CONDITION

Arhinencephaly

Learn what arhinencephaly means, how it relates to forebrain development, possible symptoms and causes, and how affected children are evaluated and supported.

WHAT IT IS
Rare developmental abnormality of the front brain

BODY SYSTEM
Nervous system

MAIN SYMPTOMS
Reduced sense of smell, developmental delay, seizures, feeding problems

WHAT CAUSES IT
Genetic or chromosome changes, sometimes unknown

HOW IT IS DIAGNOSED
Prenatal ultrasound, fetal MRI, brain MRI

MAIN TREATMENT
Supportive care and symptom management

CAN IT BE CURED?
No, brain structures cannot be recreated

IS IT AN EMERGENCY?
Sometimes, severe trouble breathing

LONG-TERM OUTLOOK
Varies widely with the full brain-development pattern

Overview

Arhinencephaly is a rare developmental abnormality involving the front part of the brain. The term literally refers to absence or severe underdevelopment of the "smell brain," including structures called the olfactory bulbs and olfactory tracts. These structures normally help carry information about smell from the nose to the brain.

The term is mainly historical. It has sometimes been used broadly for holoprosencephaly , a group of conditions in which the developing forebrain does not divide completely into right and left sides. Today, clinicians usually describe the exact structures affected rather than relying on the term arhinencephaly alone.

The medical impact depends on the full pattern of brain development. Some people mainly have absent or underdeveloped smell structures. Others have a wider form of

holoprosencephaly that affects movement, learning, feeding, hormone control, or facial development. Severity can vary greatly, even among relatives with the same genetic change.

Arhinencephaly begins before birth and is not caused by anything a child or parent did after delivery. Because it can occur as part of a broader brain-development condition, evaluation usually looks beyond the sense of smell. Brain imaging, genetic testing, hormone assessment, and developmental evaluation may all be important.

Symptoms

Symptoms depend on how much of the brain is affected. An absent or reduced sense of smell may occur when the olfactory bulbs and tracts are missing. This can be difficult to recognize in babies and young children, who cannot reliably describe what they smell.

When arhinencephaly is part of holoprosencephaly, possible findings include:

Facial differences are not present in every person. Their appearance also does not always predict the severity of the brain findings.

Hormone-related symptoms can include unusually frequent urination, excessive thirst, dehydration, low blood sugar, poor growth, or problems with puberty. One possible problem is central diabetes insipidus , in which the body cannot properly conserve water. Despite its name, this is different from diabetes mellitus, the condition involving high blood sugar.

Symptoms may change as a child grows. Feeding concerns may be most important during infancy, while learning, mobility, communication, behavior, or puberty may become more prominent later.

- Developmental delay or intellectual disability
- Muscle stiffness, low muscle tone, or unusual movements
- Seizures
- Feeding or swallowing problems
- Slow growth or difficulty gaining weight
- Differences in head size
- Vision or hearing problems
- Sleep, breathing, or temperature-control difficulties
- Hormone problems caused by abnormal development of the hypothalamus or pituitary gland

- Differences in the formation of the eyes, nose, upper lip, palate, or teeth

Causes and risk factors

Arhinencephaly results from a disruption in very early brain development. The forebrain begins organizing and separating into two sides during the first weeks of pregnancy, often before a person knows they are pregnant.

Many cases are related to genetic or chromosome changes. Genes associated with holoprosencephaly include SHH , ZIC2 , SIX3 , and TGIF1 , among others. These genes help direct early development of the brain and face. A change in one of them can affect people differently, so the same genetic finding may cause severe symptoms in one person and mild or no obvious symptoms in another.

Chromosome conditions can also be involved. Holoprosencephaly is particularly associated with trisomy 13, in which there is an extra copy of chromosome 13. It can also occur with other chromosome changes or genetic syndromes, including disorders that affect cholesterol production.

Not every affected person receives a specific genetic diagnosis. In some cases, available testing does not find a cause. This does not mean that a parent caused the condition.

Some gene-related forms can be inherited in an autosomal dominant pattern. This means one altered copy of a gene may be enough to increase the chance of the condition. However, reduced penetrance means some people with the genetic change have no clear symptoms, while variable expression means symptoms can differ widely. Other associated syndromes may follow different inheritance patterns.

Pre-existing diabetes in the pregnant parent is a recognized risk factor for holoprosencephaly. However, most pregnancies affected by diabetes do not result in holoprosencephaly, and the condition can occur without this risk factor.

A clinical geneticist or genetic counselor can review the person's test results and family history. They can explain whether testing relatives or discussing future pregnancies may be useful.

Diagnosis

Arhinencephaly may be detected before birth or after delivery. Prenatal ultrasound can identify major abnormalities in the developing brain and face. A fetal MRI may provide more detailed images when ultrasound findings are unclear or when specialists need to define the

anatomy more precisely.

After birth, brain MRI is generally the most detailed imaging study for examining the olfactory bulbs, olfactory tracts, cerebral hemispheres, pituitary region, and other structures. Computed tomography, or CT, may show some abnormalities but provides less detail about soft brain tissue and uses radiation.

The evaluation may involve several specialists. A neurologist assesses brain development, movement, muscle tone, and seizures. An endocrinologist checks hormone control. A genetics professional reviews possible inherited or chromosome-related causes. Feeding, vision, hearing, and developmental specialists may also participate.

Genetic testing may include chromosome analysis, a chromosomal microarray that looks for missing or extra pieces of DNA, or a multigene panel. Broader testing, such as exome or genome sequencing, may be considered when initial tests do not identify a cause. Testing does not find an explanation in every case.

Other assessments are guided by the person's findings. They may include:

Testing the sense of smell may be useful in an older child or adult who can understand and complete the task. It is usually less reliable in very young children.

- An electroencephalogram, or EEG, when seizures are suspected
- Blood and urine tests for pituitary hormone or water-balance problems
- Swallowing evaluation when coughing, choking, or poor weight gain occurs
- Vision and hearing testing
- Developmental, speech, movement, and learning assessments

Treatment and management

There is no treatment that can recreate brain structures that did not develop before birth. Care instead focuses on protecting health, supporting development, and treating the person's specific symptoms. The care plan should be based on actual findings rather than the name arhinencephaly alone.

Feeding support may include help with positioning, food texture, pacing, or swallowing therapy. Some children need tube feeding when eating by mouth does not provide enough nutrition or cannot be done safely. A dietitian can help monitor calories, fluids, growth, and nutritional needs.

Seizures may be treated with antiseizure medicine selected by the clinical team. Families may

also receive a written seizure action plan explaining what to do during a seizure and when to seek emergency care.

Pituitary hormone problems require assessment and treatment by an endocrinologist. Management may include replacing a missing hormone or closely controlling fluid intake and water balance. These treatments need regular laboratory monitoring and should not be adjusted without medical guidance.

Physical, occupational, speech, and feeding therapies can support movement, daily activities, communication, and safe eating. Communication support may include gestures, picture systems, or electronic devices when speech is limited. Early-intervention and school-based services can help match education to the child's strengths and needs.

Other treatment may address reflux, constipation, sleep problems, abnormal muscle tone, dental differences, or vision and hearing concerns. Surgery is not routinely needed for arhinencephaly itself, but it may be considered for a related problem such as hydrocephalus, cleft lip or palate, or a feeding-access need.

Children with severe forms of holoprosencephaly may have complex medical needs. Pediatric palliative care can be added at any stage to improve comfort, communication, and family support. It can be provided alongside treatments intended to prolong life and does not mean that other care must stop.

Complications

Possible complications depend on the wider brain and hormone findings. Feeding and swallowing problems can lead to poor growth, dehydration, or aspiration. Aspiration means food, liquid, saliva, or stomach contents enter the airway instead of the esophagus. Repeated aspiration can contribute to lung infections.

Seizures may affect safety and development. Abnormal muscle tone can lead to pain, joint stiffness, hip problems, or difficulty with positioning. Limited mobility can also increase the risk of skin pressure injuries.

Pituitary dysfunction may disturb growth, stress-hormone production, thyroid function, puberty, or the body's control of water. Untreated water-balance or adrenal hormone problems can become serious, which is why regular endocrine follow-up matters when the pituitary region is affected.

The ability to smell also has practical safety effects. A person with little or no sense of smell may not notice smoke, leaking gas, or spoiled food. Working smoke and gas detectors, food-date checks, and help from others can reduce these risks.

The outlook varies widely. It depends more on the full brain-development pattern, seizures, breathing and feeding safety, hormone function, and associated genetic condition than on absent olfactory structures alone.

Follow up

Routine follow-up should be individualized. It may include monitoring growth, nutrition, hydration, development, movement, seizures, vision, hearing, sleep, dental health, and hormone function. Medication and feeding plans should be reviewed as the child grows.

Families should contact the clinical team promptly for new feeding difficulty, repeated coughing with meals, unexplained weight loss, a clear increase in seizures, unusual thirst or urination, repeated vomiting, worsening sleepiness, or loss of previously gained skills. These concerns may need urgent assessment, but they are not always emergencies.

Seek emergency help for severe trouble breathing, blue or gray lips, unresponsiveness, a first or prolonged seizure, repeated seizures without recovery, serious choking, or signs of severe dehydration. Families of a person with known seizures or adrenal hormone deficiency should follow the emergency plan provided by their medical team.

Genetic counseling can be revisited over time. Updated testing may become useful as genetic knowledge and laboratory methods improve. Counseling may also help relatives understand whether testing or pregnancy-related consultation is appropriate.

Sources

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