Over the past several decades, the availability and use of vaccines for companion animals have become more widespread, enabling the animals to live longer, healthier lives. Yet for unvaccinated dogs, infectious diseases such as canine infectious respiratory disease complex (CIRDC) still pose a significant threat. Clients’ first visit with a new dog or puppy provides the optimal time for veterinary nurses, working along with veterinarians, to thoroughly discuss the principles of immunization and the value of vaccines for their dog’s wellbeing.

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THE DISEASE
CIRDC (also known as infectious tracheobronchitis or kennel cough) is one of the most common respiratory diseases in dogs. It is a highly contagious, multifactorial disease characterized by acute or chronic inflammation of the upper respiratory system. Historically, the most common pathogens associated with CIRDC have been canine parainfluenza virus (CPIV), canine adenovirus type 2 (CAV-2), canine herpesvirus type 1 (CHV-1), canine influenza virus (CIV) subtypes H3N8 and H3N2, and Bordetella bronchiseptica (BOX 1). Dogs can be infected with one pathogen or concurrently with several. CIRDC is transmissible via the oronasal route through mucosal secretions, inhalation of airborne virus, direct contact, and contaminated fomites. Most CIRDC pathogens are moderately stable outside the host, surviving in the environment for no more than a few hours to several weeks. All CIRDC pathogens except for CAV-2 are readily susceptible to routinely used disinfectants; CAV-2 requires disinfection with 5% sodium hydrochloride diluted 1:32.

A diagnosis of CIRDC should be suspected for a dog with an acute onset of coughing and a history of exposure to other affected dogs. CIRDC spreads rapidly among susceptible dogs within close proximity (e.g., in places such as dog parks) or housed in close confinement (e.g., shelters and boarding kennels). Incubation periods for the various causative pathogens range from 2 to 10 days. Clinical signs can vary from mild or none to an acute-onset, dry, “honking” cough followed by gagging or retching and expectoration of mucus. Other signs may include sneezing, nasal and/or ocular discharge, and sometimes lower respiratory and/or systemic disease. Although CIRDC is typically a mild, self-limiting disease, it may progress to a fatal bronchopneumonia in puppies younger than 6 months of age and can develop into chronic bronchitis in debilitated adult dogs. Clinical signs and virus shedding typically last for 5 to 10 days; however, some pathogens, such as B bronchiseptica, Mycoplasma cynos, and canine distemper virus (CDV), can be shed for prolonged periods.

For ruling out other causes of coughing or determining the severity of disease, thoracic radiographs can be useful. Diagnostic testing for bacterial and viral pathogens and obtaining samples for bacterial culture can be performed, but results vary because many of the pathogens can be isolated from both healthy and diseased dogs and co-infections are common. Because of the self-limiting course of the disease, most dogs with CIRDC do not need antimicrobial drugs or hospitalization. However, if clinical signs persist and a fever develops past a 10-day observation period, further diagnostic workup and antimicrobial treatment are recommended.

BASIC IMMUNOLOGY
The adaptive immune system (also called acquired immune system) responds to microbial invasion by producing protective antibodies (humoral immunity) or protective cells (cell-mediated immunity) or both. Active immunity occurs when the body produces antibodies to antigens after either exposure via natural infection through the environment or injection with a noninfectious form of the antigen in a vaccine.
Modified live virus (MLV) vaccines contain live organisms and are more effective at triggering cell-mediated and humoral immune responses; however, live organism used for vaccines must be attenuated (made to be noninfective) so that the organism is stable and able to pass through the animal and replicate but is no longer pathogenic.8 With current manufacturing technology, reversion of an attenuated virus to a virulent, disease-producing state is exceptionally low to nonexistent.9 Use of MLV vaccines can cause adverse events, but such events are generally uncommon.

Inactivated vaccines are vaccines in which the target pathogen is “killed” and unable to replicate in the host; they often contain adjuvants and other excipient (inactive vehicle) proteins to promote an adequate immune response.10 The use of inactivated vaccines has been implicated in acute and delayed adverse reactions; compared with MLVs, inactivated vaccines produce weaker immune responses of shorter duration and may require more frequent boosters (generally annually).10

Recombinant vaccines are created through manipulation of the deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) of a pathogen to reduce pathogen virulence.10 The isolated genetic material is then recombined with the DNA or RNA of a nonpathogenic organism.10 After inoculation, the immunizing antigen is expressed by the recombinant DNA or RNA and subsequently induces an immune response.10

THE VACCINES
Vaccines for many of the CIRDC pathogens are available in the United States (BOX 2).3 A parenteral vaccine for the prevention of CIRDC often includes modified live CAV-2, modified live or recombinant CDV, modified live canine parvovirus (CPV), and sometimes leptospiral antigens,3,10 and may or may not include modified live CPIV.10 In older dogs with no circulating maternally derived antibodies, protective immunity is achieved 7 to 10 days after the second dose of the vaccine.10 Vaccination against CAV-2 reduces the signs of respiratory disease and also cross-protects against infectious canine hepatitis (ICH), which is caused by canine adenovirus type 1 (CAV-1).11 An intranasal product that contains CAV-2, CPIV, and B bronchiseptica can be used to decrease the severity of CIRDC but should not be used as the only vaccine to prevent ICH; for this purpose, the parenteral modified live CAV-2 should also be given.11 The trivalent CDV/CAV-2/CPV is a core vaccine; often CPIV is added. The associated acronyms for the various vaccines are DAPP (distemper, adenovirus types 1 and 2, parainfluenza, and parvovirus), DHLP (distemper, hepatitis, leptospirosis, parainfluenza, and parvovirus), and DHPP (distemper, hepatitis, parainfluenza, and parvovirus).

When to Administer
Because the agents of CIRDC are so infectious and highly contagious to other dogs, the trivalent core vaccine is recommended for dogs as young as 6 weeks of age; it is administered subcutaneously.10 The American Animal Hospital Association does not provide official guidelines as to specifically where, anatomically, the vaccine should be administered; the guidelines state only that the site should be accurately documented in the patient’s medical record.10

The goal is to vaccinate at the earliest possible opportunity to stimulate active immunity.7 Vaccinating puppies younger than 6 weeks of age will probably be ineffective due to circulating maternally derived antibodies.7 It is difficult to identify the precise time when a puppy loses this passive immunity (generally 6 to 12 weeks) and when the immune system is mature enough to actively respond to vaccination.7 Typically, the combination vaccine is administered to puppies as young as 6 weeks of age, in sequential doses at intervals of 2 to 4 weeks until the puppy is at least 16 weeks of age.10 Dogs that are approximately 16 weeks of age or older when presented for initial vaccination and dogs for which vaccination history is unknown should receive 2 doses of the combination vaccine 2 to 4 weeks after the initial dose.

BOX 2
CIRDC Pathogens for Which Vaccines Are Available in the United States3

Viral
- Canine parainfluenza virus (CPIV)
- Canine adenovirus type 2 (CAV-2)
- Canine distemper virus (CDV)
- Canine influenza virus (CIV) subtypes H3N8 and H3N2

Bacterial
- Bordetella bronchiseptica
apart. Within 1 year after the last dose of the initial vaccination series, dogs should receive a single dose of the combination vaccine, followed by boosters at intervals of 3 years (or longer). Vaccine administration by off-label routes is not recommended because it will not provide adequate immunization.

Who Can Administer
Each state must follow the Model Veterinary Practice Act (avma.org/sites/default/files/2019-11/model-veterinary-practice-act.pdf), a set of guidelines for credentialed veterinary personnel, created by the American Veterinary Medical Association. Under the Model Veterinary Practice Act, each state indicates which member of the team is allowed to administer vaccines and whether direct supervision by a veterinarian is required. All members of the veterinary healthcare team should be familiar with the Model Veterinary Practice Act as well as their state’s practice act.

Adverse Reactions
Although licensed vaccines are subjected to rigorous safety and quality control standards and are very safe, they are not always innocuous. Adverse reactions to vaccines can and do occur, albeit rarely. A vaccine adverse reaction refers to any undesirable or unintended effect associated with the administration of vaccines, including failure to achieve immunity.

During an initial vaccine appointment, clients should be informed of the potential for adverse reactions to the canine core trivalent vaccine, and this thorough discussion should be documented in the patient’s medical record. During future visits, a less extensive discussion is appropriate. Most adverse events are transient, lasting only a few days, and are not life-threatening. Mild side effects that do not require treatment can include lethargy, low fever, soreness at the injection site, and/or decreased appetite. Clients should be instructed to contact a veterinary healthcare member if clinical signs last longer than 2 or 3 days or their dog’s health progressively worsens. They should contact the veterinary office immediately if the dog experiences a severe allergic reaction (e.g., facial swelling, difficulty breathing, vomiting, diarrhea, urticaria, and/or seizures). Severe allergic reactions can lead to systemic anaphylaxis, in which the dog may experience cardiovascular collapse, respiratory arrest, and/or death if it does not receive immediate treatment.

Treatment can involve an injection of an antihistamine and/or steroid; more severe reactions may require epinephrine and intravenous fluids. Other adverse events can occur days to weeks (or more) after vaccination, and can include immune-mediated hemolytic anemia, immune-mediated thrombocytopenia, immunosuppression, hypertrophic osteodystrophy, and thyroiditis. For dogs that have experienced vaccine reactions, and depending on the type of previous reaction, the veterinarian has several options: administer an antihistamine injection before the next vaccination, use a different brand of vaccine, or extend the time between immunizations. Alternatively, the client and veterinarian may elect to forgo vaccination if the dog has adequate antibody titer levels, which can be measured to determine whether they are adequate to provide protective immunity against the disease.

Regardless of whether an association between adverse events and vaccination is recognized or only suspected, adverse events should be reported to the vaccine manufacturer and/or local regulatory authority. Veterinarians are encouraged to report adverse events to the vaccine manufacturer(s), who are required to maintain files of any reported vaccine adverse event. After reporting a known or suspected vaccine adverse event to the manufacturer(s), veterinarians practicing within the United States may contact the U.S. Department of Agriculture Animal Plant and Health Inspection Service Center for Veterinary Biologics and veterinarians practicing in Canada may contact the Canadian Food Inspection Agency’s Canadian Centre for Veterinary Biologics. The reported information provides a baseline against which future reports can be compared and may lead to detection of previously unrecognized reactions or increases in known reactions, identification of risk factors associated with reactions, and identification of vaccine lots associated with unusual events or higher numbers of adverse events; reported information can also stimulate clinical, epidemiologic, or laboratory studies.

The trivalent CDV/CAV-2/CPV is a core vaccine; often CPIV is added.
ANTIBODY TITERS
Antibody titers can be useful for assessing the immune status of a puppy after completion of the initial series (wait at least 2 weeks after the last dose of the initial canine core trivalent vaccine series), assessing whether an adult dog has maintained an antibody titer since previous vaccination, determining whether an adult dog is overdue for a booster or assessing the immune status of dogs with an undocumented vaccination history. Titer testing can also help assess the immune status of shelter-housed dogs, of dogs before breeding, or of dogs of advanced age or with unique health problems; it can also be used to identify genetic nonresponders (a limited number of dogs that do not respond to vaccination by producing CPV antibodies).

Antibody titers measured in commercial laboratories and in-clinic antibody test kits can use serum or plasma samples depending on the test format used. Results can be recorded as positive or negative, yes or no, a dilution (e.g., 1:80, 1:256), or a titer (e.g., 80, 256) and can include a brief description of the result’s significance (BOX 3). Infection and serologic challenge studies have indicated that after the initial vaccination series with the core trivalent MLV vaccine has been completed, duration of immunity is a minimum of 3 years but can be as long as 9 years. When antibody testing is used, it should be performed at least as often as the booster vaccination interval (i.e., every 3 years).

CLIENT COMMUNICATION
Some clients may have a limited understanding of the value of vaccines; they can be misled by reports of vaccine complications and antivaccination sentiments spread on the internet, on social media, or by word of mouth. As veterinary nurses, we are at the forefront of providing client education and can identify clients who will benefit from more discussion of the value of vaccinating their pet against a preventable disease.

Client Communication Points
- Immunization helps animals live longer, healthier lives and improves their quality of life because immunization can prevent or mitigate disease that would otherwise be very costly to treat.
- CIRDC is found worldwide, and routine vaccination of dogs that are at increased exposure risk is advised.
- Vaccination is not a guarantee that the dog will not contract CIRDC because co-infections may be present. Vaccination does, however, reduce the severity of clinical signs and virus shedding, and contribute to herd immunity among unvaccinated dogs.
- Although vaccination carries risk for potential adverse reactions, the risks should be weighed against the benefits of protection from a preventable disease.

At subsequent vaccination appointments, briefly reminding clients that they are providing the best care to their dog by vaccinating and asking if they have any questions are useful, as is documenting all discussions in the patient’s medical record.

SUMMARY
During an initial visit with clients, veterinary nurses, working along with veterinarians, can help determine whether CIRDC presents a risk to the patient and whether administering the canine core trivalent vaccine

BOX 3
Interpretation of Antibody Titer Test Results (Applies to CDV, CPV, and CAV Types 1 and 2 Antibodies Only)
- Positive: The patient has protective levels of antibody against the virus; results correlate with protection from infection if exposed.
- Negative: The patient does not have protective levels of circulating antibody; results do not always correlate with susceptibility to infection. (Note: circulating antibodies may fall below detectable levels in the absence of exposure, including revaccination. For adult dogs that have been shown to have had protective titers in the past, exposure to the pathogenic virus is likely to induce a humoral immunity memory response.)
- Negative or weak: Further vaccination may help re-establish humoral response above the immunity threshold. (Note: a previous positive result indicates that immune memory exists and that if exposed to the virus, the patient is expected to mount a rapid, protective response regardless of whether detectable levels of antibody are present at the time of the exposure.)
- False-negative: This uncommon result can be associated with low test sensitivity, insufficient time after vaccination for a detectable antibody response to develop, procedural errors, etc.

Infection and serologic challenge studies have indicated that after the initial vaccination series with the core trivalent MLV vaccine has been completed, duration of immunity is a minimum of 3 years but can be as long as 9 years. When antibody testing is used, it should be performed at least as often as the booster vaccination interval (i.e., every 3 years).
would help prevent the patient from contracting the disease. The various antigens in the MLV vaccine should be discussed, and it should be stressed that vaccinating against one pathogen does not eliminate the chances of their dog contracting other co-infections. Clients should be advised that if any adverse clinical signs develop within a few days to weeks after vaccination, it is important to inform their veterinarian so it can be determined whether those clinical signs were caused by the vaccine. Veterinarians may choose to measure titers rather than administer booster vaccines for several reasons: the patient is geriatric, the patient has a history of vaccine reactions, the patient has received treatment for and recovered from an immune-mediated disorder, to manage infection outbreaks, or at the request of clients concerned with overvaccination. Veterinary nurses play a key role in helping clients separate facts from fiction in regard to CIRDC as well as other vaccine-preventable diseases.

References