Neuroprotective Agents Show Promise
Optic Nerve Protection Offers Hope for Saving Vision

Glaucoma, multiple sclerosis (MS) and traumatic optic nerve injury would seem to have little in common except that all are conditions that lead to vision loss because of cell death within the optic nerves. When the cells of the optic nerve, which carry all the visual information from the eye to the brain, are injured, a destructive chain of events is set in motion, leading to the self-inflicted death (apoptosis) of the injured cells. If the cells can be protected, they may recover and vision may be spared. This area of research, known as neuroprotection, has great potential for treating conditions affecting the optic nerve and other parts of the brain.

Glaucoma is responsible for 95% of all optic nerve damage; the other 5% is due to optic neuritis, trauma, cancer, stroke, circulatory problems, infection and inflammation combined. Penn ophthalmologists are participating in clinical trials to evaluate new treatments for many conditions affecting the optic nerve. Since the common thread in these treatments is protecting the optic nerve, progress in treating one disease may have application to others.

BASIC RESEARCH
Neuroprotective agents fall into two broad categories: (1) substances that protect cells indirectly by blunting or blocking an insult or toxin, and (2) substances that act directly on cells already injured, making them more capable of withstanding the insult (Figure 1). During the past 15 years, scientists observed that some injured cells die while others survive, leading to the idea that certain molecules already present in the body can help cells stay healthy despite injury or stress.

Alan M. Laties, M.D., and Rong Wen, M.D., Ph.D., are testing peptide molecules on animal models of retinal degeneration and finding that they exhibit a remarkable protective effect.

GLAUCOMA
In glaucoma, increased eye pressure combined with poor circulation and an imbalance in chemical messengers that allow cells to talk to one another (regulatory neurotransmitters) cause injury to the optic nerve. Lowering the eye pressure is the only proven treatment for glaucoma. Glaucoma specialist Jody R. Piltz-Seymour, M.D., is participating in a multi-center trial to assess memantine in patients with glaucoma. The FDA recently approved memantine for treatment of Alzheimer’s Disease. Studies are underway to determine whether or not this benefit extends to glaucoma.

MULTIPLE SCLEROSIS
MS, a disease of the central nervous system, is characterized by inflammation and demyelination, a loss of the protective insulation (myelin) surrounding nerve fibers. Inflammation of the optic nerve, or optic neuritis, can present as vision loss or pain with eye movements and is a common first symptom of MS. Fifty percent of patients with optic neuritis either have MS or will develop it later. Recent advances in diagnosis, risk assessment and therapy have substantially improved the prognosis of MS.

Continued on page 2
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In 1998, a microscopic study showed that MS-related disability is caused by actual loss of nerve fibers. The next step was to develop drugs to prevent optic nerve cell death. Steven L. Galetta, M.D., and his collaborators in a multi-center clinical trial documented that immunomodulating drugs such as Avonex may delay the onset of MS over a period of 5 years. “This is great news for people at risk for developing MS. In the future, we hope to have a host of new treatments to block nerve damage, not just control symptoms,” says Galetta.

Kenneth S. Shindler, M.D., Ph.D., is conducting research on optic nerve ganglion cells in an animal model of MS to determine whether nerves are being damaged directly or being damaged because of the loss of myelin. Shindler will evaluate treatments to prevent the damage.

**Optic Nerve Trauma**

Acute injury to the optic nerve from head trauma or stroke results in immediate death of cells directly involved (primary injury). Secondary injury to surrounding cells also occurs from within hours to days after the acute injury (Figure 2). Neuroprotection therapy seeks to prevent secondary injury and subsequent death of nerve cells. Since many factors, such as release of toxins from dying cells, inflammation and interruption of circulation from swelling, are responsible for secondary injury, scientists are studying many different neuroprotective strategies with promising results.

Nicholas J. Volpe, M.D., specializes in the diagnosis and treatment of all...
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diseases involving the optic nerve, with a research interest in correlating anatomic changes in the optic nerve to functional deficits in patients with optic atrophy. Volpe regularly evaluates new technologies for assessing vision loss in patients with optic nerve problems with the goal of finding an effective screening tool.

Tools to Diagnose and Evaluate Optic Nerve Damage

One way of assessing the health of the optic nerve is to measure its circulation. Jody Piltz-Seymour, M.D., in collaboration with Juan E. Grunwald, M.D., Director of Scheie’s Vivian Simkins Lasko Retinal Vascular Research Laboratory, measured optic nerve circulation in patients with glaucoma. They found that patients with abnormal circulation in the optic nerve had more rapid worsening of their glaucoma than patients with normal circulation. Using such techniques to identify patients at increased risk of vision loss will facilitate earlier recognition and treatment.

Patients with MS often complain of vision problems despite being able to read 20/20 on the standard eye chart. Laura J. Balcer, M.D., is developing a new tool for measuring vision using low contrast eye charts with gray letters instead of black letters on a white background. (Figure 3) This sensitive vision test monitors progression of disease and response to treatment. Balcer expects that the low contrast sensitivity test will become a standard MS Outcomes Tool.

With so many advances in basic and clinical neuroprotection research, Penn neuro-ophthalmologists are optimistic that patients with conditions affecting the optic nerve can look forward to keeping their vision intact.

Figure 3: The Pelli-Robson Contrast Sensitivity Chart used to test patients with MS is shown next to the ETDRS Visual Acuity Chart.

The Jody Lynn Sack Memorial Fund Supports Optic Nerve Research at Scheie

In August 1990, Jody Lynn Sack was a vibrant, athletic and optimistic 17-year-old looking forward to entering the University of Virginia to play lacrosse that Fall. Coming home one night, she lost control of her car on a rain-slicked road and sustained severe head injuries which crushed her optic nerves, leaving her blind in one eye and with only 20% vision in the other. Despite her visual impairment, Jody threw herself back into life. She was fearless. She resumed her participation in sports, even completing a marathon and participating on the crew team at University of Virginia. She graduated with a degree in English in 1995. Her courage, sense of humor and enthusiasm were an inspiration to her friends and family. She never gave up the hope that her sight would be restored. In 1997, a few days before she was to start a job in New York City, Jody died in a tragic fall from a friend’s rooftop deck. In her memory, her grandfather left a $500,000 gift from his estate to Scheie Eye Institute for research on optic nerve injury. His goal was to keep Jody’s hope alive.

For more information on the Jodi Lynn Sack Memorial Fund and Neuroprotection Research at the Scheie Eye Institute, call Ann Sacks at (215) 662-8774, e-mail ann.sacks@uphs.upenn.edu or visit our website www.penneye.com.
**F.M. Kirby Center Scientists . . .**

**Archives of Ophthalmology**
This cover image from the November 2002 issue of Archives of Ophthalmology illustrates work done at the F.M. Kirby Center for Molecular Ophthalmology by Joshua L. Dunaief, Tzvete Dentchev and Ann H. Milam.

The accompanying paper described apoptosis, or cellular suicide, a mechanism of retinal cell death in AMD and suggests that drugs that target the apoptotic pathway might preserve vision in patients with AMD. *Arch Ophthalmol.* 2002;120:1435-1442.

**Neuron**
Using high-powered confocal imaging, this cover from the November 2002 issue of Neuron shows how the axons in the brain are delineated through adeno associated virus-mediated delivery of green fluorescent protein.


**Gene Therapy**
The image shows the immune response after delivery of transgenes to the retina through viral vectors. The sketch portrays cell-specific transgene expression after virus delivery. The accompanying article summarizes the biology of and immune responses to intraocular injection of three different recombinant viral vectors: adenovirus, adeno-associated virus (AAV), and lentivirus. Unlike the adenovirus, neither the AAV nor the lentivirus elicit a cell-mediated response making them promising vectors for treatment of chronic ocular (retinal) diseases.

This cover represents work done at the F.M. Kirby Center for Molecular Ophthalmology by Jean Bennett, “Immune response following intraocular delivery of recombinant viral vectors.” *Gene Therapy*, 10(11) 977-982 (2003).
**Journal of Virology**

This July 2003 cover of the *Journal of Virology* is composed of 2 histological sections showing that delivery of AAV/21-CMV-EGFP to the retina of a fetal mouse on embryonic day 14 results in the presence of green fluorescent protein in the retinal pigment epithelium. This is apparent at birth through analysis of histological sections. These studies pave the way for *in utero* retinal gene therapy in mice.


**Investigative Ophthalmology and Visual Science**

From the August 2003 issue of Investigative Ophthalmology and Visual Science, this image shows extra photoreceptor vision cells (red and green circles over blue background at top of image) which would normally die, but survive in the adult mouse retina because two pro-death genes are deleted. Thus, these genes play a role in developmental photoreceptor death. Therapies that inhibit the function of these genes may similarly protect diseased photoreceptors in patients.


By Jenny Bartelle
**Whatever Kids Need, CHOP Ophthalmology Delivers**

Faculty members in pediatric ophthalmology participate in research that has direct impact on the care of children. **Brian J. Forbes, M.D., Ph.D.**, has been a principal investigator for the Philadelphia center in the Amblyopia Treatment Studies (ATS) that have changed the treatment of children with amblyopia. Parents and ophthalmologists may now choose between patching an eye and instilling eye drops for children with moderate amblyopia. In addition, the ATS has shown that patching for as little as 2 hours a day is as effective as patching many more hours for children with mild to moderate amblyopia. **Graham E. Quinn, M.D., MSCE**, a leader in national clinical trials of retinopathy of prematurity, is the principal investigator for the Philadelphia center in the Early Treatment of Retinopathy of Prematurity (ETROP) study which announced in December 2003 that many babies with severe ROP should receive laser treatment earlier than is currently recommended.

Faculty members also conduct research into basic mechanisms of conditions that affect the vision of children. **Terri L. Young, M.D.**, is searching for genes involved in severe nearsightedness; identifying the genes may lead to treatments to prevent this condition that not only requires wearing glasses or contact lenses, but also predisposes the patient to vision-

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**Pediatric ophthalmology capitalizes on the special areas of interest of the CHOP faculty.**

**James A. Katowitz, M.D.**, performs reconstructive surgery on children with deformities of the head and face and has a special interest in improving the care of children born with a very small eye or without an eye. **Grant T. Liu, M.D.**, a neuro-ophthalmologist, cares for children with vision problems or with abnormal eye movements due to conditions that affect the optic nerve, the brain, and/or the pathway of nerves between the eye and the brain. Vitreo-retinal surgeon **Albert M. Maguire, M.D.**, performs delicate surgery in infants and young children to repair damage caused by retinopathy of prematurity, trauma, or other conditions.

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**Whichever kids need!** explains **Monte D. Mills, M.D.**, Director of Ophthalmology at Children’s Hospital of Philadelphia (CHOP), when asked about the clinical services provided by his division. Children receive expert, state-of-the art care whether they have relatively common conditions, such as amblyopia (lazy eye), strabismus (eye misalignment), or rare childhood conditions such as cataract (cloudy lens) or retinopathy of prematurity (abnormal blood vessel growth in premature infants).

Evaluating infants and young children, especially those with additional medical problems, requires special methods of evaluation. Small size is not the only challenge; a child’s short attention span and inability to speak demand that examiners be especially resourceful. The division has testing facilities for electroretinography, ultrasonography, visual fields, and other tests of visual function and all are customized for young children.

Pediatric ophthalmology capitalizes on the special areas of interest of the CHOP faculty. Internationally recognized oculoplastic surgeon **Monte D. Mills, M.D.** examines a child in the Pediatric Ophthalmology outpatient practice.
threatening complications such as retinal detachment.
Eric A. Pierce, M.D., Ph.D., studies the molecular basis for inherited retinal degenerations and for abnormal growth of blood vessels such as those involved in the retinopathy of prematurity. Dr. Quinn and Ellie L. Francis, O.D., Ph.D., collaborate with other investigators in the Penn Department of Ophthalmology to investigate the factors that influence eye growth and shape. They combine information obtained by questionnaires, visual function tests, and highly precise measurements of the eye to explore the possible influence of such factors as near work, daily fluctuation in eye length, and the light/dark cycle.

Other efforts by CHOP faculty are aimed at determining how to maximize the usefulness of existing examination tests and treatments. Drs. Quinn and Francis participate in the Vision in Preschoolers (VIP) Study that is investigating the best tests for screening preschool-aged children for amblyopia, strabismus, and severe refractive error. Dr. Quinn serves as the medical adviser for the multicenter study and also serves on the Executive Committee along with Dr. Maureen Maguire, head of the Coordinating Center and Professor of Ophthalmology at U Penn. Dr. Mills is exploring whether retinal photographs taken in the nursery can provide more objective and quantitative information about whether infants should be treated for retinopathy of prematurity.

Clearly, Dr. Mills was correct in his assessment that pediatric ophthalmology provides whatever eye care children may need. In addition, the faculty research ensures that eye care for babies and children will continue to improve.

By Maureen Maguire

Alice Borowik 1932 - 2003

The Scheie Eye Institute family lost a loyal and long-time friend. Alice C. Borowik, registered nurse, ophthalmic technician and Air Force veteran, died on September 11, 2003 after a long illness. Dr. Harold G. Scheie hired Mrs. Borowik nearly forty years ago, and she performed her job with characteristic devotion and unwavering zeal until a few weeks before her death.

Mrs. Borowik loved coming to work at Scheie; indeed, she never wanted to retire. As a nurse technician, she was so quick and efficient that she ran circles around everyone else, and patients would affectionately kid, “Where’s Sarge?” Doctors and patients alike appreciated her formidable skill at refraction. She was extremely proud of her family, showing off giant photographs of her granddaughters to the Scheie staff. In her quiet way, Mrs. Borowik made an important contribution, not only because of her technical competence but also because of her sincere compassion for patients. Her dedication and professionalism were an example for all of us to follow and her presence will be missed.
Scheie Alumni Reception
American Academy of Ophthalmology meeting
November 15, 2003, Grand Californian, Anaheim, CA

 Franz Michel, SEI ’01, Thomas Bersani, SEI ’86 and his wife Joan Christy and Robert Weisenthal, SEI ’86

 Richard Kresloff, SOM ’70, SEI ’78, Randi and Michael Kresloff, SEI ’00 and Steve Orlin, SEI ’86, SEI Faculty

 Prithvi Sankar, SEI Faculty, and Madhu Gorla, SEI ’98

 Robert Rubenstein, SEI ’63 and Marie Raftery

 Ronald Pruett, SOM ’63, Harry Carrozza, SEI ’69, and Bernard Schneider SEI ’64

 Class of 1999: Tushar Patel, Nicole Delarato, John Butler, Christine Langell and Richard Kaiser

 Vanessa Trice and Veronica English, SEI ophthalmic technicians
ACADEMIC HIGHLIGHTS 2004

Spring is an exciting time in the educational activities division of the department! In addition to grand rounds and visiting professors, we look forward to welcoming several invited guests for the Saturday morning continuing medical education series, the named lectureships, and the annual Spring Alumni Meeting.

New Ideas in Glaucoma Management
February 21, 2004
Joel S. Schuman, M.D.
Professor and Chairman of Ophthalmology and Eye Center Director, University of Pittsburgh Medical Center
• Laser Trabeculoplasty
• Imaging in Glaucoma

5th Annual Louis A. Karp Lectureship
March 25, 2004
Sander R. Dubovy, M.D.
Assistant Professor of Ophthalmology and Pathology
University of Miami, Bascom Palmer Eye Institute
• Ophthalmic Pathology 2004

27th Annual Francis Heed Adler Lectureship
April 3, 2004
Thomas A. Weingeist, Ph.D., M.D.
Professor and Chair of Ophthalmology
University of Iowa Hospitals and Clinics
• Uveal Melanoma 2004: Diagnostic Challenges and Future Management
• Case Studies in Ophthalmology

130th Anniversary Meeting
May 21-22, 2004
Donald L. Budenz, M.D.
Associate Professor of Ophthalmology
University of Miami, Bascom Palmer Eye Institute
• OCT in Glaucoma
• Glaucoma Filtering Bleb Leaks - Prevention and Repair

130th Anniversary Meeting
May 21-22, 2004
Daniel F. Martin, M.D.
Associate Professor of Ophthalmology
Director, Retina Service
Emory University
• Diagnosis & Management of Posterior Uveitis
• New Information from the Age-Related Eye Diseases Study (AREDS)
The National Eye Institute (NEI) has awarded the Department an Institutional Mentored Clinical Scientist Development Program (K12). The award is made to institutions with well-established vision research programs to support the career development of clinician scientists and patient-oriented clinical investigators. Between 8 and 10 candidates, who have recently completed their clinical training, will be selected over the next 5 years. The first candidates will begin in July 2004. Maureen G. Maguire, Ph.D., Director of the Center for Preventive Ophthalmology and Biostatistics, is the Program Director.

James Katowitz, M.D., Director of Pediatric Oculoplastic Surgery, delivered the keynote address, “Congenital Eyelid Abnormalities,” for the oculoplastic section of the German Ophthalmologic Society in Berlin on September 26, 2003. He was awarded the 2003 Orkan George Stasior, M.D. Outstanding Contribution and Leadership Award for his contributions to ophthalmic plastic and reconstructive surgery. Katowitz’s textbook, Pediatric Oculoplastic Surgery, with contributions from all past oculoplastic fellows, won first prize from the National Society of Medical Illustrators.

Maureen G. Maguire, Ph.D., received the Secretariat Award in recognition of her contributions to the American Academy of Ophthalmology. Maguire has served on the editorial board of the Academy’s journal, Ophthalmology, since 1994 and served as a panel member for the Academy’s Preferred Practice Pattern for Cataract in the Adult Eye.

Robert L. Peiffer, D.V.M., Ph.D., one of our ophthalmic pathologists, received the Waltham International Award for Scientific Achievement at the World Small Animal Veterinary Association meeting in Bangkok, October 24-27, 2003, in recognition of his outstanding scientific contributions to ophthalmology.

Jody Piltz-Seymour, M.D., a member of the American Glaucoma Society (AGS) Executive Committee, has been appointed to the AGS Program Committee for the 2004 Annual Meeting. Piltz-Seymour served on the NEI Special Emphasis Panel to review RO3 grants in July 2003. That same month, she delivered the Robert Mason, Sr., M.D. Memorial Lecture at the National Medical Association Annual Meeting, July 2003.

Michael Sulewski, M.D., received the American Academy of Ophthalmology - State Governmental Affairs Veterans Service Award for his Advocacy in Support of Quality Eye Care for America’s Veterans in Anaheim, CA on 10/15/2003. Sulewski won a 3-year position as the Counselor to the AAO for VA-related issues at the Association of Veterans Ophthalmologists.

Terri L. Young, M.D., received a physician-scientist award from Research to Prevent Blindness. She was appointed to serve on the Board of Directors for National Women in Ophthalmology, Inc. for 2003-2006 and featured in a video, “Women are Researchers,” sponsored by the Department of Health and Human Services, National Institutes of Health, Office of Research on Women’s Health.
University of Pennsylvania Department of Ophthalmology
Lectures and Seminars
January 2004 - June 2004

Visiting Professor Lectures are on Thursdays:
7:45-8:30 AM (Scheie Eye Institute Auditorium-Lower Level)
Noon-1:00 PM (Talley Conference Room, 5th Floor)

JANUARY 8, 2004
Thomas A. Ciulla, M.D.
Midwest Eye Institute
7:45 A.M.: The Role of Corticosteroids in the Treatment of AMD
Noon: The Role of Macular Pigments in the Pathophysiology of AMD

JANUARY 10, 2004
Ethics Symposium:
8:30 A.M.-Noon
Samuel Packer, M.D.
Cornell University Medical College
Are Gifts From the Industry Really Gifts? Do the Residents Need Some Reading Material?

JANUARY 15, 2004
Ophthalmic Heritage Lecture
Moderators: William C. Frayer, M.D., and Nicholas J. Volpe, M.D.
Speaker: Charles E. Letocha, M.D.
7:45 A.M.: Did George McClellan Commit Malpractice? (1829 lawsuit involving cataract surgery)

JANUARY 23, 2004
Susan B. Bressler, M.D.
The Johns Hopkins University School of Medicine
7:45 A.M.: Clinically Relevant Results from AREDS
Noon: Diabetic Macular Edema: OCT or Fundus Biomicroscopy?

FEBRUARY 5, 2004
Dwight E. Stambolian, M.D., Ph.D.
F.M. Kirby Center for Molecular Ophthalmology
Scheie Eye Institute/University of Pennsylvania
7:45 A.M.: Genetic Studies of Myopia

FEBRUARY 12, 2004
Elias I. Traboulsi, M.D.
Ohio State University
Cleveland Clinic Foundation, Cole Eye Institute
7:45 A.M.: Limited Eye Movements in Childhood
Noon: An Overview of the Genetics of Ocular Malformations

FEBRUARY 19, 2004
Joshua L. Duniael, M.D., Ph.D.
F.M. Kirby Center for Molecular Ophthalmology
Scheie Eye Institute/University of Pennsylvania
7:45 A.M.: Oxidative Stress Induced Cell Death in AMD

FEBRUARY 21, 2004
Glucoma CME (8:00 AM - Noon)
Joel S. Schuman, M.D.
Univ. of Pittsburgh School of Medicine
UPMC Eye Center
Laser Trabeculoplasty, Imaging in Glaucoma

MARCH 4, 2004
Robert E. Gausas, M.D.
Scheie Eye Institute/University of Pennsylvania
7:45 A.M.: New Monoclonal Antibody Identification of Lymphatics: It’s Relevance to the Orbit and Eye

MARCH 25, 2004
4th Annual Louis Karp Lectureship
Sander Dubovy, M.D.
Bascom Palmer Eye Institute
University of Miami School of Medicine

APRIL 3, 2004
Francis Heed Adler Lecture
8:00 A.M. - Noon
Thomas A. Weingeist, Ph.D., M.D.
Department of Ophthalmology
Univ. of Iowa Hospitals and Clinics
Uveal Melanoma 2004: Diagnostic Challenges and Future Management
Case Studies in Ophthalmology

APRIL 15, 2004
Alfredo A. Sadun, M.D., Ph.D.
USC Keck School of Medicine
Doheny Eye Institute
7:45 A.M.: New Findings in Leber’s Hereditary Optic Neuropathy: Comparing Brazil to the Lab
Noon: A Neuro-Ophthalmologist’s View of RGC Apoptosis and Neuroprotection

APRIL 22, 2004
Jody R. Piltz-Seymour, M.D.
Scheie Eye Institute/University of Pennsylvania
7:45 A.M.: Evidence Based Medicine in Glaucoma

MAY 6, 2004
Eric A. Pierce, M.D., Ph.D.
F.M. Kirby Center for Molecular Ophthalmology
Scheie Eye Institute/Univ. of Pennsylvania
7:45 A.M.: rRNA for the Treatment of Ocular Neovascularization

MAY 13, 2004
Allan D. Jensen, M.D.
The Wilmer Ophthalmological Institute
Johns Hopkins University School of Medicine
7:45 A.M.: An Update on Activities of the American Academy of Ophthalmology
Noon: Demands for Demonstrating Maintenance of Competence

MAY 20, 2004
Maureen G. Maguire, Ph.D.
Scheie Eye Institute/Univ. of Pennsylvania
7:45 A.M.: Comparison of Vision Screening Tests for Preschool Children: Results from Phase I of the Vision in Preschoolers (VIP) Study

MAY 21-22, 2004
130th Anniversary Meeting
Daniel F. Martin, M.D.
Emory Eye Center
Emory University School of Medicine
Diagnosis and Management of Posterior Uveitis
New Information from AREDS
Donald L. Budenz, M.D.
Bascom Palmer Eye Institute
University of Miami School of Medicine
OCT in Glaucoma
Glaucoma Filtering Bleb Leaks - Prevention and Repair

MAY 27, 2004
J. William Harbour, M.D.
Washington University School of Medicine
7:45 A.M.: Contemporary Management of Uveal Melanoma
Noon: Uveal Melanoma: From Bedside to Bench to Bedside

JUNE 3, 2004
Michael J. Tolentino, M.D.
F. M. Kirby Center for Molecular Ophthalmology
Scheie Eye Institute/Univ. of Pennsylvania
7:45 A.M.: siRNA for the Treatment of Ocular Neovascularization

JUNE 17, 2004
Ophthalmic Heritage Lecture:
Moderators: William C. Frayer, M.D., and Nicholas J. Volpe
Speaker: William S. Tasman, M.D., F.A.C.S.
7:45 A.M.: Eye disorders and how they have affected history and the arts

For more information, please contact
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To remove name from mailing list, call above number.