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Pathobiology: A Multidisciplinary Teaching and Research Group

Bellwether

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Pathobiology— a multidisciplinary teaching and research group

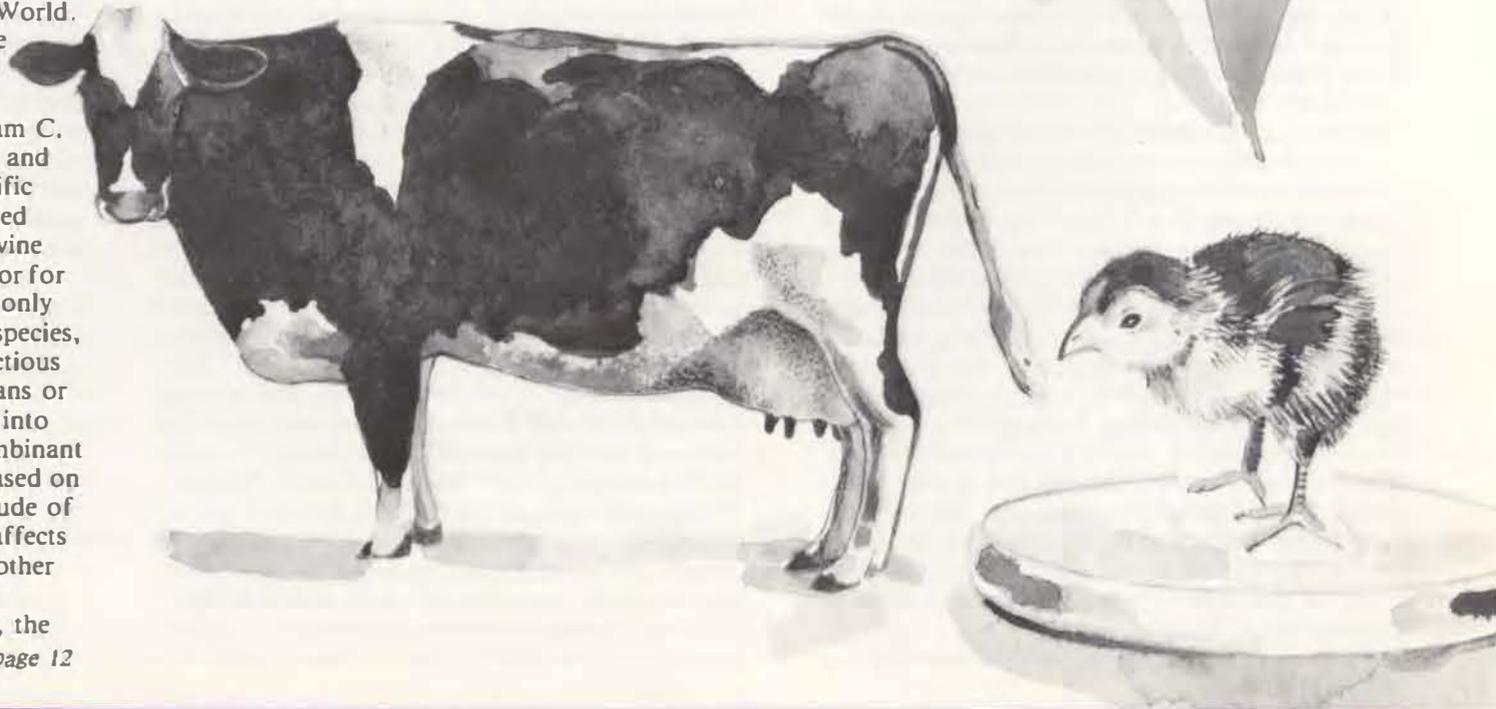
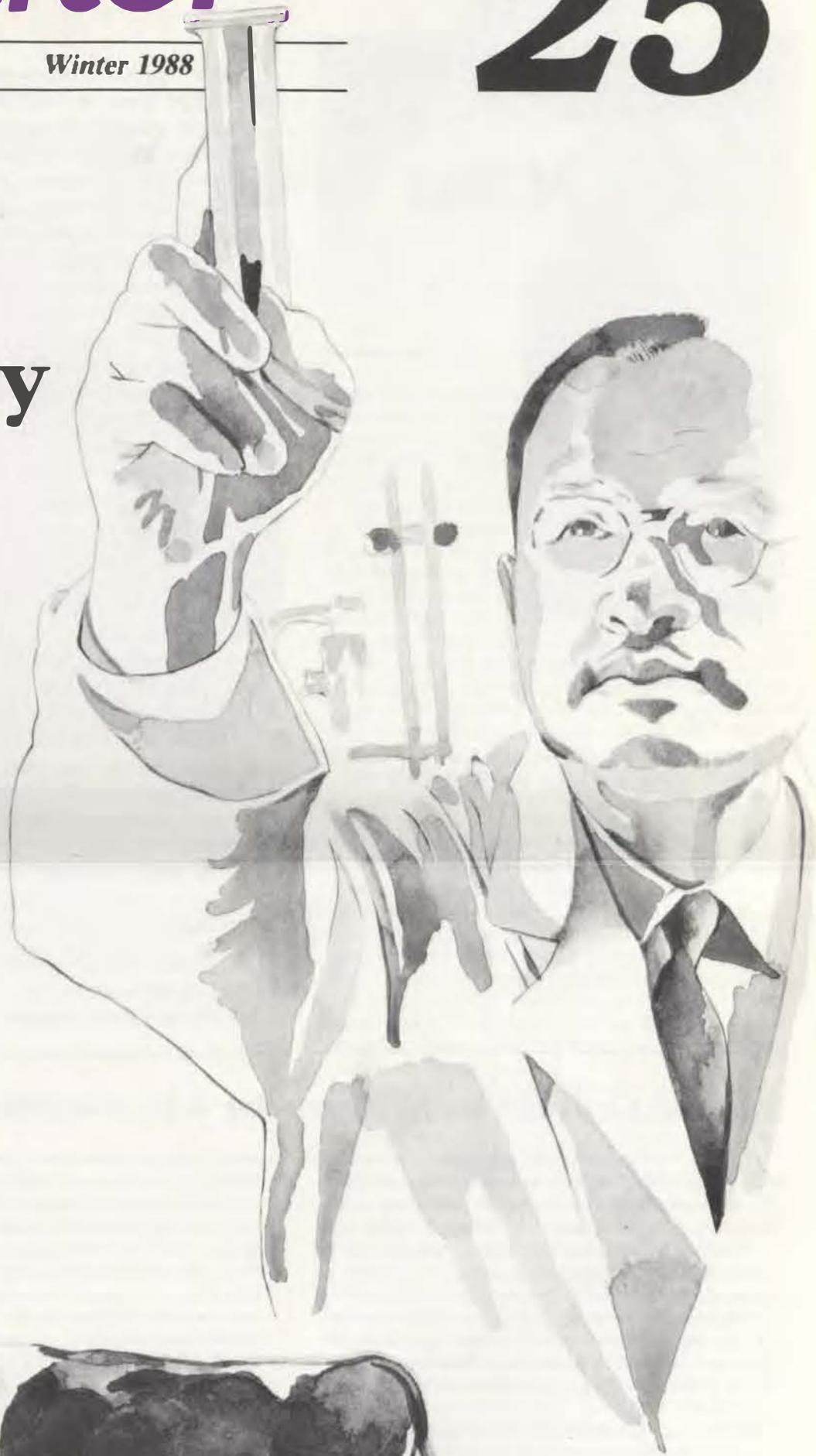
The department of pathobiology, one of four major departments in the School of Veterinary Medicine, includes the laboratories of microbiology and immunology, pathology, parasitology, large animal pathology, and avian medicine and pathology. For the past decade, the department has been chaired by Dr. Wilfried T. Weber, professor of pathology. As elsewhere in the School, significant and important changes have occurred in the department during this period. As examples, one can point to a more than six-fold increase in research funding since 1978, an increase of faculty participation in funded research from 38 percent to more than 90 percent, important changes in the teaching program, a significant increase in diagnostic capabilities, and substantial improvements and upgrading of equipment and research space. In the latter category one of the more notable additions is the construction of a new state-of-the-art, multi-user laboratory of more than 2,000 ft², which will be most useful in attempts to recruit additional faculty.

At present, a search for a new chairman is underway, as Dr. Weber will step down from the chairmanship at the end of the academic year to again devote his full time to scholarly activities. Studies by the multi-disciplinary faculty range from the development of recombinant vaccines to eradication methods of parasites in the Third World. The above mentioned laboratories within the department all are in the forefront of research within their respective fields.

Recently Drs. Leonard J. Bello and William C. Lawrence of the laboratory of microbiology and immunology developed the first species-specific recombinant vaccine. By utilizing sophisticated biotechnology, they were able to modify Bovine Herpes-virus I (BHV1) and employ it as a vector for genes of other pathogens. This virus affects only cattle and possibly a few other closely related species, and it causes bovine rhinotracheitis, an infectious respiratory disease. It has no effect on humans or other non-ruminant species, thus a spillover into other populations cannot occur. "Other recombinant vaccines utilizing a viral vector have been based on the vaccinia virus which may affect a multitude of species," explained Dr. Lawrence. "BHV1 affects only bovines and poses little, if any danger to other species."

When a virus infects an animal or human, the

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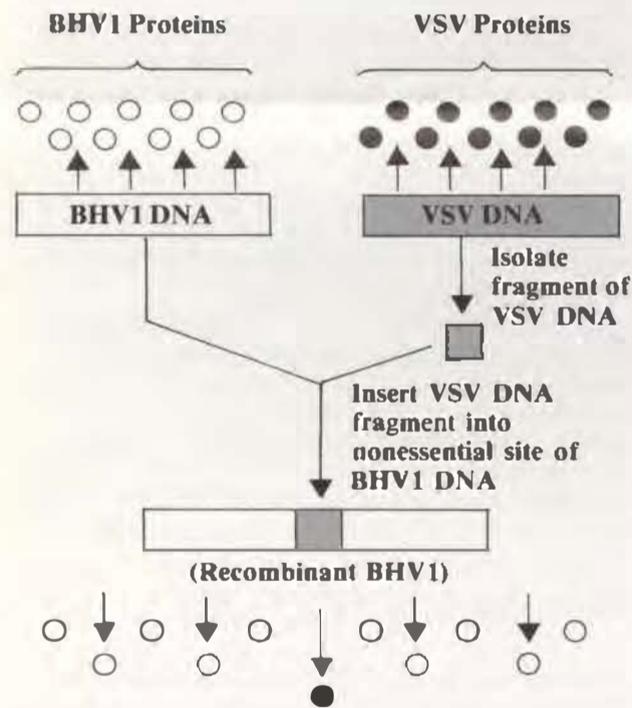


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immune system produces antibodies in reaction to proteins contained in the virus. The antibodies then attack the virus and render it ineffective. Vaccination against a disease stimulates the immune system into producing antibodies against specific viruses, creating protection against the disease and priming the immune system for future infections.

Recombinant technology allows for the production of "tailored" viruses. BHV1 has been studied extensively and an attenuated vaccine against it has been in use for a long time. "By using recombinant techniques the BHV1 strain can be made even safer," said Dr. Lawrence. "We studied the virus, mapped its genes and determined the sites of nonessential genes which could serve as locations for the insertion of genetic material from other pathogens." The pathogen selected was vesicular stomatitis virus which causes a disease prevalent in cattle in Central and South America. The gene for a protein of this virus had been cloned and was available.

To produce the recombinant vaccine, the researchers inserted the cloned vesicular stomatitis gene into a nonessential site in the BHV1 virus. "You don't just put a gene into place," said Dr. Bello. "For it to function within the host virus, a promoter gene has to be attached. We had to identify the promoter and attach it to the gene; this package is called an expression cassette. Once it is inserted into



BHV1 = Bovine herpesvirus 1
VSV = Vesicular stomatitis virus

the virus, we have a recombinant." This is then purified and cloned. The researchers tested the recombinant and found that the inserted gene was being expressed. "Adding new material to a virus is tricky because the addition should not render the virus ineffective, it still must function normally."

"We can add genes from other pathogens," said Dr. Lawrence. "In essence recombinant technology will allow us to create a polyvalent vaccine, one which combats more than one disease. We have applied for a patent." Drs. Bello and Lawrence feel that recombinant vaccines may soon be seen in veterinary clinics. Such preparations are less expensive to produce and will provide an efficient way of delivering vaccinations. They pointed out that other species-specific vector viruses have to be identified to provide safe vaccines for humans and other species.



Bovine herpesvirus 1

Dr. Charles Benson, head of the laboratory of microbiology and immunology, in collaboration with Dr. Robert Eckroade, is studying *Salmonella* strains, in particular, *Salmonella enteritidis*, an organism recently identified in eggs. He hopes that a vaccine can be developed, preventing infection in egg-laying chickens. Dr. Benson is also developing a rapid diagnostic test to facilitate diagnosis of Potomac Horse Fever and a more rapid procedure to determine antibody titers to *Ehrlichia risticii*, the organism causing the disease. Together with Dr. Robert Eckroade, head of the laboratory of avian medicine and pathology, and Dr. Linda Keller, Dr. Benson is developing a procedure which will provide the ability to distinguish vaccine strains from field strains of laryngotracheitis, a viral disease of poultry.

Dr. Roselyn Eisenberg, another researcher in the laboratory, is focusing on herpes simplex virus, also with the goal of developing a vaccine, in addition to studies of gene regulation. Much of this work is basic science, laying the groundwork for future treatment of diseases.

The focus of the laboratory for parasitology is not so much on parasites affecting domestic animals in the United States, but on parasites and their effects in third world countries. The laboratory is the center for parasitologic studies in the University. It has acquired an international reputation from its studies in the field of immunoparasitology, research which focuses on the interactions between host and parasite, and particularly on the antigens parasites produce at various stages of their life cycle. The

Stubbs Laboratory Dedicated

The Stubbs Laboratory was dedicated on September 22, 1988 at the New Bolton Center campus. The building, funded by the Commonwealth of Pennsylvania, is designed as a facility where researchers can safely deal with and manage research with infectious organisms, primarily of poultry. A limited access building, it has an impressive array of safeguards such as air-locks, shower areas, one-way air flow and two air-handling systems equipped with special filters for the complete removal of all microorganisms, including viruses. A special pathological incinerator and a chemical treatment retention tank for effluent waste are also part of the equipment.

The building was named in honor of Evan L. Stubbs V.M.D., Class of 1911, "avian pathologist, gentleman, veterinarian." Dr. Stubbs, the oldest living graduate of the Penn's Veterinary School and Emeritus Professor of Pathology, served on the faculty from 1927 to 1960. During his long career, he made many major contributions to the field of avian medicine, particularly through his studies on avian

mechanism controlling host immunologic responses to parasite infections are also under investigation. Much of the work has important public health implications, for in many instances animals act as reservoirs for human parasite infection.

Among the parasitic diseases studied are leishmaniasis, caused by protozoa, onchocerciasis, Lyme disease, trichinosis, hookworm, and gastrointestinal nematodes in sheep and cattle.

Like the laboratory of microbiology and immunology, the laboratory of pathology has facilities at the Philadelphia campus and at New Bolton Center. Research in this laboratory ranges from studies on the molecular level to classical histopathology. The laboratory now operates the largest biopsy service of any veterinary school in the United States with more than 18,000 animal tissue samples being analyzed annually. Dr. Helen Acland, head of large animal pathology, is working on a variety of projects, including ovine progressive pneumonia.

Dr. Samuel Chacko, professor of pathology, has received worldwide recognition for his studies of the biochemical mechanisms which regulate blood pressure through arterial wall contraction and relaxation in normal and hypertensive animals.

Genetic diseases and their treatment through gene therapy are the focus of Dr. Mark Haskins and Dr. John Wolf. Other research in the pathology laboratory include studies on lymphocyte biology and development of the immune system, investigation of the development of skeletal muscle, the influence of the nervous system on muscle, studies of diseases like tuberculosis, rabies, Potomac Horse Fever, and avian influenza, to name a few.

Aside from research, the responsibilities of the faculty in pathobiology includes teaching and providing diagnostic services to the two hospitals and to practitioners. Faculty teach core courses and offer laboratory experience in pathology, microbiology, immunology, and parasitology to provide the students with the scientific background so necessary in today's veterinary practice.

The research funding in pathobiology comes from many sources, among them the NIH, World Health Organization, National Science Foundation, USDA, Pennsylvania Department of Agriculture, and industry.

influenza and avian tumors.

Infectious diseases of poultry will be studied in this new laboratory, and the School has assembled an avian infectious disease research team. The Stubbs Laboratory is part of the Cooperative Poultry Diagnostic Laboratory at New Bolton Center and it will greatly enhance the School's ability to serve agriculture in the Commonwealth.

