

Childrens Hospital Los Angeles
CONSENT/PERMISSION FOR CHILD TO PARTICIPATE IN RESEARCH

A CLINICAL RESEARCH STUDY PROGRAM FOR PRENATAL AND CLINICAL RISK
FACTORS OF OPTIC NERVE HYPOPLASIA

Subject's Name:	_____
CHLA#:	_____ Birth Date: _____

• INTRODUCTION

Your child is asked to participate in a research study conducted by Mark Borchert, M.D., Mitchell Geffner, M.D. and Nina Ma, M.D. from the Departments of Ophthalmology and Endocrinology at Childrens Hospital Los Angeles. Your child has been asked to participate in this study because your child has been diagnosed as having optic nerve hypoplasia. Participation in this study is completely voluntary. Please read the information below, and ask questions about anything you do not understand, before deciding whether or not to allow your child to participate.

• PURPOSE OF THE STUDY

Your child has been diagnosed as having optic nerve hypoplasia. This is a disease of improper formation of the optic nerve prior to birth. It causes a variable degree of visual loss from very severe to very minimal. It is known to be associated with learning disabilities, malformations of parts of the brain, and hormone imbalances in some patients. The cause of this condition is not known, but certain illnesses or the use of certain medications during pregnancy have been implicated. This research study is designed to provide preliminary data about the factors that may be involved in the formation of optic nerve hypoplasia prior to birth. It is also designed to correlate those factors with the severity of the disease and its associated medical conditions.

• PROCEDURES

If you allow your child to volunteer to participate in this study, we would ask you and/or your child to do the following things:

Your child will have a complete examination of his/her eyes and photographs will be taken of his/her optic nerves. If your child has had a recent eye examination by Dr. Borchert, this part will not be necessary for your initial study visit. If so, it will be necessary to access information from his/her medical record about previous examinations. Your child will receive a complete eye examination (at no cost to you) every year until he/she is five years old.

He/she will have a pattern visual evoked potential (VEP) test performed. This involves recording brain waves through electrodes, which are painlessly attached to the scalp while your child is watching TV. This gives an estimate of your child's potential vision. At the same time, electrical signals made by the retina will be recorded. This is called an electroretinogram (ERG). To do the electroretinogram, an anesthetic drop will be placed in your child's eyes. Then, a thin wire, slightly larger than a hair, will be placed inside your child's lower eyelids. This causes no known



discomfort. If your child is too young to cooperate with these tests, he/she will be sedated for it. We will administer chloral hydrate for the sedation. This will require that you withhold food from your child six hours before the test and any liquid two hours prior. These tests will be performed free of charge.

A neuropsychologist who specializes in children will study your child's development as well as observing your child perform play-like tasks. These tests will take about an hour and will be performed at Childrens Hospital. They will be repeated every year around the time of your child's birthday until he/she is five years old. These tests will be free of charge.

If your child has not yet had the appropriate MRI scan or evaluation by an endocrinologist, these will be arranged in the usual manner, and you or your insurance company will be charged for them. It will be necessary to access your child's medical record to collect information about previous endocrine or radiographic tests. If any new medical or neurological problems are identified in your child, they will be treated in the appropriate manner.

Tests for 4 hormone-like substances, which are not normally performed as part of the evaluation for optic nerve hypoplasia, will also be done. These tests involve the removal of approximately ½ tsp. of blood. If at all possible this will be done at the time of blood removal for other tests so as to avoid an additional needle stick. This sample may be taken while your child is sedated for the VEP and ERG so he/she won't experience any discomfort during the blood draw.

If your child is diagnosed with hypothyroidism or has been treated for hypothyroidism for less than six months, tests for two hormones will be repeated every 6-12 months until your child is stabilized on the appropriate dose of medication. This will involve the removal of less than ½ tsp. of blood for each blood draw. If at all possible this will be done at the time of blood removal for other tests so as to avoid an additional needle stick.

If your child has not had a growth hormone stimulation test, this will be performed when your child reaches the age of 4 years, or sooner if clinically indicated. The growth hormone stimulation test measures how well your child's pituitary gland releases growth hormone. This is a hormone that is required for normal growth as well as for normal metabolism of fat and sugar. Nearly all children with hormone imbalances due to optic nerve hypoplasia have insufficient production of growth hormone. However, in some children with isolated growth hormone deficiency, problems with growth may not be apparent. We wish to determine how many children with optic nerve hypoplasia have growth hormone deficiency that is not clinically apparent and whether or not this deficiency correlates with the development of other problems such as learning disabilities, behavioral problems, or obesity.

The growth hormone stimulation test that we use is called the glucagon tolerance test. Glucagon is a natural occurring hormone that the body produces in response to low blood sugar. It stimulates the release of other hormones such as growth hormone and cortisol. To perform the glucagon tolerance test, a small amount of glucagon will be injected into your child's skin (upper arm). The amount of glucagon will depend on your child's weight. For example, approximately 1/4tsp will be injected if your child weighs 25lbs and approximately 1/2tsp will be injected if you child weighs 50lbs. One-half tsp. of blood will then be taken from your child 5 times over a period of 3 hours after administration of glucagon to measure for growth hormone and cortisol production. This blood will be taken from a needle inserted into your child's vein (intravenous line) that will be maintained over the course of the test so that your child will need only one needle stick for blood draws. The results of this test will be provided to you and to your

endocrinologist. The decision to treat inadequate growth hormone production, which was previously unsuspected, will be made by you and your endocrinologist. Some of the endocrine tests done prior to, or at your initial visit will be repeated at the time of the growth hormone stimulation test. This will require approximately ½ teaspoon of blood to be taken from the intravenous line so another needle stick will not be required. If the results of this test are inconclusive or the test is not complete, your child will return for a second growth hormone stimulation test. The need for a repeat test very rarely occurs.

At your child's final study visit (at age 5) you will be asked to complete a questionnaire. The questionnaire will ask you to assess your child's behaviors and social interactions. This should take you approximately 20 minutes.

The above tests will allow us to estimate the severity of your child's disease. The results of the above tests will be provided to you if you desire.

A member of the ophthalmology staff will ask you, if you are the mother, questions from a questionnaire about your diet, habits, substance use, and medical problems prior to your child's birth. You will also be asked about your child's early development. This may take forty to fifty minutes. The questionnaire may be administered over the telephone or face-to-face. Results of this questionnaire will be compared with the results of medical tests, vision tests, and neuroradiographic studies (MRI) which will be performed on your child.

If you are traveling from outside the Los Angeles area for the study, you will be given the option to have your child admitted to the hospital overnight.

● **POTENTIAL RISKS AND DISCOMFORTS**

There are no risks to you other than the inconvenience of helping us complete the questionnaires. Though not intentional, you may find some of the questions offensive or bothersome.

If your child needs laboratory tests, there is very little risk for having blood drawn. However, veins vary in size from one patient to another and obtaining a blood sample from some children may be more difficult than from others. The risks, although uncommon, include excessive bleeding, feeling faint or light-headed, having multiple punctures to locate a vein or infection.

If your child requires sedation for any of the tests, there is a very remote risk that he/she will stop breathing and require resuscitation. The sedation medication is chloral hydrate and will be used for sedation during the VEP and ERG exam and while we take photographs of your child's eyes. There is also a slight risk that your child will experience nausea from the sleep medication. For this reason it is important that your child not have anything to eat six hours before and nothing to drink two hours prior to the sedation, since vomiting could cause lung damage.

Placing an intravenous line in order to obtain blood samples for the glucagons tolerance test may be uncomfortable and/or require more than one needle stick. Occasionally the glucagon tolerance test causes nausea and vomiting. Rarely glucagon causes low blood sugar approximately 2 hours after its administration. Low blood sugar causes sweating, increased heart rate, and, if severe, may cause low blood pressure and seizures. Your child will be monitored throughout the course of the glucagon tolerance test for evidence of low blood sugar including occasional analysis of a few drops of blood from the intravenous line to insure that the blood sugar is normal. Low blood sugar will be treated appropriately with food, drink, or intravenous fluids.

- **ANTICIPATED BENEFITS TO SUBJECTS**

Your child may benefit from early diagnosis of medical neurologic problems, or learning disabilities that may be associated with optic nerve hypoplasia. Results of neuropsychologic testing, which may be of benefit in educational planning, will be made available to you. Otherwise, there is no direct benefit to you or your child for participation in this study.

- **ANTICIPATED BENEFITS TO SOCIETY**

Future patients with this problem may benefit from this study because of improved ability to identify and treat the medical and neurologic problems early. In addition, identification of prenatal risk factors may allow us to prevent this disease in the future.

- **ALTERNATIVES TO PARTICIPATION**

You have the option of not participating (not having your child participate) in this study or withdrawing at any time. The tests done for this study (e.g. neuropsychological test, MRI scan, hormone test) may also be performed if you do not participate in this study.

- **FINANCIAL OBLIGATION**

This research study is partially funded by the National Institute of Health. Services that are experimental are of no cost to you. However, if your child has not had endocrine testing or an MRI, you or your insurance company will be billed for these services. This is because these services are routine for evaluation of children with optic nerve hypoplasia. You will not receive reimbursement for your participation in this study. There is no financial benefit to the investigator for your participation.

- **EMERGENCY CARE AND COMPENSATION FOR INJURY**

If injury were to occur as a result of participating in this study the General Clinical Research Center (GCRC) will provide appropriate medical care. However, the duration and extent of any medical treatment will be determined by the GCRC Local Advisory Committee of the General Clinical Research Center. Additionally, Childrens Hospital Los Angeles and the physician investigators each maintain professional liability insurance to compensate patients for injuries caused by the fault of Hospital employees or physicians. The physicians are not employees or agents of the Hospital and are separately insured. If an injury is not caused by the fault of a Hospital employee or a physician, neither the Hospital nor the physicians provide reimbursement for treatment expenses or other compensation for the injury, and payment for care of such injury will be billed to you and/or your health benefit plan. You are not waiving any legal claims, rights or remedies because of your child's participation in this research study.

If you believe that physical injury has been suffered as a result of participation in this study, you should contact Dr. Mark S. Borchert at (323) 361-4510.

- **PRIVACY AND CONFIDENTIALITY**

Members of the research team and, if appropriate your physicians and nurses will know that your child is a research subject. All results will be kept confidential, but may be made available to you,

and/or your child's physician if you wish. Authorized representatives of the Food and Drug Administration (FDA), the Department of Health and Human Services, the General Clinical Research Center (GCRC) and the CHLA Committee on Clinical Investigations may need to review records of individual subjects. As a result, they may see your name and your child's name; but they are bound by rules of confidentiality not to reveal your identity to others. No information about you, or provided by you during the research, will be disclosed to others without your written permission, except:

- if necessary to protect your child's rights or welfare (for example, if he/she is injured and need emergency care); or
- if required by law (i.e., child abuse, reports of certain infectious diseases).

When the results of the research are published or discussed in conferences, no information will be included that would reveal your child's identity. If photographs will be used for educational purposes, your identity will be protected or disguised.

Because this study involves the diagnosis of a medical condition, a copy of this consent form will be placed in your child's medical record. This will allow the doctors that are caring for your child to obtain information about what medications or procedures your child is receiving in the study and treat him/her appropriately.

Neither your name nor the child's name will be on the questionnaire. The questionnaire will not be a part of the medical record.

● **PARTICIPATION AND WITHDRAWAL**

Your child's participation in this research is VOLUNTARY. Your choice about whether or not to participate will have no affect your child's care, services or benefits at Childrens Hospital Los Angeles. If you agree to participate, but later decide to remove your child from the study, you may do so without affecting you or your child's rights to health care, services or other benefits at Childrens Hospital Los Angeles. If you decide to remove your child from the study, the information we collected on your child during participation, up to the point in time you requested removal from the study, will be used in study analyses.

● **HOW TO OBTAIN INFORMATION**

In the event of a research-related injury or if your child experiences side effects, please immediately contact the investigator listed below.

Daytime, Monday through Friday, 8:00 A.M. through 4:30 P.M. you may call Dr. *Mark Borchert* at (323) 361-4510. You may also call the study coordinator, Cassandra Fink, MPH, at any time for questions or concerns relating to your child and his/her participation. Her phone number is (323) 361-2267.

Evenings, nights, weekends or holidays you may call the hospital number 323/660-2450 and ask for the Ophthalmology Service doctor on-call.

If your questions are not an emergency, you can obtain better information by calling Dr. Mark Borchert, Monday through Friday, 8:00 a.m. through 4:30 p.m., than by calling Childrens Hospital Los Angeles on call service after hours.

- **FINANCIAL INTEREST OF THE INVESTIGATOR**

Funding for this research study is partially provided by the National Institute of Health. The funding is used to support the activities of the Division of Ophthalmology and to reimburse the Division for the costs of the study personnel. Compensation is *not based* upon the number of research subjects enrolled. Neither the principal investigator nor the research staff receives a direct financial incentive from your participation. If your physician is an investigator for this study s/he is interested in both your healthcare and the conduct of this research. You are not under any obligation to participate in a research study conducted by your doctor.

- **RIGHTS OF RESEARCH SUBJECTS**

You may withdraw your permission for your child's participation at any time and discontinue participation without penalty. You are not waiving any legal claims, rights or remedies because of your child's participation in this research study. If you have questions regarding your child's rights as a research subject, you may contact the CHLA Office for Human Subjects Protections at 323/361-2265.

As a participant in a GCRC sponsored study you have the right to speak with the Research Subject Advocate for the GCRC. Dr. Alan B. Lewis or a member of his staff is available to discuss the study with you privately and answer any questions you may have prior to enrolling in the study or at any time during or following completion of the study. The discussion will remain confidential. Dr. Lewis and his staff can be reached at 323/361-2265.



SIGNATURE OF RESEARCH SUBJECT OR LEGAL REPRESENTATIVE

Your signature(s) below indicate

- You have read this document and understand its meaning;
- You have had a chance to ask questions and have had these questions answered to your satisfaction;
- You consent to your child's participation in this research study; and
- You will be given a copy of the signed permission form and of the *Experimental Subject's Bill of Rights*.

Name of Subject

Name(s) of Parent(s)/Guardian

Signature of Parent (Guardian)

Date

Signature of Parent (Guardian)

Date

SIGNATURE OF INVESTIGATOR

I have explained the research to the subject's parent(s)/guardian and answered all of his/her questions. I believe that he/she understands the information described in this document and freely gives permission for his/her child to participate.

Name of Investigator

Signature of Investigator

Date (must be the same date as subjects)

SIGNATURE OF WITNESS (if applicable)

My signature as witness certified that the parent(s)/guardian signed this permission form in my presence as his/her voluntary act and deed.

Name of Witness

Signature of Witness

Date (must be the same date as subjects)



SIGNATURE OF INTERPRETER (if applicable)

Name of Interpreter

Signature of Interpreter and Date (must be the same date as subject's)

Please check appropriate box and sign below.

Investigator's Statement of Certification for Subjects less than Seven Years of Age (Assent)

The undersigned investigator, Mark Borchert, M.D., hereby certifies that he has discussed the information contained in the study consent to the subject, including any risks that may reasonably be expected to occur. The undersigned further certifies that the subject was encouraged to ask questions, that all questions were answered, and that assent was obtained.

Assent was not obtained for a subject under 18 years of age. *(Please state the reason. Examples include: child is an infant; child is comatose; child lacks cognitive abilities to understand the information.)*

Date: _____

Time: _____ Signature _____

Routing of signed copies of the consent form:

- 1) Give to parent
- 2) Place in the CHLA Medical Record
- 3) Place in the Principal Investigator's research file.

