



University of Missouri-Columbia College of Veterinary Medicine and Cooperative Extension Service

VETERINARY MEDICAL REVIEW

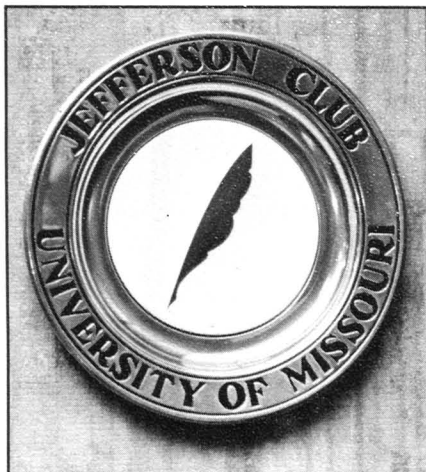
N.S., Vol. 5, No. 4, 1984.

PHARMACY & CENTRAL STORE

HOURS

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8:30 AM to 5:30 PM

CLOSED SATURDAYS,
SUNDAYS & HOLIDAYS



Don Connor, photo

Kansas City Kennel Club Donates

Paul Keene, president of the Kansas City Heart of America Kennel Club presented Dr. M.J. Bojrab a check for \$2500.00 to be used by the College Teaching Hospital for guerneys and other essential equipment. The presentation was made at the Kennel Club's annual Christmas party following a program Dr. Bojrab gave on "New Ideas in Pet Health".

cover story

The Veterinary College Pharmacy is undergoing many changes these days. Pictured behind the pharmacy counter is the newly appointed pharmacist, Mr. Bob Schultz, R.Ph. Mr. Schultz and the College pharmacy is highlighted in an article on page 3.

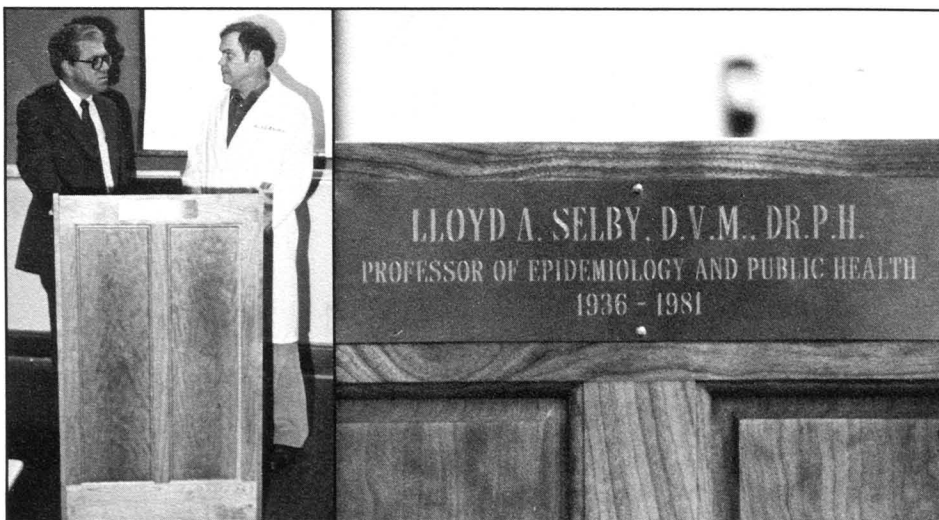
—Photo taken by Don Connor.

New Jefferson Club Members

Seven new members joined the UMC Jefferson Club, Veterinary Medicine Chapter in 1984. To achieve club membership, \$10,000 or more was pledged by each individual to the College of Veterinary Medicine.

The new members include Dr. and Mrs. M.J. Bojrab, Professor in the Department of Veterinary Medicine and Surgery, Columbia, Missouri; Dean and Mrs. Robert F. Kahrs, Dean of the Veterinary College, Columbia, Missouri; Mr. George Menos, St. Louis, Missouri, a Friend of the College and past giver of the Oscar Anesthesia Research Fund; Dr. and Mrs. Bernie Lauhoff (UMC '62), Rancho Palace Verdes, California; Dr. Jack Stephens (UMC '72), Villa Park, California; Dr. and Mrs. Theodore Trimmer (UMC '68), Las Vegas, Nevada; and Dr. Gary Weddle (UMC '78), Henderson, Nevada.

Memorial To Dr. Selby



This past fall a dedication was made at the College in the memory of Dr. Lloyd A. Selby. Dr. Niemeyer (left) and Dr. Blenden are seen at the dedication pictured above left.

Dr. Selby, a nationally recognized epidemiologist and one of the foremost specialists on birth defects of animals and children from environmental factors, taught microbiology in the UMC College of Veterinary Medicine and taught family and community medicine in the UMC School of Medicine until his death in 1981. Dr. Selby's life and his work touched many people.

Friends and fellow faculty members had a handmade cherrywood lectern made in Dr. Selby's memory. The lectern now stands in room 204 Connaway Hall where Dr. Selby taught many of his veterinary classes. It's presence will be a wonderful reminder of Dr. Selby's excellence and his love for the classroom.

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Canine Atopy

by Julie Ellis (VM 3)

Canine atopy is a genetically determined tendency to develop antibodies, IgE, having the property of specific tissue fixation. The target tissue in the dog is the skin where the condition manifests itself as pruritic dermatitis. The disorder is commonly known as allergic inhalant dermatitis, but this term is falling from favor although the allergens are believed to enter the body via inhalation of biogenic particles measuring 2 to 60 in diameter. Associated with these particles are the allergens (antigens that produce clinical allergic reactions) themselves - proteins or glycoproteins with molecular weights of 20,000 to 40,000 daltons. The upper size limit is considered 60,000 daltons because large molecules cannot readily penetrate mucous membranes. Common allergens are: pollens, fungal spores, house dust, kapok, wool, cotton, and epidermal products (dander, feathers); there are probably many others as well. It is postulated that these allergens are absorbed through the respiratory tract into the body where they encounter specific IgE fixed in the skin of the previously sensitized, atopic dog. The presence of specific IgE in the skin of affected dogs has been demonstrated by radioallergosorbent testing (RAST) and immunofluorescent assays. IgE is associated with the surface of mast cells and degranulation is triggered by complexing of the allergen and IgE. Although histamine is released it is not the primary mediator of the intense pruritis which characterizes the atopic phenomenon since pruritis is not controlled by administration of antihistamines. Suspicion falls on the proteolytic enzymes as mediators; and the role of bradykinins and slow reacting substance of anaphylaxis need further clarification. This is classified as a type I (immediate) hypersensitivity. There is some thought that allergens may be introduced to the body also through inoculation by scratching.

As much as 10% to 15% of the canine population may be atopic, and may provide up to 30% of the case load in a dermatology practice. Dogs with atopy commonly first show signs at 1 to 3 years of age, though they may not be presented until later as the course is somewhat progressive and lesions are not evident at the outset. Pruritis is intense and may be seasonal (associated



with pollens) or nonseasonal (associated with household items). Scratching and self mutilation generate the lesions including erythema, alopecia, papules, wheals, excoriation, hyperpigmentation and lichenification. These are seen in the axilla, on the face, paws, ears and ventrum. In chronic cases the lesions may be generalized. A seborrheic syndrome, otitis externa, conjunctivitis pyoderma and/or folliculitis are commonly seen with atopy. Gastrointestinal disorders have been reported rarely but the relation between food allergy and atopy is not clear cut. The skin of atopic people has been shown to carry higher populations of *Staphylococcus aureus* though this has not been demonstrated in the dog. Irregular estrus cycles and a high incidence of pseudopregnancy are occasionally observed in atopic, intact females. The sneezing, wheezing and runny noses that are familiar signs of atopy in man have been reported to exist in dogs but are very rare. An atopic dog remains so for life.

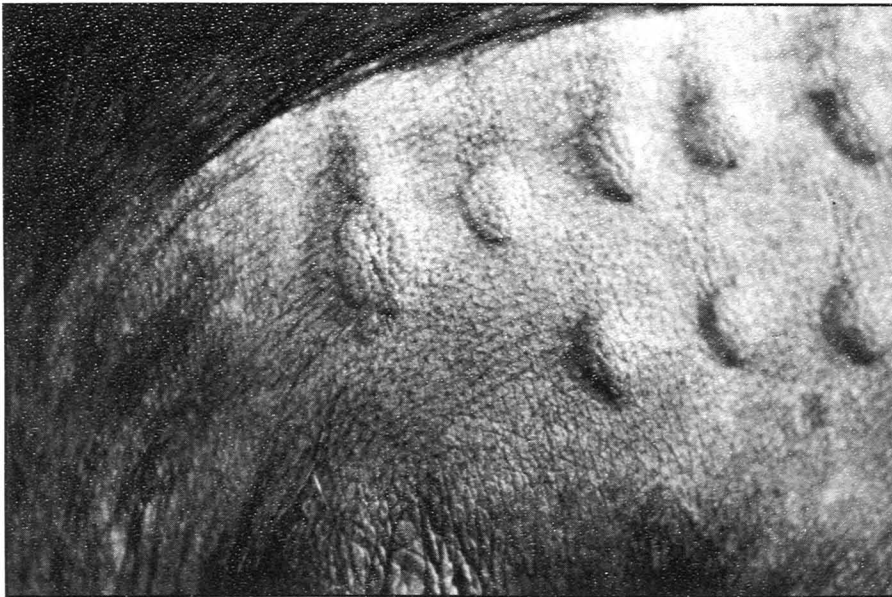
Breed predilection is generally recognized in Dalmatians, Irish and English Setters, many of the terriers, Lhasa Apsos, Miniature Schnauzers, English Bulldogs and Beagles, although dogs of any breed, including mongrels, may be affected. A 2.5 times greater incidence has been reported in females. There is some genetic basis for atopy though the mode of inheritance is unknown. Attempts at the University of Pennsylvania to establish an inbred line of atopic dogs failed though this may have been the result of experimental design and not just heritability (or lack thereof).

Reported matings of atopic sire and dam have produced litters in which the majority of pups became atopic. Atopy is generally acknowledged to run in families, and clients should be advised to avoid breeding atopic dogs.

At the microscopic level, lesional skin in one intensive study exhibited the following epidermal changes: mild to moderate hyperkeratosis (in approximately 20% of dogs), mild, focal parakeratosis (25%), rete ridges (pegging) (15%), hypergranulosis (15%), follicular keratosis (50%), mild, focal spongiosis (10%), leukocytic exocytosis (25%), melanosis (15%), focal ulcers (5%), exudative crusts (10%) and pyoderma (folliculitis and/or epidermitis) (15%). The most common epidermal change was mild to severe acanthosis (95%). These changes correlate well with the clinical appearance of affected skin which becomes thickened and roughened with the dog's constant scratching and chewing.

In the dermis the same study observed these changes: dilatation of superficial dermal blood vessels (80%), edema (40%), and perivascular cuffing in 100% of the cases. The cuffing consisted of mononuclear cells in all cases, plus neutrophils in 80% and plasma cells in 70%. Oddly, the population of mast cells was variable; they were increased in number in 35%, decreased in 5% and normal in 60%.

Unfortunately for diagnostics, higher levels of IgE in the serum of atopic dogs has not been demonstrated. In addition intestinal parasitism and dirofilariasis greatly influence IgE. Therefore, a simple diagnostic test is not on the horizon.



Intradermal Testing

C.B. Chastain, DVM, photo

We must continue to rely on history and clinical signs most strongly to provide a diagnosis of atopy. Skin scrapings should always be done to rule out parasitic causes of pruritis. A few, similar appearing, differentials are:

Sarcoptic mange

(First rule out) - skin scraping history of exposure response to steroids is poor

Superficial pyoderma

(May occur *with* atopy) - papular and pustular eruptions precede pruritis responds to antibiotic therapy

Bacterial folliculitis

(May occur *with* atopy) - papular eruptions precede pruritis more common under one year of age partly steroid responsive requires long term antibiotic therapy

Allergic contact dermatitis

occurs especially on ventral body surface and digits, rarely facial

Flea bite dermatitis

history of exposure response to environmental control of fleas usually includes dorsum of pelvis and rarely facial

Dogs affected with atopy and one or more of the above conditions are not uncommon and may present a real diagnostic challenge.

If all other causes for pruritis can be ruled out and atopy is suspected, elimination of allergen from the dog's environment and provocative exposure may provide valuable information. This probably works best when allergy is of the nonseasonal type due to household products, such as kapok, wool, house dust and human dander. Careful hospitalization for a week or so would work well.

Seasonal pruritis is most often due to pollen and at this time the only method of determining the specific pollens responsible for a case of atopy is intradermal testing. Such testing may also be done for household allergens. It must be stressed that a diagnosis of atopy must already have been made and that intradermal testing serves only to identify antigens responsible for producing signs in that particular case - positive reactions must also correlate with history of exposure. It is beyond the scope of this paper to discuss more than the basic principles of intradermal testing, and treatment by hyposensitization, which follows. For specific regimes the reader is referred to the articles listed at the end and to manufacturer's recommendations in the use of these biologicals.

Antigens for testing are supplied in aqueous suspensions with concentrations expressed as protein nitrogen units (PNU)/ml or as antigenic protein weight/volume. True potency may not be accurately reflected by these concentrations as the antigenicity of the specific antigen plays a large part in the outcome of testing. One ml of a 1:50 W/V pollen

extract is roughly equivalent to 10,000 PNU. Test concentrations most commonly used are 1000 to 1500 PNU/ml, and these may be supplied as individual antigens or a mixture of related ones such as mixed weed pollens or mixed grass pollens. The concentration of each component in these mixes would be less, but in many instances the individual allergens at 1000 PNU/ml are too concentrated anyway and produce false positive reactions due to their irritating nature. Examples are house dust, mold spore mixes, wool, feathers, tobacco and cat dander. These should be diluted 250 to 500 PNU/ml. Recommended volumes of allergen injected per site varies from 0.02 ml to 0.1 ml. Histamine phosphate 1:100,000 and saline are used as positive and negative controls, respectively. Testing should be done without tranquilization, but it has been reported that xylazine does not interfere with test reactions. The lateral thorax is clipped and the injection sites indicated with an ink pen.

The reactions are generally read twice, at 15, 20, or 30 minutes post injection. Positive sites exhibit a wheal and flare reaction diameter equal to or greater than the average of the positive and negative controls. Reactions may also be graded as to their degree of positivity, some react much more strongly. False negatives may result from improper technique, injection must be intradermal; immunosuppressives, or omission of the specific offending allergen. False positives may result from contamination, high concentration or volume or cross reactivity with related antigens.

Therapy of atopy may be divided into 3 areas: avoidance, symptomatic and hyposensitization. While avoidance may be the ideal method of management it is difficult to achieve in actual practice. Some success may be achieved in removing household allergens but such things as pollen are beyond practical control.

Symptomatic therapy is aimed at controlling physiologic mechanisms of pruritis. The mainstay of this line of treatment is judicious use of glucocorticoids. Prednisolone 0.25 to 0.50 mg/lb/day divided BID for 5 to 7 days will suppress pruritis in most cases, the dose may then be tapered to lower maintenance levels and an alternate day schedule instituted. Topical glucocorticoids such as high potency triamcinolone cream may be applied to localized lesions TID. Antihistamines are useless against atopy-continued on page 6

Atopy _____

ic dermatitis but are reported to help the occasional case of respiratory allergy.

Apparently, areas of atopic dermatitis have a lower itch threshold. Stimuli that might not initiate the itch-scratch cycle in normal skin can cause frantic bouts of self-mutilation in atopic skin. Antihistamines and barbiturates reduce the psychological urge to scratch but have side effects such as sedation and ataxia. Hydroxyzine hydrochloride (Atarax) is a centrally acting CNS drug used in the management of anxiety, tension and psychomotor agitation. It has been recommended as an adjunct to reduce self-mutilation tendencies at a dose level of 50-100 mg/day divided TID.

Hyposensitization injection regimes were developed for, and work fairly well in atopic humans. Some success has been achieved in dogs with this treatment. Success rates of 25% to 100% have been reported, but definitions of success vary from reduction in steroid usage to elimination of steroids altogether. The theoretic mechanism of hyposensitization is this: increasing dose of parenterally administered allergens (selected based on the results of intradermal testing) induces formation of IgG which specifically binds allergens in the circulation thus intercepting them before they encounter tissue-fixed IgE. Hyposensitization may also stimulate suppressor T-lymphocytes to reduce IgE production.

Hyposensitization may be considered for a dog who is pruritic more than four months of the year, in whom steroids are not efficacious or produce side effects, and it is recommended that these candidates not test positive for many more than ten allergens. The owner must understand the procedure, the requirement for maintenance boosters, the short and long-term costs (which may be considerable) and the variable prognosis.

Two types of antigens are available: alum-precipitated extracts and aqueous suspensions, which require more frequent administration. Individual allergens may be selected, or mixes such as those employed in testing may be used. Antigens selected should be strongly suspected of being responsible for the clinical allergy based on intradermal testing, a correlating history of exposure and season of affliction.

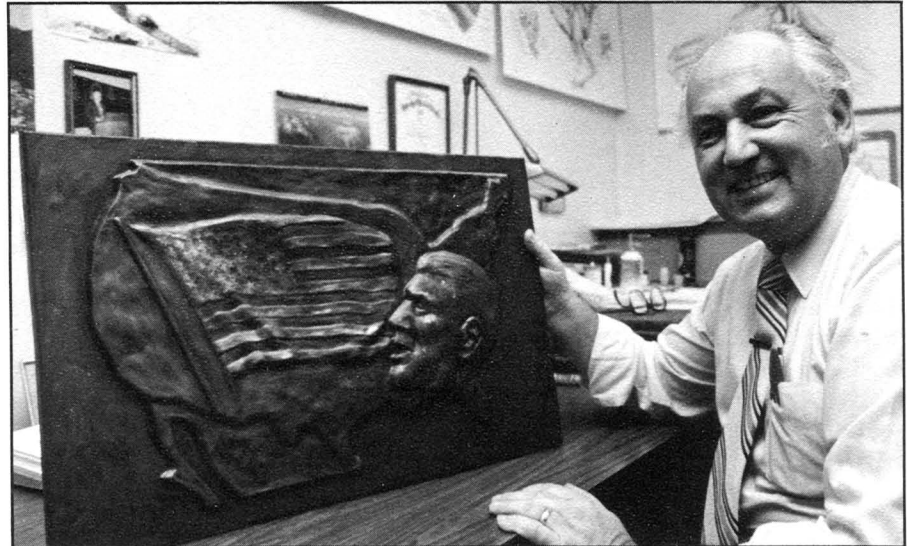
One illustration of a protocol is: nine injections of alum precipitated allergen

Dr. Constantinescu Honors the President

Dr. Gheorghe M. Constantinescu, Associate Professor in Veterinary Anatomy and a native of Romania, is proud to reside now in the United States. To demonstrate this pride, Dr. Constantinescu used his talents as an artist to

produce a most patriotic sculpture (shown below) which he sent to President Ronald Reagan.

President Reagan's reply is also included below.



THE WHITE HOUSE

Dear Dr. Constantinescu:

You were good to think of me and I want you to know how pleased I am by your kindness. Thank you for remembering me with your special sculpture. I truly appreciate the warm friendship conveyed by your thoughtful gesture.

Nancy joins me in sending you our best wishes.

Sincerely,

Ronald Reagan

over a 24-week period, beginning with 50 to 100 PNU and gradually increasing to 200,000 total PNU per injection. Dogs with perennial pruritis generally require high-dose boosters at regular intervals throughout life. Dogs with short, seasonal pruritis may be maintained by booster injections during the non-allergic period.

Pruritis may occur immediately following allergen injections if the tolerance level has been exceeded. This reaction may be prevented by administering antihistamines just before the injections. Steroid therapy may need to be continued well into the hyposensitization program in less responsive cases.

Collaboration Leads to New Sensing Devices

by Fred Goss

Reprinted from Missouri Tech Net News

Sensing devices of potential value have resulted from cooperative research efforts among three University of Missouri campuses.

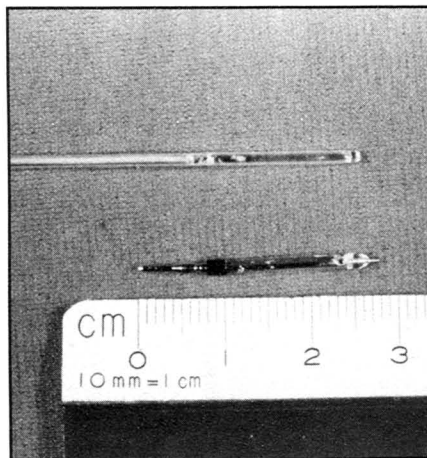
The first of these devices is designed to measure the oxygen level of blood and other fluids, according to Allen W. Hahn, professor of veterinary medicine/surgery and bioengineering at the College, and associate director and research investigator at Dalton Research Center. Its original mission was as a biomedical implant. "Oxygen concentration is a crucial factor," Hahn explained. "Knowing the level, a lot of important information about bodily functions can be determined. This becomes vital in situations like those faced in critical care. A low blood oxygen level indicates that something is going wrong that needs attention and correction."

According to Michael F. Nichols, research associate at Dalton and co-inventor of the new device, medical science has relied on one particular electrode for oxygen concentration measurement for many years. This is a wire sensor and reference electrode covered with a relatively thick polymer membrane. "This was the state-of-the-art for quite some time," he explained, "and it was designed to circumvent a major problem inherent in such devices."

That problem was the poisoning effect. The sensing surface, if unprotected, soon becomes contaminated with sulfur-containing amino acid molecules from the internal environment. These contaminants inhibit current flow and quickly make readings very unreliable. According to Nichols, unprotected electrodes are soon sufficiently contaminated to make the uncertainty of their readings climb to as high as 50 percent. "A possible error of that magnitude, makes them practically worthless unless they can be recalibrated," he pointed out.

According to Hahn, poisoning and the associated drift of readings was previously reduced by coating the sensing electrode with a relatively thick polymer membrane. This membrane, usually silicon rubber or a similar material, would allow oxygen diffusion to the sensor but keep out the larger contaminating protein molecules.

The thickness of the membrane, how-



Close-up on oxygen electrode (top) and pH electrode (bottom).
—Actual electrodes to be used in practice can vary considerably from design shown.

ever, led to additional problems of response time. According to Hahn, the traditional electrode typically took up to a minute to correctly read oxygen levels. In addition, it was for use outside the patient, necessitating the drawing of samples and their transport to the device. Working from the need for a significantly improved design, therefore, the Dalton Research Center became involved in the development of a contaminant-free, fast responding, implantable sensor.

The Dalton Center, which specializes in biological research, especially in cardiovascular disease and instrumentation, is a suitable location for the kind of multidisciplinary effort the sensor project demanded, Hahn said. "We are an organization under the UM-Columbia graduate school and can easily involve other departments and campuses in our activities. The Dalton Center was established in the late 1960s. It cooperates with the University of Missouri-Rolla Materials Research Center."

In working on developing the oxygen sensor, Hahn called upon the special talents of Eckhardt W. Hellmuth, professor of chemistry, and Ashock Sharma, then a graduate student in chemistry, both of UM-Kansas City. Later, as the project developed, Hahn enlisted the support of H.K. Yasuda and William J. James, both of the UMR Materials Research Center, who were joined by Sharma when he continued his studies on the Rolla campus.

"What we were looking for," Hahn went on, "was a way to protect the electrode's metal sensing surfaces, to keep it free of contaminants, but still keep it responsive and small enough to be useful as a permanent or semi-permanent implant. An ultra-thin film polymer membrane applied through glow discharge technology (see IncuTech News No. 1) seemed like the way to go."

Time proved this assumption correct, and a glow discharge polymer coated oxygen electrode was eventually developed, patented and licensed for commercial development to a Minnesota firm.

"The original concept was for a medical sensor," said Hahn, "but when the patent was filed, we chose to leave application options as broad as possible. This device could be used in many environments where an in-place measurement of the oxygen concentration of a fluid is needed. It could easily be adapted, for example, to provide monitoring information in a wastewater treatment stream."

The second device, a miniature, dry, ion-sensitive electrode, came to development through a somewhat similar chain of collaborations.

"We were looking for a stable, dry device to measure the pH of body fluids," Nichols explained. "As with the oxygen sensor, this device would be valuable for use in organs and tissues where collecting fluid samples was impossible or infeasible. With it, we hoped to be able to measure the acidity or alkalinity of blood, muscle tissue and other internal organs."

Previously used sensors consisted of electrode wires capped with a thin layer of glass. A high conductivity fluid was used in these devices to bring ions from the glass interface to the electrode's wire surface. While this system works well, its size and the presence of internal fluids limit its usefulness as an implant, according to Hahn.

"We felt that if we could eliminate the conducting fluid, we could make an electrode small enough for a wide variety of implant uses and Nichols accomplished these goals," said Hahn.

Nichols, the inventor of the new device, obtained the expertise of Delbert E. Day, Curator's professor of ceramic engineering and director of the Materials Research Center at UM-Rolla. "With Day's expertise in the area of

continued on page 8

College Briefs

The Dean's Corner

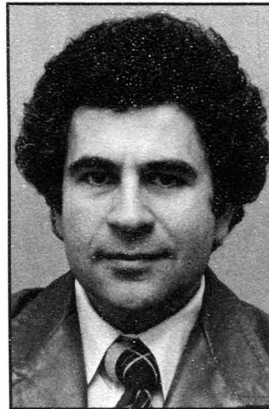


Associate Dean Niemeyer

Dr. Bojrab Presented Purdue's Distinguished Alumnus Award

Dr. M. J. Bojrab, professor in the Department of Veterinary Medicine and Surgery, was presented the Distinguished Alumnus Award by Purdue University's School of Veterinary Medicine. Dr. Bojrab is a 1964 graduate of Purdue.

The award was given to Dr. Bojrab "in recognition of his outstanding accomplishments in and contributions to the field of veterinary surgery exemplified by the superb training of surgical residents, by authorship and editorship of highly acclaimed and widely used veterinary surgery textbooks, and by his untiring efforts in the arena of continuing education which have contributed significantly to the advancement of veterinary surgery both nationally and internationally and to the ultimate benefac-



Don Connor, photo

tors . . . our friends, the animals."

The award was presented at Purdue University on the 20th day of September, 1984.

Sensing Device continued

glass membranes, Nichols eventually produced the ion-sensitive electrode," said Hahn.

Though the device was originally meant for the measurement of pH in medical applications, it could be modified to measure the levels of other ions such as sodium or potassium. Through changes in the glass membrane or a coating, it can be selectively tuned for a number of different sensing applications. "Nichols has even had a few inquiries from the oil industry where the device's tolerance to high pressures might make it a valuable tool for work within wells,"

said Hahn.

This sensor too has been patented by the University of Missouri and preliminary licensing negotiations are under way.

For additional information about this or other multi-disciplinary research projects and capacities at the Dalton Research Center, contact:

Allen W. Hahn
Associate Director
Dalton Research Center
University of Missouri-Columbia
Columbia, MO 65211
(314) 882-7586

The College would like to take this opportunity to thank alumni, friends and private organizations who have given support through the Annual Giving program. While we don't have the final figures for 1984, it appears the Annual Giving will be above our expectations.

Last year we were able to purchase items such as ophthalmology, surgical and equine equipment. We also acquired new anesthesia and heart simulator machines.

The Annual Giving program has provided some funds toward the purchase of a much needed electron microscope. The campus agreed to fund half the microscope. Your College, because of your generosity was able to fund the remainder. Bids will go out soon.

In past years we have remodeled the small animal receiving area, some reception rooms and the large animal seminar area which is used for teaching purposes.

In addition, the student lounge was originally furnished with annual giving funds.

You have enabled some faculty to conduct small research projects because your specific instructions directed it to a particular project or individual.

From your College, we thank you.

Veterinary Medical Review

College of Veterinary Medicine
and Cooperative Extension Service

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