

The Follow-up of Congenital Hypothyroidism Cases: A Pilot Study

**Developed by the Michigan Department of Community Health Newborn
Screening Program
In cooperation with the Michigan Pediatric Endocrine Advisory Committee
As a project of the Region 4 Genetics Collaborative**

**Steven Korzeniewski, MSc, MA¹
William Young, PhD²
Charles Mundt, MA³
Mary J. Kleyn, MSc¹**

August 17, 2009



Region 4

¹Maternal and Child Health Epidemiology Section, Michigan Department of Community Health

²Newborn Screening Program, Michigan Department of Community Health

³Institute for Health Care Studies, Michigan State University

Funded by HRSA/MCHB Cooperative Agreement 422MC03963

Table of Contents

Background	3
Methods.....	4
Preliminary Results	5
Conclusion	6
Contact	6
Acknowledgements.....	7
Appendix A: Michigan’s Three-Year Follow-up Flow	8
Appendix B: CH Clinician Survey	9
Appendix C. CH Script for a Clinician Phone Contact	13
Appendix D: CH Script for Parent Phone Call	16

A Tool-Kit for the Follow-up of Congenital Hypothyroidism Cases
Developed by the Michigan Newborn Screening Program, MDCH
In cooperation with the Michigan Pediatric Endocrine Advisory Committee
As a project of the Region 4 Genetics Collaborative

Background

Although newborn screening for congenital hypothyroidism (CH) was adopted several decades ago and is now nearly universal in the United States¹, several problems still exist. These include: 1) no consensus on a screening method, screening algorithm and case definition for CH (state detection rates vary from 0.7/10,000 to 94/10,000); 2) false positive rates averaging 1.5% (0.04-9.0%) for CH as compared to a cumulative false positive rate of 0.3-0.4% for all disorders detected by tandem mass spectrometry²; and 4) the complexity of detecting CH in the Neonatal Intensive Care Unit (NICU) due to the effect of gestational age (birth weight) on false positives and false negatives.

In an effort to reduce these problems, the Region 4 Genetics Collaborative engaged in an epidemiological evaluation of CH screening in Region 4 states. This included 1) determining case definitions used in each state; 2) describing current screening, follow-up and diagnostic methods; 3) evaluating and comparing false positive and false negative rates, positive predictive values (PPV), and detection rates; and 4) providing consensus recommendations for improving detection rates and reducing false positive (FPR) and negative rates in the region.

In 2006, the Region 4 Genetics Collaborative initiated an effort to explore issues related to the detection and follow-up of cases identified by endocrine newborn screening tests. During the following year, five states contributed their initial thyroid stimulating hormone (TSH) screening results. Several states also contributed information related to their diagnosed cases of Congenital Hypothyroidism (CH). The primary purpose for collecting TSH data from Region 4 states was to compare screening algorithms and performance metrics (detection rate, PPV, FPR). The data also allowed comparison of trends in mean TSH and 17-OHP values over time by state.

Subsequent discussions with participating endocrinologists who reviewed and provided comments on these preliminary screening and diagnosis results, supported the hypothesis that lack of a “Gold Standard” for the diagnosis of CH might contribute to difficulty in accurately determining the screening detection rates and the diagnostic verification of the newborn screening and diagnostic process. Infants must be quickly and properly identified and treated to prevent permanent cognitive and physical developmental delays. In addition, proper diagnosis of transient or permanent CH is essential to condition treatment and management to improve outcomes for these children. The American Academy of Pediatrics (AAP) guidelines³ recommend standard of care is to follow-up CH cases until at least the age of three. In response

¹ National Newborn Screening and Genetics Resource Center. All states screen for CH. <http://genes-r-us.uthscsa.edu/nbdisorders.doc> (Last retrieved from on 07/08/2009).

³http://www.guideline.gov/summary/summary.aspx?doc_id=9383&nbr=005029&string=congenital+AND+hypothyroidism (last retrieved 6/18/2009).

to the concerns regarding detection, diagnostic verification and crucial three year follow-up, the Michigan Newborn Screening Program in cooperation with the Michigan Pediatric Endocrine Advisory Council (PEAC) engaged in a three-year follow-up activity. A description of the project, tools used and findings are described in this tool kit.

Methods

The Michigan Newborn Screening Program developed and tested a survey in collaboration with the Michigan PEAC. The initial objective was to obtain information about the current treatment status of “Borderline” CH cases, defined as having pre-treatment serum TSH values below the 15th percentile of all diagnosed cases. This was done in part to initially concentrate on the diagnosed cases that had the lowest pre-treatment TSH serum values. The second reason for limiting the study to this sub-group was because it was not certain what resources would be required to conduct this follow-up. After initial survey results were obtained, the inclusion criteria were expanded. All diagnosed CH cases in Michigan were included in the study in 2009.

In many cases, the children with CH were receiving active treatment by the endocrinologist or the pediatrician of record in the newborn screening system. For the cases that were no longer being seen by the endocrinologist, pediatrician, or primary care physician of record and were considered lost to follow-up, the newborn screening program explored alternative sources for case finding. Several sources for contact information were evaluated. The Michigan Care Improvement Registry (MCIR), which includes information about providers of childhood immunizations and was readily accessible, was selected as a potential source for alternative contact information. Contact was made with providers identified through MCIR to determine whether testing and/or treatment for CH was continuing. In a few cases where current care providers could not be identified, the program made direct contact with the parents to obtain the information.

In order to standardize data collection, a simple flow chart and several collection instruments were developed. This flow chart (Appendix A) and three survey/script forms (Appendices B-D) are provided as a part of this Tool Kit.

Following is a brief description of how the appended forms were used:

Appendix A: Michigan’s Three-Year Follow-up Flow Chart. This one page outline provides an overview of the steps followed in conducting the three-year follow-up.

Appendix B: CH Clinician Survey. This survey is sent to physician of record after patient is 3 years of age.

Appendix C: CH Script for a Clinician Phone Contact. This is the instrument for collecting the information from the treating endocrinologist or the primary care provider by phone.

Appendix D: CH Script for Parent Phone Call. In cases where current provider contact information is not known and the Newborn Screening Program has the parent/guardian’s contact information, this survey is used to guide the telephone conversation with the parent/guardian.

Preliminary Results

As of August 12, 2009, results of follow-up efforts are available for 15 children with TSH < 15th %; 6 children with TSH 15-25th %, and 24 children with TSH > 25%. Preliminary data indicate that some children in all three groups are no longer in treatment and, for most, the decision to discontinue treatment was made without a re-evaluation by TSH challenge (Table 1).

For children with TSH < 15th %

- 8 of 15 children were still being treated (53%)
- Of the 7 children no longer being treated, 1 had been re-evaluated by TSH challenge

For children with TSH 15-25%

- 4 of 6 children were still being treated (66%)
- Of the 2 children no longer being treated, 1 had been re-evaluated by TSH challenge

For children with TSH > 25%

- 20 of 24 children were still being treated (83%)
- Of the 4 children no longer being treated, none had been re-evaluated by TSH challenge

Table 1. Number of children being/not being treated by pre-treatment TSH

TSH <15th%	
# of children with complete follow up data	15
<i># still being treated</i>	8
# still being treated who were re-evaluated by TSH challenge	5
<i># no longer in treatment</i>	7
# no longer in treatment who were re-evaluated by TSH challenge	1

TSH 15-25th%	
# of children with complete follow up data	6
<i># still being treated</i>	4
# still being treated who were re-evaluated by TSH challenge	2
<i># no longer in treatment</i>	2
# no longer in treatment who were re-evaluated by TSH challenge	1

Group 3 (TSH >25th%)	
# of children with complete follow up data	24
<i># still being treated</i>	20
# still being treated who were re-evaluated by TSH challenge	7
<i># no longer in treatment</i>	4
# no longer in treatment who were re-evaluated by TSH challenge	0

Conclusion

Based on Michigan's data, a surprising number of children diagnosed with CH during the newborn period are no longer being treated for CH at three years of age without re-evaluation. While a re-evaluation by TSH challenge is recommended practice, only two of the 13 children no longer being treated had been re-evaluated using the challenge. At least 8 families stopped treatment on their own accord. Most of these had normal Free T4 values, suggesting transient CH.

These preliminary results suggest several next steps:

- Newborns diagnosed with CH who have not been confirmed to have permanent CH should be followed for three years by the state newborn screening program and then re-evaluated to assess if original diagnosis should be changed to transient CH and treatment discontinued.
- The follow-up study should be expanded to include the additional Region 4 states. This would increase the number of cases for analysis and would allow for results to be compared across states.
- The expanded follow up study should include questions that elucidate the limited use of re-evaluation at age three years.
- Methods to increase the use of re-evaluation by TSH challenge should be explored. For example, state newborn screening programs could systematically contact doctors of children diagnosed with CH when they reach their third birthdays. Another approach could be to develop and disseminate materials for families and primary care providers that explain the importance of re-evaluation.
- A search for funds should be undertaken to support additional data collection; develop guidelines for state newborn screening programs to follow children for three years; and develop and implement methodologies to increase re-evaluation.

Contact

For further information, contact:

William Young, PhD, Manager, Newborn Screening Program, Michigan Department of Community Health.
(517) 335-8938
youngw@michigan.gov

Steven Korzeniewski, MSc, MA, Manager, Maternal and Child Health Epidemiology Section, Michigan Department of Community Health.

(517) 335-8202
Korzeniewskis@Michigan.gov

Acknowledgements

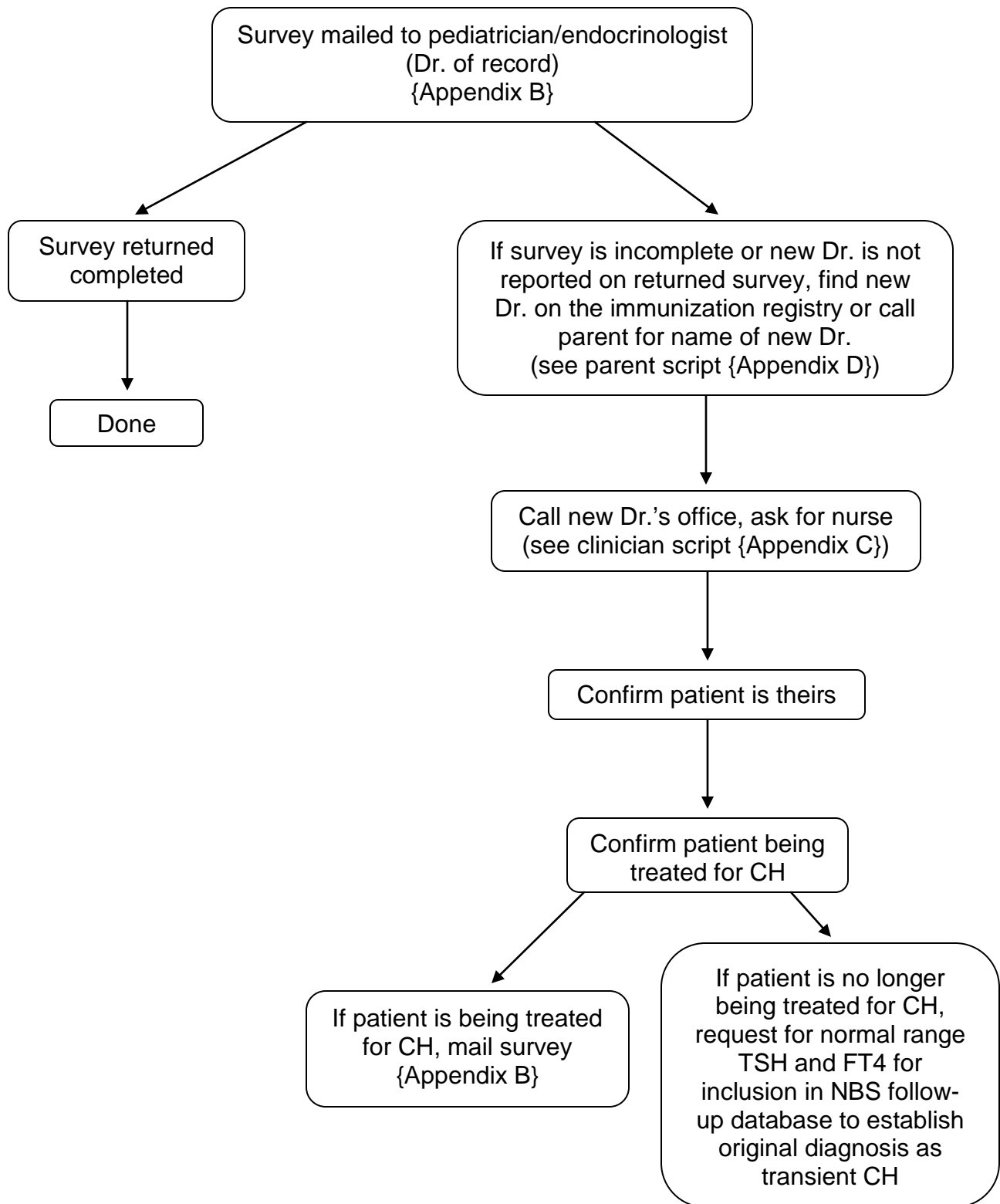
Violanda Grigorescu, Director, Division of Genomics, Perinatal Health & Chronic Disease Epidemiology, Michigan Department of Community Health.

Karen Andruszewski, Data Coordinator, Michigan Newborn Screening Program, Michigan Department of Community Health.

The Region 4 Endocrine Project Workgroup and the Region 4 Short Term Follow-up Workgroup.

Funding provided by Cooperative Agreement U22MC03963, the Region 4 Genetics Collaborative, from HRSA/MCHB through the Michigan Public Health Institute.

Appendix A: Michigan's Three-Year Follow-up Flow Chart



Appendix B: CH Clinician Survey

Dear Dr. _____,

The Michigan Department of Community Health's Newborn Screening Follow-up Program and the Pediatric Endocrinology Medical Management Center at the University of Michigan are interested in follow-up of congenital hypothyroidism (CH) patients at three years of age who had borderline elevations of serum thyroid stimulating hormone (TSH) levels when diagnosed. This survey is intended to inquire about treatment and diagnostic re-evaluation.

Data collected by this survey will be used to determine the rate of transient CH among cases identified by Michigan Newborn Screening. We hope to use these data to inform both diagnostic and treatment standards for CH in Michigan. Your participation in this survey is extremely important and will contribute to our understanding of transient vs. chronic CH.

Please provide the information requested below and return via fax or mail to:

Newborn Screening Follow-up Program,
Michigan Department of Community Health
P.O. Box 30195
201 Townsend St.
Lansing, Mi 48909
Phone: 517-335-6567
Fax: 517-335-9419

We sincerely thank you for your participation,

William I. Young, Ph.D., Manager, Newborn Screening Program, Bureau of Epidemiology, Division of Genomics, Perinatal Health and Chronic Disease Epidemiology, Michigan Department of Community Health, P.O. Box 30195, 201 Townsend St., Lansing, Mi 48909

Steven Korzeniewski, M.A., M.Sc., Epidemiologist, Maternal and Child Health Epidemiology Section, Bureau of Epidemiology, Division of Genomics, Perinatal Health and Chronic Disease Epidemiology, Michigan Department of Community Health, P.O. Box 30195, 201 Townsend St., Lansing, Mi 48909

Chris Hoeft-Loyer, M.S., Newborn Screening and Coordinating Program, Endocrine Follow-Up Office, UMMC-MPB, D1225, Box 0718, Ann Arbor, MI 48109-0718

Diagnostic Verification Survey of Endocrinologists Treating Children Identified by Michigan Newborn Screening as Having Congenital Hypothyroidism and Borderline Thyroid Function

Patient Information:

Child's Birth Date	Child's Name		Parent's Name	
	Last	First	Last	First
DD-Mon-YY	LastName	FirstName	LastName	FirstName

1) Are you or your group's practice providing care for the patient listed in the above table [check one]?

Yes (if yes, proceed to question 2)
 No (proceed to 1.1)

1.1 If no, do you know the patient's current health care provider?

Name: _____

Address: _____

Phone: _____

Fax: _____

2) Is the patient currently being treated for CH [check one]?

Yes (proceed to 2.1)
 No (proceed to 2.2)

2.1 If on treatment,

2.1.a What is the patient's current CH medication dosage? _____

2.1.b Has the treatment dosage increased over the past 3 years [check one]?

Yes (proceed to question 3)
 No (proceed to question 3)

2.2 If not on treatment,

2.2.a Why was the treatment stopped?

2.2.b When was the treatment stopped (mm/dd/yyyy)? _____

2.2.c What is your protocol for following up patients after treatment cessation? _____

3) Does the patient have a sibling with CH [check one]? Yes No

4) Has the patient's CH diagnosis been re-evaluated [check one]?

Yes (proceed to question 4.1) No (proceed to 5)

4.1 If the patient's CH diagnosis was re-evaluated, what was the result [check one]?

Diagnosis Confirmed or Diagnosis Not confirmed

4.1.a How did you make your decision to re-evaluate the patient's CH diagnosis?

4.1.b How was the patient's diagnosis re-evaluated [check one]?

Thyroid challenge was conducted by decreasing the dosage of levothyroxine and then evaluating thyroid function (Free T4/ Serum TSH levels).

Other (specify): _____

4.1.c At what age was the patient's CH diagnosis re-evaluated? _____

4.1.d What is your protocol for follow-up after re-evaluating the CH Diagnosis?

5) If you have not re-evaluated the patient's CH diagnosis, do you plan to do so [check one]?

Yes (proceed to question 6) No (proceed to 7)

If you plan to re-evaluate the patient's CH diagnosis,

6) How will you re-evaluate the patient's CH diagnosis [check one]?

Conduct a thyroid challenge by decreasing the dosage of levothyroxine and then evaluating thyroid function (Free T4/ Serum TSH levels).

Other (specify): _____

6.1 When do you plan to re-evaluate the patient's CH diagnosis?

If you do not plan to re-evaluate the patient's CH diagnosis,

7) Why do you not intend to re-evaluate the diagnosis [check one]?

- Pre-treatment thyroid scan revealed abnormal thyroid anatomy
- Medication dosage and/or serum TSH levels increased over time
- Lost to Follow-up
- Parental refusal
- Other _____

Appendix C. CH Script for a Clinician Phone Contact

INTRODUCTION

- I. Hello, my name is _____, and I am calling from the Michigan Department of Community Health. May I please speak to a nurse?

IF A NURSE IS NOT AVAILABLE:

- II. When would be a good time to call back?
Date/Time: _____

END CALL. CALL BACK AT THE RECORDED DATE/TIME.

IF A NURSE IS AVAILABLE:

- III. My name is _____, and I am calling from the Michigan Department of Community Health's Newborn Screening Follow-up Program.

The Michigan Department of Community Health's Newborn Screening Follow-up Program and the Pediatric Endocrinology Medical Management Center at the University of Michigan are interested in follow-up of congenital hypothyroidism patients at three years of age to confirm patient has been evaluated for permanent CH.

You are being contacted because your practice has been listed as a healthcare provider for a child was diagnosed with CH.

I would like to ask you a few questions about a specific patient. I can call you back when you have had a chance to review the patient's records or if you would prefer I can FAX you the survey questions. The patient's name is First Name Last Name, and the patient's parent is First Name Last Name. This patient was born on Child's Birth Date.

Patient Information:

Child's Birth Date	Child's Name		Parent's Name	
	Last	First	Last	First
DD-Mon-YY	LastName	FirstName	LastName	FirstName

SURVEY

1) Is your practice providing care for this patient?

Yes (PROCEED TO 2)

No (PROCEED TO 1.1)

1.1 Do you know the patient's current health care provider? Please provide the name, address, phone number, and fax number if possible.

Name: _____

Address: _____

Phone: _____

Fax: _____

PROCEED TO END

2) Do you have a record of the patient having CH?

Yes (PROCEED TO 3)

No (PROCEED TO END)

3) Is the patient currently being treated for CH?

Yes (PROCEED TO 3.1)

No (PROCEED TO 4)

3.1 We would like to mail you a brief survey regarding the treatment and diagnostic evaluation of this patient. The entire survey should take about 5 minutes to complete. What is your address? _____

PROCEED TO END

4) Do you have serum TSH and/or free T4 values obtained after treatment cessation?

Yes (PROCEED TO 4.1)

No (PROCEED TO 4.2)

4.1 Please provide the date and serum TSH and free T4 values obtained after treatment cessation.

Date (mm/dd/yyyy): _____ TSH: _____ free T4: _____

PROCEED TO END

4.2 Please obtain a serum TSH and free T4 value at the patient's next appointment. When is the patient's next appointment?

Date (mm/dd/yyyy): _____ (PROCEED TO END. CALL BACK AFTER APPOINTMENT.)

END:

THANK YOU FOR TAKING THE TIME TO ANSWER THESE QUESTIONS. IF YOU HAVE ANY QUESTIONS, PLEASE DIRECT THEM TO First Name, Last Name AT XXX-XXX-XXXX. GOODBYE.

Appendix D: CH Script for Parent Phone Call

For parents who are contacted to find current health care provider or who have been determined to have stopped treatment without proof that child does not have permanent CH.

INTRODUCTION

- I. Hello, my name is _____, and I am calling from the Michigan Department of Community Health. May I please speak to _____ Parent Name_____?

If _____ Parent Name _____ IS NOT AVAILABLE:

- II. When would be a good time to call _____ Parent Name _____ back?
Date/Time: _____

END CALL. CALL BACK AT THE RECORDED DATE/TIME.

If _____ Parent Name _____ IS AVAILABLE:

- III. My name is _____, and I am calling from the Michigan Department of Community Health's Newborn Screening Follow-up Program.

You are being contacted because your child was diagnosed with CH at birth. For some children treatment is required for life but for others treatment is ended after 3 years of age following further testing.

I am going to ask you a few questions about your child's past or current treatment for congenital hypothyroidism or CH. The entire survey will take about 5 minutes.

SURVEY

I am going to ask about the health of your child, FirstName LastName, who was born on Child'sBirthDate.

Patient Information:

Child's Birth Date	Child's Name		Parent's Name	
	Last	First	Last	First
DD-Mon-YY	LastName	FirstName	LastName	FirstName

1) Is your child currently being treated for CH?

Yes (PROCEED TO 1.1)

No (PROCEED TO 2)

1.1 Do you know your child's current health care provider? Please provide the name, address, phone number, and fax number if possible.

Name: _____

Address: _____

Phone: _____

Fax: _____

PROCEED TO END

2) When did your child stop taking medication for CH (mm/dd/yyyy)? _____

3) Why did your child stop taking medication for CH? _____

END:

THANK YOU FOR TAKING THE TIME TO ANSWER THESE QUESTIONS.