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Strides in Biomedical Research

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In Nolan's lab, 90% of cases of Toxocara canis, roundworm, have been found to occur in puppies less than one year old, and virtually all cases where disease has resulted have been in puppies. Adult worms are found in the small intestine. In puppies less than six weeks old, larvae penetrate the intestinal wall into a blood vessel. They travel via the blood stream to the lungs. They are coughed up and then swallowed, to return to the small intestine to mature. Here, they hatch from the eggs and migrate to the small intestine to mature, or penetrate the placenta and settle in the puppies' livers or migrate to the mammary glands, where they are transmitted to sucking puppies.

Symptoms in puppies are coughing, vomiting worms, diarrhea and malnourishment that sometimes causes a potbelly appearance. Treatment, which prevents symptoms, should occur in the bitch prior to parturition. Puppies should be treated within the prepatent period, which is the time from initial infection in offspring to the time at which the larvae have matured and are reproducing. This is normally 4-5 weeks after the puppies are born.

Though quite resilient, Toxocara eggs are subject to desiccation. Dr. Nolan recommended keeping the area dry and clean. These eggs are found in the feces in approximately two weeks, so the feces should be removed immediately. Concrete runs are very effective in preventing the eggs from washing into the ground and are easy to clean. Hookworm, Uncinostoma canis, ranked second highest in frequency at VHUP last year. Normally transmitted when puppies ingest infectious soil, they hatch from the eggs and migrate throughout the body. In adult dogs, they either arrest in the tissues or go back to the small intestine. While females, the larvae become active late in pregnancy, and migrate to the mammary glands or, less often, the placenta.

Adult worms use their large, toothed mouths to feed on the intestinal lining. These eggs can result in bloody diarrhea and weight loss. However, symptoms only occur when many worms are present.

The hardy whipworm eggs can survive in the environment for as long as two years, so it is important to remove the feces promptly and keep the dog's area dry. The prepatent period is three months, and drugs can be administered four times per year as a prophylactic if there is no way to prevent re-infection because of a severely contaminated environment. Some drugs are effective when the worms are still in their larval stages.

Dipylidium caninum, the common tapeworm, uses suckers to attach itself to the small intestine lining, but it rarely causes tissue damage. Its segmented body, which appears ribbon-like, is comprised of proglottids, motile sections of reproductive organs which are full of eggs. Upon hatching, the millimeter-long proglottids break off and pass out with the feces. They quickly crawl out of the feces and rupture, releasing their eggs, which are eaten by larval fleas. Once mature, an infected flea jumps on the dog, and the dog, in being back, ingests the larval tapeworm which is within the flea.

No disease symptoms are displayed in an infected dog. The only signs are minor intestinal disturbances, and little weight is gained. In puppies, the dog ingests cysts from the feces. The cysts hatch in the small intestine, where they invade the lining of the intestine. Most veterinarians won't treat adult dogs because their immunity to coccidia is more effective than a drug.

Usually, no symptoms are evident in puppies, although minor gastrointestinal bleeding and diarrhea sometimes occur. Within two weeks after infection, the puppy's immune system is usually able to purge itself of coccidia. The cysts are very susceptible to desiccation, so it is important to keep the dog's area dry and remove the feces quickly.

Guardia are transmitted by ingestion of waterborne cysts. They hatch and replicate in the small intestine, on which they form a tight layer. They may cause malabsorption in the dog, because food cannot filter through the wall of Guardia to reach the intestine. Fats, least likely to be absorbed in this scenario, are usually washed out, causing the stool to appear full of mucus. Malabsorption occurs only in extreme circumstances, because older dogs usually develop cysts by eating infected fleas. It normally doesn't even cause much damage in puppies, who usually contract it from their mothers, although chronic diarrhea may occur. The most important control measure is to keep the dog's area dry and prevent the dog from drinking from streams and puddles. Also, timely feces removal is crucial.

Worming should be done when puppies are about one week old, but Dr. Nolan advises caution against overwarming, which can cause other health problems.

The ectoparasites Dr. Nolan discussed were mites, fleas, ticks, and lice. Mites - those that live in the skin and cause mange and wet lesions, and those that live in the fur and frequent the skin only to eat. Mites complete their life cycle on the dog. For prevention and treatment of mites, Dr. Nolan suggested dipping the dog, and also keeping its area clean.

Fleas lay their eggs on the dog or in the environment. The eggs are very resistant to chemicals, so it is necessary to spray with a chemical that will instigate the attack period, anywhere from two days to two weeks, or to spray weekly. Vacuuming is somewhat effective. Adult fleas can jump a foot or more in one jump. If no food is available, so vacant homes were infested should be treated if they are going to be inhabited in the same year.

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Cardiovascular Disease
Renowned open-heart surgery pioneer Dr. Michael DeBakey describes the link between animal research and heart disease in these terms: "Every major advance we've had in cardiovascular research from surgery to the heart-lung machine to coronary bypass was a result of research in which it was necessary to use animals."

Dr. DeBakey, chairman of the department of surgery and director of The DeBakey Heart Center at Baylor College of Medicine, said neither the heart-lung machine, used for open-heart surgery, nor angioplasty, which is used to open and widen clogged arteries, would exist today without animal research. The heart-lung machine required over 20 years of experimental work before it was perfected for use in human beings, Dr. DeBakey said. "Even with today's technology, I would not have used a computer to develop a new, high pressure pump that made open-heart surgery possible, or the artificial heart that restored life to previously dead patients with heart failure. Nor could we have attempted the first successful coronary artery bypass or implanted the first temporary mechanical heart, with which we saved a patient's life two decades ago. Think of all the infants born with congenital heart failure who have died. Now, 90 percent of all congenital heart cases are cured."

Most cardiovascular treatments were obtained through research on a variety of animals, including rodents, dogs, cats, rabbits, and sheep. Scientists have used dogs to develop the cardiac pacemaker and surgical techniques used in coronary artery bypass surgery and heart transplantation. Rats are the most important model for researchers studying hypertension, because certain types of rats develop hypertension spontaneously. Research with rabbits has pointed to the relationship between genetics and blood pressure, and aided researchers in the study of stress-induced cardiomyopathy and atherosclerosis.

Dr. DeBakey emphasized that current research in a permanent heart-lung machine works for calves and pigs because the animals have cardiac systems that resemble those in humans. "The truth is that there are no satisfactory in-sentient models at present for certain cardiovascular research and testing," Dr. DeBakey said. "A computer is not a living system and could not alone have produced the dramatic medical advances of the past decades."

Cancer
In the early 1900s, few cancer patients had any hope of long-term survival. The disease is still a major killer, with an estimated 1,375,000 people a day dying of cancer in the United States. But due to treatments developed through animal research and testing, about 44% of patients are expected to live four out of 10 cancer patients, will be alive five years after diagnosis. A decade ago many patients with cancers such as Hodgkin's disease, Ewing's sarcoma (a form of bone cancer), and lymphocytic leukemia had a poor prognosis. Today, many of those patients are cured.

Animal research led to the discoveries of most cancer treatments. Most of the first studies on chemotherapy were done with tumors in mice. Rats have played an important role in the treatment of breast cancer, due to similarities between human breast cancer and rodent mammary carcinoma. Rats, with the help of chemicals that are common to both, have helped scientists identify the types of tumors and which treatments work best. Scientists have tested on animals new therapies, such as interferon, interleukin-2 and other biologic response modifiers, which researchers hope will enhance the body's own disease-fighting systems.

According to Dr. Heiner Fiebig, who conducted research for the National Cancer Institute (NCI), animal models play a major role in the testing of new drugs and compounds to treat cancer. "Between 1955 and the mid-1970s, 40 promising compounds were identified using animal models," he said. "Animals have also helped us come to the use of chemotherapy." Animal research helped NCI make significant strides in the areas of leukemia, lymphoma and testicular cancer, Dr. Fiebig noted.

Diabetes
Researchers Sir Frederick Banting and Charles Best used dogs in their experiments that eventually identified insulin as an important hormone in carbohydrate metabolism. Their work led to the discovery of insulin for diabetes in 1922.

Research with rodents is helping scientists understand the causes of diabetes, and in particular, insulin-dependent (juvenile) diabetes. A group of Stanford University Medical Center made significant strides in 1988 when it engineered an antibody that causes the destruction of insulin-producing cells of mice. A year-long study demonstrated that a special monoclonal antibody could block the destructive action of a T-cell lymphocyte that is believed to help trigger diabetes. Researchers continue to study the role of diabetic studies of diabetes, including work on pancreatic transplants, and ocular and vascular complications associated with the disease. However, the number of dogs used in diabetes research is declining as the knowledge gained through earlier work allows researchers to use their techniques and models.

Alzheimer's Disease
Current research on Alzheimer's disease, a degenerative brain disorder affecting about 2.5 million Americans, has focused on both discovering its causes and potential treatments. Estimates show that one in 20 people over the age 65 and one in 5 people over age 85 has the disease.

Research has produced an important characteristic of the disease, which is the abundance of neurotic plaques, or clumps of nerve endings, in the cerebral cortex. A small number of elderly dogs have been studied because they often exhibit these neurotic plaques.

Researchers in California and Massachusetts have done studies with rats that may help avoid memory loss, a major effect of Alzheimer's. Researchers discovered that it is possible to keep memory-related cells in the brain from dying by injecting the cells with nerve growth factor.

Research for the Benefit of Animals
Animals have also benefited from medical breakthroughs. Veterinarians use many techniques and treatments to save animals, including orthopedic surgery, pacemakers, transplants and radiation therapy.

Most drugs, diagnostic tests and surgical techniques used in veterinary medicine today come directly from research or from human medical or surgical practice that was originally based on animal research. "Dr. Michael DeBakey of Tufts University School of Veterinary Medicine. "The discovery process is often worked out on animals with the specific intent of being used on people, and if it is successful, veterinarians often find it economically feasible to use the same techniques on animals. Hip replacements are a good example. Over 100,000 hip replacements are done in the U.S. each year, due to research first done on dogs. Now this technique is being used on pets."

Animal research has led to preventive treatments, including medications to kill parasites, such as heartworms and hookworms that can infect pets, and vaccines to avoid rabies, feline leukemia, distemper and hepatitis. Research led to the development of a vaccine against parvovirus, a new disease that killed thousands of young dogs in the 1970s.

Approximately half of all pets over the age of 10 died from leukemia or brain, skin or breast cancer. However, new surgical techniques, radiation therapy, chemotherapy, cryosurgery and hyperthermia have helped many animals live longer.

Kidney failure, another cause of death in dogs and cats, is treatable with new micro-surgical techniques and organ transplants using the latest immunosuppressive drugs to prevent rejection.

Domestic animals, such as horses, cattle, sheep, hogs and chickens also benefit from research on breeding and nutrition. New vaccines helped protect against influenza and encephalomyelitis in horses, rinderpest in cattle, and gastroenteritis in pigs.

Biomedical research has also had a lasting effect on wildlife. Research on reproduction, nutrition, toxicology and medicine has helped save endangered species, such as the bald eagle, alligator, red wolf and Florida panther.

Significant Medical Advances Using Animal Models
Animals have played an integral role in the discovery of medical cures, treatments and vaccines. Since 1901, 57 Nobel Prizes in Physiology and Medicine have been awarded for research done with animals. The following is a sampling of some of the major medical breakthroughs that have been made using animal models.

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(Sources: JAMA, Perspectives in Biology & Medicine, Newsweek)

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