The CHOC Children’s Specialists Division of Metabolic Disorders is available for consultation and provides diagnostic services, medical treatment and follow-up for newborns, infants, children, adolescents and adults who have suspected or confirmed inborn errors of metabolism.

We are an approved CCS-metabolic center for the California Department of Public Health/Newborn screening program. Our team manages a variety of patients including those with phenylketonuria (PKU), urea cycle disorders (UCD), organic acidemias, fatty acid oxidation defects, glycogen storage diseases (GSD), lysosomal storage disease (LSD), mitochondrial dysfunction, neurometabolic defects and many other types of inherited metabolic disorders.

All of our metabolic physicians are Board-certified by the American Board of Medical Genetics and Genomics (with special qualifications in clinical/medical biochemical genetics). Our division has a CAP/CLIA certified Biochemical Genetics Laboratory, and is staffed by a multidisciplinary team of metabolic dieticians, genetic counselors, nurse practitioner, registered nurses / case managers and social worker, with expertise in the care of patients with metabolic disorders.

Our Metabolic team works with primary care physicians and other specialists to manage metabolic patients with complex and chronic medical issues.
Metabolic Conditions

Inborn Errors of Metabolism (IEM) seen by our clinic include, but are not limited to the following:

**Urea Cycle Disorders:** N-Acetylglutamate Synthase (NAGS) Deficiency, Carbamoyl Phosphate Synthase I (CPS-I) Deficiency, Ornithine Transcarbamylase (OTC) Deficiency, Citrullinemia Type I, Arginosuccinic Aciduria, Argininemia, Citrullinemia Type II, HHH Syndrome

**Organic Acidurias:** Glutaric Acidemia Type I (GA1), Propionic Aciduria (PA), Methylmalonic Aciduria (MMA), Isovaleric Aciduria (IVA), 3-Methylglutaconic Aciduria, 3-Methylcrotonylglycinuria (3MCC), HMG-CoA Lyase Deficiency.

**Amino Acid Disorders:** Maple Syrup Urine Disease (MSUD), Phenylketonuria (PKU), Tyrosinemias Type I, II and III, Alkaptonuria, Non-Ketotic Hyperglycinemia (NKH), Homocystinuria, Lysinuric Protein intolerance

**Vitamin and Cofactor Disorders:** Biotinidase deficiency, Cobalamin defects, Biotin / Thiamin transporter defects.

**Carbohydrate Metabolism Disorders:** Galactosemias, Hereditary Fructose Intolerance, Glycogen Storage Diseases (GSD), Glucose transport defects.

**Fatty Acid Oxidation Disorders:** Deficiencies of Carnitine transport, Carnitine Palmitoyltransferase I (CPT-I) and II (CPT-II), Translocase, Very Long Chain Acyl-CoA Dehydrogenase (VLCAD), Medium Chain Acyl-CoA Dehydrogenase (MCAD), Short Chain Acyl-CoA Dehydrogenase (SCAD), Multiple Acyl-CoA dehydrogenases.

**Mitochondrial Disorders:** Defects in mitochondrial DNA (mtDNA) and nuclear DNA including: mitochondrial DNA depletion, Alpers, Leigh’s Disease, MELAS, Leber’s Hereditary Optic Neuropathy, Kearns-Sayre, Pearson, tRNA synthetase deficiencies, Ethylmalonic Encephalopathy and others.

**Lysosomal Storage Diseases:** Pompe, Fabry, Gaucher Disease, Mucopolysaccharidoses such as Hurler (MPS-I), Hunter (MPS-II), Morquio (MPS-IV) and others.

**Neurotransmitter Disorders:** Deficiencies of Tetrahydrobiopterin (BH4) synthesis, Tyrosine Hydroxylase, Sepiapterin Reductase, Aromatic amino acid decarboxylase.

**Peroxisomal Disorders:** Adrenoleukodystrophy (ALD), Zellweger spectrum disease, D-Bifunctional Protein Deficiency

**Other Inborn Errors of Metabolism:** Creatine disorders, Purines & Pyrimidines disorders, Congenital Disorders of Glycosylation (CDG)
# Metabolic Disorders Referral Guidelines

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For appointments, please call the Patient Access Center at 888-770-2462 (888-770-CHOC)
Fax ALL pertinent medical records to 855-246-2329 (855-CHOC-FAX)
To speak with a CHOC Children’s Specialist in Metabolic Disorders, please call 714-509-8852

August 18, 2015
A. Developmental Regression / Cognitive Impairment  

[ICD-9 Codes: 331.83]  [ICD-10 Codes: G31.84]

Reason for Referral and Clinical Findings

- Developmental regression, which may be transient or progressive.
- Cognitive deterioration after intercurrent illness.
- Unexplained altered mental status, transient (during acute illness) or progressive.

Pre-Referral

► Provide clinical notes, laboratory records, imaging reports. Growth chart and dietary records if available.
► Refer the patient to the Regional Center for evaluation, and to start services if needed.

Consider

► Additional referral to CHOC Children’s Specialists Neurology (888-770-2462), if seizures are present / suspected.
► Brain MRI with and without contrast if not previously done.

Resources for Healthcare Providers

  http://pediatrics.aappublications.org/
B. Hypotonia  [ICD-9 Codes: 779.89]  [ICD-10 Codes: P94.2]

Reason for Referral and Clinical Findings

- Unexplained hypotonia.
- Concomitant developmental delay, seizures, micro or macrocephaly.
- Worsening of symptoms (lethargy) with intercurrent illness.
- Abnormalities / dysfunction of other organs / system (i.e. cardiac, renal, liver, endocrine, vision, hearing).

Pre-Referral

- Provide clinical notes, laboratory records, imaging reports. Include growth chart and dietary records if available.
- Refer the patient to the Regional Center for evaluation, and to start services if needed.

Consider

- Referral to CHOC Children’s Specialists Neurology: 888-770-2462 (if seizures are present and/or suspected)
- Brain MRI with and without contrast if not previously done
- Suggested initial work-up: chemistry panel, CK, electrocardiogram - echocardiogram.

Resources for Healthcare Providers

C. Stroke-Like Episodes, Intermittent Ataxia, Altered Mental Status

[ICD-9 Codes: 277.87, 780.97] [ICD-10 Codes: E88.4*, H49.8*, R41*]

Reason for Referral and Clinical Findings

- Unexplained stroke-like symptoms.
- Intermittent ataxia, associated with intercurrent illness / fever / emesis.
- Unexplained change in mental status.
- Positive family history, associated symptoms of dev. Delay / regression, feeding difficulties (anorexia, vomiting), hearing, vision abnormalities.

Pre-Referral

▶ Provide clinical notes, laboratory records, imaging reports.
▶ Include growth chart and dietary records if available.

Consider

▶ Referral to CHOC Children’s Specialists Neurology: 888-770-2462 (according to history and clinical findings)
▶ Brain CT / MRI with and without contrast if not previously done.
▶ Urgent ED referral and metabolic consult for laboratory work-up at the time of acute symptoms. CHOC Emergency Department: 714-509-9095

Resources for Healthcare Providers

D. Recurrent / Refractory Seizures [ICD-9 Codes: 345.*] [ICD-10 Codes: G40.A*]

Reason for Referral and Clinical Findings

- Seizures that are unexplained and difficult to treat. Specially:
  - Early / Neonatal onset
  - Myclonic
  - EEG with burst suppression pattern
  - Hypsarrhythmia
- Associated developmental delay / regression, macro-microcephaly, MRI abnormalities.
- Altered mental status / abnormal liver enzymes after initiation of treatment with Valproic acid.
- Associated symptoms of failure to thrive, feeding intolerance, vision / hearing abnormalities.

Pre-Referral

- Provide clinical notes, laboratory records, imaging reports. Include growth chart and dietary records if available.

Consider

- Brain MRI with and without contrast, if not previously done.
- Urgent ED referral and metabolic consult for laboratory work-up at the time of altered mental status. CHOC Emergency Department: 714-509-9095

Resources for Healthcare Providers

E. Failure to Thrive [ICD-9 Code:783.41] [ICD-10 Codes: R62.51]

Reason for Referral and Clinical Findings

• Persistent failure to thrive that does not respond to increased energy intake through diet

• Persistent / unexplained feeding difficulties (anorexia, GI dysmotility, recurrent emesis)

• Associated signs / symptoms:
  ▪ Unexplained life-threatening event
  ▪ Acute metabolic crisis (ie. acidosis, ketosis, hypoglycemia), change of mental status
  ▪ Liver dysfunction, Developmental delay / regression, cardiomyopathy and/or myopathy, organomegaly

Pre-Referral

► Provide clinical notes, laboratory records, imaging reports.
► Growth chart and dietary records

Consider

► Simultaneous referral to CHOC Children’s Specialists Gastroenterology 888-770-2462

Resources for Healthcare Providers

F. Hypoglycemia / Recurrent Hypoglycemia [ICD-9 Code: 251.2] [ICD-10 Code: E16.1]

Reason for Referral and Clinical Findings

- Unexplained symptoms suggestive of hypoglycemia: pallor, tremors, irritability, sweating, change in mental status, seizures, etc.; after prolonged fasting.

- Documented hypoglycemia (glucose < 50 mg/dl) in a fasting or post prandial sample.

- Associated metabolic acidosis, increased lactic acid, abnormal ketone bodies (low or high), hepatomegaly (with or without liver dysfunction), nephromegaly and microcephaly.

- Positive family history.

Pre-Referral

- Provide clinical notes, laboratory records, imaging reports.
- Growth chart and dietary records.

Consider

- Simultaneous referral to CHOC Children’s Specialists Endocrinology: 888-770-2462.
- Urgent ED evaluations and consult for critical samples at the time of acute episode. CHOC Emergency Department: 714-509-9095

Resources for Healthcare Providers


### G. Abnormal Laboratory / Imaging [ICD-9 Code: 790.6] [ICD-10 Code: R79.89]

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<td>• Hyperammonemia</td>
<td>► Abnormal MRI:</td>
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<td>• Metabolic acidosis with elevated anion GAP</td>
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<td>• Cholestasis</td>
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<td>• Abnormal genetic testing for a metabolic disease</td>
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#### Resources for Healthcare Providers


H. Family History of Other Endocrine and Metabolic Diseases [ICD-9 Code: V18.19] [ICD-10 Code: Z83.49]

Reason for Referral and Clinical Findings

- Family history of an inborn error of metabolism: fatty acids oxidations disorders, glycogen storages diseases, urea cycle disorders, mitochondrial disorders, lysosomal storages disorders, etc. (pg. 3)

- Family history of Sudden Infant Death - ALTE

Pre-Referral

- Provide clinical notes, laboratory records, imaging reports.
- Include growth chart and dietary records if available.

Resources for Healthcare Providers

I. Other Inborn Errors of Metabolism (positive newborn screening)  [ICD-9 Code: V77.7] [ICD-10 Code: Z13.228]

Initial Management

- After a baby is flagged as “presumptive positive” by the CA NBS program, an area service center coordinator will contact our division as well as the patient’s primary care provider (NICU or Nursery unit if patient is still in the hospital).

- Our metabolic NBS coordinator will recommend / coordinate confirmatory testing with the treating physician. Depending on the suspected metabolic condition, we could advise:
  1. To send the patient to the ED for evaluation and lab testing.
  2. To refer patient for metabolic clinic visit
  3. To perform confirmatory testing as outpatient by PCP.

- Once the confirmatory testing results are completed, our NBS coordinator will contact the PCP, to recommend treatment and scheduled follow-up, OR to inform that the case is closed and no further follow up is necessary. (NBS) Newborn Screening, (NICU) Neonatal Intensive Care Unit

Follow the recommendations by the metabolic team

► Advise patient to go to the ED at CHOC’s Children Hospital or the nearest medical center as recommended.
► Assist with the referral of the patient for the outpatient metabolic appointment.
► If confirmatory testing is required as outpatient, a pre-filled laboratory requisition form and instructions will be faxed to the PCP office (or NICU-Nursery unit).
► Provide initial education about newborn screening and discuss the possibility of a false positive result with parents.
► Obtain samples from the patient’s mother, when advised.
► Instruct parents about recommended feedings, fasting precautions, as well as monitoring for symptoms like, emesis, lethargy, etc. as indicated.
► The recommendations will change depending on the suspected disorder.

Resources for Healthcare Providers

- California Newborn screening information for healthcare providers:  http://www.cdph.ca.gov/programs/nbs
- Introduction to the Newborn Screening Fact Sheets, form the AAP:  http://pediatrics.aappublications.org/