

ORGANIC ACIDEMIAS:

After Childhood...

Mark S. Korson, M.D.

Tufts-New England Medical Center

Boston, MA

Organic Acidemias

Phenotypes

- Neonatal metabolic crisis
- Late-onset metabolic crisis
- Chronic metabolic toxicity
- Chronic neurologic presentation
- Pre-symptomatic

NEONATAL METABOLIC CRISIS

A 5 day old male presents to the ER with a 3-day history of POOR FEEDING and SPITTING. The pregnancy / labor / delivery were normal. During the previous 24 hours, the patient was LETHARGIC; the following morning, he was found LIMP and BREATHING RAPIDLY.

On exam, the patient is DEHYDRATED, UNRESPONSIVE, PALE, with RAPID HEART RATE, and LOW BLOOD PRESSURE. His LIVER is ENLARGED. He is noted to be HYPOTONIC.

Blood tests show a METABOLIC ACIDOSIS and his AMMONIA level is ELEVATED. His urine shows significant KETONURIA (3+). He has a LOW WHITE BLOOD CELL and PLATELET COUNT.

Diagnosis: Methylmalonic acidemia

LATE-ONSET METABOLIC CRISIS

An infant female is growing and developing well aside from MACROCEPHALY (LARGE HEAD), first identified at 2 months of age. At 6 months, she develops vomiting, a cough, congestion and a low grade fever. Her oral intake drops. On day 3, she becomes very IRRITABLE and she becomes very STIFF. She is referred to the ER for ?seizures.

Biochemical testing on admission shows a mild METABOLIC ACIDOSIS.

On admission, she is noted to be IRRITABLE, HYPOTONIC with HYPERACTIVE REFLEXES, and moving all LIMBS in a WRITHING fashion. A CT scan of the head shows BILATERAL INFARCTIONS of the BASAL GANGLIA.

Diagnosis: Glutaric acidemia type I

CHRONIC METABOLIC TOXICITY

A 7 month old male presents with FAILURE TO THRIVE. For several months, he has FED POORLY with significant spitting following feeds, prompting numerous formula changes and initiation of anti-reflux therapy. These interventions have not been successful. In addition, he has had RECURRENT INFECTIONS, especially chronic YEAST INFECTIONS of the mouth and peri-anal area.

The patient is admitted with failure to thrive and is noted to resist feedings, resulting in POOR CALORIE INTAKE. He is also found to be HYPOTONIC and globally DELAYED.

Biochemical work-up reveals a microcytic ANEMIA, mild METABOLIC ACIDOSIS and KETONURIA. An immunology work-up is inconclusive.

Diagnosis: Propionic acidemia

CHRONIC NEUROLOGIC **PRESENTATION**

A 31 year old is well until age 28 when he becomes CONFUSED and WITHDRAWN. His MEMORY DETERIORATES slowly and he develops INVOLUNTARY MOVEMENTS of the HANDS and FACE. His BEHAVIOR is occasionally BIZARRE. He had occasional episodes in infancy of VOMITING and LETHARGY treated with clear liquids only. Those symptoms resolved over 2-3 days.

An examination shows only INVOLUNTARY MOVEMENTS of the LIMBS and TORSO.

Routine biochemical testing shows no abnormalities; specifically blood gases and ammonia are normal. Urine organic acid testing is abnormal.

Diagnosis: Propionic acidemia

ASYMPTOMATIC / PRESYMPTOMATIC PT

A healthy infant female is born to a 21 year old woman. The stay in the newborn nursery is unremarkable, and the baby feeds on cow's milk formula feedings. A newborn screening specimen is obtained prior to discharge on day 2 of life.

In clinic, the infant is evaluated and found to be HEALTHY. A biotin supplement is prescribed.

Diagnosis: Biotinidase deficiency

Symptoms of Metabolic Crises

	Childhood	Adult
Nausea, Vomiting	+++	++
Lethargy	+++	++
Cog/mental disturbance	Probably	++
At risk – brain damage	Yes	+/- Yes

Biochemical Features of Metabolic Crises

	Childhood	Adult
Metabolic Acidosis	Yes	No
Ketosis	Yes	Yes
High Ammonia	Yes	Yes
Bone Marrow Suppression	Yes	No?

Don't expect crises at older ages to necessarily resemble crises when younger.

Organic Acidemias

Complications in adulthood

- Pancreatitis (PPA, MMA, GA type I)
- Kidney complications including failure (MMA)
- Dystonia, involuntary movements (PPA, MMA)
- Iatrogenic (obesity from excessive calories, deficiencies from overzealous restriction)

Progression of neurologic disease or of renal disease can also occur post-liver transplant (MMA).

Organic Acidemias

No Complications

- Asymptomatic even in adulthood (so far) – PPA, MMA, 3-MCC deficiency, GA type I, biotinidase deficiency, others?

ORGANIC ACIDEMIAS:

Transition of Care

The Pediatric Patient Persona

- Depends on her/his parents for instruction and supervision.
- Participates with prodding and teaching.
- Attains over time the knowledge and skills to manage the disorder.

The Adult Patient Persona

- Knowledgeable about the disorder.
- Interacts freely with available resources, especially clinic staff.
- Advocates for coverage.
- Fashions a lifestyle that suits his/her life stage, and makes changes as needed.

What Do Adult Patients Want?

(Brenton DP, et al, 2000)

- Physicians, dietitians with metabolic expertise.
- Good communication and availability by telephone between clinic visits.
- Opportunities to meet other affected individuals and families.
- Assistance around health, education, employment issues.
- Counseling during difficult times (e.g., adolescence).

What Do Adult Patients Want?

(Adult PKU list-serv)

- “Not to sit on little chairs and watch Barney in the waiting room”.
- “Be involved in making decisions”.
- “Not having to come to clinic so often”.
- “To be acknowledged as people, not just people with PKU”.

Model for Care I

- Lucy begins in a pediatric center.
- Lucy continues in a pediatric center with more of an “adult approach”, i.e., attention to adult issues, as she grows older.
- Adult consultants are called upon as needed. The pediatric experts are resources about metabolic disease for these consultants.

Model for Care II

- Bobby begins in a pediatric center.
- Bobby moves to a transitional program in a pediatric center or adult center with involvement of both the pediatric experts and the adult-trained professionals.
- Bob continues in an adult center with input as needed from the pediatric experts. Consultants are called as needed.

Model for Care III

- Caren begins in a pediatric facility within a general hospital.
- Caren moves to a permanent, shared pediatric-adult clinic within the hospital. Both the pediatric expert and adult-trained professional continue to follow Caren.
- Consultants are called in as needed; the clinic acts as a resource regarding the disorder.

Requirements for any Clinic Managing Adults with IEMs

- *Metabolic professionals:*
- Must have an expertise.
- Must act as resources to adult health professionals.
- Must identify adult health professionals familiar/comfortable with IEMs.
- Must be proactive and assertive; the adult health care system is not “warm and fuzzy”.

Requirements for any Clinic Managing Adults with IEMs

- *The Clinic:*
- Must make sure the environment (outpatient and inpatient) acknowledges the age and maturity of the patient.
- Must emphasize autonomy and find ways for patients to resolve problems based on developmental level of the patient.
- Must recognize that patients are working, have families, and live at a distance from the clinic.

Recommendations - Child

- Initiate developmental achievement programs during childhood to promote participation and decision-making.
- Make patients and parents aware of how their care will change as children grow to adolescence and adulthood.

Recommendations - Adolescent

- Develop methods for adolescents to learn about and assume their own care:
 - programs with other teenagers.
 - coordinated educational ventures with school or college.
 - no lectures!
- Acknowledge the teenager's need for privacy and confidentiality.

Recommendations - Adult

- Develop methods for long distance care to reduce the intrusiveness of care:
 - More care by phone/EMail with (known) patients around routine care issues.
 - Get insurance to support routine, off-premises care.

Recommendations - Adult

- Encourage participation in regional conferences and get-togethers to maintain social contacts and keep up to date about new developments.
- Complement this with Emailing to keep people involved and informed.
- Provide a list of adult professionals who are familiar/comfortable with metabolic disease.

And... adjust all recommendations according to the developmental level of the patient.