

**Citrulline (Urea Cycle Disorder) Screening Fact Sheet for Health Care Providers**  
Newborn Screening Program of the Oklahoma State Department of Health

**What is the differential diagnosis?**

Citrullinemia type I, Argininosuccinic Aciduria; Citrullinemia Type II (citrin deficiency)

**What are the characteristics of urea cycle disorders?**

- Autosomal recessive genetic conditions.
- Most infants are born to parents who are both unknowingly asymptomatic carriers and have NO known history of a urea cycle disorder in their family.
- Disorders of citrulline metabolism are included in a larger group of disorders, known as urea cycle disorders.
- The incidence of all urea cycle disorders is estimated to be about 1/8,000 live births. In citrullinemia and in argininosuccinic acidemia (ASA), the accumulation of ammonia and other toxic metabolites occurs during the first few days of life.
- Newborns with these disorders often appear normal initially but rapidly develop cerebral edema and the related signs of lethargy, anorexia, hyperventilation or hypoventilation, hypothermia, seizures, neurologic posturing, and coma.
- Urea cycle disorders **are life threatening**. Immediate intervention is warranted to prevent hyperammonemia and death.
- Lifelong treatment includes a special diet, and special care during times of illness or stress.

**What is the screening methodology for citrulline?**

1. An amino acid profile by Tandem Mass Spectrometry (MS/MS) is performed on each filter paper.
2. Citrulline is the primary analyte.
3. If citrulline is elevated the citrulline/arginine ratio will also be evaluated.

**What is an in-range (normal) screen result for citrulline?**

Citrulline less than 55 µmol/L is NOT consistent with a disorder of citrulline metabolism.  
See Table 1.

**What is an out-of-range (abnormal) screen for citrulline?**

Citrulline > 55 µmol/L is out of range.

**What screen results will require diagnostic testing?**

All out-of-range Citrulline screens will require immediate action. The follow-up program will provide detailed guidance on required actions and an *Emergency Management Protocol* will be provided.

**What are the follow-up needs?**

The follow-up program will provide detailed guidance on needed actions. The following metabolic specialists have approved all recommendations:

Metabolic Specialist in Oklahoma

Klaas Wierenga, M.D. (405) 271-8685

Susan Palmer, M.D. (405) 271-8685

**What is my role in screening?**

If you are listed as the infant's planned health care provider on the filter paper requisition, you are required by the *Newborn Screening Program Regulations* to initiate follow-up activities.

TABLE 1. In-range Citrulline Newborn Screening Results		
Primary Analyte	In-Range	(µmol/L)
Citrulline	<	55

Secondary Analytes <sup>1</sup>	In-Range
Citrulline/Arginine ratio	< 6.5

<sup>1</sup> Elevations of the secondary analytes are reported as "not consistent with an amino acid disorder" if the primary analyte is in-range.