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Identification of Gene Defect Leads to Cystinuria Test

Avian Influenza Vaccination

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Avian Influenza (AI) is a viral respiratory disease of many species of domestic and wild birds. Historically, in commercial poultry flocks, turkeys are most commonly affected due to the practice of range rearing and comingling with wild birds. While only six outbreaks of AI have occurred in commercial chickens in the United States prior to the current 1997 outbreak, when they occur they can be devastating. The 1983-1984 AI outbreak in Pennsylvania resulted in the depopulation of 17 million birds with a cost to the federal government of $60 million.

The recent AI outbreak in Pennsylvania began in December 1996 when a live bird market dealer's flock in Lebanon County was found to be positive for nonpathogenic AI (H7N2). Subsequent to that, a flock of commercial layers in the same vicinity was diagnosed with nonpathogenic AI (H7N2). Then in April 1997, a flock of commercial layers was diagnosed with AI in Lancaster County. A quarantine was placed on poultry facilities in a five mile radius of the index flock in Lancaster County. To date, a total of 19 commercial layer flocks, two commercial layer pullet flocks, and a commercial meat turkey flock have been diagnosed with non-pathogenic AI (H7N2) viral infection.

Control of avian influenza includes depopulation, quarantine and vaccination. Research and field experience (Mexico and the United States) has shown that vaccination for avian influenza can decrease the clinical signs of avian influenza, decrease the viral shed from known infected birds and therefore decrease the potential transmission of the disease to surrounding flocks.

Avian influenza vaccination has not been approved for use in the United States in chickens unless the virus is highly pathogenic. The use of vaccine in Pennsylvania during the 1997 avian influenza outbreak was denied because the virus was classified as nonpathogenic. Currently, the only available vaccine for use in commercial poultry is a killed product. Additional vaccines under development are the fowl pox viral vectored vaccine and sub-unit protein vaccines.

Major advances in our understanding of vaccines have occurred due to basic molecular studies, and are currently being applied to the improvement of vaccines against many human diseases. One of the most exciting advances in the development of new vaccines has been the discovery that injection of DNA-encoding viral antigens that are known to be protective — can induce protection that is equivalent to, or superior to, that obtained following immunization with killed whole organisms, purified proteins, or subunit vaccines.

There are several notable advantages to using DNA vaccines over conventional protein antigens, some of which include: 1) the ease of manufacturing the vaccine; 2) the stability of the vaccine; 3) providing long-term antigen expression that continuously stimulates the immune response; 4) the lack of a requirement for a traditional adjuvant; 5) the ability of DNA vaccines to stimulate both strong antibody responses, T cell responses and the generation of cytotoxic T cells; and 6) the ability to co-deliver the vaccine with plasmid-DNA-encoding cytokines to enhance the immune response. Of particular interest has been the inclusion of cytokines, one of the most important of which is interleukin-12 (IL-12) which, when administered in a vaccine, dramatically improves the efficacy. Unfortunately, these advances have been slow to be applied to food animals, where they could make a major impact in the agricultural industry. Our research will focus on the development of a molecularly defined avian influenza vaccine that incorporates IL-12, and compare the efficacy of such a vaccine with a commercially available killed vaccine. Development of a DNA vaccine will provide the basic information and tools necessary to offer the poultry industry of Pennsylvania the most effective vaccine available against avian influenza.

Identification of gene defect leads to cystinuria test

The gene defect for cystinuria in Newfoundlands has been identified by Dr. Paula Henthorn, associate professor of medical genetics, and colleagues in the Section of Medical Genetics at Penn's School of Veterinary Medicine. The team, which includes Drs. Urs Giger and Jung Long Lin, has developed a test to identify carriers, affected, and normal dogs for the disease in Newfoundlands. Cystinuria, which also affects many other breeds, is an autosomal recessive trait.

The molecular test is the sixth such test the Penn group has developed. Newfoundland breeders can now screen their breeding stock for this disease to reduce the number of affected animals. If all breeding animals are screened, the disease can be eliminated from the Newfoundland population in the relatively short period of one to two generations.

Cystinuria is caused by excessive urinary excretion of cystine and other amino acids due to a defective transport system for these substances in the kidney. It leads to crystal and eventual stone (bladder and kidney stones) formation in the urinary tract and is particularly problematic in male dogs.

Dr. Henthorn and her colleagues are now working to identify the gene defects causing cystinuria in other affected breeds so that additional tests can be developed. Unfortunately, in genetic diseases, the gene defect for a disease and its location vary from breed to breed, requiring much painstaking research to develop tests for each breed.

Dr. Henthorn's work on cystinuria is supported by grants from the National Institutes of Health and the AKC Canine Health Foundation. The test for cystinuria in Newfoundlands is one of the many tests for canine and feline genetic diseases available through the Josephine Deubler Genetic Disease Testing Laboratory in the Section of Medical Genetics, School of Veterinary Medicine, University of Pennsylvania. For additional information, contact Dr. Urs Giger at 215-898-3375(phone), 215-573-2162 (fax) or via e-mail at<penngen@vet.upenn.edu>.