Thrombophilia and hypofibrinolysis: Pathoetiologies of Amaurosis Fugax

A free, new (11/3/03) clinical research study at the Jewish Hospital Cholesterol Center, 3200 Burnet Avenue, Cincinnati, OH, 45229
Phone 513-924-8250 Fax 513-924-8273
email glueckch@healthall.com.

Contact us by email, fax, phone or by snail mail if you are interested in participating.

Principal Investigators: CJ Glueck MD, Howard Bell MD, Carl Golnik MD, Robert Hutchins MD, Naila Goldenberg MD, James E. Lang MD.

I: Purpose: Our specific aim is to assess major thrombophilic and hypofibrinolytic pathoetiologies of amaurosis fugax.

Amaurosis fugax is characterized by a sensation of visual "shooting stars" with short bursts of bright lights in the visual fields, unrelated to what you are currently looking at. Amaurosis fugax can be associated with transient cerebral ischemic attacks, in which you feel transiently dizzy, have one-sided tingling or weakness, often with associated very short term confusion. Amaurosis fugax can be associated with ischemic stroke, in which the symptoms of dizziness, one-sided tingling, one-sided weakness, and confusion do not clear up after 30 to 45 minutes. Amaurosis fugax can be caused by thromboemboli from atherosclerotic lesions in the carotid and/or vertebral arteries, or by thrombi (blood clots) alone. Because a majority of people with amaurosis fugax will, over time, subsequently develop severe ischemic strokes, the diagnosis requires careful medical evaluation. Evaluation of amaurosis fugax typically includes examination by an ophthalmologist or neuro-ophthalmologist to determine whether the "shooting star" sensation might be caused by a problem within the eye including retinal artery thrombosis, non-arteritic ischemic optic neuropathy (NAION), retinal vein thrombosis, or other retinal ocular problems. Careful neurological assessment is almost always done, including Doppler sonograms of the carotid and vertebral arteries to determine if there are atherosclerotic lesions in these areas which could give rise to thrombemboli which then end up in the brain. Commonly, neurological examination may include magnetic resonance imaging (MRI), and less commonly MRA and MRV, magnetic resonance arterial and venous imaging using MRI and non-invasive contrast material to look for ischemic infarction in the brain.

We have preliminary evidence that many cases of amaurosis fugax are caused by inherited clotting disorders which are either thrombophilic (loves to clot), or hypofibrinolytic (reduced ability to dissolve clots). We postulate that when exogenous thrombophilic factors (estrogen-containing oral contraceptives, estrogens, corticosteroids) are superimposed on heritable thrombophilic and/or hypofibrinolytic coagulation disorders, very small thrombotic ischemic cerebral strokes occur, leading to the symptoms of amaurosis fugax. Later in the development of the disease state, larger thrombotic ischemic strokes may occur, leading to transient cerebral ischemic attacks (TIAs) or frank major stroke.

II. Significance in Relationship to Human Health: 

Since amaurosis fugax is very closely associated with and predicts later severe ischemic strokes, better understanding of the causes of amaurosis fugax should allow physicians to prevent ischemic stroke, primarily through anticoagulation and through treatment of risk factors for atherosclerosis which commonly involves the carotid and vertebral arteries.

Most cases of amaurosis fugax are seen by ophthalmologists, some by neurologists, and some by family physicians/internists. Historically, no concerted effort has been made to assess the interactions of coagulation disorders, exogenous thrombophilic vectors, and atherosclerotic risk factors with the development of amaurosis fugax. The diagnosis is important for the following reasons:

1. It allows safe, successful treatment of the underlying conditions with thromboprophylaxis (anticoagulation), and/or treatment of atherosclerosis risk factors.
2. It protects the eyes which are commonly injured by retinal artery thrombosis and/or NAION.
3. It facilitates preventive measures to protect against other venous thrombosis (thrombophlebitis, pulmonary emboli,
stroke, etc).

III. Method of Study:  

III a. Patients:  
We plan to study 30 new patients seen by ophthalmologists, neurologists, or family physicians because of amaurosis fugax, irrespective of whether they had overt ischemic strokes.

III b. Entry Criteria:  
Amaurosis fugax must be diagnosed by ophthalmologists, neuro-ophthalmologists, neurologists, or family physicians. To enter the study, we will need to have copies of records documenting the the diagnosis of amaurosis fugax as well as reports from carotid and vertebral Doppler studies.

III c. Exclusions:  
Patients whose amaurosis fugax events were secondary to embolus (from atrial fibrillation, cardiac myxoma, cholesterol embolus after carotid endarterectomy, bypass surgery, etc) will be excluded as will all patients with hemorrhagic stroke.

III d. Protocol:  
Each patient will be seen at the Jewish Hospital Cholesterol Center by Dr Glueck and/or one of the Jewish Hospital resident co-investigators. The outpatient visit will take approximately 90 minutes. A detailed medical, ophthalmologic, and neurologic history will be taken along with a history of exogenous oral contraceptives, estrogen replacement therapy, SERM use, or corticosteroids.

A detailed family history will be done, focusing on ischemic stroke, stroke of any type, venous thrombosis, arterial thrombosis, and/or myocardial infarction.

Fasting blood samples will be obtained for measurement of major thrombophilic and hypofibrinolytic risk factors for amaurosis fugax, as well as major risk factors for atherosclerosis.

A brief physical examination will be carried out. Measures of height, weight, and blood pressure will be obtained. Blood samples will be obtained for a state-of-the-art measurement of thrombophilia and hypofibrinolysis.

A full written report will be provided to each patient and to their physicians after each individual’s laboratory tests are complete. Suggestions for followup therapy will be provided as well. All information is absolutely confidential, and will be released only by the patients’ request, with a signed ARelease of Medical Records@ form.

The outpatient visit to the Jewish Hospital Cholesterol center is free of charge, as is the state-of-the-art coagulation evaluation (which otherwise would cost ~$2,500). These costs are covered by our research grant. The grant cannot, however, pay for transportation costs from the patient’s home to the Center and return.

The state-of-the art coagulation evaluation includes the following tests:

cDNA-PCR:  

Serologic tests for thrombophilia:  
Resistance to activated protein C, Protein C, Protein S (total and free), Antithrombin III, anticardiolipin antibodies (IgG, IgM), lupus anticoagulant, homocysteine, Factors VIII and XI.

Serologic tests for hypofibrinolysis:  
Plasminogen activator inhibitor activity (PAI-Fx), lipoprotein (a).
Atherosclerosis risk factors:
Low, very low, and high density lipoprotein cholesterol (LDLC, VLDLC, HDLC), homocysteine, Lp(a), insulin, c-peptide, high specificity C reactive protein.

IV. Risks and benefits:
Benefits:
Documentation of an underlying heritable coagulation disorder will benefit the patient by either initiating appropriate anticoagulation, by directing family studies of first degree relatives, and by education in avoidance of precipitating environmental factors like estrogens. Knowledge of heritable coagulation disorders should facilitate prevention of thrombotic events in other arterial and venous beds.

Risks:
Documentation of coagulation disorders of a heritable nature, might, were they known to medical insurance companies, be identified as a pre-existing risk for thrombosis. However, the information for the current study will be processed following strict confidentiality rules and will be released only with signed patient consent.

Payment:
There will be no financial remuneration. Parking will be free in the Alliance ABC garage.

Subject costs:
There are no anticipated costs for the patients involved with their clinical and laboratory evaluation at the Jewish Hospital Cholesterol Center. The grant cannot, however, cover travel costs to the center.

References:


Amaurosis Fugax associated with antiphospholipid antibodies

Amaurosis fugax associated with thromboembolism
Amaurosis fugax associated with thrombophilia

Associations of coagulation disorders with NAION, pseudotumor cerebri

E-mail: glueckch@healthall.com
or cgglueck@fuse.net
Fax: 513-924-8273