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| **Disease Name** | **Propionic academia** |
| **Alternate name(s)** | Propionyl-CoA carboxylase deficiency, PCC deficiency, Ketotic hyperglycinemia |
| **Acronym** | PA |
| **Disease Classification** | Organic Acid Disorder |
| **Variants** | Yes |
| **Variant name** | Late onset (> 6weeks) |
| **Symptom onset** | Neonatal |
| **Symptoms** | Episodic crises leading to neurologic damage, coma and death. |
| **Natural history without treatment** | Metabolic crises may lead to neurologic damage including mental delays, movement disorders, seizures. Coma and sudden death are also possible. |
| **Natural history with treatment** | If treatment instituted before metabolic crisis, normal IQ and development may be seen. Treatment may improve some symptoms of affected individuals. |
| **Treatment** | Protein restricted diet with supplementary medical formula, carnitine supplementation, ketone monitoring, avoidance of fasting, cornstarch supplementation, and biotin supplementation. Antibiotic (metronidazole and neomycin) treatment. Human growth hormone therapy. |
| **Physical phenotype** | Characteristic facies including frontal bossing, widened depressed nasal bridge, epicanthal folds, long philtrum, upturned curvature of the lips and possible hypoplastic/inverted nipples. |
| **Inheritance** | Autosomal recessive |
| **General population incidence** | 1:35,000 to 1:75,000 (may be underestimate as infants may die undiagnosed) |
| **Ethnic differences** | Yes |
| **Population** | Saudi Arabia |
| **Ethnic incidence** | 1:2000 to 1:5000 |
| **Enzyme location** | Mitochondria |
| **Enzyme Function** | Intermediary in the metabolism of isoleucine, valine, threonine and methionine. |
| **Missing Enzyme** | Propionyl-CoA carboxylase |
| **Metabolite changes** | Increased glycine in blood and urine, 3-hydroxypropionic acid in blood and urine, methylcitrate, tiglic acid, tiglylglycine butanone and propionyl glycine in urine. |
| **Prenatal testing** | Enzyme activity in amniocytes. GCMS assay in amniotic fluid. If DNA mutations known, DNA testing is possible. |
| **MS/MS Profile** | N/A |
| **OMIM Link** | http://www.ncbi.nlm.nih.gov/omim/232000 |
| **Genetests Link** | www.genetests.org |
| **Support Group** | Organic Acidemia Association<br>www.oaanews.org<br>Save Babies through Screening Foundation<br>www.savebabies.org<br>Genetic Alliance<br>www.geneticalliance.org |

# Newborn Screening ACT Sheet
# [Elevated C3 Acylcarnitine]
## Propionic Acidemia and Methylmalonic Acidemia

**Differential Diagnosis:** Propionic acidemia (PA); Methylmalonic acidemias (MMA) including defects in $B_{12}$ synthesis and transport; maternal severe $B_{12}$ deficiency.

**Condition Description:** PA is caused by a defect in **propionyl-CoA carboxylase** which converts propionyl-CoA to methylmalonyl-CoA; MMA results from a defect in **methylmalonyl-CoA mutase** which converts methylmalonyl-CoA to succinyl-CoA or from lack of the required $B_{12}$ cofactor for methylmalonyl-CoA mutase (cobalamin A, B, C, D, and F).

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***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).
- Consult with pediatric metabolic specialist.
- Evaluate the newborn; check urine for ketones and, if elevated or 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 hyperammonemia and metabolic acidosis (poor feeding, vomiting, lethargy, tachypnea).
- Report findings to newborn screening program.

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**Diagnostic Evaluation:** Plasma acylcarnitine confirms the increased C3. Blood amino acid analysis may show increased glycine. Urine organic acid analysis will demonstrate increased metabolites characteristic of propionic acidemia or increased methylmalonic acid characteristic of methylmalonic acidemia. Plasma total homocysteine will be elevated in the cobalamin C, D and F deficiencies. Serum vitamin $B_{12}$ may be elevated in the cobalamin disorders.

**Clinical Considerations:** Patients with PA and severe cases of MMA typically present in the neonate with metabolic ketoacidosis, dehydration, hyperammonemia, ketonuria, vomiting, hypoglycemia, and failure to thrive. Long-term complications are common, early treatment may be lifesaving and continued treatment may be beneficial.

**Additional Information:**

Emergency Protocols (New England Consortium of Metabolic Programs)
- PA
- MMA

Gene Reviews
- PA (Organic Acidemias Overview)
- MMA

Genetics Home Reference
- PA
- MMA

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

Testing
- PA
- MMA

Clinical Services