Management of the Patient Receiving Parenteral Biologic Therapy

Abstract

Biologic therapies are becoming the preferred treatment option for many complex medical conditions, especially in the areas of oncology and immunology. Cytokines, monoclonal antibodies, and immunomodulators all have their own specific roles, clinical applications, mechanisms of action, and side effects. As newer biologic agents are approved and used for treatment, the nurse involved in the care of the patient receiving parenteral biologic therapy or in the administration of parenteral biologic therapies must know and understand the technology and mechanisms of action associated with these agents as well as guidelines for their safe administration to ensure positive patient outcomes. This article discusses biologic therapies, focusing on monoclonal antibodies used in oncology and immunology. The indications, use, and administration of parenteral biologic therapies, as well as the nursing management of the patients receiving the therapies, are presented.

Biotechnology encompasses a multitude of different applications that use living organisms or their parts to produce or modify chemical compounds. It began with simple and traditional processes such as the production of beers, wine, and cheeses. Currently, biotechnology has evolved to highly complex molecular processes such as the use of recombinant DNA to yield new drugs and to introduce new traits into commercial crops and animals.

Biotechnology-derived products currently account for 5% of the value of the world market in medicines, and

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their share is expected to increase. By 2010, between 325 and 400 biotechnology drugs could reach the market, with the promise of better health outcomes. More than 325 million people worldwide have benefited from more than 155 biotechnology drugs and vaccines approved by the United States Food and Drug Administration (FDA). More than 370 biotechnology drug products and vaccines are currently in clinical trials targeting more than 200 diseases. Revenues for these products in 1992 were $8 billion. This figure increased to $34 billion in 2001 and is projected to exceed $56 billion by 2006.

Biologic therapy includes the use of agents derived from biologic sources or agents that affect biologic responses. Primarily, these are products derived from the mammalian genome, but chimeric and xenogenic sources are becoming more common.

Traditionally, biologic therapies were used to modify the body’s immune responses. Although modulation of the immune response remains a main focus, the term “biotherapy” has replaced “immunotherapy” because the scope of the field has widened. Other names for biologic therapies include “biologic agents,” “biologics,” “biologicals,” and “biological response modifier therapy.”

Biologics include a diverse range of products such as bacterial and viral vaccines, tissues, human blood, plasma, plasma derivatives, and certain products produced by biotechnology. These cells and biologic molecules are extraordinarily specific in their interactions. Because of this specificity, the tools and techniques of biotechnology are precise and tailored to operate in known, predictable ways.

**IMMUNE SYSTEM REVIEW**

To understand how biologic agents interact with the immune system, it is important to recall how the immune system functions. There are two types of immunity: innate and adaptive immunity. Innate immunity, also termed nonspecific immunity, is the first line of defense against antigens, which are foreign substances that induce an immune response. Innate immunity is present before exposure to an antigen, and is not enhanced by subsequent exposures. The innate immune system’s first lines of defense are mechanical barriers such as intact skin and mucous membranes. If these defenses fail, the innate immune system has other components, including complement, phagocytes, and natural killer cells, as a second line of defense.

Adaptive immunity, also known as specific or acquired immunity, is characterized by specific recognition of foreign organisms and a memory response. This allows the immune system to increase its ability to respond and defend the body with successive exposures to infectious organisms. There are two major branches of the adaptive immune responses, humoral immunity and cell-mediated immunity, depending on the components of the immune system involved in the response to the antigen. Humoral immunity involves the production of antibody molecules in response to an antigen and is mediated by B-lymphocytes. Cell-mediated immunity, on the other hand, involves the production of cytotoxic T-lymphocytes, activated macrophages, activated natural killer cells, and cytokines in response to an antigen and is mediated by T-lymphocytes. The major difference between humoral immunity and cell-mediated immunity is that with the latter, the immune response does not involve antibodies, but rather the activation of macrophages and natural killer cells, the production of antigen-specific cytotoxic lymphocytes, and the release of various cytokines in response to the antigen.

A most remarkable feature of the immune system is its ability to distinguish between the self-antigens, which are part of the host, and foreign antigens, which may present a threat to the host. The immune system does not normally respond to self-antigens. This immunologic unresponsiveness to self-antigens is known as tolerance, and it is an important factor in understanding autoimmune disorders. The failure of this tolerance, because of interaction between the wrong environment and the wrong genes, results in autoimmune disease. Unfortunately, when a self-antigen becomes immunogenic, it cannot be eliminated, and the resulting inflammation becomes persistent and destructive. This is evident in autoimmune disorders such as rheumatoid arthritis, Crohn’s disease, and psoriatic arthritis, to name a few. Examples of autoimmune diseases by the main target organ are listed in Table 1.

**BIOLOGIC AGENTS**

Biologic therapy uses a variety of agents, frequently derived from the cells of the immune system, for a variety of different clinical applications. Table 2 outlines examples of biologic agents and their clinical applications. Many of the biologic agents currently in clinical use are cytokines, a broad class of protein cell regulators produced by the immune system and manufactured using recombinant DNA technologies. Monoclonal antibodies also are used widely in biologic therapies for cancer and immune-mediated disorders. They are produced using the hybridoma technique developed by Kohler and Milstein in 1975. This technique fuses an antibody-producing cell with a myeloma cell line that results in an “immortal hybrid” cell, which produces a single antibody recognizing only a single antigen.

The hybridoma technique made it possible to produce an unlimited batch of pure monoclonal antibody that varied little and was highly specific for a single antigen. The generic drug names of monoclonal antibodies end with the suffix “mab.” The infixes preceding the suffix stem identify the target disease state and the product source. Thus, the “tu” in the drug name rituximab indicates that the drug is for “tumor”; the “xi” indicates that the drug is a...
chimeric monoclonal antibody, meaning it is derived from two or more genetically distinct sources; and the “mab” indicates that the drug is a monoclonal antibody.

The use of biologic therapy to treat malignant disease can be traced back to the 19th century and earlier. With scientific advancements in the way biologic agents are identified, produced, and used to improve tumor responses, biologic therapy currently is a viable treatment method for cancer. As a result of this success, the use of biologic therapy for a variety of diseases besides cancer has been investigated and researched intensively. These efforts have resulted in regulatory approval of several biologic agents for numerous autoimmune diseases, for cardiovascular diseases to prevent blood clots, and for treatment of organ transplant rejection. This discussion on the clinical use of biologic therapy focuses on monoclonal antibodies and their application in oncology and for immune-mediated inflammatory disorders.

### THE CLINICAL USE OF BIOLOGIC THERAPY

The use of biologic therapy to treat malignant disease can be traced back to the 19th century and earlier. With scientific advancements in the way biologic agents are identified, produced, and used to improve tumor responses, biologic therapy currently is a viable treatment method for cancer. As a result of this success, the use of biologic therapy for a variety of diseases besides cancer has been investigated and researched intensively. These efforts have resulted in regulatory approval of several biologic agents for numerous autoimmune diseases, for cardiovascular diseases to prevent blood clots, and for treatment of organ transplant rejection. This discussion on the clinical use of biologic therapy focuses on monoclonal antibodies and their application in oncology and for immune-mediated inflammatory disorders.

### Monoclonal Antibodies in Oncology

Traditional treatments for cancer have included surgery, radiation, and chemotherapy. All these treatments attack the tumor cells directly, but often are nonspecifically accompanied by serious side effects. The trend of using biologic therapy to promote the patient’s own immunologic response against the cancer, or to target the cancer cells specifically, is increasing. Cancer cells have antigens specific to the tumor, termed tumor-specific antigens, or antigens present in greater concentrations than normal, referred to as tumor-associated antigens.

One biologic agent used in oncology is the monoclonal antibody. Two types of monoclonal antibodies are used...
in cancer treatment. The first type includes monoclonal antibodies without any drug or radioactive material attached to them, often referred to as “naked” or “unconjugated.” Unconjugated monoclonal antibodies either attach themselves to specific antigens on cancer cells and mark the cancer cell for the immune system to destroy or attach themselves to certain antigen receptors, preventing cells from attaching to the receptors that stimulate cancer cell growth.

The second type, termed “conjugated,” includes monoclonal antibodies joined to a chemotherapy drug, a radioactive particle, or a toxin. Antibodies of this type are used as a delivery vehicle to take the substances directly to the cancer cells, minimizing damage to normal cells in other parts of the body. The actual therapeutic effects depend on the type of substance to which the antibodies are attached. Table 3 lists the FDA-approved monoclonal antibodies for cancer therapy.

**Monoclonal Antibodies for Immune-mediated Inflammatory Disorders**

Immune-mediated inflammatory disorders (IMIDs), a group of diseases that share common inflammatory pathways, are characterized by immune dysregulation that causes acute or chronic inflammation, resulting in organ damage, increased mortality, or morbidity. A shared underlying manifestation of IMIDs is inappropriate inactivation of inflammatory cytokines such as interleukin 12 (IL-12), interleukin 6 (IL-6), or tumor necrosis factor-alpha (TNFα). Disorders referred to as IMIDs include, but are not limited to, sepsis, rheumatoid arthritis, inflammatory bowel disease such as Crohn’s and ulcerative colitis, inflammatory skin conditions such as psoriasis, transplant-related diseases such as multiple sclerosis. The traditional symptom-based treatment of IMIDs includes the use of antiinflammatory drugs, corticosteroids, immunosuppressants, and even surgery, which result in limited control and effectiveness often accompanied by safety and tolerability issues. It was this limitation and ineffective treatment together with a greater understanding of the underlying IMID mechanisms that facilitated the development of new drugs and revolutionized treatment.

The monoclonal antibodies for IMIDs include anti-TNFα agents known as TNF antagonists. For certain varieties of IMID-like rheumatoid arthritis and Crohn’s disease, scientific evidence indicates that TNFα, a proinflammatory cytokine released by activated monocytes, macrophages, and T-lymphocytes, serves as a central factor in the development of both diseases. Findings show that TNFα binds to its receptors cells, and that

**TABLE 3**

**Monoclonal Antibodies Used in Cancer Therapy**

<table>
<thead>
<tr>
<th>Drug Name (Generic/Trade)</th>
<th>Manufacturer</th>
<th>Year</th>
<th>Indications</th>
<th>Dosing/Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituximab/Rituxan</td>
<td>Genentech/Biogen Idec</td>
<td>1997</td>
<td>• CD20+ B cell non-Hodgkins lymphoma</td>
<td>375 mg/m² IV 4× per week or 8 doses</td>
</tr>
<tr>
<td>Trastuzumab/Herceptin</td>
<td>Genentech</td>
<td>1998</td>
<td>• Metastatic breast cancer</td>
<td>4 mg/kg IV over 90 minutes, then 2 mg/kg over 30 minutes weekly maintenance</td>
</tr>
<tr>
<td>Gemtuzumab ozogamicin/Mylotarg</td>
<td>Wyeth</td>
<td>2000</td>
<td>• CD33+ acute myeloid leukemia</td>
<td>9 mg/m² IV over 2 hours, second dose in 14 days</td>
</tr>
<tr>
<td>Alemtuzumab/Campath</td>
<td>Berlex/Ilex</td>
<td>2001</td>
<td>• B cell chronic lymphocytic leukemia treated with alkylating agents and failed fludarabine</td>
<td>2-hour IV infusion starting with 3 mg escalating to 30 mg 3 days a week up to 12 weeks</td>
</tr>
<tr>
<td>Ibritumomab tiuxetan/Zevalin</td>
<td>Biogen Idec</td>
<td>2002</td>
<td>• Relapsed or refractory non-Hodgkins lymphoma</td>
<td>First dose: rituximab then In-111 Ibritumomab followed in 7-9 days by rituximab then Y-90 Ibritumomab</td>
</tr>
<tr>
<td>Tositumomab/Bexxar</td>
<td>Glaxo Smith Kline/2003</td>
<td>2003</td>
<td>• Non-Hodgkins lymphoma</td>
<td>IV administration: dosimetric step, followed in 7-14 days by therapeutic step.</td>
</tr>
<tr>
<td>Cetuximab/Erbitux</td>
<td>Imclone Systems/Bristol Meyers Squibb</td>
<td>2004</td>
<td>• Metastatic colorectal carcinoma</td>
<td>400 mg/m² IV over 120 minutes, then 250 mg/m² over 60 minutes weekly</td>
</tr>
<tr>
<td>Bevacizumab/Avastin</td>
<td>Genentech</td>
<td>2004</td>
<td>• Metastatic carcinoma of colon or rectum</td>
<td>5 mg/kg IV once every 14 days</td>
</tr>
</tbody>
</table>
A high concentration of TNFα is responsible for the inflammatory pathogenesis by mediating leukocyte recruitment and inflaming the synovial membrane of the joint and intestinal mucosa.\textsuperscript{12,13} TNFα antagonists work by impairing the binding of TNF to its receptors and lyse cells that express TNFα on their surface.\textsuperscript{11} Studies have shown that TNFs are implicated in a wide spectrum of diseases beyond rheumatoid arthritis and Crohn’s disease including sepsis, diabetes, cancer, osteoporosis, and multiple sclerosis.\textsuperscript{14} Table 4 outlines the monoclonal antibodies currently in clinical use for IMID.\textsuperscript{15,16}

### Adverse Events of Monoclonal Antibodies

Adverse events occur with all medical therapies and are expected to occur whether the monoclonal antibodies are used for cancer therapy or for immune-mediated inflammatory disorders. In cancer therapy, the type and severity of adverse events depends on whether the monoclonal antibody is administered unconjugated or conjugated to radioisotopes, chemotherapy drugs, or immunotoxins. Compared with standard chemotherapy, the adverse effects of monoclonal antibodies usually are mild and manageable, and do not affect the patient’s positive clinical response.

With IMIDs, the use of monoclonal antibodies, particularly TNFα antagonists, is associated with a wide range of adverse events. Because the actions of the monoclonal antibodies affect the immune system and its components, adverse events may include infections, malignancies, injection-site or infusion reactions, cardiac events, neurologic events, hepatic involvement, hematologic changes, and immune and autoimmune responses.\textsuperscript{11} Table 5 is a summary of the adverse events reported with monoclonal antibodies used for cancer therapy, and Table 6 is a summary of the adverse events reported with monoclonal antibodies used for the treatment of IMIDs.

#### THE ROLE OF THE INFUSION NURSE SPECIALIST

The advances in drug technology and increased understanding about the immune basis of many diseases led to the expansion of the clinical application for biologic agents. This advancement can become an ongoing challenge for both experienced and new infusion nurses as they provide care and manage patients receiving parenteral biologic therapies. The discussion on the role of the infusion nurse specialist in managing patients receiving parenteral biologic therapies includes patient assessment; patient education; drug handling, preparation, and administration; monitoring and management of adverse events such as infusion reactions, and reimbursement.

### Patient Assessment

One of the greatest contributions nurses make to patient care is patient assessment. For the patient receiving biologic therapy, patient assessment is performed before initiation of therapy for baseline information and screening, then with each scheduled visit before the infusion to obtain updated or new information. Before initiation of therapy, the patient’s medical history is obtained, including any significant illnesses or diseases such as cancer or malignancies, cardiac or pulmonary problems, neurologic disorders, hepatic or liver disorders, hematologic disorders or blood dyscrasias, diabetes, hypertension,

#### TABLE 4

Monoclonal Antibodies Used in Immune-mediated Inflammatory Disorders\textsuperscript{15,16}

<table>
<thead>
<tr>
<th>Drug Name (Generic/Trade)</th>
<th>Manufacturer</th>
<th>Year</th>
<th>Indications</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humira/Adalimumab</td>
<td>Abbott Labs</td>
<td>2002</td>
<td>Rheumatoid arthritis</td>
<td>40 mg SC every other week</td>
</tr>
<tr>
<td>Remicade (Infliximab)</td>
<td>Centocor Inc.</td>
<td>1998</td>
<td>Rheumatoid arthritis; Crohn’s disease; fistulizing Crohn’s disease; Ankylosing spondylitis; Psoriatic arthritis</td>
<td>For RA, 3 mg/kg IV at 0, 2, and 6 weeks then every 8 weeks. For patient with incomplete responses, dose at 10 mg/kg or treat as frequent as every 4 weeks. For CD and fistulizing CD, 5 mg/kg IV at 0, 2, and 6 weeks then every 8 weeks. For AS, 5 mg/kg at 0, 2, and 6 weeks then every 6 weeks. For PsA, 5 mg/kg at 0, 2, and 6 weeks then every 8 weeks</td>
</tr>
</tbody>
</table>

SC, subcutaneous; RA, rheumatoid arthritis; CD, Crohn’s disease; AS, ankylosing spondylitis; PsA, psoriatic arthritis.
or serious viral, fungal, or bacteria infections. Information about the patient’s medical history helps the nurse be aware of factors that may place the patient at a higher risk for developing adverse events associated with biologic therapy. For patients receiving biologic therapy that suppresses TNFα, the nurse must screen for a history of tuberculosis and other infections such as histoplasmosis and coccidiomycosis as well as active infections. A tuberculin skin test, chest x-ray, or both must be administered and the results read before initiation of therapy. The presence of TNFα is critical for containing and killing mycobacterium and other intracellular pathogens, and chronic suppression of TNF by anti-TNF agents appears to remove these protections and may reactivate latent tuberculosis.10

A medication and allergy profile must be obtained, including a history of prior treatments as well as current symptoms related to the prior treatment or the underlying disease process. Nurses must always be aware of any allergies to drugs or food the patient may have, and special attention must be paid to allergic reactions associated with biologic therapy. It is important to conduct a detailed review of the patient’s medication history, with close attention paid to concurrent medications for possible interactions.1 Patients are discouraged from taking medications similar to the parenteral biologic therapy they will be receiving because of the increased risk for potential side effects with no additional medical benefit.

After a detailed medical history is obtained, the patient’s current health status and condition must be assessed. The patient’s current weight, vital signs, hydration status, and skin integrity and appearance must be noted at baseline and before each treatment. It is important to establish the baseline status and function of the renal, hepatic, hematologic, cardiovascular, and pulmonary systems. Laboratory assessments may be necessary depending on the biologic agent and the underlying disease process. Laboratory tests may include a complete blood count with differential, platelet, and reticulocyte count; prothrombin time; partial thromboplastin time; and liver and kidney function tests, including electrolytes and a thyroid panel.1

Special considerations must be remembered for the elderly. They are more likely to have alterations in renal

### TABLE 6

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Humira (Adalimumab)</th>
<th>Remicade (Infliximab)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergic reactions</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Local injection site reactions</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Malignancies (lymphoma)</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Lupus-like syndrome</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Aseptic meningitis</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Serious infections</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Liver disease</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Demyelinating disease</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Hematologic</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

GI, gastrointestinal.
and hepatic functioning as well as a decrease in cardiac function, which may affect dosing, clearance, and tolerance of the biologic agents. Special attention to their medication profile is required because they often are taking several medications.¹

The patient’s response to treatment should be assessed continually, and nurses should pay particular attention to the patient’s progress or lack of progress or response. For certain diseases such as rheumatoid arthritis, a patient self-assessment tool such as a health assessment questionnaire, which measures disability index and pain scale,²⁵ can be valuable in providing the patients’ perspective on their own progress. A reduction in the health assessment questionnaire score over time indicates improvement. A similar self-administered health-related quality-of-life assessment tool is available for use with patients who have Crohn’s disease and other inflammatory bowel diseases.²⁶ As a result of the assessments by both the patient and the healthcare provider, the patient may need treatment manipulation related to drug dose or schedule.

**Patient Education**

The purpose for therapy, the treatment schedule, the potential side effects, and cost and reimbursement concerns are discussed with the patient before the initiation of therapy.¹ Possible adverse events associated with the biologic agents should be discussed along with recommendations for preventing, minimizing, or alleviating them. The nurse should assess what the patient has been told by others regarding his or her disease and possible treatment to avoid misunderstanding and confused expectations. It is important for the nurse and other healthcare providers to work together in order to give the patient accurate information. With all the new and ongoing therapies reported by the media in newspapers, on the Internet, and on national television, patients may have many questions about current therapies and new therapies that are not yet approved. It is the responsibility of the nurse to be aware of and have access to educational material and information in order to answer questions appropriately. Proper patient preparation through patient education and effective communication is instrumental in promoting quality of life and compliance with the prescribed therapy.

**Drug Preparation, Handling, and Administration**

Depending on the setting in which the therapy will be given, the nurse also may be responsible for drug preparation, handling, disposal, and administration. Biologic agents generally are a protein powder preparation, which must be reconstituted by closely following the procedure recommended by the manufacturer. The nurse must be cognizant of the drug dosage and the maximum concentration recommended for proper administration. The drug, before and after reconstitution, must be handled properly to avoid destabilization of the protein. It must not be shaken or subjected to heat because this can destroy some of the drug’s sensitive protein components.

Throughout the reconstitution and preparation, it is necessary to observe sterile technique, particularly if the drug is not reconstituted in the pharmacy. Currently, there are no Occupational Safety and Health Administration guidelines for the handling and disposal of biologic agents. Monoclonal antibodies by themselves are not mutagenic because they do not alter DNA. Thus they are not considered genotoxic substances.²⁷ However, monoclonal antibodies conjugated with chemotherapy drugs or radioactive substances should be handled in the same manner as chemotherapy or radiotherapy.

Biologic therapies usually are administered through either intravenous infusion or subcutaneous injection. If they are given intravenously, a venous access must be established, which may become a challenge to the nurse. Many of the patients requiring biologic therapy have been on high-dose steroids or other medications causing skin changes that can make vein assessment and access difficult. Patients with a history of diabetes may have thicker vein walls and sensitive or rough skin surfaces. Hypertension also may have thicker vein walls that may not constrict or dilate.

During the infusion, nurses must follow the manufacturer’s recommendations for rate, volume, duration, frequency, and need for a filter during the infusion as well as the type of administration set to be used. If the drug is to be administered subcutaneously, the injection will be either weekly or biweekly and may be administered by the nurse or self-administered by the patient. For self-administration, the patient must be educated in drug preparation, how to administer subcutaneous injections, the importance of site rotation, what to do for missed doses, and what to monitor or report during and after the injection. Compliance is extremely important for patients receiving self-administered subcutaneous injections to prevent worsening of the disease attributable to missed doses.

**Patient Monitoring**

During the infusion, many manufacturers recommend that the patient be monitored closely for any problems, including monitoring of vital signs before and after infusion or as frequently as every 15 to 30 minutes. As with any infused agents, the potential for infusion reactions exists with the intravenous delivery of many protein-
derived drugs and biologic agents. The types, severities, and manifestations of infusion reactions vary among biologic agents, but have some commonality. These include symptoms such as dizziness, headaches, and chest tightness, or signs such as rash or hypotension.

In a retrospective study of 165 consecutive patients with Crohn’s disease who received a total of 429 infliximab (Remicade, Centocor, Horsham, Pa) infusions during the period of July 1, 1998 through January 2001, Cheifetz et al28 described the severity of infusion reactions as mild, moderate, or severe and classified the type as acute (occurring within 1 to 2 hours of an infusion) or delayed (occurring up to 14 days after treatment). Treatment protocols were developed on the basis of the commonly reported symptoms associated with mild, moderate, or severe acute infusion reactions and the corresponding treatment and prophylaxis. Infusion reactions were commonly controlled by slowing or stopping the infusion and by treatment with acetaminophen, antihistamines, corticosteroids, and epinephrine.10,28

The nurse should be prepared to manage acute infusion reactions by having the knowledge, the treatment orders, and the equipment needed. Ideally, biologic agents should be infused separately via a side port or low Y-site of a primary administration set so that in the event of an acute infusion reaction, the infusion of the biologic agent can be stopped and intravenous fluids can be initiated immediately. Medications for treating infusion reactions can be administered intravenously through an injection port.

Although many infusion reactions occur during the first infusion, they also can develop during subsequent exposures.1 The use of routine prophylaxis protocols, such as the use of acetaminophen and antihistamines before the infusion, will allow patients to be retreated safely, but prophylaxis does not always prevent subsequent infusion reactions.28 Although Cheifetz et al28 stated that most acute infusion reactions are not immunoglobulin E (IgE)-mediated, the risks and benefits of retreating a patient after a severe infusion reaction should be carefully considered because biologic agents still will be perceived as “foreign” by the patient’s immune system.

Delayed infusion reactions are generally manifested as arthralgia, myalgia, malaise, fever, urticarial rash, fatigue, and gastrointestinal symptoms. Together, these clusters of constitutional signs and symptoms are called flu-like syndrome. The pathophysiology of the flu-like syndrome resulting from biologic infusion therapy is unclear and dependent on the type of biologic agent used. For patients receiving monoclonal antibodies, recent reports suggest that the flu-like syndrome probably is related to elimination of the circulating target antigen.1 Although the flu-like syndrome is not life threatening, it can contribute substantially to the debilitation already experienced by the patient, and can adversely affect quality of life. The management of flu-like syndromes includes the use of hydration and medications such as acetaminophen, antihistamines, and steroids as well as nursing comfort measures to decrease chills and fever.1

Because many biologic agents interact with the immune system, several have the potential to increase the risk or severity of infections. Common infections such as upper respiratory tract infections (sinusitis, pharyngitis, and bronchitis) or urinary tract infections do occur, but more severe infections may develop in some patients. For the patient receiving anti-TNF therapy, the risk of more serious infections such as tuberculosis, histoplasmosis, coccidiomycosis, and reactivation of hepatitis B is increased due to the suppression of TNFα when it normally would protect the patient. Patients should be instructed to avoid areas where they may be exposed to these infections. Their symptoms should be monitored, and they should immediately report to or see a doctor if any symptoms are present.

Reimbursement

The advent of biologic products represents both a clinical opportunity and a financial challenge for payers and health plans. With the expanded use of biologic products to treat familiar chronic conditions besides cancer, autoimmune diseases, and HIV/AIDS to date, few payers have figured out how to make such treatment available without “breaking the bank.”2 The vast majority of biologic therapies are administered as an outpatient service. Thus, reimbursement depends on whether the policy covers prescriptions or self-administered drugs.3 However, reimbursement for biologic therapies still is limited, restricted, or nonexistent, and the effect is felt directly by the patient seeking treatment and the healthcare providers. The nurse caring for the patient receiving biologic therapy has a responsibility to be informed about the reimbursement for a recommended therapy such as biologic infusion. Nurses can become knowledgeable about the process of working with insurers or payers by developing a working relationship with case managers or medical directors. They also can assist patients by educating them about financial responsibilities for specific aspects of the therapy, by discussing reimbursement issues related to the “off-label” use of drugs, and by providing them with pharmaceutical company-sponsored reimbursement services or patient assistance programs. Additionally, nurses may use cost-effective plans when making clinical decisions for equipment and treatment strategies, balancing cost and quality clinical care.

Nurses should exercise their power as professional healthcare providers to help patients by participating in professional organizations involved in influencing national reimbursement for healthcare services. The collective voice of many healthcare professionals can make a difference.
THE FUTURE OF BIOLOGICS

Approximately 300 new medications are in the biotechnology pipeline.\(^29\) Developing technologies, which have not yet resulted in an approved drug, include the use of antisense agents, which interfere with the production of proteins, and gene therapy. With the explosive growth in genomics, sequencing of the entire human genome, and new strides in medical informatics, the area of biologic therapies will continue to grow at a pace that healthcare providers will find challenging.

SUMMARY

Biologic therapies are a rapidly growing field in the treatment of many common and serious diseases. Initially used in cancer therapy, these drugs have found a role in the management of autoimmune diseases and other common disease states. For the nurse providing care for the patient receiving parenteral biologic therapy, an understanding of the basic principles of these agents, the specific administration protocols and monitoring parameters, and the management of potential adverse events is crucial to ensuring positive patient outcomes.

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