BARE YOUR RARE
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PATIENT & CAREGIVER GUIDE

Hajdu-Cheney Syndrome (HCS)

A practical guide to living with an ultra-rare bone disorder.

Built from published case literature, anesthesia guidelines, and the lived experience of a 45-year HCS patient. Designed to be printed, marked up, and brought to every specialist appointment.

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<100
documented cases worldwide

NOTCH2
causative gene (exon 34)

Autosomal Dominant
inheritance pattern

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A NOTE BEFORE YOU READ

There is no HCS clinic. There is no published multidisciplinary care guideline. There is no disease-specific specialist who will coordinate your care. What exists is a patchwork of published case reports, anesthesia literature, genetics papers, and the accumulated knowledge of patients who have spent decades navigating a system that has almost certainly never encountered their condition before.

This guide is built from that literature and from 45 years of lived experience with HCS. It is designed to be printed, marked up, and brought to appointments. It is not a substitute for medical care — it is a map to help you ask the right questions.

The most protective thing you can do

Build a team. Specialists who each see one piece of you need someone coordinating the whole picture. That someone is usually you — at least until they understand what HCS is. This guide is designed to help you make that case.

SECTION 01

Building Your Care Team

With fewer than 100 known HCS patients in the literature, every specialist you see will almost certainly be encountering this condition for the first time. Your job is to help them understand what they're looking at — and to ensure every piece of your care connects to every other piece.

En
Endocrinologist

Your quarterback for bone health. Manages bisphosphonates, denosumab, or romosozumab. Orders and interprets DEXA scans. Tracks bone turnover markers (CTX, P1NP) to gauge treatment response. Note: romosozumab (Evenity) carries a black-box cardiovascular warning requiring careful risk assessment in HCS.

Ne
Neurosurgeon / Neurologist

Basilar invagination and Chiari malformation occur in roughly half of HCS patients and can be life-threatening. Neurological consultation is not optional — it is baseline care. Skull base CT or MRI every 1–2 years.

Ca
Cardiologist

Congenital heart defects and valve disease are documented in HCS. Annual echocardiogram is appropriate as a baseline. One patient in the literature required mitral valve replacement.

Re
Nephrologist

Polycystic kidney disease appears in an estimated 10% of HCS patients. Annual renal ultrasound and function panel. What was once called "serpentine fibula-polycystic kidney syndrome" is now recognized as the same disease.

De
Dental Specialist / Oral Surgeon

HCS causes progressive alveolar bone atrophy, severe periodontal disease, and premature tooth loss. Every six months — not annually. Your dentist must know about bisphosphonate use before any invasive procedure.

Au
Audiologist

Hearing loss — both sensorineural and conductive — is a recognized feature of HCS. Annual audiometry is the only way to catch decline before it significantly impacts daily life.

Pu
Respirologist

Thoracic deformities cause restrictive lung disease. Basilar invagination can cause central respiratory compromise during sleep. Baseline pulmonary function testing; sleep study if apnea is suspected.

Ge
Clinical Geneticist

Confirms diagnosis via NOTCH2 exon 34 sequencing. Essential for family planning discussions and coordinating across specialties. First-degree relatives should be offered testing regardless of whether the patient's mutation was inherited or de novo.

Carry your full medication list to every appointment.

No single specialist can manage HCS alone. They each see one organ system. You see the whole person. Make sure the cardiologist knows what the endocrinologist prescribed. Print a one-page summary and hand it over at every new consult.

SECTION 02

Monitoring Schedule

There is no published surveillance protocol for HCS. The schedule below is derived from the clinical literature and reflects the organ systems documented to be at risk. Adapt it with your care team based on your specific findings.

Test	Purpose	Frequency
DEXA Bone Density Scan	Quantifies osteoporosis severity, tracks treatment response	**Annual**
Bone Turnover Markers (CTX, P1NP)	Tracks osteoclast activity and treatment response	**Every 6 months**
Hand & Foot X-rays	Documents acro-osteolysis progression in digits	**Annual**
Skull Base CT or MRI	Screens for basilar invagination and Chiari malformation	**Every 1–2 years**
Spine X-ray Series	Compression fractures, kyphosis, scoliosis, cervical instability	**Annual**
Echocardiogram	Valvular disease and congenital cardiac defects	**Annual**
Renal Ultrasound + Function Panel	Polycystic kidney disease (~10% of HCS patients)	**Annual**
Audiometry	Progressive sensorineural and/or conductive hearing loss	**Annual**
Pulmonary Function Tests	Restrictive lung disease from thoracic deformities	**Baseline + as indicated**
Dental Exam with Panoramic X-ray	Alveolar bone atrophy, periodontal disease, root resorption	**Every 6 months**

With fewer than 100 known cases, your specialists will be encountering HCS for the first time.

Keep a binder. Bring copies of every scan, every lab result, and every note. You are the most complete record of your own case that exists.

SECTION 03

Emergency Red Flags

Some HCS complications develop slowly. Others do not. These are the signs that mean you need emergency care immediately — not a call to your specialist next week.

- ! **Severe sudden headache** with neck stiffness, vomiting, or vision changes — may indicate hydrocephalus from basilar invagination
- ! **New weakness, numbness, or coordination loss** in arms or legs — spinal cord compression
- ! **Difficulty swallowing or breathing** that worsens rapidly — upper airway obstruction or brainstem compression
- ! **Sleep apnea that suddenly worsens** — central respiratory arrest from basilar invagination is a documented cause of death in HCS
- ! **Chest pain, palpitations, or fainting** — cardiac valve disease can worsen unpredictably
- ! **Blood in urine or severe flank pain** — may signal renal cyst complication
- ! **New seizures** — documented in HCS patients with neurological involvement
- ! **Sudden severe back pain with height loss** — vertebral compression fracture

In an emergency room, the team treating you will almost certainly not know what HCS is.

Carry a medical ID card that states: "Hajdu-Cheney Syndrome (NOTCH2 mutation) — difficult airway, severe osteoporosis, potential basilar invagination, bleeding risk. Contact [your specialist] before intubation or any surgical procedure."

SECTION 04

Surgical & Anesthesia Safety

HCS is classified in the anesthesia literature as one of the most difficult airway-related syndromes. The combination of micrognathia, short neck, cervical instability, severe osteoporosis, and restricted thoracic movement creates a surgical risk profile that requires specialist planning — not last-minute improvisation.

A Airway Challenges — Why Intubation Is Dangerous

Micrognathia, abnormal dentition, short neck, and cervical spine deformities combine to create a textbook difficult airway. The anesthesia literature specifically recommends video laryngoscopy or fibreoptic intubation as the primary approach. Standard intubation carries real risk of failed airway or cervical injury. Your anesthetist must be briefed before the day of surgery.

B Bleeding Risk & Coagulation

NOTCH2 mutations are associated with bleeding risks. The anesthesia literature recommends a preoperative coagulation profile assessment for all HCS patients undergoing surgical procedures. Inform every surgeon and dental specialist.

P Positioning & Fracture Prevention

Severe osteoporosis and joint laxity mean that positioning during surgery can itself cause fractures — documented in the literature. Pressure points need extra padding. The surgical team needs to be briefed before the patient is moved into position, not after.

S Spinal Surgery — Why HCS Makes It Harder

Spinal surgery in HCS is documented as exceptionally challenging. Distorted anatomy, reduced bone stock for fixation, fragile bone quality, and the presence of wormian bones all affect surgical planning. Basilar invagination repair requires neurosurgical expertise in complex craniocervical procedures.

R Respiratory Considerations

HCS patients may have severe restrictive lung disease from thoracic deformities. Pulmonary function testing before any planned surgery allows the team to plan ventilatory support appropriately. Basilar invagination can affect brainstem respiratory control independently.

Share these recommendations with your surgical team before the procedure — not the morning of.

Print this section and give it to your surgeon and anesthetist at the pre-op consultation. Ask them to document their airway plan in your chart.

SECTION 05

Dental Management — The Bisphosphonate Paradox

HCS attacks your teeth from below. The alveolar bone progressively atrophies, causing severe periodontal disease and premature tooth loss. Root resorption has been documented. These changes are progressive and cannot be fully reversed.

The paradox: bisphosphonates — the most commonly prescribed medications for HCS osteoporosis — carry a risk of osteonecrosis of the jaw (ONJ) following invasive dental procedures. The treatment for the bones complicates the treatment of the teeth.

P Preserve — Do Not Extract Where Avoidable

The literature explicitly recommends conservative, non-invasive dental approaches where possible in patients on bisphosphonates. Extraction creates ONJ risk. Every extraction should be a deliberate decision made with your endocrinologist and oral surgeon aware.

B Bisphosphonate Coordination Is Not Optional

If you are on bisphosphonates, your dentist must know before any invasive procedure. Timing relative to bisphosphonate dosing matters. Some protocols involve a drug holiday before invasive dental work — discuss with your endocrinologist.

M Frequent Monitoring Protocol

Dental exams every six months with panoramic X-rays. Aggressive preventive care — professional cleaning, fluoride application, and meticulous home hygiene — is far preferable to intervention. Consider a dentist with experience in medically complex patients.

SECTION 06

Beyond Bones — Heart, Kidneys & Lungs

NOTCH2 signaling is involved in the development of the heart, kidneys, and other organs. The extraskeletal complications of HCS are not rare secondary findings — they are core features of the disease that can be life-limiting if undetected.

H Cardiovascular Complications

Documented findings include patent ductus arteriosus, ventricular septal defects, and valve abnormalities including mitral valve disease. One case required valve replacement. Annual echocardiogram is appropriate baseline monitoring. Romosozumab (Evenity) carries a black-box cardiovascular warning particularly relevant in HCS.

K Kidney Involvement — The SFPKS Connection

What was once called serpentine fibula-polycystic kidney syndrome (SFPKS) is now recognized as the same disease as HCS. Polycystic kidneys appear in an estimated 10% of patients. Renal disease has progressed to end-stage in documented cases. Annual renal ultrasound and function panel from the time of diagnosis.

L Respiratory System — Three Separate Threats

Thoracic deformities create restrictive lung disease documented by pulmonary function testing. Recurrent respiratory infections are reported. Basilar invagination can cause central respiratory compromise during sleep, independent of the thoracic component. A sleep study is warranted if symptoms suggest apnea.

SECTION 07

Hearing & Voice Changes

A deep, gravelly voice is one of the recognized clinical features of HCS. It is caused by structural changes in the laryngeal cartilages and is sometimes the finding that first prompts investigation.

Hearing loss is more consequential. Both sensorineural and conductive loss are documented. Sensorineural loss reflects nerve damage and is not reversible; conductive loss may have treatable components. The pattern varies between patients.

Annual audiometry — without exception.

Hearing loss in HCS tends to progress gradually and is easy to miss without formal testing. Most patients adapt to incremental decline without noticing until the loss is significant. An audiogram takes 20 minutes and catches decline early enough to plan intervention — hearing aids, then cochlear implant if needed.

SECTION 08

How HCS Changes Over Time

HCS is present from birth, but it does not look the same at every age. Understanding the typical progression helps patients and families know what to watch for and when.

Age	Stage	What Typically Emerges
Birth – 2 yrs	**Infancy**	Cleft palate, congenital heart defects, open cranial sutures, wormian bones. Most children have normal cognitive development. Diagnosis is often not made at this stage.
2 – 12 yrs	**Childhood**	Skeletal manifestations become apparent: short stature, joint hypermobility, early fractures, acro-osteolysis beginning in the fingers. Abnormal dental eruption and early periodontal disease.
12 – 25 yrs	**Adolescence**	Osteoporosis accelerates: vertebral compression fractures, progressive height loss, worsening kyphosis. Many patients are first diagnosed in this period. Hearing loss may begin. Basilar invagination surveillance becomes critical.
25+ yrs	**Adulthood**	Progressive complications accumulate: continued bone density loss, ongoing acro-osteolysis, progressive hearing loss, worsening dental disease, voice changes. Renal and cardiac monitoring becomes increasingly important.

Early diagnosis matters.

Not because HCS has a cure, but because starting treatment earlier — bisphosphonates before compression fractures, surveillance before basilar invagination becomes symptomatic — preserves more function for longer. The age-dependent pattern is the argument for early NOTCH2 testing in at-risk children.

SECTION 09

Family Planning & Inheritance

HCS follows autosomal dominant inheritance. If one parent carries the NOTCH2 variant, each pregnancy carries a 50% chance of the child inheriting it. This applies equally to men and women. The severity can differ significantly between parent and child.

50%	NOTCH2 Exon 34	De Novo Possible
chance per pregnancy if one parent is affected	causative mutation in the NOTCH2 gene	30–50% of cases arise without family history

Many cases of HCS arise as a *de novo* mutation — meaning the variant occurred spontaneously and was not inherited from either parent. If your child has HCS and you have tested negative, the mutation is de novo in them. Their children would then each carry a 50% risk.

There is nothing a parent did to cause this. It is not caused by anything during pregnancy, diet, environment, or lifestyle. It is a random genomic event.

Preimplantation Genetic Testing (PGT-M)

Families who wish to have children without HCS can use PGT-M. This involves creating embryos through IVF, testing each for the NOTCH2 variant, and transferring only unaffected embryos. Ask your clinical geneticist for a referral, or contact your provincial or state genetics program directly.

A genetic counselor is your best resource.

Ask your geneticist for a referral to a genetic counselor who can walk you through testing options for family members and reproductive planning. Provincial genetics programs in Canada can facilitate NOTCH2 testing for at-risk relatives.

For more on the NOTCH2 pathway and current preclinical research, visit **bareyourrare.org/resources/#res-conditions**

You Found This Place.

Bare Your Rare exists because patient experience is expertise.
This guide was built to make what took years of lived experience
and thousands of pages of literature to understand,
findable in one evening — for the person who needs it tonight.

Share it freely with your specialist, your family,
or anyone navigating this diagnosis.

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