SPRING 2010

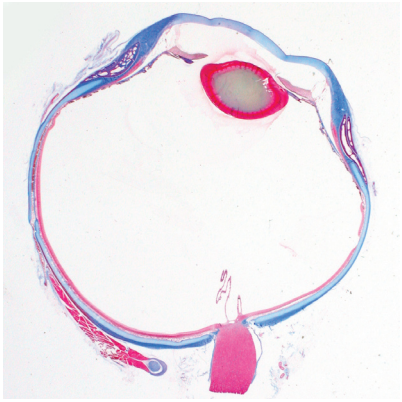
Point of View
THE EYE RESEARCH INSTITUTE UNIVERSITY OF WISCONSIN–MADISON

Through Many Lenses

From domestic, agricultural, and exotic animal species across the country and the world—including dog, cat, horse, cow, sheep, walrus, walleye, gecko, giraffe, sturgeon, sandhill crane, polar bear, penguin, bat, boa constrictor, octopus, owl and more—

—nearly 29,000 ocular specimens have been sent directly to Richard Dubielzig, DVM, DACVP, professor in the department of pathobiological sciences in the School of Veterinary Medicine and member of the UW Eye Research Institute. The charter faculty member in his department when UW-Madison established its veterinary school in 1983, Dubielzig initiated a mail-in eye pathology service for veterinary ophthalmologists. Under his direction for the past twenty-seven years, the Comparative Ocular Pathology Laboratory of Wisconsin (COPLOW) has amassed an extensive collection of both normal and abnormal vertebrate and invertebrate eyes, the largest in the world, and has become a unique resource for teaching and research focused on understanding eye disease.

A veterinarian might need to remove a painful or diseased eye to benefit an animal's health or well-being. The eye, already chemically fixed in formalin to prevent decay and to firm the tissues, is then sent to COPLOW. Each specimen is carefully opened, and findings are described and noted by the pathologist. The eye is then photographed, after which the globe is embedded in a paraffin block (allowing the tissue to be stored forever without drying or desiccating). Very thin slices of tissue are then mounted on glass slides and stained to enhance the visibility of cells and cell components for microscopic viewing. Reports of the findings are sent to the submitting veterinarian to provide a timely and accurate diagnosis for their animal "patients."

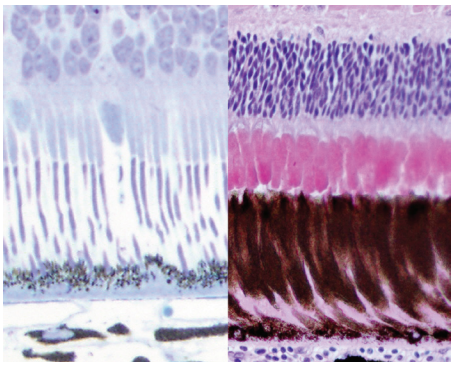


This low magnification view of a normal loon eye shows the entire eye in cross section. A very thin tissue slice, slide-mounted and stained, is representative of those of each species in the collection.

The cumulative result of these detailed specimen examinations is an unparalleled histopathology collection and photographic record. Indexed by animal species, age, gender, breed, disease, specimen submission reports, and the lab's diagnostic summary, information is widely searchable within the fully archived collection. Lab scientists are also involved in investigating distinctive and relevant aspects of ocular disease processes to better comprehend disease origins, effects, and progression.

Due to a steadily increasing caseload, Dubielzig relinquished his longstanding diagnostic and teaching role conducting biopsies and necropsies in the Veterinary Medical Teaching Hospital in order to direct full attention to his COPLOW activities. He remarks, "I'm pleased to have the opportunity to devote more time to my central research focus, cataloging and teaching about the pathology of spontaneous disease of the eye in animals. In addition to collaborating with the clinical veterinary ophthalmologists throughout the world who submit specimens, I also work with ophthalmology residents from many places who use the archival resource to compile a case series for research projects."

Richard Dubielzig, DVM, DACVP, reviewing pathology submissions at a teaching microscope in his veterinary pathology lab.



Dubielzig's photographs capture the innate beauty in eye structure. This high magnification view shows retinal layers in macaque monkey (left) and walleye (right) eyes.

Investigators can request a "case series" to work up, usually comprised of five or more instances of a particular disease for study along with access to the full range of information and photographic images. Archived tissues for further evaluation are also available. Because tissue structure and proteins are maintained, scientists can extract genetic material and can look at proteins one by

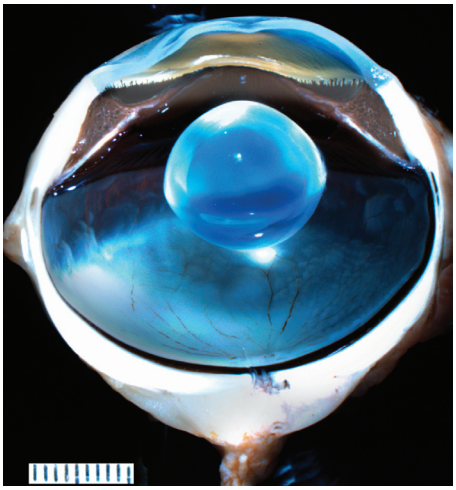
Dubielzig with some of his former Comparative Ocular Pathology Fellows. Back row: Christiane Kafarnik, Tricia Mundy, Chris Pirie. Front row: Carol Naranjo, Mitzi Zarfoss, Dick Dubielzig, Gia Klause, Chris Reilly.

one to see if they are expressed. They can also perform polymerase chain reaction studies, looking for specific genetic markers. "Our collection is a resource to be used to investigate the pathogenesis, prognosis, effectiveness of treatment, and epidemiology of spontaneous ocular disease in animal species," states Dubielzig. And for researchers interested in comparative ocular anatomy or in ocular evolution, there are nearly 1,200 normal eye specimens available. "Using our collection, we can catalog ocular morphology (structure) in comparison to evolution of the eye," he notes. "To that end, we're now working to gather a collection of morphologically different blind cave fish from around the world."

Employing a comparative ocular pathology pathway has been key to discovery, as Dubielzig has utilized the collection to focus on characterizing the morphological changes observed in animal diseases. Discerning patterns, parallels or contrasts within and across species and breeds has led to first-time recognition of a number of ocular diseases, the following among them: canine ocular gliovascular syndrome; neovascular vitreoretinopathy in young cats; corneal squamous cell cancer in dogs with chronic keratitis; and the causal relationship between trauma and ocular cancer in cat eyes. Wider areas of ongoing interest include ocular neoplasia, glaucoma in dogs and cats, ocular trauma, and inflammatory disease.

A dedicated mentor, Dubielzig founded a pre-residency fellowship in comparative ocular pathology and vision science available to either future veterinary or physician ophthalmology trainees. Recognizing the study of animal and human eyes as mutually informative and richly complementary, he worked with ERI Director Daniel Albert (Ophthalmology and Visual Sciences) to structure a learning environment for their respective fellows to participate reciprocally in the daily "read out" of the slides of newly-received specimens in both the veterinary and physician pathology labs. Currently training his fifteenth fellow, Dubielzig has required each to write a research case report for publication—using specimens and data accrued within the COPLOW collection as primary resources. Studies have included retrospectives analyzing various ocular cancers in equine and canine species; identification of morphologic features of degeneration and cell death in the retina in dogs with acute glaucoma; discovery of a cancerous spindle cell tumor that affects only blue-eyed dogs; and a first report of feline intraocular tumors arising from lens epithelial cells.

A true scholar-scientist with broad knowledge and expertise in art as well, Dubielzig brings his considerable photography skills to his scientific interests, capturing remarkable views of animal eyes that simultaneously engender insight and appreciation. His carefully crafted images, often superimposed multiple exposures of the same specimen in order to intensify coloring or structural differentiation, are much more than teaching tools. When asked how his art and science perspectives interface, Dubielzig responds: "I attempt to create an image that tells a story about the disease beyond simply recording the morphology—an image that is engaging in itself and facilitates a deeper understanding of the disease process."



Challenges in ocular specimen photography arise from tissue depth and contrast and their variable light reflectivity. Dubielzig shoots multiple images with dramatically varying light intensities and then selectively merges them using the Photoshop layering tool. The round lens and relatively flat cornea are morphologic features affecting the sea lion's ability to see both above and below water.

Many of his images illustrate a new pathology text, a synthesis of what Dubielzig has learned about veterinary eye pathology during the course of his career and the first to compare eye diseases in animals to those in humans in a systematic way. Titled *Veterinary Ocular Pathology: A Comparative Review*, co-authored with Kerry Ketring and with ERI members Gillian McLellan and Daniel Albert, the book will be released by Elsevier in June. It will provide tangible evidence of the multidisciplinary approach and collaborative spirit Dubielzig brings to his many interactions with veterinary and physician ophthalmologists and pathologists, and with the broad spectrum of basic scientists, humanists and engineers within the ERI. With the philosophy that knowledge gained in one species benefits all, Dick Dubielzig serves as a reserve of deep experience and myriad ideas for continued collaborative explorations—a resource as rich as the collection he has nurtured, sustained and advanced.

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