



CdLS

DIAGNOSIS

Distinguishing Features

The de Lange Syndrome is most commonly referred to as the Cornelia de Lange Syndrome (CdLS) but is also known as the Brachmann-de Lange Syndrome. Dr. Cornelia de Lange first described this syndrome in 1933 although Dr. Brachmann wrote about a similar child in 1916. CdLS is a syndrome with estimated birth prevalence between 1:10,000 and 1:30,000 live births.

Although several genes have been found to be involved CdLS (NIPBL, SMC1A and SMC3), they have only been implicated in around 60% of patients. At the present time diagnosis is made on the basis of clinical observations. The most frequently observed facial characteristics include thin, downturned lips; low set ears; long eyelashes; and eyebrows that meet in the middle.

Other characteristics often associated with this syndrome include delayed growth and small stature; language delay, even in the more mildly affected; microcephaly (small head size); hirsutism (excessive body hair); and simian creases. Low birth weight is typically a feature of this syndrome with the average birth weight being five pounds and one ounce. Individuals may also be tactilely defensive or show a lack of sensitivity to pain. There is often a characteristic vocal quality in the crying of babies, which has been described as feeble or low-pitched.

Although mental retardation is typically present in this syndrome, there are some people who have nearly normal intelligence.

FAMILY ISSUES

Whether an individual is diagnosed at birth, or at age two, five or twenty, receiving a diagnosis of CdLS can be overwhelming. A lifelong process of challenging and re-challenging feelings, thoughts, actions and beliefs may begin. There will be sadness, but there will also be joy. There will also be many decisions to be made, but they do not need to be made in isolation. There are many families and professionals ready to offer information, support and encouragement to people who request it.

Families may struggle to accept the diagnosis of Cornelia de Lange Syndrome. Shock, anger, denial, guilt, and sadness are common early responses. Most families adjust to their new situation, but protracted grief or depression in a family member should be treated. In addition to the initial adjustment, intermittent stresses throughout the life of the child may temporarily destabilize a family. The primary care providers should periodically inquire about family adjustment and continue to provide emotional support for the family.

Children may qualify for special services such as CAP/MR (Community Assistance Program for the Mentally Retarded) through the division of developmental disabilities at their local mental health center. Most children should be eligible for Medicaid (independent of parents' income) which provides prescription coverage as well as physical, occupational and speech therapy. In addition, respite care should be suggested in cases where the care-taking burden is high. The Association of Retarded Citizens often has a respite program and also provides support for families.

GROWTH AND DEVELOPMENT

Growth

Individuals with CdLS have proportionate small stature. Specific growth charts are available for height, weight and head circumference parameters of boys or girls with CdLS at different ages. Using these, the practitioner can follow growth as compared to other affected individuals rather than the unaffected population. If an individual deviates from the CdLS curve, then specific investigation for occult pathology may be warranted. The term "failure to thrive" is not appropriate, and may generate the use of unnecessary calorie supplementation, which results in no increased rate of growth and considerable parental anxiety. Pubertal growth spurts occur at comparable ages to unaffected individuals. Some individuals with CdLS have been found to have growth hormone deficiency, requiring exogenous growth hormone administration, however, without a documented deficiency, the use of growth hormone most likely does not increase final adult height.

Puberty

Puberty appears to be a difficult period for many individuals with CdLS. The onset and course of puberty appears similar to unaffected individuals, not only physically, but also emotionally and behaviorally. Some characteristics have included mood swings, irritability, unexplained pain episodes, contrariness, worsening behavioral problems, and aggression. In females, premenstrual syndrome occurs and may be treated symptomatically (e.g. Tylenol or non-steroidal anti-inflammatory agents).

Menstruation may be a problem for caretakers, especially in females with communication difficulties. In addition, protection from potential pregnancy may be indicated, since for both males and females fertility appears to be normal or slightly decreased. Several therapeutic modalities have been utilized including synthetic hormonal treatment (e.g. oral contraceptives or Depo-Provera injection) and surgery (e.g. tubal ligation, hysterectomy). Together, the individual with CdLS, the family and the practitioner should determine the most appropriate course of action.

The secondary reason is for the fertility issue, which may or may not be a factor in an individual with CdLS, depending on the level of function. The earlier the procedure can be done (e.g. by age 2), the less are the psychological effects of the surgery, but it should be performed prior to puberty, since that is when the risk for cancer rises.

Undescended testicles are at increased incidence in males with CdLS. Nearly 70% of affected males have one testis or both testes undescended, compared with less than 2% of the unaffected male population. In general, surgery is definitely recommended following failure of medical treatment (hormone injections) to bring down the testicles. The primary reason is because testicles that remain in the abdomen are at higher risk for developing malignancies than those that are in the scrotum, even though this is a fairly low percentage.

Growth Hormones

There is not much factual information available at this point regarding the issue of growth hormone testing and therapy. In the meantime, growth in CdLS can be monitored by using the CdLS specific growth charts. If growth is below the lower curve, then other factors may need to be taken into account (e.g. growth hormone deficiency). Several cases of growth hormone deficiency have been documented, probably higher than the incidence in the unaffected population, but this has not been studied carefully. Certainly with documented growth hormone deficiency, replacement hormone may be appropriate.

Development

Developmental skills are often delayed in individuals with CdLS. Because of this, early intervention is indicated as soon as a diagnosis is made, since it appears to play a major role in the level of developmental achievement. An average IQ score in individuals able to be tested has been found to be 53, which is within the mild to moderate range of mental retardation. Acquisition of new skills continues throughout life without regression. Developmental areas of strength include visual-spatial memory and perceptual organization, and thus the use of computers, using visual memory, may be of benefit over standard methods of verbal instruction, as may tactile stimulation. Language is an area of weakness, and may be compounded by hearing abnormalities. Fine motor activities should be stressed in education, especially those related to activities of daily living. A developmental chart specific for CdLS is available, and can be used by practitioners and therapists to monitor progress, and potentially even to confirm diagnosis.

SPEECH AND LANGUAGE

One of the most challenging issues for caregivers or people with CdLS is determining the best communication tool available for their use: speech, signing, communication boards, computer programs, or some other means. While it is not clear why some children talk and others do not, particularly among the children without obvious differences in physical appearance, it is very clear that all individuals do communicate.

For a small percentage of individuals with CdLS, speech develops normally. For most, however, the ability to communicate is greatly influenced by the developmental factors related to the syndrome, as well as access to early intervention programs and speech therapy. One research study¹ indicated that children with CdLS who exhibited good social relatedness were more likely to talk than children who exhibited behaviors seen in autism. Social relatedness included factors such as the child's overall ability to relate to people and to share reactions with caregivers. It also included eye contact, the appearance of

comfortableness, and alertness. This research study also indicated that children who had no, or only a mild, hearing loss, who had no severe upper-limb malformations, who sat by the age of 18 months or walked by the age of 30 months and who weighed at least 5 pounds at birth, were much more likely to acquire expressive language skills than those who did not meet these criteria.

Characteristics of Speech, Language and Hearing

The absence of speech or the development of only minimal speech has been well documented, even in the more mildly affected. There is often a characteristic vocal quality in the crying of babies, which has been described as feeble or low-pitched. The low-pitched cry frequently present at birth and early infancy often disappears by 12 months.

Most children with CdLS exhibit errors in articulation, with sound substitutions and distorted or missing consonants. These errors are the result of a number of factors, including the overall developmental delay, the smaller oral cavity and retruded lower jaw, a tendency toward lower muscle tone, and possible hearing impairment.

In addition, most children with CdLS exhibit childhood apraxia of speech (CAS)ⁱⁱ. The American Speech-Language-Hearing Association defines childhood apraxia of speech as a neurological childhood (pediatric) speech sound disorder in which the precision and consistency of movements underlying speech are impaired in the absence of neuromuscular deficits (e.g., abnormal reflexes, abnormal tone). CAS may occur as a result of known neurological impairment, in association with complex neurobehavioral disorders of known or unknown origin, or as an idiopathic neurogenic speech sound disorder. The core impairment in planning and/or programming spatiotemporal parameters of movement sequences results in errors in speech sound production and prosodyⁱⁱⁱ.

There are confirmed reports of children who unexpectedly utter a meaningful word or phrase only once or twice, using completely clear articulation and often performing at a level higher than previously observed. This performance is rarely, if ever, repeated. This behavior is also seen in adults who have acquired apraxia as a result of a brain trauma.

In almost all individuals the ability to produce language is remarkably inferior to the ability to comprehend language. There is also considerable discrepancy between vocabulary measures and syntactic skills, in that people who have highly developed vocabulary usually do not exhibit the expected syntactic skills. Similarly, children who are using an average utterance length of 4-5 words per utterance typically are not using question transformations.

The majority of individuals are very quiet. They often make eye contact, and there is often a sense they understand what is being said, but they are not usually vocal or verbal. Even among individuals who have good language skills, there are few who can be described as talkative.

The decision to begin speech therapy should not be delayed. Some parents have reported they were told speech therapy could not begin until their children were talking! Additional parents reported they were told their children could not receive speech therapy or learn to talk until their gastric tubes were removed and their children were eating normally. This of course is not true. Some children who are talking have never received nourishment except through their gastric tubes. When appropriate, it is beneficial to consult with a speech-language pathologist who is familiar with feeding therapy so the oral mechanism functions as normally as possible.

Augmentative and Alternative Communication (AAC)

For some people with CdLS, non-vocal or nonverbal strategies will need to be considered. For these individuals it may not be possible to achieve normal or even adequate speech for communicative purposes. Instead an immediate goal should be to communicate some form of yes-no response. A good example of an early communication system is what parents do when they learn to recognize some of the vocalizations or nonverbal movements their babies make.

Examples of more formalized available AAC strategies include communication boards; American Sign Language; American Indian Hand Talk or Amer-Ind gestural code; Blissymbolics; Total Communication; Pantomime; a manual alphabet; eye-blinking encoding; or electronic communication aids. For children with severe upper-limb malformations there are gestural-assisted and neuro-assisted strategies available. Unfortunately almost all augmentative communication strategies are difficult to learn for children who have difficulty understanding nonverbal or gestural communication.

Before considering the use of augmentative or alternative communication, a number of factors need to be considered. These include the level of cognition, motor abilities, receptive language abilities, and the motivation to communicate. It will often be most beneficial when speech-language pathologists function as communication therapists rather than as speech therapists and consult as appropriate with professionals such as physical therapists, occupational therapist, physicians, psychologists, social workers, vocational counselors, nurses, and teachers.

ⁱ Goodban, M.T. (1993) Survey of speech and language skills with prognostic indicators in 116 patients with CdLS. *Am J MedGenet* 47:2059-2063.

ⁱⁱ *Setting goals for speech development*. Reaching Out: The Newsletter of the Cornelia de Lange Syndrome Foundation. XIV: 2, 1995, p. 10-11.

ⁱⁱⁱ American Speech-Language-Hearing Association (2007) Childhood Apraxia of Speech[Position Statement]. Available from www.asha.org/policy.

HEARING

Almost all children with CdLS are diagnosed with mild to moderate hearing loss or even severe hearing loss; however interviews with caretakers reveal that these hearing test results are sometimes unexpected. Many caretakers report that their children were diagnosed as severely hearing impaired at birth, moderately impaired at 12 months, and mildly impaired or without impairment at age 2 years. Since it is unusual for hearing to improve rather than worsen, it seems that obtaining a correct hearing assessment is difficult. This may be due to the fact that Individuals with CdLS may have narrow ear canals and difficult behaviors, making examinations a challenge. Because of this, it is advisable to consult an audiologist and/or otolaryngologist who is familiar with CdLS or who is experienced in working with infants.

Parents often report their children seem to hear much better than their test results would indicate. Considerable confusion exists regarding hearing ability for some children. In addition, many CdLS children fitted with hearing aids do not tolerate the use of them or do so only sporadically. For these individuals, retesting is often important to insure that the aid is truly beneficial.

Children with narrow ear canals may also have a problem with chronic ear drainage or cholesteatoma (a collection of skin cells in an abnormal location). They may also have recurrent ear infections or chronic ear fluid just like all children. Ear tubes, or pressure equalization tubes, may be useful for these conditions. However, the placement of ear tubes should be performed by a doctor experienced in working with small infants or syndromic children with small ear canals.

If a hearing loss is suspected, a hearing test should be carried out by an audiologist and an ear evaluation should be carried out by an otolaryngologist. Further hearing testing (such as an ABR) may be recommended based on this initial evaluation. Hearing aids may be prescribed for infants and children. Even a mild hearing loss can result in a speech and language delay. Smaller aids are available so it is not necessary or advisable to use an adult-sized aid. If the child will not leave on the aid, an audiologist or behavioral therapist may be helpful. While the child's personal hearing aid may be sufficient some of the time, the use of an FM system for amplification may be necessary in other situations.

OPHTHALMOLOGY

All children with a new diagnosis of CdLS should be referred for a complete ophthalmic assessment. This should take place with a medical doctor specializing in eyes, also known as an Ophthalmologist or Eye MD. An Eye MD can check for several problems found in patients with CdLS. While some of these conditions may be easily detected by the family, others may be quite hidden. Therefore, the exam should take place even if the family has no evidence of an eye concern. These paragraphs will clarify several eye concerns for CdLS patients and families. Strabismus is a misalignment of the eyes, most commonly turning in or wandering out. While casual observation may detect a 'large degree' of misalignment, an exam can detect small amounts that may still be visually significant to the patient. Glasses or sometimes surgery can be recommended to fix the problem. Sometimes, the amount of strabismus is small and does not require either treatment.

Nystagmus or 'shaky eyes' can also occur and may be readily detected by the family at home. While some cases of nystagmus are congenital and evident immediately at birth, others are not detected until early childhood. An exam can help determine if the nystagmus may be due to a correctable problem.

Nearsightedness or myopia is usually not noted by the family because there are often no outward signs of it. While older children occasionally squint to see more clearly, younger children may not. This is because the condition may 'creep up' on them gradually. Patients with CdLS may have very severe myopia, with either no outward signs or with lack of visual attention as the main sign. An exam by an ophthalmologist will detect myopia, which may be corrected with glasses. Because myopia increases with age, a normal initial eye exam should be followed with periodic exams in the future.

Many children with CdLS may not engage in normal gaze behaviors. This problem is quite upsetting to caregivers if they do not understand the cause. Gaze averting (looking away from a parent or object) may happen for a number of reasons. It may give the child time to process visual information, it may mean the child perceives the task as too difficult, or it may mean the child is feeling uncertain or stressed. Children with CdLS may also use peripheral vision more frequently than central direct gaze because they have greater difficulty choosing which of the varied stimuli should receive their attention. Simply put, they may get visually overwhelmed more easily than other kids. Parents and teachers may find that presenting toys or objects more slowly or given the child fewer visual choices is helpful.

CdLS patients may develop self-injurious behavior which can seriously damage the eye. Any signs of self-induced eye injury should prompt an ophthalmic referral. The ophthalmologist can rule out treatable eye-related causes, although they are rare. If no direct eye cause is found, your child's neurologist or psychologist may be able to assist with some medications to attempt to decrease this difficult to control behavior.

Ptosis (pronounced TOE-sis, the p is silent) is a drooping of one or both eyelids. If mild or moderate in nature, children may lift their chin to "look under" the drooping lid. Parents may notice their child's eyebrows are arched upward in an effort to use their forehead muscles to raise their lids. In severe cases, the ptosis may cover the center visual axis and prevent the development of good vision. If the ptosis is severe enough, eyelid surgery will be recommended at a very early age. If it is mild or moderate, surgery is often performed when the child is older. Your Eye MD can help determine whether early surgery, late surgery or simple observation is the best option. That choice may be made based on the child's vision and development, so the recommendation may change as your child grows.

CdLS patients who develop recurrent red eyes, crusting on the eyelashes, itchy eyes, tearing, or eye discharge should also see an ophthalmologist. In infants, this symptom may indicate a blocked tear duct (nasolacrimal duct obstruction). Your pediatrician or family practice doctor will be familiar with this problem, as nearly 3% of the population has it in infancy. However, these same symptoms are also due to blepharitis: an idiopathic condition in which the 20-30 glands normally present in each eyelid have sub-optimal flow. While rather rare in the general pediatric population, this condition is extremely common in CdLS patients: almost 50% have it. Rather than surgical treatment for a tear duct problem, eyelid shampooing or gentle eye lid scrubs at home can often result in dramatic improvement of the blepharitis symptoms. Your Eye MD can distinguish which condition your child has, and is available to treat both.

In summary, there are many eye issues that can be detected and successfully treated in CdLS patients. The partnership between caregiver and an ophthalmologist is one that should start early on. If no issues are found at an initial exam, yearly follow-up is recommended.

Vision

It is not unusual for children with this syndrome to be nearsighted, have recurrent redden, discharge or tearing or have ptosis of the eyelids. If ptosis is severe the children may lift their chins or arch their eyebrows in order to improve their vision. Many parents opt for surgery to correct the ptosis.

Many children with CdLS may not engage in normal gaze behaviors. Gaze averting may happen for a number of reasons. It may give the child time to process visual information, it may mean the child perceives the task as too difficult, or it may mean the child is feeling uncertain or stressed. Children with CdLS may also use peripheral vision more frequently than direct gazing because they have greater difficulty choosing which of the varied stimuli should receive their attention. It also tends to be true that children who are lower functioning show greater sensory rejection and sensitivity to stimulation in their environment.

DENTAL

Dental problems can include small jaw development, poor oral hygiene, crowded teeth, small teeth, periodontal disease, and the erosion of teeth caused by stomach acids from reflux. Children diagnosed with CdLS require early dental evaluation, treatment, planning and preventative home care. The oral structures are greatly affected with this syndrome. Growth and development concerns of the jaws and teeth must be assessed at a young age in order that therapeutic measures can be instituted.

Clefting of the palate is common in patients with CdLS. This condition would necessitate pediatric dental involvement shortly after birth. Feeding obturators and surgical stents may be of great assistance to the craniofacial surgeons. The early introduction to dental care allows for baseline documentation of the oral soft and hard tissues. Clefts should be repaired as early as possible. Not only does this repair improve the ability to eat and reduce the likelihood of ear infections leading to hearing loss; it also enhances the speaking process.

Oral hygiene practices can be taught to caretakers, thus, preventing infant bottle cavities and other common dental problems. Routine six-month check-ups can assist in monitoring changes, detecting pathology and reinforcing appropriate home care. Orthodontic evaluation should take place by the 7th year.

Pediatric dental specialists are trained in the specific dental requirements and treatment of children, especially in the area of children with special health care needs. The American Academy of Pediatric Dentistry recommends regular professional attention beginning with patient oral evaluation and parental counseling no later than 12 months of age with a pediatric dentist.

Pediatric dentistry educators and practitioners throughout the country are advocating a preventative approach, which has been termed the "no-cavity plan". In addition to water fluoridation, optimal systemic supplemental and topical fluoride, the daily use of appropriate amounts of a fluoride dentifrice and the placement of pit and fissure sealant, the no-cavity approach utilizes nutritional counseling, strict home oral hygiene care, the maintenance of existing restorations and biannual professional cleanings.

When indicated, using conscious sedation and performing a number of tasks at one time may optimize dental care as well as care for other medical conditions for certain individuals. Individuals who are unable to communicate pain or discomfort and who are uncooperative in the dental office may need to be sedated in order to provide quality care. Remember, whenever an

individual has anesthesia for dental care, consider other procedures that could be done concurrently (endoscopy, ENT exam, eye exam etc).

ORTHOPEDICS

In the more mildly affected children curving of the fifth finger (clinodactyly), small hands, a short thumb placed closer than usual to the wrist and some limitation of elbow motions are often present, with webbing of one or more fingers (syndactyly) less common. Abnormalities of the hip occur in five to ten percent of the children with CdLS and may interfere with the ability to walk. Surgery may be used to correct this condition.

Of greater relevance to communication because of the interference in the use of sign language or other augmentative strategies for communication are the more severe upper-limb malformations. In some cases fingers, metacarpals and the long bones of the arm are absent.

GASTROESOPHAGEAL REFLUX DISEASE (GERD)

The successful management of the gastrointestinal complaints of patients with CdLS remains a challenge. Problems based in the gastrointestinal tract exist in a very high percentage of patients with CdLS. Complaints can originate from the upper GI tract, including the esophagus, stomach, and upper small intestine. Problems from these areas can be mild and easily manageable, such as occasional symptoms of vomiting, belching, heartburn, or intermittent poor appetite. As these symptoms become more severe, more consistent, and more difficult to overcome, they require a more comprehensive evaluation.

Complaints can also originate from the lower GI tract, including the large intestine, the rectum and anus. These complaints also can be mild and easily manageable, or severe, requiring evaluation. Problems with the lower areas of the GI tract typically involve the formation and passage of stool. Constipation, diarrhea, and gaseous distension with cramping are common problems.

Formal assessments of problems can be done by your primary care physician and, if needed, by a consulting gastroenterologist. Common studies done for both upper, and lower GI tract problems can involve blood tests, stool tests, X-ray studies, and endoscopic studies. Even though we have a great deal of knowledge about these common disorders, accurate and timely diagnosis, cannot always be assured, even in the hands of consulting specialists.

The normal process of eating and digestion is very complex. The stomach secretes a strong acid that begins the process of digestion. Since the esophagus is not designed to tolerate the effects of acid exposure, stomach acid that washes back up continuously onto the esophagus can cause an injury known as reflux esophagitis. This simple act of acid regurgitation has also been implicated in a large number of other problems. Many different diseases of the lung, as well as feeding difficulties and diseases of the ear, nose and throat, are now thought to stem from the process of regurgitation of acid. Gastroesophageal reflux disease (GERD) is the term that collectively describes all of these different diseases. Sandifer Syndrome which is sometimes seen in individuals with CdLS is characterized by severe gastroesophageal reflux and unusual body movements such as wiggling and moving constantly, turning the head to one side or throwing the head back.

If GERD with esophagitis is suspected, an upper endoscopy is commonly performed. It is important that patients with CdLS who present with chronic pain, thought to be related to the GI tract, undergo a standard acid-reflux evaluation. The treatment for reflux usually consists of special diets, medications, and elevating a child after eating. When these treatments are not successful surgical procedures such as a Nissen fundoplication and a gastrostomy may be necessary. The Nissen results in a narrowing of the lower esophagus and the gastrostomy provides a hole in the stomach, thus allowing for feeding by a G-tube and providing an outlet for stomach gases.

Presenting symptoms in people with CdLS may be classified as straightforward acid reflux, but they may not respond in the same way as other patients. Local consultants, skilled in the evaluation and treatment of acid-induced reflux disease, but inexperienced with CdLS patients, may unintentionally mislead parents. In CdLS, these symptom complexes may be multifactorial. If standard treatments for reflux are unsuccessful, discussions involving other options may be helpful.

Behavioral Indications of GERD

People who can tell us about their GI symptoms might report severe heartburn, vomiting, or abdominal pain. This pain can interfere with appetite, with participation in desired activities, or with restful sleep. If a person with CdLS cannot accurately report symptoms, they might only demonstrate changes in behavior that reflect chronic pain, such as irritability or even self-injurious behaviors. It is common, therefore, for behavior based practitioners who are evaluating patients with self-injury to ask if all causes of chronic pain have been properly evaluated. GERD with esophagitis is commonly suspected in patients with difficult behaviors.

THE ROLE OF ULTRASOUND IN THE PRENATAL DIAGNOSIS OF CdLS

For parents who already have a child with Cornelia de Lange Syndrome (CdLS) and who want to have more children, prenatal ultrasound can provide a helpful evaluation of subsequent pregnancies. Research continues to support the low reoccurrence risk for CdLS and ultrasound can be a source of reassurance and comfort to some parents.

Ultrasound is currently our best - and possibly our only - tool for prenatal diagnosis. There are a number of findings in CdLS that can be recognized prenatally. Probably the most reliable indicator is poor growth in a small fetus. Poor growth can be detected at ages greater than 25 weeks of gestation for most babies with CdLS, especially if there has been accurate dating with an earlier ultrasound.

For parents who have had a child with CdLS, an initial ultrasound examination may be recommended for all subsequent pregnancies at 18 weeks. The timing of this scan will allow a thorough study of the anatomy of the fetus, and also provide accurate dating of the pregnancy. In addition to the routine survey, the anatomy that should be examined particularly carefully includes the face, the hands, the heart, the arms, and the ventricles of the head. A second ultrasound study at 30 weeks could provide added reassurance that the fetus has grown normally, if needed.

An initial scan at 8 weeks would provide a very accurate estimate of the fetus' age, and this would allow a close monitoring of the growth. In addition a scan would also have to be performed at 18 weeks because the organs of the fetus are not completely formed and fetal anatomy cannot be seen clearly at eight weeks.

Anatomic abnormalities that have been described on prenatal studies of babies with CdLS include: limb abnormalities (particularly of the upper limbs), abnormal hearts, cleft lip, abnormal facial profile, diaphragmatic hernia, mild enlargement of the ventricles of the head, and gastrointestinal abnormalities.

The most distinctive of these abnormalities are those of the upper limb. Arm bones and fingers should be carefully examined and counted because these may be missing or abnormally short. The femur, feet, and arm bones should be measured to ensure that their lengths are within the normal range. There are tables of normal measurements that the person performing the ultrasound study should have.

In the face of a baby with CdLS, one might find cleft lip or palate, long eyelashes, a small chin, and a small upturned nose. In many of the children, there are abnormalities of the heart (ventricular septal defects, atrial septal defects, hypoplastic aorta, persistent left superior vena cava, and tetralogy of Fallot).

The head of the baby with CdLS will tend to be short and small (microbrachycephaly) and so should be measured and compared to tables of non-normal measurements. The person performing the ultrasound study should also check to be certain that the baby does not have a diaphragmatic hernia or abdominal calcification (meconium peritonitis).

In many cases, babies with CdLS move much less than normal babies. The person doing the scan could perform a biophysical profile to provide an evaluation of the babies behavior and responses.

Ultrasound is not a perfect tool to diagnose CdLS, nor is it a perfect tool to exclude the possibility of CdLS. Nonetheless, most children with CdLS have fairly severe abnormalities that can be detected prenatally by careful radiologists or obstetricians. It is anticipated that in almost all cases, scans performed on subsequent pregnancies will be normal. This should help parents find considerable joy and hope with these pregnancies, rather than anxiety and fear.

BEHAVIOR

Although many children with CdLS have no significant behavioral problems, there are some conditions, which make self-injurious behavior more likely to occur: pain, discomfort, frustration or dismay. The typical young person with CdLS may be described as hypersensitive and dysrhythmic. He/she may be hypersensitive in he/she may have strong reactions to ordinary stimuli and these reactions may continue long after the stimulus is gone. He/she is sometimes dysrhythmic, that is having irregular patterns of behavior in the areas of eating, sleeping and emotional response.

The lack of sensitivity to pain and/or heightened sensitivity to touch suggests some individuals may have neurological impairment. They may also be prone to behavioral problems such as hyperactivity, short attention span, and oppositional or repetitive behavior.

Psychiatric Evaluations

Many of ordinary problems that children have can be dealt with by a pediatrician who has some developmental or behavioral experience. These would be minor problems with eating or sleeping, tantrums, or even hyperactivity. Many pediatricians are quite skilled in the first and second line drugs for impulsive and hyperactive behaviors.

Persistent behavioral difficulties including hyperactivity that does not respond to medication, severe impulsive behavior oppositional behavior aggression, or self injury, are very common in CdLS and may require the kind of treatment that includes the attention of a specialist in behavioral psychology or a child psychiatrist who has experience with the developmentally disabled. Sometimes, individuals need referral to an epilepsy specialist first, if there is suspicion of seizures. But the long-term treatment of serious behavior or emotional problems in individuals should almost always be the responsibility of a specialist in child and adolescent psychiatry and/or a behavioral specialist with experience in developmental disabilities, who has the appropriate background.

EDUCATION

Cornelia de Lange Syndrome (CdLS) has great variability in its manifestation, from those individuals who are visually recognizable as having CdLS to those who, to the uninitiated observer, display no unusual physical and/or behavioral characteristics. A common characteristic, however, is that numerous infants, preschool and school-age children with CdLS have a range of significant medical and health issues that consume parental physical, emotional and financial energy and the attention of numerous professional disciplines. Many children diagnosed with CdLS also present another set of concerns, namely in the areas of communication, learning styles, learning needs and behavior. Planning and providing appropriate quality educational services for children who have CdLS must consider the influence and interplay of both sets of issues and concerns.

Education is a cultural activity with schools charged to prepare children for the life they will lead in the culture they will live. Education can be thought of as the other side of the coin from medical and health-related issues and, as such, needs to be addressed simultaneously. This means issues of assessment, individualized education plan (IEP) development, educational placement, curriculum adaptation and teaching techniques require special consideration and, in many situations, unique and creative modifications.

Physical, Environmental, Instructional & Social Considerations

Factors to consider in educational planning include: The child's medical and health status, stamina, ability to manage sensory-motor demands, levels of arousal, communicative status, need for structure and organization, relevant goals and objectives, motivating and understandable activities, and appropriate adaptations. Moreover, the child with CdLS needs to be an equal partner in interactive and satisfying social experiences. Social equality rests, in part, on helping oneself as much as possible, communication abilities, contribution to others, and shared experiences. Medical-Health Related Issues: There is a critical need for family, medical-health personnel and school staff to communicate with each other around issues affecting health. Many students with CdLS have a range of medical-health issues. For example, school staff need to be aware of the student's visual and auditory status, if a seizure condition exists and/or if the student suffers from pain in their joints. Staff need to be sensitive to those periods when there is a flare-up of gastro-esophageal reflux. Staff also should be informed of food allergies and strictly adhere to dietary limitations. Lastly, staff need to distinguish between those periods of fidgeting and non-attentiveness due to discomfort and pain vs. those periods when the behaviors are due to other causes. The situation, of course, is somewhat easier to understand and manage if the student has expressive language.

Communication: Any discourse on education must involve the discussion of communication. We cannot transmit or receive information unless we communicate. Children with CdLS are at risk for delayed or absent speech, difficulty in understanding the subtle nuances and pragmatics of language and/or auditory sensitivity to a barrage of speech and environmental sounds. Speech is very difficult for many individuals with CdLS due to oral-motor apraxia. These children do not choose not to talk but find the coordination and production of the motor actions extraordinarily difficult – especially under typical school-like demand situations. Thus, some students with CdLS may talk more at home than in school. Parents and school staff might find it helpful to consider the following:

- While speech may be the ultimate goal for those children who currently do not talk or find talking difficult, they need a way to express themselves now so they may be more active participants in the educational process. There are a variety of educational techniques that can be employed to help these children communicate right now while they simultaneously work on the higher goals of speech production.
- Speech may not be a realistic goal for some children with CdLS. There are, however, a great many other educational techniques that can be employed for very effective communication. These techniques are very reliable regardless of the country, culture and/or the education program.
- Signing may/may not be an effective route for some children due (a) receptive difficulties related to poor visual attention, a visual handicap and the transient/ spatial/speed nature of sign, or (b) expressive difficulties such as upper limb malformations, dyspraxia (difficulty in performing smooth, rhythmical and sequential hand motions) or memory for motor movements. On the other hand, many students with CdLS who have little or no speech may develop some idiosyncratic gestures for requests that are of importance to them. Recognizing these gestures requires meaningful

others to make systematic observations to determine if the child is using such gestures and, if so, what the child is requesting. Needless to say, interpreting and responding to such idiosyncratic gestures involves a lot of trial and error.

- Although most children with CdLS are said to have visual-perceptual strengths, this does not necessarily mean they understand all forms of visual stimuli. Visual regard for two-dimensional representation (pictures, line drawings, icons, photographs, print) does not automatically mean there is understanding of this form of symbolic representation. An assessment of such understanding is critical in determining what mode(s) of communication have the best chance of being successful effective.
- Technology provides many options for augmenting communication and has been a major boon for persons who have disabilities. However, computers and other high tech devices are not the answer for every child. There are basic skills that must be learned in order to use this technology effectively as communication and learning devices. Students need both a basic understanding of the communication process and of the concrete world of objects before they are able to manage the abstract world of symbols. Again, an assessment of such understanding is recommended to determine if communication devices will be effective for individual students. Many, but not all, students with the more classic type of CdLS have rejected the use of communication devices. At this time, we do not know if such rejection is due to the type of device, the readiness for the device when first introduced, the manner of training to use the device and/or other factors.
- In general, children who have multiple disabilities are at very high risk for missing out on numerous incidental learning experiences that typical children pick up so easily. These types of experiences center around the concrete world and bring together the visual, hearing, touch, "doing" foundation necessary to manage the abstract world of symbols.

Vision: Myopia (near sighted), amblyopia (lazy eye affecting depth perception), chronic conjunctivitis-appearing eyes, and dry eye syndrome (making the eyes feel as if they have sand in them), photophobia (light sensitivity) and ptosis (droopy eye lids) are common visual problems. Students with these symptoms may need drops for lubricating their eyes and eye washes done in school. They also may need (a) preferential seating close to the center of action, (b) assigned seating facing away from the windows or other sources of glare due to their light sensitivity, (c) adapted but non-glare lighting to highlight the specific work area, (d) special printed materials if vision is limited even with corrective lenses, and (e) alternating work requiring fine visual functional skills from work requiring less fine visual performance in order to reduce fatigue. Fatigue may result from the need to constantly shift head positions to accommodate to the ptosis. Teachers should know if glasses have been prescribed for the student and what is the recommended pattern for wearing them. Sometimes glasses are prescribed for specific activities. If the student has use of only one eye, it may be helpful to know if safety glasses should be worn during certain activities. Some students may have a documented visual handicap and will require the services of a trained teacher of the visually impaired.

Hearing: Students may have a documented hearing loss or fluctuating hearing requiring close communication and coordination with the pediatrician and with the audiologist. Such students may require use of hearing aids, a FM system and/or preferential seating near the teacher. If either hearing aids or a FM system are prescribed, staff should be aware how to adjust the settings, how to work with the ear molds, and the best times to use the equipment. Other children with CdLS may have delayed responses to auditory stimuli which require that they be given time to process the auditory information and plan their response. Some students will require the services of a trained teacher of the hearing impaired. Of particular importance is the fact that many students with CdLS are very sensitive to sound and easily may become overly aroused or agitated in situations of auditory confusion and noise.

Vision & Hearing: Some students with CdLS have both a vision and a hearing impairment. These students are considered deafblind and require very specialized teaching. Deafblindness is not a simple "one plus one equals two" but rather, presents significant risks in learning due to the impact of the dual sensory disability on the development of a language system. Teaching techniques oriented toward children who are visually handicapped rely on intact hearing and touch. Teaching techniques oriented toward children who are hearing impaired rely on vision. When neither sensory modality is intact or reliable, alternative communication techniques need to be utilized. Moreover, the efficiency in which a deafblind individual is able to use their residual vision and hearing is highly influenced by stress, health, medications, fatigue, background noise/visual clutter, size/distance/plane of presentation/etc of the visual stimulus, speed of presentation, competing sensory stimuli and many, many other factors interwoven with each other. All children who have combined visual and auditory disabilities require the services of a trained teacher of the deafblind.

Visual & Auditory Processing: Many students with CdLS children have associated problems in processing and understanding visual and auditory messages. Cortical visual processing problems are the biggest single cause of visual handicaps in the United States. In most of these situations, central auditory processing problems also exist. At this time, we do not have enough data to provide information on the incidence of these cortical processing problems as related to students with CdLS although there is evidence that sensory processing and motor planning are slower. This means that parents and educators need to allow the student time to process the sensory information and plan/implement the motor responses. To do otherwise may result in significant communication and behavioral difficulties.

A Few Educational Strategies:

- A well-organized routine and predictable, calm, organized environments seem most conducive for students with CdLS. Schedule and calendar systems via objects, pictures, line drawings, icons and/or words, as appropriate, can help the student anticipate and prepare for changes in the routine.
- Allowing time for the student to process, plan and implement a response to sensory information is essential. The number and pacing of activities may have to be individualized – especially for those students who have limited stamina, endurance and ability to control their own state of arousal. Take advantage of the visual strengths the student may have by orally giving the directions, then visually present the questions and/or demonstrate the method, and end

by giving the oral directions again. Time constraints potentially may add to the stress, which, in turn, will reduce processing time further.

- Many of the students perform better with concrete learning experiences. For example, applying math principles by going into the community to shop for needed items involves planning, reading, mobility, safety, social etiquette and so forth. Enhance literacy via creating opportunities of interest and using these experiences of interest to promote communication, reading and writing – in whatever format the student is able to use.
- If handwriting is laborious, investigate the advantages of computer use for the student.
- Some students in academic programs may need rest breaks to reduce their level of arousal. Simultaneously, many need specific tutoring or pre-teaching, in a resource room, to deal with subjects they find difficult in the mainstream environment.
- Some of the students have a difficult time taking the initiative and making their needs known. They may find casual, recreational times with typical peers difficult because of communication difficulties and the unpredictable nature of social events. Communication and social differences generally become more apparent and more difficult during the middle and high school years without early proactive social skills training

CARDIOLOGY

CONGENITAL HEART DISEASE

Babies born with CdLS have a higher likelihood of having congenital heart disease compared to the general population. Studies have shown that the incidence of congenital heart disease in CdLS children is as high as 20 – 30% (compared to 0.8% for all births). The severity of heart defects seen in CdLS individuals cover the full spectrum from relatively minor defects (e.g. atrial septal defects) to more serious forms (e.g. Tetralogy or Fallot).

Some heart defects have obvious signs and symptoms at birth that will prompt an evaluation by a pediatric cardiologist. Other defects are more subtle and are not always recognized at birth. Detection of congenital heart disease in people with CdLS may be delayed. Short stature and failure to thrive may be attributed solely to the CdLS, when in fact congenital heart disease may be playing a role as well. It is therefore recommended that every individual diagnosed with CdLS be evaluated by a pediatric cardiologist with an echocardiogram.

If a congenital heart defect is detected, treatment options may include surgery, medications, or merely observation. Treatment options of heart defects in people with CdLS should not differ from other individuals. In general, it is thought that the outcomes of congenital heart disease in children with CdLS are not significantly different than the general population.