

Immune Deficiency Foundation

Patient & Family Handbook

For Primary Immunodeficiency Diseases

.....

Chapter 27

Immune Deficiency Foundation

Patient & Family Handbook

For Primary Immunodeficiency Diseases

6th Edition

The development of this publication was
supported by Shire, now Takeda.



110 West Road, Suite 300
Towson, MD 21204
800.296.4433

www.primaryimmune.org
idf@primaryimmune.org

Chapter 27

Infections in People with Primary Immunodeficiency Diseases: Antibiotic and Antifungal Therapy

Niraj Patel, MD, Levine Children's Hospital, Charlotte, North Carolina, USA

Infections are the hallmark of a primary immunodeficiency disease (PI). For many individuals, a PI diagnosis is suspected and made only after the individual has had recurrent infections or infections that are uncommon or unusually severe. This section discusses common infections and their treatment.

Infections in a Person with PI

Anyone can get an infection, and everyone does. But an infection in a person with PI may require different treatment than a similar infection in a person with a normal immune system. For example, the person with a PI may require a longer course or higher dose of antibiotics than someone who does not have a PI.

An individual's primary care provider should be the first point of contact when a person with PI is ill. The provider may then want to confer with the immunologist about the management and treatment of a particular infection. The immunologist needs to know about the infections, as this knowledge may affect treatment. For example, individuals with antibody deficiency who receive immunoglobulin (Ig) replacement therapy may need to have their dose adjusted if they are experiencing frequent breakthrough infections.

The goals of medical treatment and supportive care are to reduce the frequency of infections, prevent complications and prevent an acute infection from becoming chronic and potentially causing irreversible organ damage. The affected individual, family/caregivers, and members of the healthcare team must work together and effectively communicate among each other if these goals are to be accomplished.

A description of several kinds of infections and their treatment follows. Many other infections including skin infections, deep abscesses, bone infections, meningitis, and encephalitis (infections of the brain) are not covered here, but these may also occur in individuals with PI.

Remember that the suffix “itis” means an inflammation of a particular body part, like tonsillitis (inflammation of the tonsils) or appendicitis (inflammation of the appendix). The inflammation is usually caused by an infection but not always.

Eye Infections

Conjunctivitis

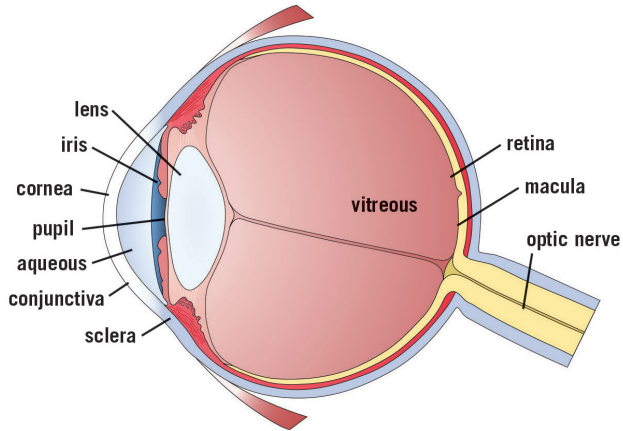
Conjunctivitis, or pink eye, is an inflammation or infection of the lining of the eyelid and of the membrane covering the outer layer of the eyeball (conjunctiva). It can be caused by bacteria, viruses, environmental allergies, or chemical irritants such as smoke or soap. Conjunctivitis may occur by itself or in association with other illnesses, such as the common cold. The symptoms commonly associated with conjunctivitis are redness and/or swelling of the eyelids, tearing, and discharge of mucus or pus. These symptoms are frequently accompanied by itching, burning, and sensitivity to light.

In the morning, it is not unusual to find the eyelids stuck together from the discharge that has dried while the eyes were closed during sleep. These secretions are best loosened by placing a clean washcloth or cotton ball soaked in warm water on each eye. After a few minutes, gently clean each eye, working from the inner corner to the outer corner of the eye. **Meticulous hand washing is necessary for anyone coming in contact with the eye discharge in order to prevent the spread of the infection as conjunctivitis is usually very contagious.**

It may be necessary to be seen by a physician if vision is significantly affected or if symptoms persist, in order to determine the type of conjunctivitis.

The eye discharge may be cultured to determine if the infection is bacterial or viral. Topical antibiotics (ointment or eye drops) may be prescribed if the infection is bacterial in nature. If the inflammation is caused by an irritant, avoidance of that irritant will be important.

Figure 27:1 The Eye



Ear Infections

Otitis Media

Otitis Media is an infection of the middle ear and is usually caused by bacteria or viruses. A small tube called the Eustachian tube connects the middle ear with the back of the throat and nose. In the infant and small child, the tube is shorter and more horizontal than in the adult, and provides a ready path for bacteria and viruses to gain entrance into the middle ear and not drain out. In some infections and allergic conditions, the Eustachian tube may actually swell and close, preventing drainage from the middle ear.

The characteristic symptom associated with otitis media is pain, caused by irritation of the nerve endings in the inflamed ear from inflammatory secretions or changes in ear pressure. A baby or young child may indicate pain by crying, head rolling, or pulling at the infected ear(s). The older child or adult may describe the pain as being sharp and piercing. Restlessness, irritability, fever, nausea, and vomiting may also be present. Pressure in the infected eardrum tends to increase when the individual is in a flat position. This explains why pain is often more severe at night, causing the individual to wake up frequently. As fluid pressure increases within the eardrum, pain becomes more severe and the eardrum may actually rupture. The appearance of pus or bloody drainage in the ear canal is an

indication of a possible eardrum rupture. Although pain is usually relieved when the eardrum ruptures, the infection still exists.

Whenever an ear infection is suspected, the patient should be seen by a healthcare provider. Antibiotic therapy is usually started in order to treat the infection. Analgesic (pain killing) ear drops may also be prescribed to help with pain. A follow-up examination may be recommended to be sure that the infection has cleared and that no residual fluid remains behind the eardrum. Repeated episodes of otitis media may actually cause hearing impairment or loss.

For children with repeated episodes of otitis media, a procedure called a myringotomy may be recommended. In this procedure a small hole is made in the eardrum and a tube placed in the hole, to promote drainage of fluid from the middle ear and equalize the pressure between the ear canal and middle ear.

Upper Respiratory (Sinus and Throat) Infections

Rhinitis

Rhinitis is a term used to describe an inflammation of the nose. It is usually caused by bacteria, viruses, chemical irritants, and/or allergens. Symptoms may include sneezing, difficulty in breathing through the nose, and nasal discharge (rhinorrhea). The nasal discharge may vary from thin and watery, to thick and yellow or green. It is generally accepted that green or yellow-green nasal discharge is a sign of acute infection, but this may not always be the case.

Acute Sinusitis

Sinusitis is an inflammation of one or more of the sinuses. The sinuses are small cavities, lined with mucous membranes, located in the facial bones surrounding the nasal cavities. The purpose of the sinuses is thought to be to decrease the weight of the skull and to give resonance and timbre to the voice. The basic causes of sinusitis are the blockage of normal routes of sinus drainage and infections spread from the nasal passages. Pain, particularly in the forehead and cheekbones, and tenderness over the face in these same areas are characteristic symptoms. In addition, there may be pain in and around the eyes, and in the teeth of the upper jaw. The pain and headache associated with sinusitis is typically more pronounced in the morning due to accumulated secretions in the sinuses during sleep.

Being in an upright position during the day facilitates sinus drainage and usually provides some temporary relief. Depending on the amount of sinus drainage, there may be cough, throat irritation, bad breath, and decreased appetite. Sinusitis may be accompanied by a fever.

A sinus infection can be difficult to treat in an individual with PI and may require a longer course of antibiotics than would be usually prescribed. Many individuals get benefit from the use of daily sinus rinses to keep the sinuses free of accumulating secretions. It is important to boil water or to use purchased distilled water for sinus rinses to make sure the water itself doesn't contain unwanted pathogens. Repeated or prolonged episodes of acute sinusitis may lead to chronic sinusitis and damage to the mucosal surfaces.

Acute Coryza

Coryza, also known as upper respiratory infection (URI) or the common cold, is an acute inflammation of the upper respiratory tract (nose and throat or nasopharynx). Early symptoms include a dry tickling sensation in the throat, followed by sneezing, coughing, and increased amounts of nasal discharge. There may also be symptoms of fatigue, and generalized aches and discomfort. A cold is usually caused by rhinovirus. Symptomatic treatment may bring some relief, but there is no antibiotic currently available that will kill or inactivate rhinovirus. Taking an antibiotic will not cure a cold any quicker. A cold generally lasts about a week. But if a cold lasts more than a week and is accompanied by a fever, productive cough, and/or difficulty breathing, it may be more than a cold and a primary care provider should be seen.

Influenza

Influenza, or flu (a short form of the word influenza), is a term that is often used generically to describe the fever, body and joint aches, cough, congestion, etc. that we associate with many common respiratory viruses. True influenza, however, is caused only by an influenza virus, and it may be more severe and dangerous than other common respiratory viruses. Flu season is generally in the fall and winter. Flu may occur sporadically or in epidemics. Usually epidemics occur every two to four years and develop rapidly because of the short incubation period of the disease.

The incubation period is the time from when a person is exposed to an infection to the time symptoms appear. Symptoms of the flu include sudden onset of high fever, chills, headache, muscle

ache, weakness, fatigue, and runny nose. Vomiting and diarrhea may also be present. Sometimes a bacterial infection of the ears, sinuses, or even lungs may develop during or after the flu.

There are anti-viral drugs available to treat the flu, but they must be started shortly (one or two days) after the onset of symptoms in order for them to be effective. There is also some evidence to suggest that these drugs may prevent the flu or decrease its severity if taken after someone has been exposed to the flu. Influenza can be a very serious infection, particularly in someone with PI, and seeking medical attention is highly recommended.

Pharyngitis

Pharyngitis describes an inflammation of the throat (sore throat). It is usually caused by a bacterial or viral infection but may also be caused by simple irritation. Symptoms include a raw or tickling sensation in the back of the throat, and there may be difficulty swallowing. Sometimes these symptoms are accompanied by a fever. Sore throats that are caused by *Streptococcus pyogenes* (strep throat) can cause other diseases such as rheumatic fever or kidney inflammation if they are not treated. If an individual has a sore throat, they should seek medical attention; a quick test or culture to determine if it is a strep throat infection is usually indicated.

Tonsillitis

Tonsillitis is an inflammation of the tonsils. The most common causes are viral illnesses for which antibiotics do not work. Some people have chronic tonsillar infections, and it may be recommended that the tonsils be removed (sometimes along with the adenoids).

Adenitis or Lymphadenitis

Lymphadenitis, or swollen glands, is an inflammation of the lymph nodes. Lymph nodes are present all over the body, but particularly in the neck, axillae, and groin areas. The lymph system functions to help the immune system respond to infection. For example, the lymph nodes in the neck can become inflamed as the body is recovering from an upper respiratory infection. This is called reactive lymphadenopathy because it is a normal response, or reaction, to an infection. It is also possible for the lymph nodes to become inflamed because they themselves are infected. Enlarged lymph nodes on a single side of the neck generally indicate a bacterial infection, while enlargement on both sides usually indicates a viral infection but not always.

Lower Respiratory Infections

Croup

Croup is a general term used to describe an infection, usually in children, which causes narrowing of the air passages leading to the lungs. Croup can be caused by viruses or bacteria. The child's temperature may be normal or slightly elevated. The onset of croup may be sudden or occur gradually. In some instances, the onset occurs at night, and the child may awaken with a tight barking cough and respiratory distress.

Breathing is difficult due to the narrowing of the trachea (windpipe). Croup can be a frightening experience for both the parents and child. Unfortunately, the child's anxiety may increase the severity of the symptoms. It is important for the parents to remain as calm and as reassuring as possible. Urgent medical attention may be needed. Depending on the severity of symptoms, advice may be sought from the primary care on-call provider, and sometimes an emergency room visit is in order.

Acute Bronchitis

Acute bronchitis is an inflammation of the bronchi, which are the major branches off the trachea (windpipe). It often accompanies or follows an upper respiratory infection. Symptoms include fever and cough. At the onset, the cough is usually dry but gradually becomes more productive in which the person may cough up mucus or phlegm.

Pneumonia

Pneumonia is an acute infection of the lungs and can be caused by bacteria, viruses and/or fungi. Symptoms include chills, high fever, cough, and chest pain associated with breathing. Symptoms of pneumonia should always be reported to the primary care provider. In some people with a PI, bronchiectasis may develop if there are repeated episodes of pneumonia. Bronchiectasis is an irreversible condition where the airways become widened and scarred. After this occurs, it becomes difficult to clear the airways of mucus and bacteria, which leads to even more serious lung infections.

General Care of Respiratory Infections

Respiratory infections may be merely bothersome, like a cold or more serious like pneumonia. Management of these infections is directed toward the relief of symptoms and the prevention of complications. The primary care provider may

recommend a medication to relieve fever and general body aches. Antibiotics may be prescribed to treat infections that are caused by bacteria. Expectorants may be prescribed to liquefy (water down) mucus secretions and make them easier to cough up. Decongestants to shrink swollen mucous membranes may also be recommended. Fluids should be encouraged to promote adequate

hydration. Drinking a variety of non-alcoholic beverages is important. Beverages served with crushed ice can be soothing to a sore throat. Warm beverages, such as tea, may promote nasal drainage and relieve chest tightness.

During the acute phase of any of these types of illnesses, there may be a loss of appetite. This is generally short lived. It is usually effective to have small frequent feedings of liquid and light foods. Once the appetite returns, a high-caloric, high-protein diet to replace the proteins lost during the acute phase of the illness might be recommended.

General comfort measures also include rinsing the mouth with plain water at regular intervals. This will relieve the dryness and bad taste that often accompanies illness and mouth breathing. A vaporizer may be helpful in increasing room humidity. However, if a vaporizer is used, daily cleaning is imperative to prevent contamination with molds. A coating agent (such as petrolatum or lip balm) can provide relief and protection to irritated lips and nose. Adequate rest is important. If persistent coughing or post nasal drip interferes with rest, elevation of the head and shoulders with extra pillows during periods of sleep should be attempted. Sometime a cough suppressant can be prescribed at night to prevent interruption of sleep.

Respiratory infections tend to be easily passed from one individual to another. The person who is ill should always be encouraged to cover the mouth and nose when sneezing and coughing. Soiled tissues should be promptly discarded. Hand washing is the most important method to prevent the spread of the infection. An alcohol-based hand sanitizer should be used frequently. If the hands are visibly soiled, soap and water is best. In some cases of bronchitis and pneumonia, coughing and breathing deeply at regular intervals should be encouraged as coughing protects the lungs by removing mucus and foreign particles from the air passages. Deep breathing promotes full expansion of the lungs, reducing the risk of further complications. In some situations, the primary care provider may order chest

postural drainage, chest physiotherapy, or sinus postural drainage, which are all ways of helping to loosen and clear mucus.

Gastrointestinal (GI) Infections

Diarrhea

Diarrhea is characterized by frequent, loose, watery bowel movements (stools). Diarrhea is a symptom and may indicate an infection or inflammation of the GI tract. Infections may be caused by viruses, bacteria, fungi or parasites. The primary care provider may order stool cultures to determine the cause of the infection. Certain medications may also cause diarrhea. Diarrhea may be mild to severe in nature. Whether it is mild or severe depends on the frequency, the volume and the consistency of the stools. Diarrheal illnesses may be accompanied by fever. In some cases severe diarrhea can cause dehydration. Infants, young children, and the elderly are at the greatest risk of serious problems associated with dehydration. Diarrheal illnesses may sometimes be accompanied by vomiting, further increasing risks of dehydration. Signs of dehydration can include:

- Loss of skin elasticity
- Dry parched lips, tongue, and mucus membranes
- Thirst
- Decreased urine output
- In infants, depressed or sunken fontanelles (soft spots on the head)
- An appearance of sunken eyes
- Behavioral changes ranging from restlessness to extreme fatigue and weakness

The general care of diarrhea focuses on the replacement of lost body fluids and salts, and the prevention of dehydration. When diarrhea is mild, changes in the diet and increased fluid intake may compensate for fluid losses. The primary care provider may suggest a clear liquid diet (avoiding dairy products), including weak tea, sports drinks, bouillon, and flattened soft drinks (without carbonation). As clear liquids are tolerated and the frequency and volume of stools decrease, the diet may be gradually advanced. In case of severe dehydration, hospitalization and intravenous fluids may be necessary.

General comfort measures include coating the rectal area with a petroleum jelly preparation. This will help protect the skin and reduce irritation from frequent diarrheal stools. Soiled diapers and clothing should also be changed immediately. The older child and adult may be encouraged to rinse his or her mouth with water regularly. This helps to relieve mouth dryness and bad taste associated with illness and is especially important after vomiting.

In infectious diarrhea, several measures are used to reduce the chances of spreading the illness to other family members. It may be easier for the infected person to use disposable cups, dishes, and utensils. Soiled diapers, clothing and linens should be kept separate and washed separately from other family laundry. Bathrooms should be cleaned with a disinfectant solution as often as necessary. Frequent hand washing with soap and water is essential for everyone, especially before and after handling soiled diapers or linens.

Bloody diarrhea and diarrhea accompanied by urgency and severe abdominal cramping may be signs of illnesses other than infections. These symptoms should always be reported to the primary care provider. Diarrhea can be caused by many things in addition to infections including certain drugs, malabsorption, inflammatory bowel diseases, like ulcerative colitis or Crohn's disease, etc., and additional testing may be required to determine its cause. Bacterial causes of diarrhea do not always require antibiotics, and antibiotic therapy may sometimes prolong symptoms.

Sometimes, antibiotics themselves may cause diarrhea. The job of antibiotics is to kill bacteria. In some cases, they kill good bacteria that normally live in the GI system as well as the disease causing ones. A prescriber may recommend taking a probiotic when someone is on antibiotics. The probiotic will replace some of the good bacteria that have been killed by the antibiotic.

Other GI Infections

Any of the gastrointestinal organs can become inflamed. Examples of these disorders include hepatitis (liver), gastritis (stomach), pancreatitis (pancreas), cholecystitis (gall bladder), or colitis (large intestine). This inflammation may be caused by infection. Symptoms can include pain, yellowing of the skin and/or eyes (jaundice), diarrhea, nausea, or loss of appetite. Medical attention should always be sought for these types of symptoms.

Bloodstream Infections

The blood can become infected with any kind of germ (bacteria, fungus, or virus). The general term for this is sepsis. These are extremely serious infections usually accompanied by high fever and signs of severe acute illness. It is necessary for the blood to be drawn and cultured to see if infectious organisms are present. Very often, blood stream infections require treatment with intravenous antibiotics

Infections at Unusual Locations or with Unusual Organisms

Infections that occur with defects in the innate immune system may be quite different from infections that affect individuals with defects in T cells or individuals with defects in B cells/antibody production.

For example, children with Chronic Granulomatous Disease (CGD), which is a defect in the innate immune system, are usually healthy at birth. The most common CGD infection in infancy is a skin or bone infection with the bacteria *Serratia marcescens*, an organism that very rarely causes infections in other types of PI and any infant with an infection with this particular organism should be tested for CGD. Infections in CGD may involve any organ or tissue, but the skin, lungs, brain, lymph nodes, liver, and bones are the usual sites of infection and where abscess formation is common. Infections may rupture and drain with delayed healing and residual scarring. Infection of lymph nodes (under the arm, in the groin, in the neck) is a common problem in CGD, often requiring drainage or surgery along with antibiotics. Pneumonia is also a common problem in CGD. Pneumonias due to the fungus *Aspergillus* may come on very slowly, initially only causing fatigue, and only later causing cough or chest pain. Fungal pneumonias often do not cause fever. In contrast, bacterial infections (*Staphylococcus aureus*, *Burkholderia cepacia* complex, *Serratia marcescens*, *Nocardia*) usually come on very quickly with fever and cough. *Nocardia* in particular causes high fevers and lung abscesses that can destroy parts of the lung. With CGD, it is particularly important to identify infections early and treat them completely, usually for a long period of time, so it is critical to seek medical attention early. If pneumonia is found it is very important to figure out exactly which microorganism is the cause, which may require a biopsy, usually done with a needle or a bronchoscope and not surgery. Treatment may require many weeks. Liver

abscesses occur in about a third of individuals with CGD. They can start as fever and fatigue but may also cause mild pain over the right upper abdomen. *Staphylococcus aureus* causes most liver abscesses. Abscesses can also develop in the brain or bones (osteomyelitis) and can involve the spine, particularly if a fungal infection in the lungs spreads into it. (See Chronic Granulomatous Disease Chapter.)

Treatment of Infections

There are many anti-infective drugs: antibacterial, antifungal, antiviral, and anti-parasitic. The term antibiotic usually refers to a drug that fights bacterial infections. Anti-infective drugs are very specific. Different infections require different treatment. While penicillin is an excellent antibacterial antibiotic, it does not kill every kind of bacteria and has no effect at all on a virus or a fungus. If antibiotic therapy is indicated, the antibiotic prescribed should be one that will kill or inactivate the disease causing organism. Taking the medication as prescribed is very important, and every effort should be made not to miss any doses. Every infection does not necessarily need to be treated with an antibiotic or an anti-infective. The body has many defenses and mechanisms to fight off and kill infections. These defenses are present, even in people with PI. For example, the skin and mucus membranes are the first line of defense against many infections. Phagocytes (germ-killing white blood cells) usually work very well in people with antibody deficiencies just as antibodies are produced and work effectively in people with certain phagocyte problems. Some infections are mild and will resolve on their own, even in someone with PI.

Taking anti-infectives (antibiotics) may cause unwanted side effects and may require monitoring by a physician or laboratory testing. Antibiotics can cause upset stomach, vomiting, or diarrhea when taken over short periods of time such as days to one to two weeks. Longer courses of antibiotics (several weeks) may cause decreasing blood counts and kidney irritation, or require monitoring of drug levels. Antifungal medication may cause similar side effects as antibiotics as well as liver irritation, and may interfere with other medications, causing increase or decrease levels of those medications. Doctors should be consulted about possible side effects before taking any medication.

Sometimes prophylactic (or preventive) antibiotics may be prescribed for individuals with some types

of PI. For example, people with CGD usually receive daily antibiotics to protect them against certain kinds of infections.

People with cellular immune defects may take antibiotics to protect them against a particular kind of pneumonia. Prophylactic antibiotics are not, however, routinely recommended for all people with PI. There can be risks associated with antibiotic therapy. For example, drug-resistant organisms can develop or severe diarrhea can occur if normal body, non-pathogenic organisms are killed by an antibiotic. Only an immunologist can determine if prophylactic antibiotics are appropriate.

It is always important to try and determine the cause of a particular infection in someone with a PI. In order to determine what the right drug is, it may be necessary to get a culture. For example, if an individual has a respiratory infection with a cough, sputum that is coughed up can be sent to the lab to identify what the infecting agent is and its sensitivity to different antimicrobial agents. Cultures can be obtained on any type of drainage or body fluid including the blood. Sometimes, a biopsy of a tissue needs to be done. This involves taking a sample of a particular tissue and testing it to see if infection is present. For example, during a colonoscopy, tiny samples of the tissue from the intestinal wall are taken and examined by the pathologist to determine if an infection or other kind of inflammation is present.

Figure 27:2 Infections and autoimmune and/or inflammatory complications in CVID. The predominant organisms and sites of infection are shown on the left, with the inflammatory and autoimmune complications on the right.

Infections

Rhinovirus

Streptococcus pneumoniae

Haemophilus influenzae

Staphylococcus aureus

Moraxella catarrhalis

Pseudomonas in bronchiectasis

Helicobacter pylori

Giardia enteritis

Salmonella

Campylobacter jejuni

Norovirus

Ureaplasma

Mycoplasma

Inflammatory and Autoimmune

LIP

GLILD

Lymphadenopathy

Nodules/opacities

Diarrhoea

Malabsorption

Inflammatory bowel disease

Nodular lymphoid hyperplasia

Idiopathic enteropathy

Autoimmune

Immune thrombocytopenic purpura

Autoimmune Hemolytic anaemia

Evans syndrome

Rheumatoid Arthritis

Anti-IgA antibodies


Alopecia & Other

Credit: Jolles S. The variable in common variable immunodeficiency: A disease of complex phenotypes. J Allergy Clin Immunol Pract 2013;1:545-56. <http://dx.doi.org/10.1016/j.jaip.2013.09.015>.

Summary

While infections of all kinds (acute, chronic, frequent, or recurrent) are always going to be problematic for people with PI, it is important to remember that prevention and early intervention are always the best approaches. A healthy lifestyle that includes adequate rest, nutrition, and exercise can go a long way to preventing infections. Similarly, a common-sense approach to prevention that includes such measures as frequent handwashing and avoiding others who are ill can also be highly effective. Once symptoms of an infection are present, however, seeking medical care in a timely manner is critical so that infections can be diagnosed early and treated appropriately, thereby preventing complications.

Adapted from: Chapter 22 Infections. IDF Patient & Family Handbook for PI Diseases 5th Edition. 2013.



The development of this publication
was supported by Shire, now Takeda.



110 West Road, Suite 300
Towson, MD 21204

800.296.4433

www.primaryimmune.org
idf@primaryimmune.org