

TRANSCRIPT OF THE #MDPEOPLE GROUP SESSION WITH DR. PETER GOURAS 4/24/99

(Edited for length and clarity)

Dan: Dr. Peter Gouras is a leading researcher in the field of ophthalmology, and we are honored to have him as our guest today. Dr. Gouras, thank you for agreeing to be our guest. Before I open the floor to questions, please tell us about yourself and your work.

Dr. Gouras: Thank you, Dan. I received my MD degree and surgical training at Johns Hopkins University Medical School & Hospital. I was a fellow at Cambridge University, England, and subsequently a staff member of the National Eye Institute at the National Institutes of Health. I came to Columbia University in 1978, where I am currently Professor of Ophthalmology. My major interests are in retinal function and cell transplantation. My research has concentrated on the retina.

I discovered that vitamin A deficiency was responsible for the retinal degeneration in abetalipoproteinemia, which has led to a universal therapy for this retinal abnormality. I pioneered the method of retinal pigment epithelial (RPE) cell transplantation and used it to stop the progression of the retinal degeneration in the RCS rat, a well known model of retinitis pigmentosa. This is the first retinal degeneration that has been stopped by retinal cell transplantation.

I also developed methods to transplant human fetal retinal epithelium into the human macula and have been collaborating with the Karolinska Institute, Sweden, in applying it to the treatment of ARMD.

Dan: Thank you, Dr. Gouras. You are doing impressive work. Can you bring us up to date on the progress of RPE cell transplantation? What success has there been with human subjects since the first surgeries were performed?

Dr. Gouras: There really hasn't been success, as far as helping anyone. The only successes which we have learned is in technique so that we can improve the methods, and hopefully reach our goal of influencing the course of this degeneration.

The first problem we encountered was slow rejection. This happens over several months, and the central area of vision is particularly vulnerable to rejection. The fovea is the main concern, because of its vital importance to vision.

To try to counteract rejection, we give immunosuppression drugs. In older patients, cyclosporine (CSA) can be given as a capsule which is sewn into the back of the eye. This capsule releases the drug slowly, and works better than systemic application. This has been done only in animals models so far.

Rob: Is the dosage of the immunosuppression drugs set by the danger of infection - or is efficacy to rejection suppression lost as higher dosages already?

Dr. Gouras: The dosage is set to minimize toxicity and prevent rejection. We use a standard dose which is used in kidney transplants. A group in Washington

Rob: Is the dosage of the immunosuppression drugs set by the danger of infection - or is efficacy to rejection suppression lost as higher dosages already?

Dr. Gouras: The dosage is set to minimize toxicity and prevent rejection. We use a standard dose which is used in kidney transplants. A group in Washington University has tried immunosuppression drugs with about ten patients, but they have run into problems, and I believe the study has stopped.

Rob: Is immune response the same in all organs? Or maybe are some organs "fussier"?

Dr. Gouras: I don't think anyone knows that. We know very little about immunosuppression in the retina.

Joan: Have there been trials using RPE cells from healthy, peripheral retina in the same patient? Is that an option?

Dr. Gouras: No, not yet. With Stargardt's Syndrome, it is thought that the defective photoreceptors cause damage to the epithelium in the macula; therefore, it is conceivable that a strategy of putting a healthy RPE into the central area would work. It hasn't been tried yet, but it could work. The problem is that you would have to subject a younger person to a biopsy in a totally experimental procedure. It is a complex procedure.

Joan: Do you know of specific differences between early onset and late onset Stargardt's?

Dr. Gouras: You have to realize that there are many different mutations of the Stargardt's gene, from very mild to very severe. It all depends on the specific gene defect which is traveling in your family. For your information, Randall Alikments is two floors below me here. He is the doctor who discovered the Stargardt's gene about a year ago. He believes that the Stargardt's gene may also play a role in MD, but this is very controversial at this time.

Joan: Then age of onset is less predictive of progression of the disease than is the specific mutation?

Dr. Gouras: Well, we just don't have enough info on the mutations. I would think that the earlier the onset, the more severe the disease; but there are not that many studies in this area. This situation will improve quickly over the next year or so.

Joan: Thank you. I realize the information is limited.

Dan: One of the most promising treatments for wet MD is photodynamic therapy, now in its third phase of study. What is your opinion on the success of this treatment?

Dr. Gouras: I agree that it is a promising treatment for wet MD, which is a small fraction of all MD. It is still experimental, and there are two problems with it. Number one, it is not permanent, and the vessels will grow back. The second problem is that if you use it too much, you could damage good vessels. These are

Dr. Gouras: I agree that it is a promising treatment for wet MD, which is a small fraction of all MD. It is still experimental, and there are two problems with it. Number one, it is not permanent, and the vessels will grow back. The second problem is that if you use it too much, you could damage good vessels. These are the problems that scientists are trying to work out in order to make it a routine procedure. I am optimistic about it being useful.

Dan: Would you recommend PDT over the current "hot" laser technique?

Dr. Gouras: I am not enthusiastic about the traditional laser technique, and would opt for PDT if I could.

Dan: What can you tell us about the success rate of submacular surgery? Would you recommend this treatment?

Dr. Gouras: I think the success with submacular surgery has not been good with MD. It depends on the experience of the surgeon. Unless we tie it in with transplantation in the future, I cannot see it going very far. It's greatest success has been in young people with histoplasmosis. Submacular surgery has not been that useful in older people with MD.

Linda: What are the factors in success or failure in submac?

Dr. Gouras: As I said, young people tend to do better than older people. One theory is that the epithelial layer can grow back in younger people, but it is too atrophic in older folks. That is just a theory at this time.

Linda: Can nutrition and UV protection/blue light protection help?

Dr. Gouras: I would certainly avoid blue light. That is not a bad idea. Vitamins E and C can also help, but these are minor factors in MD. It is mainly a genetic weakness which a lot of people have.

Joan: A therapy that seems promising to me (for Stargardt's) is the possibility of using a viral vector to deliver functioning genes to the retina where cells have "turned off." Do you have an opinion as to the possibility of success along this line in the near future?

Dr. Gouras: That's a great idea, but the problem is that it has to be given to the subject before he loses the photoreceptors in the macula. If they are lost, they cannot be brought back with gene therapy. We are using a retroviral HIV therapy in animals at this time, and we are hopeful of that approach.

Dan: Retinal translocation has been performed on several of the people on MDList, and they have reported good results. Please give us your opinion.

Dr. Gouras: Retinal translocation is a very complicated procedure that shifts the foveal retina to a healthier position over healthy epithelium. It works. It actually stops the degeneration from neovascularization; but it has several problems. One, it is a very complex procedure. Two, it doesn't work well if you have vision in the other eye, because it creates double vision. In the hands of a good surgeon, it is

actually stops the degeneration from neovascularization; but it has several problems. One, it is a very complex procedure. Two, it doesn't work well if you have vision in the other eye, because it creates double vision. In the hands of a good surgeon, it is probably a useful procedure.

Dan: Avoidance of smoking, good nutrition, and protection against UV rays are all recommended as ways to possibly slow down the progression of retinal disease. Would you please comment on any or all of these?

Dr. Gouras: Of course, smoking is harmful to the body. Also good nutrition is helpful, especially antioxidants. Everyone believes that an important contributing factor to the demise of the epithelial layer is oxygen damage. Our ability to handle the amount of oxygen is an important factor. There are ten or more genetic mechanisms which also come into play, so any attempt at slowing down retinal degeneration is intricate.

Regarding UV rays, they are not really getting into your macula. They are being filtered by the cornea, but you do not want them to get that far, anyhow, so good glasses are important. It is not a bad idea to wear yellow-tinted glasses to block blue light, especially in blue-eyed people. I might add that you have a natural yellow pigment in the retina which absorbs blue light, and that helps.

Dan: A 1995 NIH study showed Vitamin E to have a negative effect, and you have discovered a correlation with Vitamin A. Please comment on the use of these and other vitamins in relation to retinal disease.

Dr. Gouras: This was carried out at Harvard, and it showed that patients who took these vitamins differed in the following ways: Those who took Vitamin E progressed a little more rapidly, and those that took vitamin A progressed more slowly. 15,000 units daily of Vitamin A is recommended under the supervision of a doctor. You don't want to take too much, as it can be toxic.

Dan: Can you give us your opinion on experimental therapies which are currently being marketed as treatments for MD, specifically microcurrent stimulation and rheotherapy?

Dr. Gouras: I don't think too much of these treatments. There is no proof that they work.

Dan: Do you see any possibility that they will be proven?

Dr. Gouras: I wouldn't bet on them, as they don't show too much scientific rationale. With gene therapy and cell transplantation, you can see evidence of physiological change. With microstimulation and rheotherapy, there is no such evidence that makes good scientific sense to me.

Dan: There have been reports of work being done on microchips as replacements for malfunctioning retinas. Do you see this as a possibility in the near future?

Dr. Gouras: They are very experimental, and have not been tried in any human subjects. The closest we have come is at Hopkins, where the retina has been stimulated to see light. I think the chip has a future, but it is very far away. The

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Dr. Gouras: They are very experimental, and have not been tried in any human subjects. The closest we have come is at Hopkins, where the retina has been stimulated to see light. I think the chip has a future, but it is very far away. The problem is that you are trying to interface organic with inorganic materials with salt solutions, and that is very difficult.

Dan: Do you think there might be a cure for retinal degeneration before such things are developed?

Dr. Gouras: Yes, and I think gene therapy will be there first. After total cell degeneration, then it will have to be either a chip or a transplant.

Rob: Let me first follow up on the artificial retina. There was a piece in Forbes that says Massachusetts Eye and Ear is ready to experiment with temporary implants now. I do not have specs on the chip. Would it really be useful for high-resolution vision?

Dr. Gouras: There are various groups attempting to develop chips. The one at Mass Eye is very competent, but I don't think they will be putting a chip into a human subject in the very near future. I think we are a long way off from high resolution in a chip.

Rob: My original query was about retinal translocation. If there is a problem with binocular confusion, what is the experience with using an eye patch? Maybe shifting between eyes over weeks to keep both healthy.

Dr. Gouras: With someone who has a good eye, I don't think translocation is a good procedure. I don't think it's been tried yet with patching, but I don't think it will be easy to regain stereopsis, especially in older patients.

Rob: If the person loses the good eye in an accident, might it not be a good idea to prevent further degeneration of the other eye?

Dr. Gouras: Absolutely. For someone with only one eye left, it is worth the attempt.

Joan: Can you comment on the reluctance of ophthalmic surgeons to perform cataract surgery on patients who have some form of retinal degeneration?

Dr. Gouras: There shouldn't be any reluctance at all. The only possibility is that, if the degeneration is so advanced, it isn't going to help.

Joan: There is no expected speedup of damage to the retina then?

Dr. Gouras: No, only benefit. And there will be a sharper image.

Joan: Think I'll find me a new ophthalmologist.

Dr. Gouras: LOL

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Dr. Gouras: LOL

Joan: Thank you.

Dr. Gouras: Your welcome.

Dan: Are you familiar with the new phi-motion angiography and micro-laser treatment being performed on patients at the Glaser Murphy Retina Treatment Center in Chevy Chase, Maryland?

Dr. Gouras: I'm not sure about this, but they are good doctors there at Glaser. I think what they are doing is using highly-sophisticated methods of looking at blood vessels in the living retina and directing their lasers more accurately. I think this is good.

Dan: What is the latest on radiation therapy?

Dr. Gouras: I don't think it has been that successful. The results have not been very promising, and I think it has lost much of its appeal. PDT shows the most promise right now.

Dan: What is your opinion on the injection of corticosteroids into the tissue of MD patients?

Dr. Gouras: I have heard through the grapevine that slow release capsules in the eye are showing more promise than injecting systemically, due to the toxicity of steroids. I have heard that they are having some success with that in St. Louis.

R_Hammer: You mentioned retrovirus vector being used in animal models to treat the Stargardt's gene. How is the virus introduced? Does it effectively infect cells in the desired region? Are there a lot of procedural difficulties to overcome before clinical trials can be considered?

Dr. Gouras: So far, we have not been that successful in getting the retrovirus to transect into the human eye. A number of groups are working on that very important problem. The virus is introduced into the subretinal space by microsurgery.

Donna: Is there anything I can do to keep my wet eye damage from imaging into my dry eye?

Dr. Gouras: Donna, that is a curious question. When you close the bad eye, do you have a problem with the good eye?

Donna: Yes. I see a ghost image of the damage in my wet eye. Photos prove it is not the damage I have in my dry eye.

Dr. Gouras: are you sure that your good eye doesn't have a problem of it's own?

Donna: Yes. I know the shape of the damage in my wet eye and the shape of

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Donna: Yes. I know the shape of the damage in my wet eye and the shape of damage in the dry eye. Photos at Retinal Specialist prove this.

Dr. Gouras: It could occur, but it has to be in your brain's visual perception. It may stop with time. It would not be easy to coreect. I will have to give this some more thought.

Dan: Dr. Gouras, thank you again for being our guest today. You have really helped to bring us up to date.

Dr. Gouras: Your welcome, Dan. If anyone wants to learn more, please follow my newsletter on the web. The web site is <http://cpmcnet.columbia.edu/dept/eye/retina>. The newsletter will be updated by May or June, when I return from the Association for Research in Vision & Ophthalmology. I will have a lot of new information to dispense after that.

Dan: Ok, if there are no more questions or comments, we will close the session for today.

Dr. Gouras: Thank you, Dan, for inviting me here today.