Know the difference

Patients who present with symptoms of Hyperhomocystinemia

This is a general term for high blood homocysteine.

It *may* be an inherited metabolic disorder, but can also result from:

- Folate deficiency
- Vitamin B12 deficiency
- Inflammation
- Nitrous oxide

May actually have the symptoms of

Inherited Homocystinurias

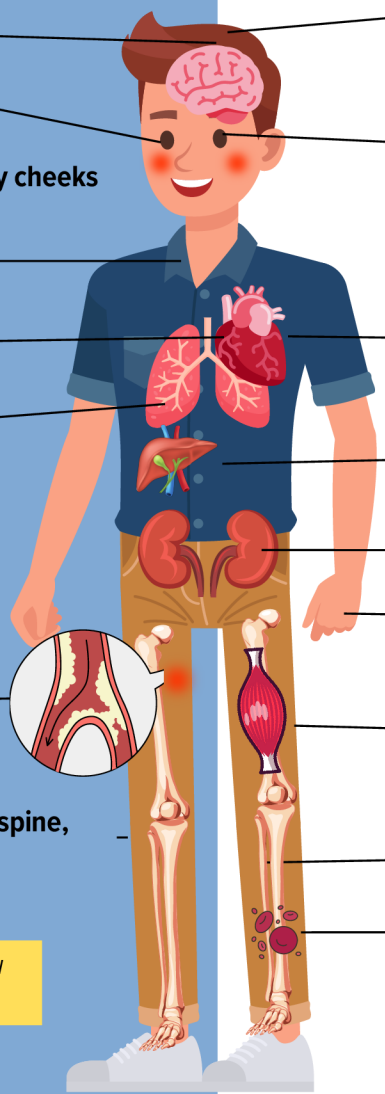
Markedly **elevated homocysteine levels** can be detected in blood and urine; testing in blood is usually performed.

It usually denotes **an inherited metabolic disorder**, such as classical homocystinuria or remethylation disorders.

Knowing when to refer a patient to a geneticist for further testing can make a world of difference for your patients.

Classical Homocystinuria (HCU)

Remethylation Disorders



Brain: developmental delay, stroke, seizures, mental health

Eyes: nearsightedness and lens issues

Skin & Hair: light color skin and hair, rosy cheeks

Chest: caved or prominent chest bone

Heart: blood clot, enlarged aorta

Lungs: blood clot

Muscle: blood clot

Skeletal: long limbs, tall stature, curved spine, low bone density

Brain: developmental delay, stroke, seizures

Eyes: vision loss, maculopathy, nystagmus

Heart: cardiac complications

Liver: liver damage

Kidneys: kidney damage, TMA, HUS

Skin: dermatitis, rash

Muscle: muscle weakness, low tone

Skeletal: small stature

Blood: anemia, especially megaloblastic

Symptoms highlighted in yellow are present in both Classical Homocystinuria (HCU) and Remethylation Disorders.

Genetics referral process

When should I refer my patient?

- If on B6 therapy, stop for one week to find the base homocysteine level. Refer if elevated.
- Check the patient's total homocysteine level. Refer if elevated.
- When B12 and Folate levels are normal, but homocysteine is high, refer.

Where do I refer them?

- As the infographic shows, patients with various forms of homocystinuria can suffer from a variety of symptoms. Clotting issues are only one symptom of many.
- Patients with HCU are seen and managed by biochemical geneticists (also called metabolic geneticists).
- Visit our website to find a provider near you. https://hcunetworkamerica.org/find-a-clinic/

Frequently asked questions and myths

My patient has a total homocysteine over 50, but had genetic testing and does not have Cystathionine Beta Synthase (CBS) Deficiency. Could they still have homocystinuria?

Yes, in fact there are more than 12 types of inherited metabolic disorders that cause high homocysteine! Here are the most frequent genes associated with homocystinuria:

- CBS
- MMACHC
- PRDX1
- HCFC1
- THAP11
- ZNF143
- MMADHC
- LMBRD
- ABCD
- MTRR
- MTR
- MTHFR

What if their genetic report reveals a variant that is classified as a Variant of Uncertain Significance (VUS)?

If a patient has a total homocysteine over 50 and they have a VUS, refer them to metabolic genetics for additional testing. A VUS often needs to be further investigated especially if clinical symptoms are present.

Myth: My patient's newborn screen was negative for homocystinuria, so they can't have it.

Newborn screening is just a screen, it's not a diagnostic tool. It's estimated that more than 50% of patients with HCU are missed by newborn screening!

Myth: Homocystinuria is a pediatric condition.

Research is finding that almost all types of homocystinuria have late-onset forms. Many patients do not become symptomatic until young adulthood.

HCU NETWORK AMERICA

For more information & resources

HCU Network America
info@hcunetworkamerica.org
(630) 360-2087
hcunetworkamerica.org