

Inside Retina

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News from the California Retina Research Foundation

A CANDID DISCUSSION WITH MOVIE ICON AND AMD PATIENT JANE RUSSELL



Jane Russell

Film icon Jane Russell became a patient at California Retina Consultants eight years ago when she presented with age-related macular degeneration (AMD). She currently receives ongoing treatment at our Santa Maria office, and at 89 years old, leads an active lifestyle despite the limitations of AMD. Her upbeat attitude and legendary career, which she hopes to continue well into her nineties, are an inspiration.

Russell graciously agreed to meet with us in her Santa Maria home to discuss her life since diagnosis.

What was your initial reaction to the diagnosis of Age Related Macular Degeneration?

Crazy! I was flying from Los Angeles to London and when I landed in Europe all of the buildings appeared slanted, like a zig-zag. I knew then that something was very wrong and I needed to see a doctor, which I did when I returned to California. It happened so quickly - I drove myself to the LAX airport for departure and by the time I returned home I knew it wasn't safe to drive anymore. I was terribly upset and worried.

What types of treatment did you receive?

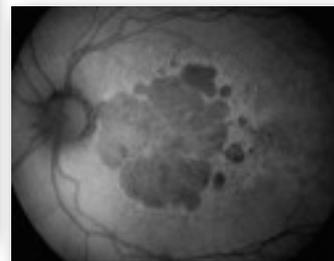
Russell began seeing Dr. Ma'an Nasir at California Retina Consultants and received photodynamic therapy (PDT) for recurrent subretinal fluid in the left eye, which helped stabilize her vision. She also enrolled in Macugen trials at UCLA, since clinical trials at California Retina Consultants were closed. She continued with Macugen for two years with relatively good outcomes. Unfortunately, her maculopathy continued to worsen in her right eye and Dr. Nasir suggested off-label Avastin injections.

*I was originally traveling three hours in each direction to UCLA and after a while it seemed the medication I received there wasn't really helping; I was thrilled to be able to stay in Santa Maria for treatment. Since receiving care in Santa Maria, I am now able to read if I have a really good light. **Continued on page 7***

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NEW TREATMENTS FOR DRY AMD



Following major advances in the treatment of wet AMD, researchers at CRRF and around the world are now focusing their attention on treating AMD at earlier stages of the disease process. Genentech, maker of Avastin and Lucentis, is developing a novel inhibitor of Factor D (a protein involved in complement

CALIFORNIA RETINA CONSULTANTS CONTRIBUTE TO THE PREVENTION OF BLINDNESS THROUGH GROUND-BREAKING RESEARCH

Treatments -Continued from page 1

activation and inflammation) for treatment of geographic atrophy, a major cause of vision loss in dry AMD. Dr. Pieramici, the principal investigator, led The California Retina Research Foundation's efforts in a Phase 1 FDA trial of this drug. Working in conjunction with other top eye institutions, including Johns Hopkins Wilmer Eye Institute, Harvard and Duke Universities, investigators hypothesize that inhibiting the complement system as discussed above might retard the progression of cellular and visual loss, and prevent the progression to more advanced stages of AMD. Dr. Avery presented the initial results at the Retina Society's annual meeting this past fall in San Francisco. He comments, "The purpose of the Phase 1 study was to test and identify any safety issues associated with the new treatment, and we are pleased to report that the drug passed this first phase successfully, leaving us very hopeful." Enrollment for Phase 2 of this study is underway.

MACULAR DEGENERATION

Anti-VEGF Research

The doctors of the California Retina Consultants and Research Foundation have had the privilege of playing a role in the advancement of the use of anti-VEGF agents in the treatment of retinal diseases. According to Dr. Pieramici, "The advent of these agents in the treatment of our patients is probably the single most significant advancement in ophthalmology in the last 25 years. Today, because of these agents millions of patients around the world will avoid blindness."

California Retina Consultants' involvement dates back to 1993 when Dr. Robert Avery began collecting intraocular samples on patients with diabetic retinopathy and retinal vein occlusions. These samples were analyzed with collaborators at the Joslin Diabetes Center, Harvard University and Johns Hopkins University to identify the growth factor, VEGF (vascular endothelial growth factor). Napoleone Ferrara, a collaborator from Genentech on this project, has recently been awarded the Lasker Award – an award which often precedes the Nobel prize. Genentech was the first pharmaceutical company to produce inhibitors of VEGF, and the doctors at CRC were among the first medical groups to adapt these agents to treat patients, first with neovascular (wet) AMD and then with other diseases. The data from California Retina's first large series of patients was collected and published in *Ophthalmology* and has become the single most cited retina paper in the last decade. Dr. Avery comments: "It has been an extremely exciting time to be a researcher in retinal diseases. Conditions that

were at one time considered irreversible and destined to lead to permanent, significant visual impairment are now treatable with remarkable results. It's been very rewarding to be involved in both discovering VEGF's role in retinal disease, and years later, pioneering the treatment of these diseases with VEGF inhibitors."

California Retina Consultants' dedication to the investigation and clinical application of new treatments continues unabated despite these advances. Much of the emphasis is now directed to extending the treatment duration and efficacy of current therapies while focusing on treating retinal diseases at earlier stages in the pathologic process.

Comparison of Age Related Macular Degeneration Treatments Trial (CATT)

There are currently two widely used drugs approved by Medicare for the treatment of wet AMD: Avastin and Lucentis. Both drugs are manufactured by Genentech, however, Avastin is not FDA approved for retinal diseases, but is commonly used "off-label." It is significantly more affordable than Lucentis which is FDA approved and is accepted by most insurance carriers. The Comparison of Age-Related Macular Degeneration Treatments Trial (CATT) is the first major clinical trial to compare these two drugs. Dr. Avery has been involved in this trial's design as a member of its executive committee. Data analysis is now beginning for the first year of this two-year trial, with results expected to be reported in the first half of 2011. Genetic analyses of blood samples collected from patients enrolled in the study were recently added to explore potential relationships between an individual's genetic composition and the degree to which an individual responds to treatment.

"It has been an extremely exciting time to be a researcher in retinal diseases. Conditions that were at one time considered irreversible and destined to lead to permanent, significant visual impairment are now treatable with remarkable results."

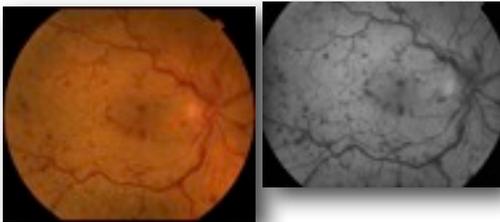
Robert L. Avery, M.D.

Complement Pathway Trials and Other Novel Treatments

Two multi-centered clinical trials at CRC are testing new combination therapies for wet AMD. Each study evaluates the efficacy of using Lucentis in combination with another treatment. By adding an additional mechanism of action, the hope is to improve the efficacy and durability over Lucentis monotherapy. The first study tests a compound designed to strip the abnormal vessels of pericytes, which act to facilitate blood vessel development, growth and stability. This compound seems to preferentially eliminate the abnormal vessels that result in retinal bleeding and scar formation. The second study tests a complement pathway inhibitor. The complement pathway is an important inflammatory pathway. Over-

activation of this pathway may lead to inflammatory damage within the outer retina, and could be an inciting and propagating factor in the development of both wet and dry AMD. Patients with genetic abnormalities predisposing to complement over action have heightened risk of developing advanced macular degeneration. Histo-chemical evaluation of drusen (deposits under the retina associated with AMD) conducted at The University of California Santa Barbara have confirmed that inflammatory proteins of the complement system are present in these deposits. This is additional evidence supporting the hypothesis that inhibiting this inflammatory system may be a rational approach to treating AMD patients.

RETINAL VEIN OCCLUSIONS

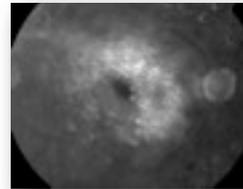


An occlusion, or blockage, of a retinal vein is a common cause for vision loss. When the central vein becomes blocked, blood flow out of the eye is reduced. This leads to bleeding and swelling of the retina, a condition known as macular edema.

Given the success of both Lucentis and Avastin in treating retinal fluid accumulation in wet macular degeneration, California Retina researchers set out to determine if these two drugs could be effective treatments for patients suffering from central retinal vein occlusions. California Retina Research Foundation began the studies in 2005 and results were presented at the Association for Research in Vision and Ophthalmology’s annual meeting. Using the data from this small clinical trial, Genentech and investigators around the country initiated large scale national clinical trials to further evaluate the treatment of retinal swelling or macular edema associated

with branch and central retinal vein occlusions using Lucentis. These trials were conducted at multiple centers across the United States, including California Retina Consultants. The majority of participants in the trials demonstrated an improvement in visual acuity and a reduction in macular edema. In June 2010, Lucentis was approved by the FDA for treating this condition.

The CRRF is conducting additional trials to find longer lasting treatments for retinal vein occlusions, testing the effectiveness of higher doses of Lucentis as well as combination therapies using Lucentis with laser.



DIABETIC MACULAR EDEMA

Swelling of the retina, or macular edema, is a major cause of vision loss in patients with diabetic retinopathy. Until recently, laser therapy was the only effective treatment for patients with diabetic macular edema. Despite this therapy, many

experienced incomplete resolution of the swelling and persistent visual loss. Newer therapies were needed.

CRRF researchers have been members of the NIH (National Institutes of Health) sponsored Diabetic Retinopathy Clinical Research Network investigating various treatments for diabetic eye diseases over the last eight years. Recently the DRCR reported favorable results using anti-VEGF agents in the treatment of diabetic macular edema. Drs. Pieramici and Nasir recently presented the findings of this trial at the Retina Society and California Retina Consultants’ annual meetings. Dr. Nasir stated, “This new treatment option will forever change the management of diabetic eye disease and potentially save the vision in thousands of our patients. We are grateful to be part of this groundbreaking study and proud to have offered patients in our various offices a chance to receive treatment before it was commercially available. We thank all of our patients who participated in these clinical research trials.”

DR. NATHAN STEINLE JOINS CALIFORNIA RETINA CONSULTANTS



Nathan and Valerie Steinle

Nathan C. Steinle, M.D. is the most recent addition to California Retina Consultants. Dr. Steinle was born and raised in South Dakota, where he met his wife of five years, Valerie. Dr. Steinle received his undergraduate and medical training in his home state, where he was named the class valedictorian and graduated summa cum laude. After completing his residency in Kentucky, Dr. Steinle performed his surgical vitreoretinal training at the renowned Cleveland Clinic. Steinle comments, “The motto of the Cleveland Clinic is to provide world-class care every single day to every patient, and I look forward to carrying forth this approach to the wonderful people of the Central Coast region. I am extremely excited to join the exceptional group of physicians and staff at California Retina Consultants where collectively we can offer patients availability to the latest clinical trials and research as well as access to cutting edge diagnostic equipment and therapeutic tools.” Dr. Steinle will be based in San Luis Obispo.

RETINA RUNS IN THE FAMILY

When Dr. Glynne Couvillion graduated medical school, he was among the first to pursue specialized retina training at Boston's prestigious Massachusetts Eye & Ear Infirmary. The field of retina was in its infant stages, with experimentation of new treatment options on the cusp of discovery. At that time there were very few retina fellowship programs offered throughout the country and Dr. Couvillion was one of only six doctors in his class.

Dr. Couvillion received the privilege of training under Dr. Charles Schepens, a revered physician widely regarded as the "father of the retina specialty" for his dramatic contributions in the treatment of severe retinal diseases. Under Schepens' tutelage, Dr. Couvillion worked with the first intraocular scissors, tested silicone oil in the eye, experimented with the vitrectomy -- a procedure that was just beginning to revolutionize retina surgery -- and, in particular, learned the modern method of repair of the retinal detachment. When he arrived on California's Central Coast in 1969, Dr. Couvillion was among the first trained retina specialists on the West Coast. He brought new treatment options, advanced instrumentation and expert knowledge gained from his Boston training.



Stephen and Glynne Couvillion

Interestingly, both of his sons, John and Stephen, followed in his footsteps when they pursued careers as retina specialists. Stephen followed his dad - literally - landing at the practice his father founded, California Retina Consultants, just three years ago. CRC met with Drs. Glynne and Steve Couvillion to learn more about this medical family.

Why did you decide to open a practice on the Central Coast?

Well, actually many people told me that California was a medical desert and I thought all the better – I'll get myself a wet suit and dive right in. I had spent three years working as a diving doctor in the Navy, stationed in San Diego, and I really wanted to get back to the California mentality. It really is a mentality.

What was the ophthalmology community like when you arrived?

Treatment was very different back then. First of all, general ophthalmologists were trained to learn the whole eye and had a limited understanding of specific retinal diseases. They questioned the necessity of targeted retinal treatments because it was such a new, burgeoning specialty. I really had to prove to them that there was a better way to treat patients. When I arrived there were about 100 ophthalmologists serving the Central Coast and I would visit each doctor and talk about retina treatments. It took a lot of convincing.

How has the retina field changed over the last two decades?

Nobody ever wanted to touch a retinal detachment. It's such a precise, delicate surgery. When I was treating patients all of our surgeries were performed on the outside of the eye, now everything is done on the inside of the eye. Patients were placed on bed rest in the hospital, while their eyes were put on ice. We also used bilateral patches. Today patients have retinal surgeries on an outpatient basis.

What do you view as the most significant change in California Retina Consultants (CRC) since you started your practice in 1969?

I am extremely proud of the research performed at CRC. It has evolved from a clinical treatment and surgical practice to a first rate academic institute with participation in national clinical trials and the discovery of revolutionary treatment options. CRC is also a training ground for new fellows. I think the crew of doctors constitutes the best practice of retinal specialists in the world. Santa Barbara has always been a town of academic excellence and this practice has attracted some of the most sought-after doctors who have been trained at some of our country's premier medical institutions: Johns Hopkins Wilmer Eye Institute, Emory University, Bascom Palmer Eye Institute and Duke University Eye Center. I don't know if patients even realize this, but these are the finest trained doctors you can get.

How do you account for the fact that two of your sons are doctors, specifically retina surgeons? Did you do anything to influence their decisions?

At a loss, Dr. Glynne Couvillion shrugs his shoulders and the question turns to his son, Dr. Stephen Couvillion, who is asked to recall any early memories that may have impacted his decision.

I remember going to St. Francis as a kid and going on rounds with my dad, seeing the patients on bed rest. I was exposed to the excitement of surgery as well as the drama and I think that held a certain appeal. I was always interested in math and science and by the time I got to high school, I had already decided on a career in surgery. His dad adds, "You were always clever with your hands."

How is it that you selected retina as a specialty?

Dr. Stephen Couvillion: Once in medical school, I was obviously familiar with ophthalmology and at the time retina surgery was at the forefront of the field with advancements in surgical tools and techniques for treating severe retina diseases. The study of retina became the highest mountain you could climb. By completing that level of training you were equipped to fix any problem in ophthalmology. You become the end of the line – doctors would send you the patients they could no longer treat. As a surgeon, you have the ability to fix someone when nobody else could and I found that very appealing.

You trained at one of the top retina fellowship programs in the country (Miami’s Bascom Palmer Eye Institute). You really could have gone anywhere. Why did you decide to return to Santa Barbara?

My wife’s family is from Santa Barbara and we both have long family ties to both Santa Barbara and Santa Maria. Of course my family is still here, and I appreciate the lifestyle. But mostly, it was the chance to be part of this world-class group of doctors. It’s akin to going back to an academic program with the benefits of a private group.



Dr. Stephen Couvillion with his wife Lisa and sons James, Thomas and Michael

It seems that medicine runs in the family. Where does your other son practice?

Dr. Glynne Couvillion: My other son, John, is also a retina specialist with a practice in Baton Rouge. And my grandfather, John James was a doctor. In fact, he delivered me in 1933 in our very small town of Plaquemine, in Louisiana’s backcountry. I also have a brother who is an oral surgeon and my brother-in-law was an OB/GYN.

That’s quite an impressive legacy. Dr. Steve Couvillion, you have three young sons and I wonder if you hold any hope of a third generation Couvillion working at California Retina Consultants?

Well, I certainly wouldn’t discourage them. It’s a lot of training but extremely rewarding. I would say if that’s what they find their interest in and that’s where their talents lie, then we would absolutely support that decision. I do bring the boys to the office with me and hope to give them the same exposure I received as a child.

ACCOLADES

Dr. Dante Pieramici and Dr. Robert Avery have been recognized by Best Doctors in America, a peer-reviewed database of the best doctors in the United States in over 400 specialties. Founded by physicians affiliated with Harvard Medical School, this compendium represents the top 5% of physicians nationwide.

Dr. Robert Avery has joined the medical Board of Directors for the Braille Institute. He has been elected to *Marquis Who’s Who in America* and *Who’s Who in Medicine and Healthcare*.

Dr. Dante Pieramici serves as President-elect of the Santa Barbara County Medical Society and continues his participation as Board member of S.E.E. International (Surgical Eye Expeditions).

MEDICAL FAMILY TIES AT CALIFORNIA RETINA CONSULTANTS

In addition to the Couvillion legacy, the physician gene seems to run in the CRC family:

Dr. Dante Pieramici has two younger brothers who are also physicians: Dr. Erik Pieramici, gastroenterologist in Denver, Colorado and Dr. Sean Pieramici, cornea specialist in Pittsburgh, Pennsylvania.

Dr. Bob See’s wife, Gina, is a gastroenterologist practicing in Lancaster, California.

Dr. Alessandro Castellarin’s father is an 81-year-old radiologist still practicing in Verona, Italy. His grandfather was a general surgeon.

Dr. Ma’an Nasir has five uncles who are doctors, 12 cousins who are doctors and a brother, Dr. Marwan Nasir, a pathologist in Tomball, Texas.

EYE SIGHTINGS

California Retina Consultants physicians continue to share their knowledge and expertise with ophthalmologic colleagues around the world, while bringing the best practices from other locations back to California's Central Coast.

Here's a sampling of where our staff has been in the past few months:

- ❖ Dr. Ma'an Nasir attended the Bascom Palmer Angiogenesis Meeting in Miami, Florida; The American Society of Retinal Specialists, Vancouver, Canada; and The American Academy of Ophthalmology, Chicago, Illinois.
- ❖ Dr. Dante Pieramici presented findings of new clinical research at Club Vit, Sorrento, Italy; ARVO, Ft. Lauderdale, Florida; American Academy of Ophthalmology, Chicago Illinois; Retina Society, San Francisco, CA; The Macula Society, Tuscon, Arizona; American Society of Retina Specialists, Vancouver, Canada; and the Wilmer Eye Institute Educational Course, San Francisco, California.
- ❖ Dr. Robert Avery presented findings of new clinical research at the Retina Society, San Francisco, CA; the Association for Research in Vision and Ophthalmology, Ft. Lauderdale, Florida; American Academy of Ophthalmology, Chicago Illinois; The Macula Society, Tuscon, Arizona; the Vail Vitrectomy Meeting, Vail, CO; and the Surgical Study Group, Tahiti.
- ❖ Dr. Alessandro Castellarin was a guest speaker at Club Vit, in Sorrento Italy; an instructor at the American Academy of Ophthalmology in Chicago and will be guest speaker this year at the international meeting on Present and Future Challenges in Severe Retinal Diseases.
- ❖ Alison Ratliff, Practice Administrator, attended a Genentech Advisory Board Meeting in New York; presented at the American Academy of Ophthalmology in Chicago, Illinois; multiple presentations addressing insurance concerns for retina practices over Southern California and Texas.

2010 CRC ANNUAL EDUCATIONAL MEETING HIGHLIGHTS



Now in its ninth year, the California Retina Consultants' Annual Education Meeting welcomed over 130 ophthalmologists, optometrists and eye care specialists throughout the Central Coast and Southern California. Dr. Dennis Clegg, co-director at UCSB Center for Stem Cell Biology and Engineering was the keynote speaker, addressing recent advances in stem cell therapies for retinal disease. Dr. Clegg is the recipient of the UCSB Distinguished Teaching Award in the Physical Sciences, and served as Chair of the Department of Molecular, Cellular and Developmental Biology from 2004-2009.



Left to Right: Dr. Pieramici, Dr. Castellarin, Dr. Kohn, Dr. Avery

In addition, Nobel Laureate, Dr. Walker Kohn spoke about the benefits of a computer program that he developed with Jim Klinghshirn to help correct distorted or wavy images using a novel algorithm. The device is still in early development and not yet ready for patient use. Dr. Kohn's wife suffers from advanced macular degeneration, and has been cared for by Dr. Avery. Dr. Kohn says he created the program to help his wife, and he has collaborated with Dr. Avery on its development – testing it on CRC patients. Dr. Kohn was awarded the 1998 Nobel Prize in chemistry for his development of the density-functional theory.

The event was held on October 2, 2010 at Fess Parker's Doubletree Resort.

Russell -Continued from page 1

How has age-related macular degeneration changed your life?

Well, I can't drive anymore which is sickening because I've been driving since I was 14 years old. I have to have a driver or rely on taxi. Thankfully, I can still read and I can see images if they are very close. I have moved the television off the pedestal in my bedroom and placed it by my bedside so that I can still watch the classic movies.

What, if anything, do you miss the most?

Driving!

You manage to stay quite active; what types of activities do you still enjoy?

I have been singing with a group called the "Swinging Forties." It started with just three women and one terrific piano player singing all of our old favorites for fun. We would sing around town in restaurants, and we have now grown to nearly a dozen male and female singers who sing regularly at the Radisson Hotel. It's wonderful - older people can hear all their old music; we sing Jimmy Dorsey, Frank Sinatra, Benny Goodman, Nat King Cole and other classic tunes. I also just returned from London and Florida where I still do singing shows and interviews. I travel a lot.

Do you use any aides that help you, particularly while you travel?

I can still travel and just returned from Europe but the key is to take someone with you. You can't travel alone. And I take my PRISMA with me wherever I go; I just love my PRISMA and think it's so wonderful.

Can you explain the PRISMA?

I have a small PRISMA that travels with me and that I use at home. It's a device that plugs into my TV and enlarges images, pages from a book, photos, or whatever you place under the PRISMA light, projecting the image onto the TV screen.

Note: The PRISMA, manufactured by Ash Technologies, is a full color video magnifier that may aide some people with low vision. There are a number of low vision aides, however, for many, these devices are still not enough to improve visual acuity. CRC has no financial interest in any low vision devices.

What advice would you give to patients who have recently been diagnosed with AMD?

Get the PRISMA - it changed my life.

Any tips on how you stay so positive?

Well, I've been pretty busy my whole life so I remain that way. I used to paint but I don't do that anymore and I no longer act but I do lots of interviews. I go to Church every Sunday and can still read my Bible. I can also still watch the Turner classic movies on TV. I've just gotten used to it, I've been living with AMD so long that it's simply part of my life.

Which of the Turner Classics are among your favorites?

Well, of the ones I was in, my favorite was "Gentlemen Prefer Blondes." We had the perfect director and choreographer. Neither Marilyn nor I knew how to dance before that movie! We got so lucky working with two extraordinary men (director: Howard Hawks, choreographer: Jack Cole).



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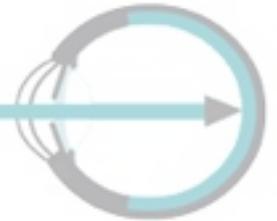
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FELLOWS RECEIVE TRAINING AT CRC

California Retina Consultants is proud to have tutored two visiting doctors this past year as part of its ongoing fellowship program. “The fellowship program is a wonderful addition to our practice as it allows us to teach advanced techniques to doctors on a global level” states Dr. Dante Pieramici, surgical training director. He adds, “There is no doubt that we learn as much from these visitors as we teach.” This past year the practice welcomed Dr. Juan Pablo Davila from Mexico City and Dr. Narcisa Ianopol from Iasi, Romania.

Dr. Davila received his medical degree from Universidad Anahuac in Mexico City, Mexico. After completing his clinical clerkship with a medical retina group in Mexico City, Dr. Davila was awarded the clinical fellowship position at CRC. During his three month visit, Dr. Davila participated in clinical research projects and observed a variety of medical and surgical cases, including retinal detachments, Baerveldt glaucoma implantation and trauma. “I had the opportunity to observe patients and procedures in Bakersfield, Oxnard and Santa Maria and I was amazed by the differences in pathology and in the severity of diseases from one office to the next,” says Dr. Davila, adding, “This was an incredibly valuable learning opportunity for me and I am so fortunate to have these well trained doctors as my teachers.”

Dr. Narcisa Ianopol has nearly twenty years of experience as a surgeon in both Romania and Germany, so in addition to receiving training locally, she also brought new ideas to the California Retina Consultants’ offices when she visited this year.

Dr. Ianopol followed the doctors on patient rounds and observed in the operating room. She commented, “I was impressed by the number of patients that these doctors and staff care for each day and by their high level of professionalism.” She continues, “I learned the art of being patient and talking with compassion, but at the same time making the best medical or surgical decisions for all ophthalmological pathologies, without any limitations.”

<p>Santa Barbara Offices 515 E. Micheltorena St.; Ste C Santa Barbara, CA 93103 (805) 963-1648</p> <p>29 W. Anapamu St. Santa Barbara CA 93101 (805) 681-8950</p> <p>Research Foundation 515 E. Micheltorena St.; Ste G Santa Barbara, CA 93103 (805) 884-5185</p>	<p>Santa Maria Office 1510 E. Main St.; Ste 103 Santa Maria, CA 93454 (805) 922-2068</p>	<p>Oxnard Office 1801 N. Solar Dr.; Ste 145 Oxnard, CA 93030 (805) 983-8808</p>	<p>Bakersfield Office 5329 Office Center Ct.; Ste 120 Bakersfield, CA 93309 (661) 325-4393</p>
	<p>Valencia Office 27420 Tournay Rd.; Ste 170 Valencia, CA 91355 (661) 253-2939</p>	<p>Lancaster Office 1505 West Ave J.; Ste 303 Lancaster, CA 93534 (661) 951-9519</p>	<p>San Luis Obispo 628 California Blvd. ; Ste D San Luis Obispo, CA 93401 (805) 781-0292</p>

Robert L. Avery, M.D. Ma’an A. Nasir, M.D. Dante J. Pieramici, M.D. Alessandro A. Castellarin, M.D.
Robert F. See, M.D. Stephen S. Couvillion, M.D. Nathan C. Steinle, M.D.

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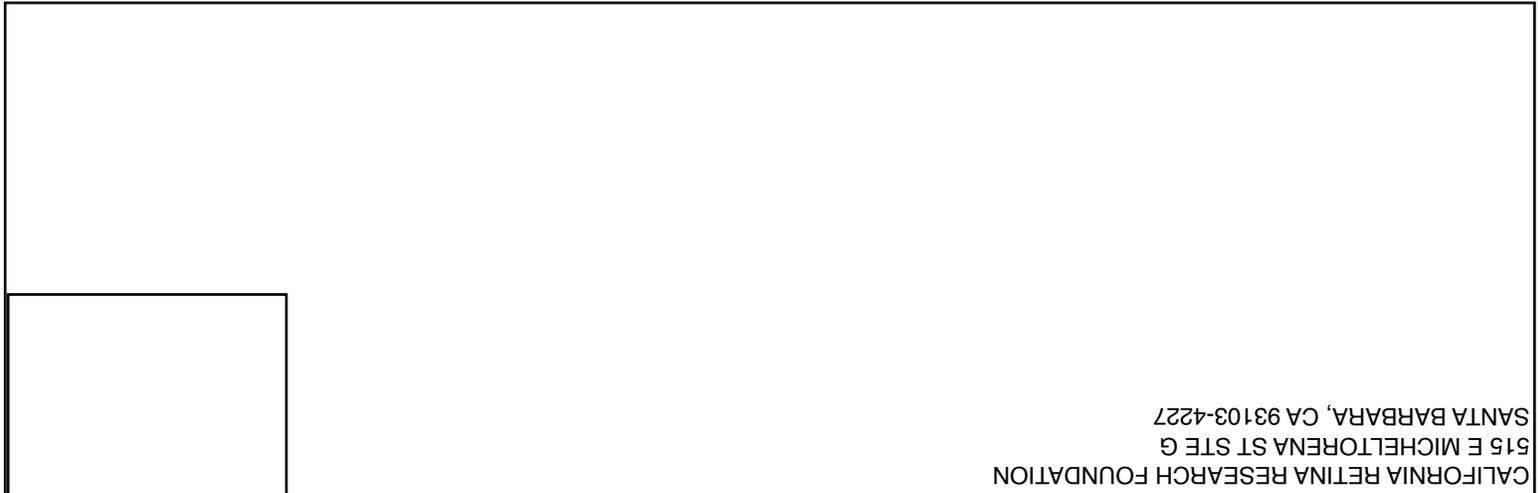
Medical Director: Dante J. Pieramici, M.D.

Editor: Ann Pieramici

Design & Production: Matthew Giust

Director of Research: Melvin Rabena

Practice Administrator: Alison Ratliff



CALIFORNIA RETINA RESEARCH FOUNDATION
515 E MICHELTORENA ST STE G
SANTA BARBARA, CA 93103-4227