

## Newborn Screening ACT Sheet [Elevated C5 Acylcarnitine] Isovaleric Acidemia

**Differential Diagnosis:** Isovaleric acidemia (IVA), 2-Methylbutyrylglycinuria (2MBG) (also referred to as short/branched chain acyl-CoA dehydrogenase deficiency or SBCAD deficiency); antibiotic-related (pivalic acid derived) artifact.

**Condition Description:** IVA and 2MBG result from different defects in the metabolism of the branched chain amino acids, leucine (isovaleryl-CoA dehydrogenase in IVA), and isoleucine (short/branched chain acyl-CoA dehydrogenase in 2MBG). In both conditions, specific metabolites accumulate and are potentially toxic.

---

***YOU SHOULD TAKE THE FOLLOWING ACTIONS IMMEDIATELY:***

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea, odor of sweaty feet).
- Consult with pediatric metabolic specialists
- Evaluate the newborn; if infant is ill, initiate emergency treatment as indicated by metabolic specialist and transport IMMEDIATELY to tertiary center with metabolic specialist.
- Initiate timely confirmatory/diagnostic testing as recommended by specialist.
- Educate family about signs, symptoms and need for urgent treatment of metabolic acidosis (poor feeding, vomiting, lethargy, tachypnea, odor of sweaty feet).
- Report findings to newborn screening program.

---

**Diagnostic Evaluation:** Plasma acylcarnitine analysis confirms the increased C5. Urine organic acid analysis will show isovalerylglycine in IVA and 2-methylbutyrylglycine in most cases of 2MBG. Urine acylglycine and acylcarnitine analysis may also be informative.

**Clinical Considerations:** Isovaleric acidemia presents in the neonate with metabolic ketoacidosis, a “sweaty feet” odor, dehydration, hyperammonemia, ketonuria, vomiting, hypoglycemia, and failure to thrive. Milder variants without neonatal illness exist. Long-term prognosis of IVA with appropriate therapy is good. The clinical spectrum of 2MBG is variable. To date, most patients identified by newborn screening with 2MBG are of Hmong descent and remain asymptomatic.

**Additional Information:**

[New England Consortium of Metabolic Programs](#)  
[Gene Reviews](#)  
[Genetics Home Reference](#)

**Referral (local, state, regional and national):**

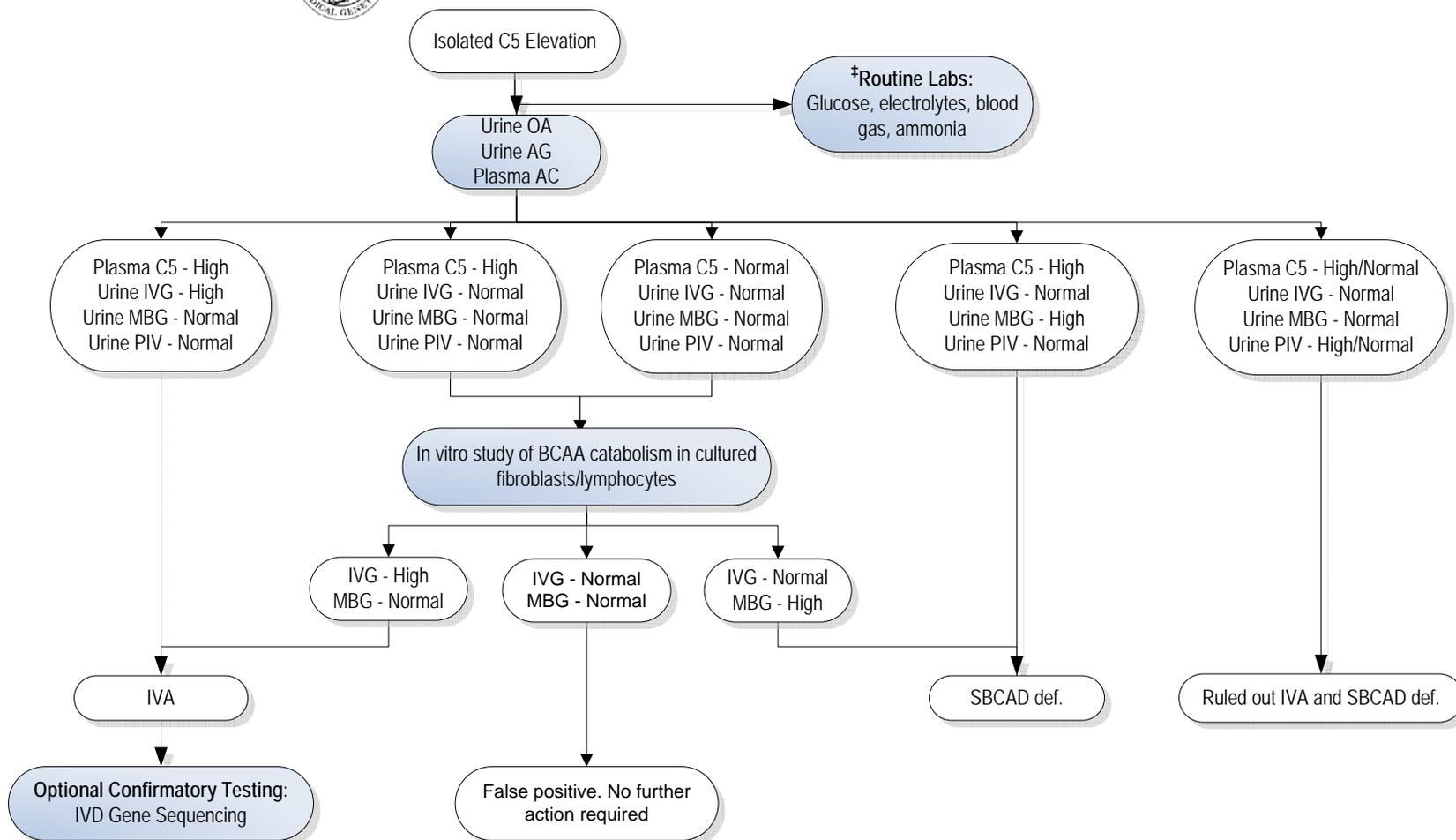
[Testing](#)  
[Clinical Services](#)  
[Find Genetic Services](#)

Disclaimer: This guideline is designed primarily as an educational resource for clinicians to help them provide quality medical care. It should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same results. Adherence to this guideline does not necessarily ensure a successful medical outcome. In determining the propriety of any specific procedure or test, the clinician should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. Clinicians are encouraged to document the reasons for the use of a particular procedure or test, whether or not it is in conformance with this guideline. Clinicians also are advised to take notice of the date this guideline was adopted, and to consider other medical and scientific information that become available after that date.

© American College of Medical Genetics and Genomics, 2012 (Funded in part through MCHB/HRSA/HHS grant #U22MC03957)



# C5 Elevated (Isolated)



### Abbreviations

- AC = Acylcarnitine
- AG = Acylglycine
- IVA = Isovaleric acidemia
- IVD = Isovaleryl-CoA dehydrogenase
- IVG = Isovalerylglycine
- MBG = 3-methylbutrylglycine
- OA = Organic acid
- PIV = Pivalic acid (antibiotic)
- SBCAD = short/branched chain Acyl-CoA dehydrogenase

### Key

‡ =When the positive predictive value of screening is sufficiently high and the risk to the infant is high, some initiate diagnostic studies that are locally available at the same time as confirmation of the screening result is done.

Actions are shown in shaded boxes; results are in the unshaded boxes.

**Disclaimer:** This guideline is designed primarily as an educational resource for clinicians to help them provide quality medical care. It should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same results. Adherence to this guideline does not necessarily ensure a successful medical outcome. In determining the propriety of any specific procedure or test, the clinician should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. Clinicians are encouraged to document the reasons for the use of a particular procedure or test, whether or not it is in conformance with this guideline. Clinicians also are advised to take notice of the date this guideline was adopted, and to consider other medical and scientific information that become available after that date.