IgA is produced at mucosal surfaces and is the predominant antibody made in response to bacterial colonization of the intestine. It serves as a first-line barrier for the intestinal mucosa, providing protection against pathogens, toxins, and allergens. IgA-producing plasma cells are numerous in the intestine, and secretory IgA is important for preventing bacterial overgrowth in the intestinal tract. The presence of secretory IgA in the bronchial lumen effectively protects the respiratory tract from bacterial and viral infections. IgA is also the antibody isotype that is present in secretions as a dimer and in blood as a monomer.

Plasma cells that secrete IgA are found primarily in the lamina propria of mucosal surfaces, such as the bronchial and intestinal epithelium. Transport of the dimeric IgA into the lumen of the gut or bronchus depends on its binding to a polymeric immunoglobulin receptor (pIgR) that is present on the overlying epithelial cells (Figure 6.1). Once the receptor has transported the IgA into the gut lumen, the receptor undergoes proteolytic cleavage and leaves the small extracellular fragment (called the “J chain”) attached to the dimeric IgA. This J chain, referred to as secretory component, helps the IgA to bind to mucins in the secretions, and in the intestinal lumen protects against proteolytic digestion by enzymes. Normal levels of IgA are in the range of 20–150 mg/dL in canine serum, 17–125 mg/dL in saliva, and 80–540 mg/dL in fecal extract. There is also age-dependent variation in these levels of IgA, with lower levels being observed in puppies less than 6 months of age compared with adult dogs. A severe deficiency in IgA production can lead to a variety of mucosal system infections.

**TOPICS BEARING ON THIS CASE:**
- Mucosal immunity
- Immunoglobulin deficiency
- Genetic causes of immunodeficiency

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**Figure 6.1** IgA is secreted into the intestinal lumen and neutralization of pathogens occurs in the gut as shown. Secretory IgA is also important in the respiratory secretions, where it can neutralize pathogens that enter through the nasal cavity. (From Murphy K & Weaver C [2017] Janeway’s Immunobiology, 9th ed. Garland Science.)
THE CASE OF DUTCHESS: A PUPPY WHO HAS HAD A RECURRENT COUGH AND FEVER FOR MOST OF HER LIFE

SIGNALMENT/CASE HISTORY

Dutchess is a 1-year-old spayed female German Shepherd (Figure 6.2) with a history of recurrent bouts of bacterial pneumonia. Since the age of 2 months she has had a moist cough. She has also failed to gain weight as expected for her age and breed. She was first seen by the veterinarian at 4 months of age, presenting with severe cough and a fever. At that time radiographs were taken and she was diagnosed with pneumonia. Treatment with antibiotics for 2 weeks resulted in improvement both clinically and on the lung radiographs. However, at 8 and 11 months, respectively, Dutchess developed pneumonia again and was similarly treated, with good results. Her failure to gain weight has been a continual problem. There is no history of vomiting, but intermittent diarrhea has been reported. She was referred to a specialty practice for further evaluation.

PHYSICAL EXAMINATION

On presentation, Dutchess was thin, with a body score of 3 out of 9,1 but bright, alert, and responsive. She did not have signs of respiratory disease at the time of her presentation. She did have a strong odor and excessive exudate in the auditory canals. Upon further questioning, the owner confirmed that the dog frequently scratched at her ears.

DIFFERENTIAL DIAGNOSIS

The early onset of recurrent bacterial infection in the respiratory tract, the failure to gain weight, occasional diarrhea, the apparent otitis externa, and the dog’s breed suggested that an immunoglobulin deficiency might be involved, particularly IgA, since it is so important on mucosal surfaces. Other possible causes of recurrent pneumonia include aspiration pneumonia due to megaeosophagus, ciliary dyskinesia, neutrophil defects, and other anatomic defects. The failure to gain weight could have a variety of causes, including pancreatic insufficiency, food allergy, parasitic infestation, and inflammatory bowel disease.

DIAGNOSTIC TESTS AND RESULTS

Differential diagnoses were ruled out by thoracic and abdominal radiographs (no significant lesions), an esophagram (negative for megaeosophagus), a fecal flotation (negative for parasite ova), and a complete blood count (CBC) and chemistry panel. The neutrophil number and morphology were within the normal range. Serum trypsin-like immunoreactivity, cobalamine, and folate levels were also in the normal range. To rule out immunoglobulin deficiency, quantitative IgM, IgG, and IgA levels were determined by single radial immunodiffusion (SRID). The serum IgG level was elevated at 32 mg/mL (normal range, 10–20 mg/mL), the IgM level was slightly elevated at 2.5 mg/mL (normal range, 1–2 mg/mL), and the IgA level was undetectable. Further diagnostics were performed to determine whether secretory IgA was similarly affected; to this end a bronchoscopy and lung lavage were performed. Despite sample concentration by 100-fold, no IgA was detected in the bronchoalveolar lavage fluid (normal control dog lavage, similarly concentrated, had a mean secretory IgA concentration of 1.8 mg/mL).

1 According to the Purina body condition scoring system.
**DIAGNOSIS**

Dutchess was diagnosed with selective IgA deficiency based on the ruling out of neutrophil defects, parasitism, defects in other immunoglobulin isotypes, and megaesophagus. The undetectable serum IgA and bronchoalveolar lung fluid levels (even after concentration) were pivotal in confirming the diagnosis.

**TREATMENT**

The inability to make IgA is a genetic defect. Functional IgG, IgM, and cell-mediated immunity are sufficient to prevent the IgA deficiency from becoming life-threatening. Treatment is generally limited to symptomatic treatment of infections with appropriate supportive care as indicated. Thus Dutchess will continue to need antibiotic therapy periodically when she develops respiratory infection and/or infection of other mucosal surfaces.

**SELECTIVE IgA DEFICIENCY**

Selective IgA deficiency is the most common primary immune deficiency recognized in dogs. It is associated with infections on mucosal surfaces, including the lung, intestinal tract, genital tract, skin, and ear canals. IgA deficiency is also inherited and has been recognized as familial in the following pure-bred dog breeds: German Shepherd, Shar-Pei, Beagle, Airedale Terrier, Basset Hound, Weimaraner, and Irish Setter. The mode of inheritance has not been determined. However, a recent genome-wide association study of four breeds (German Shepherd, Golden Retriever, Labrador Retriever, and Shar-Pei) determined that there are 35 loci associated with low IgA concentrations. The authors of the study suggested that the defect is related to genes that control B-cell development.

The incidence of allergic dermatitis is sometimes increased in dogs that have selective IgA deficiency. It is not unusual to see a compensatory increase in serum levels of the other immunoglobulin isotypes, as was observed in this case for IgG. In German Shepherd dogs an association of aspergillosis infection with low IgA levels has also been observed.

**COMPARATIVE MEDICINE CONSIDERATIONS**

Primary immunodeficiency in both humans and dogs is characterized by the appearance of infections early in life because the defect is inherited and manifests itself upon loss of maternal antibody protection. Selective IgA deficiency is the most common immunodeficiency disorder in humans, affecting approximately 1 in 700 people of European descent. It can be inherited as either an autosomal dominant or an autosomal recessive trait. Some people are asymptomatic, and others develop a variety of respiratory, gastrointestinal, skin, mouth, and ear infections. Development of autoantibodies to IgA has been reported in some people, while others may spontaneously resolve the defect and begin to produce IgA.

**Questions**

1. Describe the points during the development of an IgA response when there might be an error that results in selective IgA deficiency.

2. How might the otitis externa seen in Dutchess be related to her IgA deficiency?

3. If Dutchess develops allergies to inhaled allergens, describe how her lack of IgA might contribute to this condition.
4. Do you think that an intranasal vaccine for “kennel cough” (*Bordetella bronchiseptica*/parainfluenza-3) would be effective in a dog with selective IgA deficiency? If not, would you expect a parenteral vaccine to work better?

**Further Reading**


