HCU Network America

The HCU *Herald*

All things Homocystinuria: patient stories, resources, research, events and more!

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HCU HERO: ALAVA FROM SWEDEN

On November 1st, 2019 our precious little daughter, Alva, was born and we couldn't have been happier. I remember how we were lying in our beds at the hospital, refusing to sleep in order to just watch that beautiful little person who had entered our lives.

Two days after she was born we left the hospital, after leaving a few drops of blood for the Newborn screening, and since she is our first child our lives completely evolved around her. She was just perfect.

When Alva was 12 days old (or young I guess we should say), I woke up as my phone began to ring - and half-awake/half-asleep I picked it up. It was a doctor from the hospital here in Umeå, Sweden. She told me they had discovered that Alva had a high level of methionine in the blood test they took after she was born. She started talking about medications and diets and I just could not wrap my head around any of it. She asked us to come in and meether and a dietician that same day and so we did. That was the start of a horrific week that really made our new "baby-bubble-life" burst.

They drew blood from Alva every day for a week, after starting her on a very high dose of Pyridoxine (B6) that first day, to see if she responded to the medication. It was a real struggle to find her little veins in her chubby little baby arms/feet/hands (they even went for the skull a few times) and it usually took around 3 tries every day. It was heart breaking, but we knew it was for her own good, and she wouldn't remember any of it.

Her numbers went up for the first few days before going down; the first day her homocysteine was at 44, then 79 and 100 before going down to 65, 63 and finally 39. So, they thought she was at least partially responding to the B6. With that information they told us I could continue to breast feed her as I already did, and a little over a month later they also gave her Cystadane (betaine) that we still give her twice a day. A week or two after starting with the Cystadane her methionine peaked at 160 and homocysteine at 40, before they came back down.

She began with small portions of fruit and veggie purées when she was 4 months old and then increased the amount of food slowly as she grew. To be honest, we did not have to adjust very much at all for the first 9 months of her life while breast-feeding, except for choosing vegetarian options when we bought ready-made baby-food.

We continue to feed her vegetarian food but not 100% vegan since we use some dairy products while cooking. She is now 2 years and 3 months old and eats around 20 grams of protein per day. She has had two injections of B12 during her life, but no other supplements since her levels of all other amino acids are within "normal" ranges. When she was a little over a year our doctor wanted to try taking away the Cystadane to see if the Pyridoxine alone was enough. It was not. After being stable with homocysteine around 25-30 they went up to 52 in just a week so we went back to Cystadane and are now back

to the lower levels. Our doctor is happy with anything under 50, but we'd like to keep it a bit lower.

As for now she is eating regular kids-porridge with fruit or some oat-based yoghurt with cereals and gluten-free bread for breakfast (around 3-5 grams of protein in total), and then two cooked meals of around 10-15 grams in total (can be one that is high and one low or sometimes two medium-high meals), before having regular baby formula in bed (2-5 grams of protein depending on amount). Her higher tolerance really makes life a lot easier for us, and we feel that we have many options when cooking for her. We feel so lucky! And even if she would have had a lower tolerance, we are thankful for the months of breast-feeding since it gave us a lot of time to read and learn, and have some trial-and-error-missions in the kitchen. Cook for Love is a great website that really has helped us a lot - and also the community on Facebook. Thank you all so much for taking the time to answer our many questions.

So, how is Alva today? She is just the most adorable little girl. Besides her food there is really nothing to tell her apart from other kids her age. She took her first steps a few days before turning 11 months old and now she is running around and climbing on everything in our home and at her preschool. She is very verbal and speaks extremely well for her age. (She did not inherit that ability from me since I was a really poor speaker as a child). She is full of energy and has already given her mothers a few grey hairs. Oh, guess I forgot to mention that earlier, but yes, we are two moms - so I gave her my HCU-gene (that I did not know I had) and she got the other one from the donor.

She loves to help out in the kitchen, both when it is time to do the dishes (water EVERYWHERE) and when we cook. Her favorite food is probably avocado, but she also loves pasta in different shapes and sizes, that we often serve with vegetarian sausages or a tasty sauce with either tomatoes or mushrooms. She is also a huge fan of beetroots so we try to use it in our meals - we have a soup that all of us enjoy! Other than that, we have a great taco pie with black beluga lentils and a tasty goulash as favorite dishes.

We are still struggling a little with trusting the preschool to cook for her (in Sweden all children get free food in both preschool and "regular" school), but that is mainly due to our control issues - they are actually doing a great job and really try to learn as much as possible from us.

When Alva had just turned 2, she became the older sister to two adorable twin brothers. As I mentioned before, we are two mothers who have gotten pregnant with the help of a sperm donor and when we wanted a sibling for Alva we actually choose to use a different donor to minimize the risk of having the same diagnosis. Alva is really enjoying her baby brothers and she is very loving and caring around them - it is beautiful to watch. We really hope, and believe, that they will have great fun together.

To be honest, the thing we have struggled with the most is the lack of ”rules”. As soon as Alva was diagnosed we read about how pretty much everyone had a specific protein allowance per day. We figured that we would get one when I stopped breast-feeding - but that didn't happen. We kind of just winged it and actually still do. We usually ask for new tests of her levels every three months, and as long as her levels are fine (around 30) we continue as earlier.

After reading all of the stories here (yes, I've read every single one) we feel thankful for the fact that the cost of medication and special food is never an issue here in Sweden. Until you are 18 all prescribed medication is free, and after that the government covers everything above ~$200/12 months. Since Alva has a higher tolerance we do not get any special food from our dietician, but if I have understood it correctly - the ones who need it only pay a small price for shipping even if they get A LOT (as much as they've been prescribed) of products in each shipment (I think it is around $20/shipment).

Of course, we do worry about potential issues/symptoms down the road, but honestly - doesn't every parent? We try to control what is within our reach, and try to advocate for Alva in the best way we know how, and besides that we can only hope for the best. She is the best thing that has happened to us, and we are lucky to have a good hospital nearby with a doctor who listens to our wishes and answers all of our questions to the best of her abilities.

If you are a parent who has just found out that your child has HCU, we would say: It is okay - grieve, cry, be sad! That is part of the process. We can still feel really sad that this illness always will be a part of Alva's life, but with the help of doctors and dieticians, and especially the great low-pro-community we will try to make it as smooth as we possibly can! Like most diseases - it is not fair, but we have to work with what we've got. Reach out to people, both family and friends, and again - the community that REALLY knows what you are going through. And don't miss out on your child. Enjoy the everyday life, the moments you will treasure forever - they will all happen, and you do not want to be buried too deep in the emotions concerning HCU to miss out on all the magic that goes on in your baby's life.

July 2022, HCU and You: Ask Methia

Dear Methia

When Low Protein Diet (MMA) + Low Protein Diet (HCU) ≠ doesn't equal Low Protein diet

The diet confusion behind MMA+HCU, type CblC

I have a beautiful one-month old baby girl at home. When she was five days old, we got a call from our pediatrician that something was high on her newborn screen and that we had to take her to the emergency room. She was not sick and doing just fine, but her labs were still abnormal and she was diagnosed with methylmalonic acidemia and homocystinuria (MMA+HCU), also called cobalamin C disease. The genetics team we have been working with has been great, prescribing all of the right medications to help keep her healthy, but I still have a lot of questions about diet. Both of these conditions that she has require a protein restricted diet. However, our doctors are saying that she does not need to be restricted and can eat a completely normal diet. This is REALLY confusing to me. Can you help me understand?

Sincerely,
Confused Cobalamin Mama

Dear *Confused Cobalamin Mama,*

I'm just going to go right ahead and say it: The methylation cycle is not only one of the most important metabolic pathways, but also the most confusing. There are so many enzymes involved, and multiple conditions that can result from deficiencies in these enzymes! The underlying reason why certain labs are abnormal (elevated) for each condition are not the same, and this is why treatment is not the same. Let's dig into cobalamin C disease a little bit deeper

In cobalamin C disease, individuals are not able to convert vitamin B12 to the active forms methylcobalamin and adenosylcobalamin. Methylcobalamin is a cofactor for the enzyme that affects homocysteine metabolism, and adenosylcobalamin is important for the enzyme that regulates the breakdown of certain amino acids that, when defective, produce methylmalonic acid (MMA). As a result, individuals have both elevated homocysteine AND MMA. Amazingly enough, giving hydroxocobalamin (the most biologically available form of vitamin B12) and Betaine can reduce both homocysteine and MMA levels to a safe range (although MMA and homocysteine levels may never completely normalize).

You're probably wondering about methionine, right? Well, studies have shown that restricting protein in people with cobalamin C can actually cause LOW methionine levels (which already tends to be low)! Methionine is an essential amino acid, which means our body cannot make it and we rely on it from dietary sources. Low methionine levels can cause problems with growth and development. This is the case for other cobalamin disorders with high homocysteine as well.

In short – you can rest assured that the team is guiding your family in the right direction when they tell you that protein restriction is not part of the medical management for cobalamin C. There are papers and studies that have been done that can reassure you, so ask your team to show you the literature. Knowledge is power!

Sincerely, Methia

Zucchini Hummus

Serves 6*

Ingredients:

- 1 cup peeled & diced zucchini
- 2 tablespoons tahini
- 2 to 3 tablespoons fresh lemon juice
- 3 cloves garlic
- 2 tablespoons olive oil
- ½ teaspoon sea salt ,or to taste
- 2 teaspoons ground cumin

Instructions:

Add garlic to a blender or mini food processor and blend until garlic is diced. Add the lemon juice, and tahini.

Blend until smooth and creamy, then add zucchini and olive oil.

Blend just until smooth.

Add cumin and ½ teaspoon salt or as desired to make your perfect dip.

Stir to blend and chill in refrigerator for an hour or overnight.

Serve chilled with your favorite veggies or crackers. Enjoy!

Kcal: 81	**Protein:** 1.4 gm	**Arginine:** 19 mg	**Methionine:** 5 mg

*Nutritional information is per serving.

aeglea™

RESEARCH OPPORTUNITIES

ICYMI RESEARCH NEWS

Exciting things are happening in research for the homocystinuria community!

HCU Network America and HCU Network Australia established a research grant program and a Scientific Advisory Board (SAB) in 2017 to identify and advise on research priorities for classical homocystinuria (CBS deficiency), and in 2021 the call for proposal for new treatments was for homocystinurias in general (including classical homocystinuria, select cobalamin disorders and severe MTHFR). While we had not raised adequate funding to support a grant focused on a cobalamin disorder on our own, we reached agreement with Onlus Cblc (patient group for cblC patients in Italy) and the Organic Acidemia Association to co-fund, and in May we announced our first Cobalamin Research grant focused on identifying a chaperone therapy for cobalamin C.

Then last month, thanks to our Race for Research participants from 2021, we announced our 3rd CBS research grant!

Did you miss our press releases?

HCU Network America Announces Third Recipient of the CBS Deficiency Global Grants Program!

June 25, 2022 - HCU Network America announced the third recipient of the CBS deficiency global grants program – awarding a research grant to the Newcastle University Biosciences Institute in Newcastle, United Kingdom to explore a potential avenue for treatment for homocystinuria due to cystathionine beta-synthase (CBS) deficiency. The research, led by Dr. Thomas McCorvie, aims to identify stabilizers or activators of the defective enzyme in CBS-deficient homocystinuria (HCU). Dr. McCorvie is a Senior Research Associate at the Newcastle University Biosciences Institute

Read the full press release at: https://bit.ly/2022CBSGrant

HCU Network America, OAA and CblC Onlus Announce First Collaborative CblC Research Grant

May 13, 2022 - CblC Onlus, HCU NetworkAmerica and the Organic AcidemiaAssociation announced the recipient of their first collaborative cobalamin research grant–awarding a researchgrant to the National ResearchCouncil's Institute of Biophysics in Palermo, Italy to identifypotential treatment for cobalamin C (cblC) deficiency. The research, led by Dr. SilviaVilasi, aims to identify compoundsthat could potentially rescue MMACHC functional deficiency in cblC disease.Dr. Vilasi is a researcher at the Institute of Biophysics (IBF) in the National Research Council, and has had a longstanding interest and involvement in the studyof structure-function relationship of proteins involved in human pathologies. More recently she focused her interest in homocystinuria research.

Read the full press release at: https://bit.ly/2022CblCGrant

SEPTEMBER 1-30, 2022

More swag available for fundraisers!

Per Individual: $30

Per Family (up to 4 – 1 mailing address): $50

Registration now!

https://runsignup.com/Race/IL/Batavia/HCURaceforResearch

WALK, RUN, RIDE VIRTUAL RACE BENEFITING HCU NETWORK AMERICA

What is a virtual race?

A virtual race is a race that can be walked, ran, or biked from any location you choose. You can participate on the road, on the trail, on the treadmill (or stationary bike), at the gym or on the track (or even at another race). You get to run your own race, at your own pace, and time it yourself. You do not have to complete the miles all at once, in one day, or even a week. You can use the entire month to complete the race.

How do you know how many miles I completed?

- We rely on the honor system. You don't have to use a device to prove your miles.
- If you'd prefer to use an app to track your miles, we recommend Strava. You can join the HCU Network America Club.
- Please use intentional miles - this means no step counting
- Please log all your miles by 11:59 pm ET September, 30, 2022

How do my miles translate to money raised?

After a racer is registered, they are set up with their own personal donation page. You can direct those who would like to donate to your race link.

Learn more or register at https://runsignup.com/Race/IL/Batavia/HCURaceforResearch

info@hcunetworkamerica.org | https://hcunetworkamerica.org | 630-360-2087

HOMOCYSTINURIAS
DATA COLLECTION PROGRAM

FACEBOOK LIVE CHAT

June 7 at 8:00 PM EDT

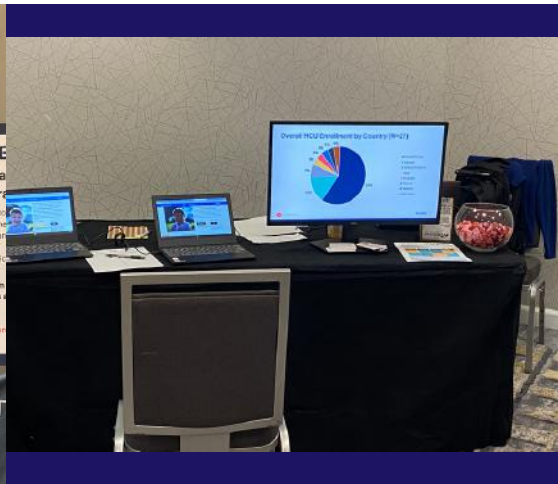
The Low Protein Diet

with Homocystinurias

HCU Network America

HCU Network Australia

POWERED BY RAREX



UPCOMING EVENTS

Find all events at: https://www.eventbrite.com/o/hcu-network-america-30163980100

Low Protein Cooking Class

July 16 | Time: 2 PM EDT

Cobalamin Disorders with HCU Community Virtual Meet-up

Online meet-ups are an opportunity to connect patients and caregivers impacted by cobalamin disorders with elevations of homocysteine to one another virtually.

Saturday, July 30, 2022 | 8 am PT | 11 am ET | 4 pm UTC+1

Classical HCU Parent-Caregiver Meetup

Parents,Grandparents and Caregivers of "kids" all ages with HCU need support too!

August 20, 2022 at 10 am CT

Come network and learn from other parents, grandparents and caregivers!

Classical HCU Community Virtual Meet-up

Online meet-ups are an opportunity to connect patients and caregivers impacted by homocystinuria to one another virtually.

Sunday, August 21, 2022 | 12 pm PT | 3 pm ET | 8 PM UTC

NOW ENROLLING: A Natural History Study on Classical Homocystinuria

Travere Therapeutics is enrolling children and adults with classical homocystinuria (HCU) in a Natural History Study. The goal is to learn more about classical HCU and course of the disease. Information gained from this study may help to improve understanding of HCU and help other patients, families, healthcare providers, and researchers to design new clinical research studies and therapies. No investigational medicine will be given to patients.

Approximately 150 patients will participate at sites in the US, Europe, and other countries around the world. The study will include three key stages (screening, enrollment, and observational follow-up) and will last approximately 6.5 years.

You (or your child) may be eligible to participate in the Natural History Study if you:

- **Have been diagnosed with HCU**
- **Are 5–65 years of age**

You (or your child) will need to meet all other study criteria to take part in the Natural History Study.

For additional information about the Natural History Study, please go to: https://www.clinicaltrials.gov/ct2/show/NCT02998710

You may be able to receive payment for time and travel when you participate in this study. Talk with your doctor and family members about joining the Natural History Study. Sites are open and currently enrolling patients.

If you have any questions, please email:

HCUConnect@labcorp.com

Visit www.hcuconnection.com for more information

MA-PE-22-0004. March 2022.

TRAVERE THERAPEUTICS

NOW AVAILABLE

Betaine Anhydrous for Oral Solution

*The **FIRST AB RATED GENERIC** Version of*
CYSTADANE® (betaine anhydrous for oral solution) Powder

NDC NUMBER	STRENGTH	FORM	TE RATING	COMPARE TO
72647-900-01	1 gm/scoopful	Powder	AB	CYSTADANE®

PRESCRIPTION ORDER FORM

PRESCRIPTION CO-PAY CARD

INDICATIONS AND USAGE

Betaine Anhydrous for Oral Solution is indicated for the treatment of homocystinuria to decrease elevated homocysteine blood concentrations in pediatric and adult patients. Included within the category of homocystinuria are:

- Cystathionine beta-synthase (CBS) deficiency
- 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency
- Cobalamin cofactor metabolism (cbl) defect

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypermethioninemia in Patients with CBS Deficiency: Betaine Anhydrous for Oral Solution may worsen elevated plasma methionine concentrations and cerebral edema has been reported. Monitor plasma methionine concentrations in patients with CBS deficiency. Keep plasma methionine concentrations below 1,000 micromol/L through dietary modification and, if necessary, a reduction of Betaine dosage.

ADVERSE REACTIONS

Most common adverse reactions (> 2%) are: nausea and gastrointestinal distress, based on physician survey.

To report SUSPECTED ADVERSE REACTIONS, contact Oakrum Pharma, LLC at 1-833-444-8010 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Click here for full prescribing information.

OAKRUM PHARMA

3636 S Geyer Road, Suite 100
St. Louis, MO 63127

Live better, together!

Contact Register

What is the contact register?

The contact register is a secured private survey that allows you to share information on you or your family member with HCU with us. This includes where you are from, your relationship to homocystinuria, the patient's birthdate, gender, their exact diagnosis (e.g. CBS, cobalamin, or MTHFR), how they were diagnosed, and if the patient was diagnosed through newborn screening. This information is kept confidential and will not be shared unless you give us permission. By registering, you will be able to identify other patients in your state and request their contact information. You will also be able to access information posted over time that can only be shared with the patient community. (For example, we may have webinars that the expert presenter does not want to be publicly available, but is willing to share with the HCU community.)

What will this information be used for?

HCU Network America strives to inform patients and families with resources, create connections, and support advancement of diagnosis and treatment of HCU and related disorders. The information you provide helps us succeed in our mission - plan events, develop resources and educational tools, and ensure everything is being done to support timely and accurate diagnosis from birth. It also allows us to have informed conversations with doctors, pharmaceutical companies, and law makers. Your information helps us understand the landscape better so we can better advocate for you!

How do I participate?

The contact register form takes approximately 3-5 minutes to complete. You can find the form either by visiting our website and clicking on the "Contact Register" tab, or you can fill it out by going directly to: https://bit.ly/3OJuF1W