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<b>MEDICAL RECORD</b>	<b>MINOR PATIENT'S ASSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY</b> • Attach to NIH-2514-2, Consent to Participate in a Clinical Research Study
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INSTITUTE: National Institute of Child Health and Human Development

STUDY NUMBER: 00-CH-0093 PRINCIPAL INVESTIGATOR: Karel Pacak, M.D., Ph.D.

STUDY TITLE: Diagnosis, Pathophysiology, and Molecular Biology of Pheochromocytoma and Paraganglioma

Continuing Review Approved by the IRB on 7/22/09

Amendment Approved by the IRB on 6/10/10 (ZZ)

Date Posted to Web: 6/15/10

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Minor

### Introduction

There is a chance that you have a type of tumor, pheochromocytoma, or "pheo" (pronounced "fee-oh"), a tumor of the adrenal glands that produces large amount of chemicals called catecholamines. The most well known catecholamine is adrenaline. Pheos can be dangerous, because they release large amounts of catecholamines into the bloodstream, and this can cause high blood pressure, a heart attack, stroke, or even sudden death. It is important that we make the diagnosis as promptly and accurately as possible.

### What We Plan to Do

We will do several tests to see if you have pheo. To do this, we will give you two drugs, glucagon and clonidine. Glucagon stimulates the tumor, and clonidine does not affect release of catecholamines by the tumor but reduces catecholamine release by normal cells. We will see what effects these drugs have on your heart rate, blood pressure, and the levels of catecholamines and related biochemicals in your blood. We will also collect some of your urine to assay these substances.

### Testing Procedures

You will come either to the clinic or to the hospital at the NIH for 1 to 2 weeks. You will stay in the hospital overnight or in a hotel or guest house with your parent/guardian. Your parent/guardian must come with you to the clinic.

We will perform a blood test for levels of catecholamines and their breakdown products. The test requires an intravenous (i.v.) plastic tube placed in an arm. A needle is put into a vein, to allow insertion of a plastic tube, which stays in the vein after the needle is removed, until the test is completed. This will hurt for only a minute, and once the i.v. is in your arm, it shouldn't hurt. You rest in a bed for 15-20 minutes. Then we draw off a 15 ml (1/2 ounce) sample of blood through the i.v. Drawing blood through the i.v. should not hurt.

You must not eat any food or drink coffee or tea after midnight the night before the blood samples are taken. You may have up to 8 ounces (1 cup) of water if you are thirsty before you come to the clinic. You must not use any drug containing acetaminophen (brand name Tylenol™) for 5 days before the blood samples are taken. Breakfast or lunch will be served after we finish these tests.

If you are a girl old enough that you could get pregnant, we will also check your urine to make sure you are not pregnant. You and your child will be notified about pregnancy test results.

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<b>PATIENT IDENTIFICATION</b>	<b>MINOR PATIENT'S ASSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY</b> NIH-2514-2 (10-09) P.A.: 09-25-0099 File in Section 4: Protocol Consent (2)
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**Glucagon Stimulation Test** In the glucagon stimulation test, you receive a small amount of glucagon (1 mg) i.v. We draw 2-5 samples blood over about 5 minutes. Glucagon may cause you to have a brief increase in heart rate or blood pressure, as well as a feeling of nervousness. This drug may also cause a cramping discomfort in your abdomen, a pounding sensation or tightness in your chest, shortness of breath, or a sensation of faintness or lightheadedness. Furthermore, this drug may also cause a brief feeling of warmth, redness of the skin, nausea or vomiting, a metallic taste in the mouth, an urge to urinate, or an urge to have a bowel movement. These effects may be like attacks that you have been having. If so, the symptoms should be much milder and of shorter duration than your attacks. We will have drugs available to control your symptoms, if necessary. Your blood pressure and heart rate will be checked before and after you receive the glucagon, using an automatic device placed on your arm.

**Clonidine Suppression Test** In the clonidine suppression test, you receive a clonidine (0.3 mg, the dose adjusted for your body weight) by mouth. The drug may make you sleepy and often causes a dry mouth. These effects wear off over a few hours. Your blood pressure and heart rate will be checked before and after taking clonidine. A doctor or nurse will be present at all times while these tests are underway. Just before and 3 hours after taking the drug, we will draw a blood sample through the i.v.

### Other Tests

We may collect blood also for other tests. The blood may be drawn using a needle or needle and then tube (i.v.) in the arm. In accordance with NIH guidelines for research subjects, no more than 5 ml/kg will be drawn for research purposes in a single blood withdrawal and no more than 9.5 ml/kg will be drawn over any eight-week period.

We may also ask you to collect your urine for up to 24 hours. The nurses will show you how to collect all of your urine in a special container. For urine collection we want you to put all of your urine into that special container for a 24-hour period. The urine sample may be collected with the help of your parents.

We will ask you to have blood pressure monitoring done for a 24-hour period. This will be done to find out if there are changes in your blood pressure you may not be aware of during the day and night. The blood pressure equipment is lightweight, small and will not limit your activities.

We may also use your blood to get a substance called "DNA." DNA contains the genes, the units of inheritance in humans and animals. Testing the DNA can identify gene changes that increase or decrease the risk of developing some diseases. We will compare the DNA from people not having pheo with your DNA to see if we can find whether your DNA is abnormal and can cause your disease. If we think you may have a genetic disease (something you would inherit from one or both parents) we would like to test your blood at NIH or at another facility for specific testing (e.g. testing for multiple endocrine neoplasia, or von Hippel-Lindau syndrome).

Other tests may be needed to localize your tumor. These are not research studies but are done to help you. These tests (MRI, CT scan, MIBG and PET scans) include images of parts of your body, taken using machines that we have in the hospital (Departments of Radiology and Nuclear Medicine). For these tests you lie on a table like an X-ray table. The scanner is like a big doughnut, and part of your body is in the hole. During these tests you cannot move the part of your body in the scanner for the time that the test lasts. For MRI imaging, your entire body may be in the scanner, and you will hear a loud sound like a drumbeat while the pictures are being taken. If you get scared or have a question, you can talk directly with the doctors, technicians, or with your parent/guardian. Another imaging test (called "ultrasound") involves only moving a metal tube over the part of the body being imaged. For ultrasound, a jelly-like substance is placed on the body. These imaging studies do not hurt. Your parent or guardian can be with you while these tests are being done.

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Some imaging tests will require an intravenous (i.v.) plastic tube placed in an arm vein, as described above, for an injection of radioactive compound. Injection of such a compound through the i.v. should not hurt.

We will discuss the results of all studies with you, your parent/guardian, and your doctor.

**What We Want You to Do**

We want you to know what we will do, why we will do it, and what things may hurt. You can ask any of the doctors or nurses if there is something you do not understand at any time. We will be happy to answer your questions. You will also fill out some forms and answer questions that will help us to figure out whether you may have a tumor.

If you agree to come to the NIH and be part of our study, then we ask you to write your name on this paper. Writing your name on this paper is a way of showing that you agree. You do not have to do this if you or your parent/guardian do not want you to. Don't write your name until you feel that you understand what will happen and you are ready to be part of our study. Even if you agree now, you or your parent/guardian can change your minds later.

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I have had this study explained to me in a way that I understand, and I have had the chance to ask questions. I agree to take part in this study.

Signature of Minor Patient: \_\_\_\_\_ Date: \_\_\_\_\_

Print Name: \_\_\_\_\_

Signature of Investigator: \_\_\_\_\_ Date: \_\_\_\_\_

Print Name: \_\_\_\_\_