous ADR reporting is a useful source of drug safety information in populations not routinely tested in RCTs, such as neonates and infants.

Recognizing ADRs in children

In the paediatric population, availability of high-quality data about the harms of medicines used can be an issue. For more established medicines, there may be limited clinical trial data supporting their use in children and young people, making recognition of potential ADRs more difficult. The lack of paediatric-specific drugs also means that off-label and unlicensed use of medicines is common in paediatrics; this type of medication use is also associated with increased ADR risk.[8-10]

The majority of ADR reports are submitted by healthcare professionals, although the proportion of reports submitted by patients, parents and carers has been

steadily increasing as a result of several public health campaigns. While spontaneous reporting systems have their advantages, and are one of WHO's five minimum requirements for a functional national pharmacovigilance system, they have their drawbacks, the principal of which is enormous under-reporting, up to 98%, of ADRs. Reasons given for under-reporting are numerous and include indifference, fear of litigation and ignorance on how to report ADRs.

Predictable ADRs are those that can be anticipated predicated on the known pharmacology of the drug. This ADR pattern is the most common type of ADR, and these ADRs tend to be less severe and often self-limited. Typical predictable ADRs include side effects which are usually off-target effects such as hand tremor associated with inhaled albuterol and secondary effects, such as pseudomembranous colitis due to lincosamide therapy. Other predictable ADRs include interactions, which may be drug-drug, drug-disease, or drug-food in nature. As noted above, the common use of polypharmacy among children with chronic disease makes an understanding of drug interactions very important for clinicians caring for children. Unpredictable ADRs are those whose evolution, while possibly understood to some degree, is not predictable based on the drug's known pharmacology. These are less common but often more severe. As an illustration, many fatal ADRs are unpredictable ADRs. Patterns of unpredictable ADRs include "intolerance," in which vulnerable subsets of patients experience disabling adverse effects at usual doses (for example, disabling tinnitus during low-dose salicylate therapy), and "allergic/pseudoallergic reactions: (such as penicillin allergy). Idiosyncratic ADRs are often very severe, for example, Stevens-Johnson Syndrome associated with sulfonamide therapy or clozapine-associated agranulocytosis. A final and very difficult to manage unpredictable ADR pattern involves psychogenic ADRs, a type of adverse event that is difficult for clinicians and disabling for patients.[11,15]

Pediatric Pharmacy and Drug Safety

Currently there are more than 3600 therapeutic products available for the treatment of children in the United States and Canada, with approximately 20 to 30 new drugs entering the market every year. The role of pediatric pharmacy becomes a more and more important part of a robust patient safety strategy. The first venue in which this applies is the clinical arena. As outlined above, a key area in which pediatric pharmacists have a major role in terms of gathering key information is the specific event in question, which is then informed by the latest drug information as to the therapeutic agent in question. For this very reason, clinical pharmacists are an essential part of pediatric care teams, notably in areas such as Neonatal Intensive Care Units and on teams managing children with complex chronic disease.

Antibiotic-resistant diseases such as MRSA (methicillin-resistant Staphylococcus aureus). The emergence of resistance to antibiotics in Gram-positive pathogens has become a major international problem as there are fewer, or even sometimes no, effective antimicrobial agents available for infections caused by these bacteria. The problem of increasing antimicrobial resistance is even more threatening when considering the very limited number of new antimicrobial agents that are in development. As rapidly as new antibiotics are introduced, Staphylococci have developed efficient mechanisms to neutralize them; inevitably this has left fewer effective bactericidal antibiotics to treat these often life-threatening infections. Multidrug-resistant (MDR) Staphylococci pose a growing problem for human health. The rise of drug-resistant virulent strains of *Staphylococcus aureus*, particularly methicillin-resistant *S. aureus* (MRSA) is a serious problem in the treatment and control of Staphylococcal infections. Methicillin-resistant Staphylococci (MRS) cause hard-to-treat infections. The most striking situation is that MRSA strains have emerged with concomitant resistance to many commonly used antibiotics of groups, aminoglycosides, macrolides, fluoroquinolones, chloramphenicol, and tetracycline.[16-18]

Common infections in children's

Chickenpox

Chickenpox is a viral infection that causes fever and an itchy rash with spots all over the body.It used to be a common childhood illness in the United States, especially in kids under age 12. It's much rarer now, thanks to the varicella vaccine.

Signs & Symptoms of Chickenpox

Chickenpox often starts without the classic rash, with a fever, headache, sore throat, or stomachache. These symptoms may last for a few days, with the fever in the 101°–102°F (38.3°–38.8°C) range. The red, itchy skin rash usually starts on the belly or back and face. Then it spreads to almost everywhere else on the body, including the scalp, mouth, arms, legs, and genitals. The rash begins as many small red bumps that look like pimples or insect bites. They appear in waves over 2 to 4 days, then develop into thin-walled blisters filled with fluid. The blister walls break, leaving open sores, which finally crust over to become dry, brown scabs.

Causes of chickenpox

Chickenpox is caused by the varicella-zoster virus (VZV). This virus also can cause a painful skin rash called shingles (herpes zoster) later in life. After someone has had chickenpox, the virus stays dormant (resting) in the nervous system for the rest of their life. The virus can reactivate ("wake up") later as shingles.

Treatment for chickenpox

In cases of severe illness, treatment with an antiviral medication may be needed. In most cases, chickenpox is mild and gets better without the need for specific treatment.

It includes

- Bed rest
- Drinking extra fluids (to avoid dehydration)
- Paracetamol to bring down the fever – aspirin should be avoided because of a possible increased risk of complications
- Lukewarm baths with baking soda or oatmeal added to the water – a cup of oatmeal can be put into an old, clean pair of panty hose, then tied and left in the bath while the water runs.
- Creams or lotions, such as calamine lotion, to reduce the itching.
- Avoidance of salty or citrus foods
- Wearing mittens to prevent scratching.

Diphtheria

A second type of diphtheria can affect the skin, causing pain, redness and swelling similar to other bacterial skin infections. Ulcers covered by a gray membrane also may be a sign of skin diphtheria.

Causes

Diphtheria is caused by the bacterium Corynebacterium diphtheriae. The bacterium usually multiplies on or near the surface of the throat or skin. C. diphtheriae spreads through:

- **Airborne droplets.** When an infected person's sneeze or cough releases a mist of contaminated droplets, people nearby may inhale C. diphtheriae. Diphtheria spreads easily this way, especially in crowded conditions.
- **Contaminated personal or household items.** People sometimes catch diphtheria from handling an infected person's things, such as used tissues or hand towels, that may be contaminated with the bacteria.

Risk factors

People who are at increased risk of catching diphtheria include

- Children and adults who don't have up-to-date vaccinations.
- People living in crowded or unsanitary conditions.

Complications

Diphtheria can lead to

- **Breathing problems:** Diphtheria-causing bacteria may produce a toxin. This toxin damages tissue in the immediate area of infection — usually, the nose and throat. At that site, the infection produces a tough, gray membrane made up of dead cells, bacteria and other substances. This membrane can obstruct breathing.
- **Heart damage:** The diphtheria toxin may spread through the bloodstream and damage other tissues in the body. For example, it can damage the heart muscle, causing such complications as inflammation of the heart muscle (myocarditis). Heart damage from myocarditis may be slight or severe.
- **Nerve damage:** The toxin can also cause nerve damage. Typical targets are nerves to the throat, where poor nerve conduction may cause difficulty swallowing. Nerves to the arms and legs also may become inflamed, causing muscle weakness.

Prevention

Before antibiotics were available, diphtheria was a common illness in young children. Today, the disease is not only treatable but also preventable with a vaccine. The diphtheria vaccine is usually combined with vaccines for tetanus and whooping cough (pertussis). The three-in-one vaccine is known as the diphtheria, tetanus and pertussis vaccine. The latest version of this vaccine is known as the DTaP vaccine for children and the Tdap vaccine for adolescents and adults. The diphtheria, tetanus and pertussis vaccine is one of the childhood vaccinations that doctors in the United States recommend during infancy.

Vaccination consists of a series of five shots, typically administered in the arm or thigh, given to children at these ages

- 2 months
- 4 months
- 6 months
- 15 to 18 months
- 4 to 6 years

The diphtheria vaccine is effective at preventing diphtheria. But there may be some side effects. Some children may experience a mild fever, fussiness, drowsiness or tenderness at the injection site after a DTaP shot.

Treatment

Treatments include

- **Antibiotics.** Antibiotics, such as penicillin or erythromycin, help kill bacteria in the body, clearing up infections. Antibiotics lessen the time that someone with diphtheria is contagious.[19]
- **An antitoxin.** If a doctor suspects diphtheria, he or she will request a medication that counteracts the diphtheria toxin in the body. This medication comes from the Centers for Disease Control and Prevention. Called an antitoxin, this drug is injected into a vein or muscle.

Hand, foot, and mouth disease

Hand, foot, and mouth disease (HFMD) is a highly contagious infection. It’s caused by viruses from the *Enterovirus* genus, most commonly the coxsackievirus. These viruses can spread from person to person through direct contact with unwashed hands or surfaces contaminated with feces. It can also be transmitted through contact with a person’s saliva, stool, or respiratory secretions. HFMD is characterized by blisters or sores in the mouth and a rash on the hands and feet.

Symptoms

Symptoms begin to develop 3 to 6 days after first getting the infection

- Fever
- Decreased Appetite
- Sore Throat
- Headache
- Irritability
- Malaise (Feeling Unwell)
- Painful Red Blisters In Your Mouth
- Drooling

Treatment

It includes

- Prescription or over-the-counter topical ointments to soothe blisters and rashes.
- Pain medication, such as acetaminophen or ibuprofen, to relieve headaches.
- Medicated syrups or lozenges to ease painful sore throats.

Hepatitis

Hepatitis is a general term used to describe inflammation of the liver. Liver inflammation can be caused by several viruses (viral hepatitis), chemicals, drugs, alcohol, certain genetic disorders or by an overactive immune system that mistakenly attacks the liver, called autoimmune hepatitis.

Types of Hepatitis

There are five viruses that cause the different forms of viral hepatitis: hepatitis A, B, C, D and E. Hepatitis A is mostly a food-borne illness and can be spread through contaminated water and unwashed food. It is the easiest to transmit, especially in children, but is also the least likely to damage the liver and is usually mild and is completely resolved within six months. Hepatitis B can be transmitted through exposure to contaminated blood, needles, syringes or bodily fluids and from mother to baby. It is a chronic disorder and in some cases may lead to long-term liver damage, liver cancer and cirrhosis of the liver after many years of carrying the virus. Hepatitis C is only transmitted through infected blood or from mother to newborn during childbirth. It too can lead to liver cancer and cirrhosis in the long term.

Types of Hepatitis

- Autoimmune hepatitis
- Hepatitis A
- Hepatitis B
- Hepatitis C
- Hepatitis D
- Hepatitis E
- Neonatal hepatitis

Symptoms

- Malaise
- Abdominal tenderness, especially in the upper right corner
- Fatigue
- Jaundice (yellowing of the skin and the white portion of the eyes)
- Dark-colored urine
- Lightly colored stools
- Abdominal pain
- Nausea with or without vomiting
- Abdominal swelling due to fluid retention

Diagnosis

It includes

- Physical exam, which may or may not reveal a swollen, enlarged liver.
- Blood tests to check liver enzymes that are elevated when the liver is damaged or infected, as well as blood tests to check for the presence of any of the five viruses causing hepatitis.
- Ultrasound of the liver to detect any changes.
- Liver biopsy to confirm suspected inflammation when other tests are inconclusive and to determine the exact degree of liver damage.

Treatment

To prevent infection, children or anyone who has not been previously vaccinated should be vaccinated against hepatitis B and hepatitis A. There are no vaccines against hepatitis types C, D and E. There is no cure for hepatitis once it occurs. Treatment focuses on preventing further damage to the liver, reversing existing damage if possible and symptom relief.

Herpes simplex

The herpes simplex virus, also known as HSV, is a viral infection that causes genital and oral herpes. Many people live with asymptomatic HSV, which means they have the virus without ever having an outbreak or active episode of herpes.

Types of the herpes simplex virus: HSV-1 and HSV-2

- **HSV-1.** This type primarily causes oral herpes, characterized by cold sores or fever blisters that appear around mouth or on your face.
- **HSV-2.** This primarily causes genital herpes, which involves sores that appear on or around genitals, anus, buttocks, and inner thighs. Sores can also develop inside the vagina.

HSV-1

You can transmit or contract HSV-1, or oral herpes, through direct contact with a herpes sore, saliva, or other bodily secretions during an episode. If you're shedding the virus, someone can contract it through direct contact with the site of the infection.

Examples of direct contact include

- Kissing
- Oral sex
- Other skin-to-skin contact

HSV-2
As with HSV-1, you can transmit or contract HSV-2, or genital herpes, through direct contact with a herpes sore, saliva, or other bodily secretions during an episode.

Direct contact might include
- kissing
- oral sex
- sharing sex toys during a sexual encounter
- penetrative sex
- other skin-to-skin contact at the infection site

Symptoms of herpes
Primary HSV symptoms
Primary episodes often include flu-like symptoms, such as:
- fever
- swollen lymph nodes
- body aches and pains, including headache
- unusual tiredness or fatigue
- lack of appetite
- shooting pain at the site of the infection

Medications
Antivirals can help reduce the number of episodes you experience and ease the severity of your symptoms.

It includes
- Acyclovir
- Famciclovir
- Valacyclovir
- Foscarnet or cidofovir

Influenza
Influenza is a viral infection that attacks respiratory system. People at higher risk of developing flu complications include
- Young children under age 5, and especially those under 6 months
- Adults older than age 65
- Residents of nursing homes and other long-term care facilities
- Pregnant women and women up to two weeks after giving birth
- People with weakened immune systems
- Native Americans
- People who have chronic illnesses, such as asthma, heart disease, kidney disease, liver disease and diabetes
- People who are very obese, with a body mass index (BMI) of 40 or higher

Symptoms
Common signs and symptoms of the flu include
- Fever
- Aching muscles
- Chills and sweats
- Headache
- Dry, persistent cough
- Shortness of breath
- Tiredness and weakness
- Runny or stuffy nose
- Sore throat
- Eye pain
- Vomiting and diarrhea, but this is more common in children than adults

Flu
The signs and symptoms include:
- Difficulty breathing or shortness of breath
- Chest pain
- Ongoing dizziness
- Seizures
- Worsening of existing medical conditions
- Severe weakness or muscle pain

Emergency signs and symptoms in children can include
- Difficulty breathing
- Blue lips
- Chest pain
- Dehydration
- Severe muscle pain
- Seizures

Risk factors
Factors that may increase your risk of developing the flu or its complications include:
- **Age.** Seasonal influenza tends to target children 6 months to 5 years old, and adults 65 years old or older[19-20].
- **Living or working conditions.** People who live or work in facilities with many other residents, such as nursing homes or military barracks, are more likely to develop the flu. People who are staying in the hospital also are at higher risk.
- **Weakened immune system.** Cancer treatments, anti-rejection drugs, long-term use of steroids, organ transplant, blood cancer or HIV/AIDS can weaken the immune system. This can make it easier to catch the flu and may also increase the risk of developing complications.
- **Chronic illnesses.** Chronic conditions, including lung diseases such as asthma, diabetes, heart disease, nervous system diseases, metabolic disorders, an airway abnormality, and kidney, liver or blood disease, may increase the risk of influenza complications.
- **Race.** Native American people may have an increased risk of influenza complications.
- **Aspirin use under age 19.** People who are younger than 19 years of age and receiving long-term aspirin therapy are at risk of developing Reye's syndrome if infected with influenza.
- **Pregnancy.** Pregnant women are more likely to develop influenza complications, particularly in the second and third trimesters. Women are more likely

to develop influenza-related complications up to two weeks after delivering their babies.
- **Obesity.** People with a body mass index (BMI) of 40 or more have an increased risk of flu complications.

Prevention
The nasal spray isn't recommended for some groups, such as:
- Children under 2
- Adults 50 and older
- Pregnant women
- Children between 2 and 17 years old who are taking aspirin or a salicylate-containing medication
- People with weakened immune systems
- Kids 2 to 4 years old who have had asthma or wheezing in the past 12 months

Controlling the spread of infection
It includes
- Washing hands often with soap and water for at least 20 seconds is an effective way to prevent many common infections.
- Avoid touching face
- Cough or sneeze into a tissue or your elbow. Then washing hands.
- Regularly clean often-touched surfaces to prevent spread of infection from touching a surface with the virus on it and then face.
- Avoid crowds

Rubella
Rubella is a contagious viral infection best known by its distinctive red rash. It's also called German measles or three-day measles. While this infection may cause mild symptoms or even no symptoms in most people, it can cause serious problems for unborn babies whose mothers become infected during pregnancy. Rubella isn't the same as measles, but the two illnesses share some symptoms, including the red rash. Rubella is caused by a different virus than measles, and rubella isn't as infectious or as severe as measles.[21-22]

Symptoms
The signs and symptoms of rubella are often difficult to notice, especially in children. Signs and symptoms generally appear between two and three weeks after exposure to the virus. They usually last about one to five days and may include:
- Mild fever of 102 F (38.9 C) or lower
- Headache
- Stuffy or runny nose
- Inflamed, red eyes
- Enlarged, tender lymph nodes at the base of the skull, the back of the neck and behind the ears
- A fine, pink rash that begins on the face and quickly spreads to the trunk and then the arms and legs, before disappearing in the same sequence
- Aching joints, especially in young women

Causes
Rubella is caused by a virus that's passed from person to person. It can spread when an infected person coughs or sneezes. It can also spread by direct contact with an infected person's respiratory secretions, such as mucus. It can also be passed on from pregnant women to their unborn children via the bloodstream.

Prevention
The rubella vaccine is usually given as a combined measles-mumps-rubella (MMR) vaccine. Babies born to women who have received the vaccine or who are already immune are usually protected from rubella for six to eight months after birth. Widespread concerns have been raised about a possible link between the MMR vaccine and autism.

Treatment
No treatment will shorten the course of rubella infection, and symptoms don't usually need to be treated because they're often mild.

Measles, mumps
Measles, mumps, and rubella are viral diseases. All can be very serious. Measles starts as a fever, cough, runny nose, conjunctivitis (pinkeye), and a red, pinpoint rash that starts on the face and spreads to the rest of the body. If the virus infects the lungs, it can cause pneumonia. Measles in older children can lead to inflammation of the brain, called encephalitis, which can cause seizures and brain damage. The mumps virus usually causes swelling in glands just below the ears, giving the appearance of chipmunk cheeks. Before the vaccine, mumps was the most common cause of both meningitis (inflammation of the lining of the brain and spinal cord) and acquired deafness in the U.S. In men, mumps can infect the testicles, which can lead to infertility. Rubella is also known as German measles. It can cause a mild rash on the face, swelling of glands behind the ears, and in some cases, swelling of the small joints and low-grade fever.

Prevention
The Centers for Disease Control and Prevention recommends that children and adults receive the measles vaccine to prevent measles.

Meningococcal meningitis
Meningococcal meningitis is a rare but serious bacterial infection. It causes the membranes that cover the brain and spinal cord to become inflamed. Each year, approximately 1,000 people in the U.S. get meningococcal disease, which includes meningitis and septicemia (blood infection). Meningococcal meningitis can be fatal or cause great harm without prompt treatment; as many as one out of five people who contract the infection have serious complications. Bacteria and viruses are the two main causes of meningitis. The bacterium *Neisseria meningitidis*, also called meningococcus, causes meningococcal meningitis.

In children and teens, meningococcus is the most common cause of bacterial meningitis.[23-26]

Symptoms
The more common signs and symptoms include:
- General poor feeling
- Sudden high fever
- Severe, persistent headache
- Neck stiffness
- Nausea or vomiting
- Discomfort in bright lights
- Drowsiness or difficulty awakening
- Joint pain
- Confusion or other mental changes

Pediatric HIV-AIDS
HIV is a virus that attacks the immune system. That makes children with HIV more vulnerable to infections and disease.

HIV symptoms in children and teens
An infant may not have any obvious symptoms at first. As the immune system weakens, you may start to notice:
- lack of energy
- delayed growth and development
- persistent fever, sweating
- frequent diarrhea
- enlarged lymph nodes
- Repeated or prolonged infections that don't respond well to treatment
- weight loss

Treatment
HIV may not have a current cure, but it can be effectively treated and managed. Today, many children and adults with HIV live long, healthy lives. The main treatment for children is the same as adults: antiretroviral therapy. Antiretroviral therapy and medications help prevent HIV progression and transmission.

Respiratory syncytial virus (RSV)
Respiratory syncytial virus (RSV) is a common respiratory virus. It affects the lungs and its bronchioles (smaller passageways that carry air to the lung). RSV is one of the most common causes of childhood illness, infecting most children by two years of age. RSV can also infect adults. Most healthy children and older adults who get RSV will get a mild case with cold-like symptoms.

Signs and symptoms
Common symptoms of RSV in infants include:
- Runny nose.
- Decrease in appetite.
- Sneezing and coughing.
- Fever (temperature above 100 degrees Fahrenheit). Fever may not always be present.

Symptoms in the youngest infants include
- Fussiness/irritability.
- Decreased activity/more tired than usual.
- Decreased appetite.
- Pauses in breathing.

Symptoms of severe RSV in infants include
- Short, shallow and rapid breathing.
- Flaring (spreading out) of nostrils with every breath.
- Belly breathing (look for a "caving in" of the chest in the form of an upside-down "V" starting under the neck).
- Bluish coloring of lips, mouth and fingernails.
- Wheezing (This can be a sign of pneumonia or bronchiolitis.)
- Poor appetite.

Treatment
Antibiotics are not used to treat viral infections, including those caused by RSV. Antibiotics may be prescribed, however, if testing shows you or your child has bacterial pneumonia or other infection[27].

Viral infections
Many viral infections are common, from influenza to herpes, and can be easily spread. Unlike bacteria, viruses need living cells to keep them alive, allowing them to reproduce and spread. These are called the hosts. Another way of looking at it is viruses enter healthy cells and "hijack" them to grow and multiply. Because viruses need those live cells for survival, they don't do well on surfaces, outside of a living being. While some bacteria can live on a doorknob or tabletop for days or weeks, viruses usually can only survive for a few hours, although there are some that may live longer. Viruses enter your body much like bacteria, through body openings, especially the nose and mouth. They can also be spread through exchange of body fluids, like contaminated blood, or through sexual activity. Hepatitis C and HIV are examples of this type of spread.

Treatment
Unlike bacterial infections, there are not a lot of cures for those caused by viruses. Antibiotics do not fight viruses, only bacteria. Some antiviral medications treat illnesses like hepatitis C.

Ear Infections
Ear infections are some of the most common childhood illnesses. According to the American Academy of Pediatrics (AAP), children are more prone to ear infections than adults. Ear infections can be caused by bacterial or viral infections. Symptoms include ear pain, fever, irritability, difficulty sleeping, and tugging at an ear.

Conjunctivitis
Conjunctivitis is known by the more common (and descriptive) name "pink eye." The telltale signs of pink eye include redness, discharge, itchiness, and swelling in

one or both eyes. There are multiple causes, but the contagious type of conjunctivitis is caused by a bacteria or virus that gets into the eye. A pediatrician may treat the pink eye with antibiotic ointment or eye drops.

Gastroenteritis

Gastroenteritis is also known as the stomach flu, but it is not the flu at all. But like the flu, it is caused by a virus that can spread quickly. Symptoms include nausea, vomiting, and diarrhea. Usually, the symptoms pass within a couple of days and treatment includes rest and giving fluids to avoid dehydration due to vomiting and diarrhea.

Sinusitis

Sinusitis is the technical term for a sinus infection. It is caused by a build-up of fluid in the sinuses, which allows germs (bacteria and viruses) to grow. Most cases of sinusitis are caused by viruses. Symptoms include runny nose, stuffy nose, headache, pressure or pain in the face, post-nasal drip (mucus dripping into the throat), sore throat, cough, and bad breath.

Strep Throat

Strep throat is caused by a bacteria called streptococcus pyogenes that gets into the nose and throat. It causes sore throat, fever, swollen tonsils, and stomach pain.

Whooping cough

Whooping cough is a bacterial infection that gets into your nose and throat. It spreads easily, but vaccines like DTaP (diphtheria, tetanus, and pertussis) and Tdap (tetanus, diphtheria, and pertussis) can help prevent it in children and adults.

Symptoms

- Mild coughing
- Sneezing
- Runny nose
- Low fever (below 102 F)

Whooping Cough Prevention

The DTaP vaccine can help protect children from whooping cough. Infants should get a dose every other month for the first 6 months, another between 15 and 18 months, then one last time between ages 4 and 6.

- Get lots of rest.
- Clean air.
- Drink fluids.

Pediatric adverse drug reactions

Asthma

Asthma is the most common, non-infective, chronic disease of childhood, affecting one in 11 children and young people. Commonly used medications include beta-agonists, inhaled corticosteroids (ICS), leukotriene receptor antagonists, xanthine derivatives and, more recently, monoclonal antibodies. Children and young people typically receive lower doses of ICS, meaning that some systemic ADRs to corticosteroids, such as striae and fat redistribution, are rarely seen in children and young people with asthma[64]. However, there are still concerns about ADRs caused by ICS in children and young people, particularly adrenal suppression[65–67]. Adrenal suppression can be difficult to identify, as the presentation can be asymptomatic; subtle (e.g. loss of growth velocity, increased lethargy, weight loss); or florid (e.g. symptomatic adrenal crisis).

Infection

After vaccines, anti-infective agents are the most commonly reported group of medicines for ADRs in children and young people (all age groups), with anti-bacterials accounting for around half of the ADR burden in children. The most common ADRs reported are nausea, vomiting, diarrhoea and skin rashes.

Allergy

Systemic antihistamines are commonly used in children for symptomatic relief in a variety of allergic diseases, including allergic rhinitis, allergic conjunctivitis, food allergy, chronic spontaneous urticaria and atopic eczema. Studies have shown that, of the major drug classes, antihistamines are responsible for around 1–3% of reported ADRs. Historically, although highly effective, first-generation antihistamines (e.g. chlorphenamine and promethazine), were associated with a greater incidence of ADRs than second-generation antihistamines, such as loratadine and cetirizine.

Pain

Pain is often undertreated in children and young people, and its management varies globally. Three groups of analgesics are commonly used in children and young people: paracetamol, NSAIDs and opioids. These account for around 10% of ADRs reported in children. Opioids were associated with markedly more adverse events than paracetamol or NSAIDs, particularly in the central nervous system (CNS), and dual therapy with a non-opioid/opioid combination conferred a protective effect for ADRs compared with opioids alone. Codeine raised particular concerns about harms in children after the deaths/serious harms reported in children given ‘standard’ doses of codeine, whom were later found to be ultra-rapid metabolisers at the CYP2D6 locus.

Epilepsy

Epilepsy is a neurological condition affecting both adults and children. The majority of patients will depend on antiepileptic drugs (AEDs) to achieve seizure control. AEDs are the second most frequently reported therapeutic class associated with ADRs in children and young people and up to 25% of AED treatment failure has been attributed to ADRs. The risk of ADRs from AEDs is almost tripled in patients prescribed more than one drug. Sodium valproate and carbamazepine account for the majority of AED ADRs; however, this is likely to be because of their widespread use among children and young people with epilepsy. The most common ADRs

reported involve the CNS and include behavioural disturbance, somnolence/fatigue and increased seizures.

Diabetes

Insulin is the primary agent used to treat diabetes mellitus in children. Various insulin products are available that vary in their time-action profiles: short-acting (including soluble insulin and rapid-acting insulin), intermediate-acting insulins and long-acting insulins. Hypoglycaemia is the most serious and potentially life threatening adverse effect of insulin and a major barrier to achieving adequate glycaemic control. Insulin is an anabolic hormone involved in promoting the uptake of fatty acid into adipose tissue; unsurprisingly, with the exception of insulin detemir, weight gain is another commonly reported adverse effect of insulin. Although the mechanisms are not entirely understood, detemir is associated with reduced food intake compared with other insulin preparations. Weight gain can be a significant barrier to adherence to insulin, especially in a teenage population.[28]

Corticosteroids

ICS have been discussed previously; however, systemic corticosteroids (e.g. prednisolone, methylprednisolone and dexamethasone) are also widely used in paediatrics for their anti-inflammatory, immunomodulatory and immunosuppressive characteristics across a range of diseases.

Management of ADRs

When managing ADRs in primary and secondary care, the WHO recommends three steps for evaluation:

1. Assess the nature and severity of the reaction;
2. Establish the cause;
3. Take corrective and follow-up action

Assessment of ADR's

Historically, none of the causality tools for assessing ADRs such as the Naranjo probability scale were designed for use in paediatrics. The Adverse Drug Reactions in Children (ADRIC) programme highlighted the difficulties in applying these existing tools within paediatric populations and the need to develop paediatric-specific methodologies. The LCAT classifies ADRs as "unlikely", "possible", "probable" or "definite" and LAAT classifies them as "unassessable", "not avoidable", "possibly avoidable" and "definitely avoidable".

CONCLUSION

Most of the research studies found that ADR's causes moderate severity. This indicates the need for a rigid ADR monitoring among pediatric patients to ensure safe drug therapy. The regular pharmacovigilance awareness programs should be conducted to increase the spontaneous reporting of ADRs. A large proportion of ADRs in children under 2 years old was mainly induced by drugs from the antibacterial for systemic use and most of the ADRs were skin reactions.[29-30]

The wide range of drugs available, the manifestations of toxicity may vary and affect any organ system. The adverse reactions have taken over from syphilis and tuberculosis as the great mimics of other diseases. The pattern of adverse drug reaction is likely to change with the introduction of new biotechnology products. Therefore the prescribing clinicians should be aware of the toxic profile of drugs they prescribe and to be ever vigilant for the occurrence of unexpected adverse reactions. Individualised therapy is becoming more of a possibility as not just pharmacogenetics but other phenotypic information can be combined to generate patient-specific advice to prescribers. For individual clinicians, achieving the best outcomes from therapies remains a key goal because avoiding or mitigating the risk of ADRs continues to challenge our everyday clinical practice.

REFERENCES

1. Chien JY, Ho RJ. Drug delivery trends in clinical trials and translational medicine: Evaluation of pharmacokinetic properties in special populations. J Pharm Sci., 2011; 100: 53–8.
2. Aagaard L, Hansen EH. Adverse drug reactions reported for systemic antibacterials in Danish children over a decade. Br J Clin Pharmacol, 2010; 70: 765–8.
3. Le J, Nguyen T, Law AV, Hodding J. Adverse drug reactions among children over a 10-year period. Pediatrics, 2006; 118: 555–62.
4. Bavdekar SB, Karande S. National pharmacovigilance program. Indian Pediatr, 2006; 43: 27–32.
5. Clavenna A, Bonati M. Adverse drug reactions in childhood: A review of prospective studies and safety alerts. Arch Dis Child, 2009; 94: 724–8. [PubMed] [Google Scholar]
6. Johann-Liang R, Wyeth J, Chen M, Cope JU. Pediatric drug surveillance and the Food and Drug Administration's adverse event reporting system: An overview of reports, 2003-2007. Pharmacoepidemiol Drug Saf, 2009; 18: 24–7. [PubMed] [Google Scholar]
7. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther, 1981; 30: 239–45.
8. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm, 1992; 49: 2229–32. [PubMed] [Google Scholar]
9. Schumock GT, Seeger JD, Kong SX. Control charts to monitor rates of adverse drug reactions. (1091-2, 1095-6).Hosp Pharm, 1995; 30: 1088.
10. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. Hosp Pharm, 1992; 27: 538.
11. Brunlof G, Tukukino C, Wallerstedt SM. Individual case safety reports in children in commonly used

drug groups - signal detection. BMC Clin Pharmacol, 2008; 8: 1.
12. Berry MA, Shah PS, Brouillette RT, Hellmann J. Predictors of mortality and length of stay for neonates admitted to children's hospital neonatal intensive care units. J Perinatol, 2008; 28: 297–302.
13. Neubert A, Dormann H, Weiss J, Egger T, Criegee-Rieck M, Rascher W, et al. The impact of unlicensed and off-label drug use on adverse drug reactions in paediatric patients. Drug Saf, 2004; 27: 1059–67.
14. Moore TJ, Weiss SR, Kaplan S, Blaisdell CJ. Reported adverse drug events in infants and children under 2 years of age. Pediatrics, 2002; 110: e53.
15. Segal AR, Doherty KM, Leggott J, Zlotoff B. Cutaneous reactions to drugs in children. Pediatrics, 2007; 120: e1082–96.
16. Dharnidharka VR, Kandoth PN, Anand RK. Adverse drug reactions in pediatrics with a study of in-hospital intensive surveillance. Indian Pediatr, 1993; 30: 745–51.
17. Rieder MJ. If children ruled the pharmaceutical industry: the need for pediatric formulations. *Drug News Perspect*, 2010; 23(7): 458–464.
18. Kauffman RE. Status of drug approval process and regulation of medicines for children. *Curr Opin Pediatr*, 1995; 7(2): 195–198.
19. Impicciatore P, Choonara I, Clarkson A et al. Incidence of adverse drug reactions in paediatric in/out-patients: a systematic review and meta-analysis of prospective studies. *Br J Clin Pharmacol*, 2001; 52(1): 77–83.
20. Mitchell AA, Lacouture PG, Sheehan JE et al. Adverse drug reactions in children leading to hospital admission. *Pediatrics*, 1988; 82(1): 24–29.
21. Thiesen S, Conroy EJ, Bellis JR et al. Incidence, characteristics and risk factors of adverse drug reactions in hospitalized children—a prospective observational cohort study of 6,601 admissions. *BMC Med*, 2013; 11: 237.
22. Posthumus AA, Alingh CC, Zwaan CC et al. Adverse drug reaction-related admissions in paediatrics, a prospective single-centre study. *BMJ Open*, 2012; 2(4): e000934.
23. Martinez-Mir I, García-López M, Palop V et al. A prospective study of adverse drug reactions in hospitalized children. *Br J Clin Pharmacol*, 1999; 47(6): 681–688.
24. Jonville-Bera AP, Giraudeau B, Blanc P et al. Frequency of adverse drug reactions in children: a prospective study. *Br J Clin Pharmacol*, 2002; 53(2): 207–210.
25. Gholami K, Babaie F, Shalviri G et al. Pediatric hospital admission due to adverse drug reactions: report from a tertiary center. *J Res Pharm Pract*. 2015; 4(4): 212–215.
26. Gallagher RM, Bird KA, Mason JR et al. Adverse drug reactions causing admission to a paediatric hospital: a pilot study. *J Clin Pharm Ther*, 2011; 36(2): 194–199.
27. Neubert A, Lukas K, Leis T et al. Drug utilisation on a preterm and neonatal intensive care unit in Germany: a prospective, cohort-based analysis. *Eur J Clin Pharmacol*, 2010; 66(1): 87–95.
28. Vernacchio L, Kelly JP, Kaufman DW, Mitchell AA. Medication use among children <12 years of age in the United States: results from the Slone Survey. *Pediatrics*, 2009; 124(2): 446–454.
29. Griesenauer RH, Kinch MS. 2016 in review: FDA approvals of new molecular entities. *Drug Discov Today*, 2017; 22(11): 1593–1597.
30. Gallagher RM, Bird KA, Mason JR et al. Adverse drug reactions causing admission to a paediatric hospital: a pilot study. *J Clin Pharm Ther*, 2011; 36(2): 194–199.