

# TESTING FOR HYPERAMMONEMIA

## The Essentials

**HYPERAMMONEMIA CAN BE A LIFE-THREATENING  
CONDITION THAT MAY AFFECT PATIENTS AT ANY AGE.<sup>1</sup>**

### ■ A LIFE-THREATENING CONDITION

Hyperammonemia is a metabolic condition characterized by excess ammonia in the blood that can affect patients at any age. **If left untreated, hyperammonemia may lead to irreversible neurological damage or death.<sup>1</sup>** Thus, particular care should be taken when sampling and handling plasma specimens to increase the positive predictive value of ammonia test results.<sup>2</sup>

### ■ SIGNS AND SYMPTOMS OF ACUTE HYPERAMMONEMIA

Signs and symptoms of acute hyperammonemia are nonspecific and are mostly neurological in origin.<sup>3</sup> Symptoms may include:

- Somnolence and lethargy progressing to coma<sup>3</sup>
- Vomiting (metabolic acidosis)<sup>1</sup>
- Seizures<sup>1</sup>
- Peripheral circulatory failure<sup>1</sup>
- Cerebral edema (respiratory alkalosis)<sup>1</sup>
- Liver failure<sup>1</sup>
- Multiorgan failure<sup>1</sup>
- Postpartum psychosis<sup>1</sup>
- In neonates: sepsis-like picture, respiratory distress, hypo/hyperthermia<sup>1</sup>

### ■ COMMON CAUSES OF HYPERAMMONEMIA

Common causes of hyperammonemia include<sup>4</sup>:

- Liver failure
- Reactions to drugs (e.g., valproic acid)
- Hemolytic disease
- Gastrointestinal bleeds
- Urea cycle disorders (UCDs)  
or other inborn errors of metabolism (IEMs)<sup>2,5</sup>

## ACCURATE BLOOD AMMONIA DRAW AND ANALYSIS: THE ESSENTIAL STEPS

## ACCURATE BLOOD AMMONIA DRAW AND ANALYSIS: THE ESSENTIAL STEPS

Levels of ammonia can be affected by sampling technique, transport, and analytical technique.<sup>6</sup> Follow these steps to ensure an accurate plasma ammonia result:

1



### STAT Lab Alert

Alert the laboratory to the incoming STAT order.<sup>2</sup>

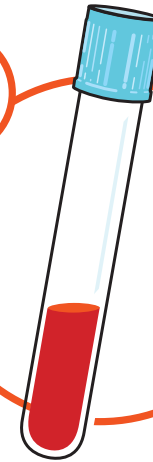
### Free-Flowing Venous or Arterial Blood Sample

Prepare to collect a free-flowing venous or arterial blood sample. Do not use a tourniquet, and keep the patient's arm as relaxed as possible.<sup>4,7,8</sup>

2



3



### Lithium Heparin or EDTA Tube

Collect the blood sample in a specimen tube (preferably pre-chilled) containing either lithium heparin or EDTA as an anticoagulant.<sup>7</sup>

4



### Ice & Transport to Lab

Place the sample on ice. Order the sample to be handled STAT (transported to lab, separated within 15 minutes of draw, and analyzed immediately).<sup>2,7</sup>

< **Newborns** who develop severe hyperammonemia after 24 hours of age usually have a UCD or an organic acidemia—both IEMs.<sup>5</sup>

< **In older patients**, liver disease is a likely cause of hyperammonemia. However, UCDs should be considered since 69% of UCD patients present with symptoms of hyperammonemia later in life.<sup>9,10</sup>

### SPEED AND ACCURACY

- The management of a hyperammonemic crisis not only demands a rapid plasma ammonia reading but also an accurate one.<sup>1</sup>
- Critical clinical decisions depend on having the right diagnostic information.
- Hyperammonemic crises can develop quickly, increasing the risk of neurological damage and death.<sup>1</sup>
- If hyperammonemia is confirmed, treatment should not be delayed.<sup>1</sup>
- Consider calling a metabolic geneticist.

## LAB PROCEDURES AND ANALYSIS

The test for ammonia should only take a few minutes after receipt of the sample, so clinicians can expect a rapid report from the laboratory.<sup>1</sup> Direct procedures, such as enzymatic methods, are more widely used than indirect procedures to measure plasma ammonia levels, as they are more easily automated.<sup>11</sup>

### NORMAL BLOOD AMMONIA REFERENCE LEVELS<sup>7</sup>

Decision limits of plasma ammonia concentrations\* (to be interpreted with the clinical situation)<sup>1</sup>:

Approximate age	μmol/L
Premature neonates	< 150
Term neonates	< 100
Infants	< 40
Adults	11-32

\*Individual laboratory reference levels may vary.

### INTERPRETATION OF RESULTS

The goal is to rule out hyperammonemia without delay.<sup>1</sup>

If hyperammonemia is confirmed, other laboratory tests that may be helpful in diagnosing a urea cycle disorder (UCD) include<sup>1</sup>:

- Blood glucose, blood gases, electrolytes, lactate, and transaminases
- Plasma amino acids and blood acylcarnitines
- Urine amino acids, organic acids, and orotic acid

Regardless of cause, any delay in recognizing or treating hyperammonemia increases the risk of irreversible brain damage or death.<sup>1</sup>

## RAPID, ACCURATE BLOOD AMMONIA DRAW AND ANALYSIS: A QUICK SUMMARY

- Alert laboratory to STAT order
- Sample free-flowing venous or arterial blood – no tourniquet
- Use lithium heparin or EDTA tube
- Immediately place sample on ice, with orders to be handled STAT

### REFERENCES

1. Haberle J. Clinical practice: the management of hyperammonemia. *Eur J Pediatr* 2011;170:21-34.
2. Broomfield A, Grunewald S. How to use serum ammonia. *Arch Dis Child Educ Pract Ed* 2012;97:72-77.
3. Haberle J, Boddaert N, Burlina A, Chakrapani A, Dixon M, Huemer M, Karall D, Martinelli D, Sanjurjo Crespo P, Santer R, Servais A, Valayannopoulos V, Lindner M, Rubio V, Dionisi-Vici C. Suggested guidelines for the diagnosis and management of urea cycle disorders. *Orphanet J Rare Dis* 2012;7:32.
4. Orton DJ, Gifford JL, Seiden-Long I, Khan A, de Koning L. Critically high plasma ammonia in an adolescent girl. *Clin Chem* 2016;62(12):1565-1569.
5. Burton BK. Inborn errors of metabolism in infancy: a guide to diagnosis. *Pediatrics* 1998;102(6):E69.
6. Galal NM, Fouad HM, Saied A, Dabnon M. Hyperammonemia in the pediatric emergency care setting. *Pediatr Emerg Care* 2010;26(12):888-891.
7. Hawke L. Ammonia (plasma, blood). The Association for Clinical Biochemistry and Laboratory Medicine. Available at: <http://www.acb.org.uk/whatwedo/science/amalc.aspx>. Published 2012. Accessed September 7, 2017.
8. Barsotti RJ. Measurement of ammonia in blood. *J Pediatr* 2001;138(1):S11-S20.
9. Roth K. Genetics of hyperammonemia. eMedicine/Medscape. Updated Mar 29, 2016. Available at: <http://emedicine.medscape.com/article/944996-overview>. Accessed September 7, 2017.
10. Batshaw ML, Tuchman M, Summar M, Seminara J. A longitudinal study of urea cycle disorders. *Mol Genet Metab* 2014;113:127-130.
11. Infinity™ Ammonia Reagent for Beckman Coulter AU Chemistry Analyzers. Available at: <https://tools.thermofisher.com/content/sfs/manuals/Infinity-Ammonia-Beckman-EN.pdf>. Accessed September 14, 2017.

VISIT CHECKAMMONIA.COM