Medical Management of Kabuki Syndrome - Part 1

Compiled by Margot Schmiedge and Peta Colton

Welcome Families and Professionals

We have come a long way in understanding what it means to have Kabuki syndrome since it was first described in 1981. Studies and their resulting published articles have given us objective data, helping to decipher what is typical for the syndrome and what is simply typical for that individual. Equally important has been the observations and sharing of information between parents and professionals.

The Medical Management Package has been a joint effort between Margot Schmiedge, founder and director of Kabuki Syndrome Network (KSN) and Peta Colton, founder and director of Supporting Aussie Kids with Kabuki Syndrome (SAKKS). It was developed to provide users with an easy to read and print alternative. This package is designed for educational purposes only. It is not intended for diagnosis or advice on medical conditions. It is not meant to endorse particular therapies, treatments and/or medicines. It is paramount that families seek care from the professionals. In addition, this package will only be updated occasionally. The best place for current, up-to-date information is at the respective websites: www.kabukisyndrome.com and http://www.sakks.org.

The articles may use medical terminology. It is difficult to avoid since one medical word often requires ten layman's words. There are many online dictionaries available or, if you prefer, you can use the one at www.kabukisyndrome.com .

The language used to describe varying disability has evolved as society has gained increased knowledge. Some terms have acquired shameful implications because of misuse. We will always refer to a child with Kabuki as just that – not a Kabuki child. The terms cognitive disability and intellectual disability are used interchangeably. 'Developmental delay' is a term often used by professionals. It usually means there are global delays present, including either or both physical and intellectual. It's a 'safe' term because 'delay' infers that the individual will eventually catch-up. After all, a delayed flight does eventually arrive! We are not suggesting that we get hung-up on the terms we use, just that they are respectful and accurate for the situation.

Many families find it helpful to keep their child's medical records and notes in a binder, which they bring with them to appointments for handy reference.

We would like to throw a word of caution, especially to new parents of children with Kabuki. In the coming years you will be inundated with research, advice, and medical procedures. Each family will find it necessary to weed out what is important and what is not for their individual child. Sometimes, though, we need a reminder that it be kept in perspective, that we don't become wholly obsessed with caloric counts, medical procedures and therapies, and in the process, forget to enjoy our children!

Inheritance

On August 15, 2010 researchers at the University of Seattle announced the discovery of the MLL2 gene mutations responsible for approximately 75% of individuals with Kabuki Syndrome. The scientists used a "second generation" technique to examine only the protein-coding gene portion of the human genome, called the exome. Since the exome constitutes only 1 - 2% of the human genome, the cost and time requirement has been greatly reduced, making it more plausible to look for gene mutations.

There are different reasons why a gene may have a mutation. In the case of Kabuki, the MLL2 gene mutations were found to be due to either nonsense or frame-shift mutation which resulted in a shortened, nonfunctional protein. To help families better understand the basics of the discovery please see *Understanding the Genetics of Kabuki*.

It is speculated that Kabuki is a heterogeneous syndrome, meaning that multiple genes could potentially be involved. It is hoped that with continued analysis, other genes will be discovered.

Due to the August 2010 discovery of the MLL2 gene mutations responsible for approximately 75% of individuals with Kabuki Syndrome, a clinical blood test is now available to help with diagnosis. The National Center for Biotechnology Information provides a database* which lists laboratories offering clinical testing. There may be other labs offering the testing which have not added their institution to this voluntary listing. If you are interested in having an individual with a clinical diagnosis of Kabuki be tested, you can ask your geneticist or another specialist to order the tests, perform the blood work (about 5 cc's of blood draw) and have it sent to one of those labs. Turnaround time to receive results is approximately 6-8 weeks. The test is called MLL2 Full Gene Sequencing and the test code is SMLL2. If applicable, it may be valuable to call your insurance company to see if the test will be covered. Some insurers cover them because they are diagnostic tests. CPT codes are 83891 (x1), 83894 (x1), 83898 (x76), 83904 (x152), 83909 (x152), 83912 (x1) and cost is approximately $2,000 - $3,000. In Canada, the test is not yet available but there have been situations where a geneticist may send the samples south of the border for testing. Please check with your geneticist to explore the options.

It is important to keep in mind that this test only diagnoses the 75% of cases that are caused by the MLL2 gene. It is possible that your result may be negative for the MLL2, but that the individual may still be believed to have Kabuki syndrome based on other presenting characteristics.

Initially, your geneticist will make a clinical diagnosis of Kabuki based on the recognition of four (out of five) main characteristics, with the distinct facial features being imperative.

- characteristic facies (long palpebral fissures with eversion of outer third, arched eyebrows with sparse outer half, prominent eyelashes, prominent and/or misshapen ears, and depressed nasal tip)
- skeletal anomalies
- dermatoglyphic anomalies
- intellectual disability (mild to moderate)
- postnatal short stature

The characteristic facies is imperative.

Associated features, which are also looked at but which are not cardinal manifestations:

- hypotonia
- feeding difficulties
- recurrent infections
- congenital heart defects
- renal (kidney) / urinary tract anomalies
- small mouth, micrognathia (smallness of the jaws), cleft/high arched palate, hypodontia (missing teeth)
- birth: normal weight, infancy & childhood: underweight, pre-teen onward: possible obesity
- early breast development (girls)
- hearing impaired and/or inner ear malformations

The occurrence of associated conditions, for individuals, varies in number and degree. Though the Kabuki population exhibits a wide spectrum of medical involvement, each patient presents a unique clinical picture.

*http://www.ncbi.nlm.nih.gov/sites/GeneTests/lab/clinical_disease_id/216289?db=genetests

Dr. Tiong Tan

What Role Does a Clinical Geneticist Play in the Lives of Children and Adults with Kabuki Syndrome

By Dr. Tiong Tan

About Author:
Tiong initially trained as a paediatrician and then as a clinical geneticist working with the fantastic team at Genetic Health Services in Melbourne. His interest lies in helping children and families affected by genetic conditions and birth defects. After doing PhD research in Melbourne, he is now pursuing further research in Hong Kong to understand the mechanisms of congenital changes affecting the head and face, such as clefting. His plan is to rejoin the team in Melbourne with this knowledge and experience and return to clinical work.

Children and adults with Kabuki syndrome often see many health professionals. These may include, but are not limited to, their GP, paediatrician, physiotherapist, heart specialist, speech pathologist, dentist, orthotist, immunologist, and eye specialist. Once every couple of years, they might see a geneticist. What does a geneticist do? And what can a clinical geneticist contribute to the lives of families affected by Kabuki syndrome?

A clinical geneticist is a medical specialist who cares for people with conditions that have a genetic component. A large part of clinical genetics practice is the management of children who are born with multiple birth defects, some of whom are diagnosed with a condition such as Kabuki syndrome. Clinical geneticists usually become involved in the lives of such children when they are asked to make a diagnosis to explain the pattern of medical problems experienced by the child. Kabuki syndrome is a rare condition that is distinctive. Its recognition allows advice and management to be tailored specifically for the affected individual. We base this advice on what we know from our collective medical experience of looking after other individuals with Kabuki syndrome.

Making the diagnosis of Kabuki syndrome does not give us the power of a crystal ball. It does not predict what problems will happen, or when they will happen. But it does allow us to draw up a plan to anticipate some of the problems that might happen, and to avoid them, or at least reduce their impact. It is somewhat like drawing up a road map for the future, to help keep the child on the healthiest route. The clinical geneticist is aware of the possible complications of Kabuki syndrome, and is able to guide the whole care team about how to keep the affected child in the best possible health.

Often a diagnosis of a condition like Kabuki syndrome means that the child will have special needs in the future. The clinical geneticist is in the position to advocate for additional help in school to maximize the learning potential of a child with Kabuki syndrome. The clinical geneticist is also in a position to offer support and care to the entire family, not just the affected child. Often parents have questions about whether they might have another affected child, or whether their other children might have an affected child. These are questions that a clinical geneticist can address. We are also aware of any new research findings, and can provide this information or facilitate involvement in an ongoing research project.

By following a child and his or her family over many years, we learn a great deal about some of the difficulties that have to be overcome, and hopefully contribute in a positive and meaningful way in the management of the family's medical and genetic health.

Margot Schmiedge

Maggie McMillin

Understanding the Genetics of Kabuki

By Margot Schmiedge

Edited by Maggie McMillin

Maggie McMillin is a clinical researcher in Human Genetics, Bamshad Lab at the University of Washington

Every cell in our body contains a full set of chromosomes and identical genes. What then differentiates our cells? What makes some of our cells become muscle and others, say, skin? This happens because only a fraction amount of genes in each cell are 'turned on' or 'expressed'. That's an interesting concept isn't it? That our blood, hormones, bones, and heart all share the exact same building blocks (genes), but only a select few are turned on in each system!

Most of us don't have an insatiable desire to understand genetics, but we all have some basic curiosity as to what our bodies are made of. How does it all work? This is particularly true when things don't work so perfectly.

Let's begin with the smallest most basic elements of the body – DNA. **DNA** is made up of 4 bases (adenine, cytosine, guanine, and thymine), each represented by the letter which they begin with. The bases pair with one another and are attached to sugar and phosphate molecules to make what looks like a ladder. *See Figure 1*

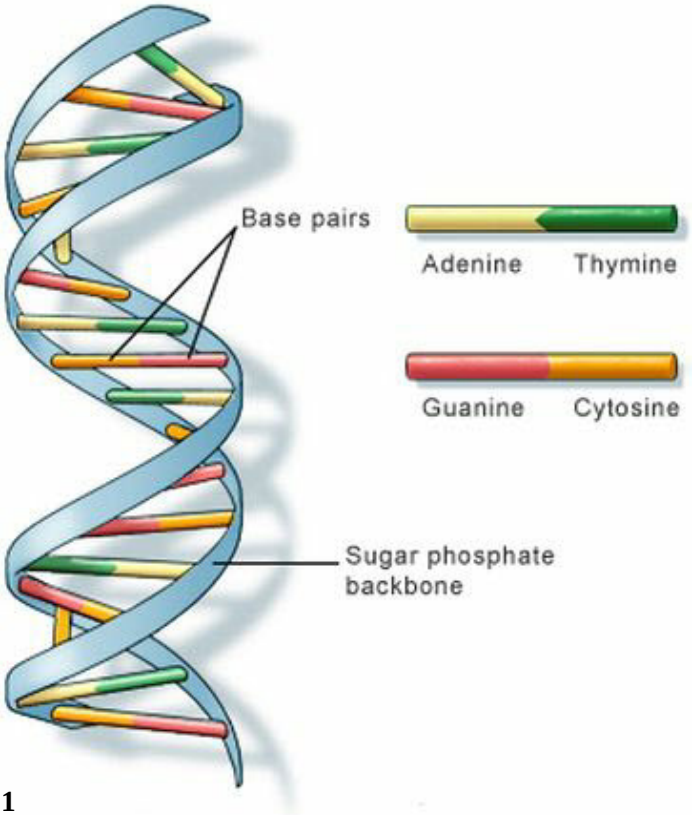

Figure 1

A **gene** is a length of DNA ladders. We have approximately 25,000 genes. The DNA ladders make up a code, similar to our alphabet. Actually, *very* similar to our alphabet. They are read 3 letters at a time to produce amino acids. Think of the amino acids like the words of a sentence. They are read similarly to the way we know that the letters *a-r-m* signifies a part of the body. These same letters put in a different order, *r-a-m*, now represents a male sheep. Since there are four different letters (A, C, G, and T), there are 64 different combinations that can be used. However there are only approximately 20 amino acids. That means that different codes can produce the same amino acid. Some of them act as punctuation for the sentence, signalling when a sentence begins and when it ends. *See Figure 2*

An example of an amino acid chain might be: CAT ATT GCA GAT TGT

Use the DNA decoder wheel on the next page to find out what your amino acid chain would look like. Start from the inside of the wheel and work outwards to the second ring for your next letter and so on till you get to the outside ring to find the name of your amino acid.

You should have decoded: Histidine-Isoleucine-Alanine-Aspartic Acid-Cysteine

Proteins are made up of many amino acids. Think of them as the sentences. It is these proteins that perform most of the critical functions of each cell. Again, some proteins will form muscle, some will work as enzymes to regulate hormonal and other chemical processes, and yet others will regulate the genes themselves.

Only about 1% of our DNA is coded by genes, which in turn make proteins. The rest is referred to as non-coding DNA and is not yet well understood. It is believed, among others, that they have an influence on our cells to know when to switch certain genes on and off.

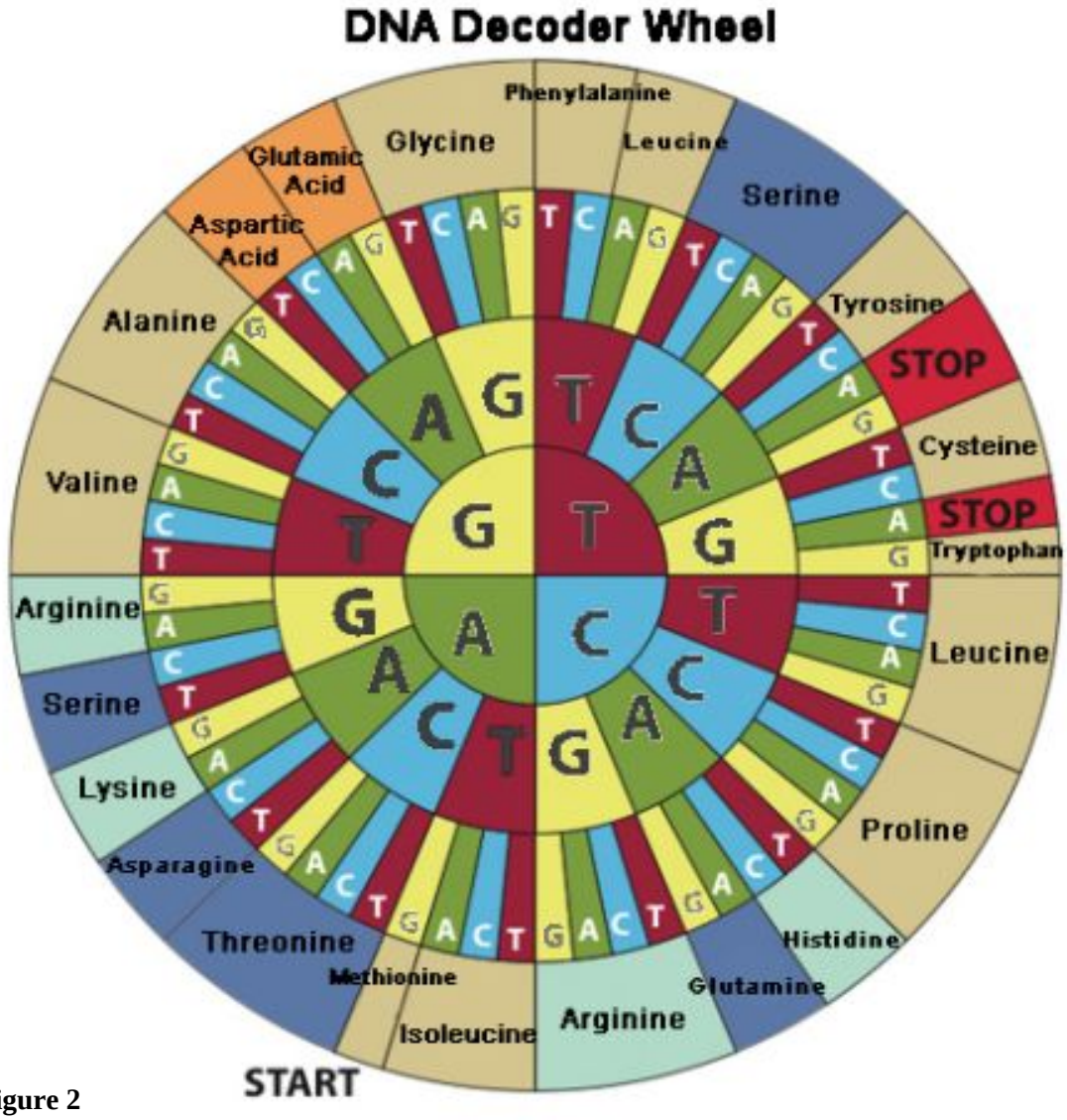

Figure 2

Chromosomes are made up of many genes. Humans have 22 pairs of chromosomes plus one pair that determines our sex. *See Figure 3*

Let's re-cap: DNA consists of 4 bases, and sugar and phosphate molecules to form ladders. Genes consist of DNA ladders and it's all tightly packaged into bundles called chromosomes.

DNA is read 3 bases (letters) at a time to produce amino acids (the words) and stops and starts (the punctuation). Many amino acids make up proteins (the sentences) which are contained in genes (paragraphs or chapters). Proteins do the work in constructing our bodies (which makes the story complete!)

So what happens in the case of disease or a syndrome? Sometimes one of the letters of the DNA is swapped for another. All of us carry some of these errors. So why do we not all have a syndrome? Remember how the four DNA letters could be coded in

64 possible combinations (4x4x4x4) but will only produce about 20 different amino acids? Some combinations can handle an error. For example if the letter T is swapped for an A in the codon GCT the resulting protein would still be the same, since both the old codon (GCT) and new codon (GCA) code for the same amino acid (see for yourself with the DNA decoder). Other error combinations may have very serious effects. Swapping an A for a T in a gene for hemoglobin results in the serious blood condition sickle cell anemia. Think of it like this: it's OK if Jane the waitress doesn't show up because we can move Mary into her position and Jack into Mary's position since they have all performed each other's tasks. However if Jessica the orthopedic surgeon doesn't show up, we can't very well have the OR nurse fill in for her! Other errors can occur as well, such as a bit of the DNA sequence is missed or a bit added, etc.

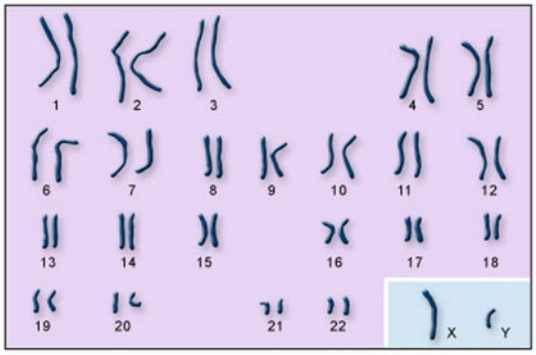

Figure 3

Karyotyping or blood chromosomal analysis is a study of our chromosomes. Cells are stained and examined microscopically to examine the size, shape and number of chromosomes in the sample. Think of it as a view of earth using a satellite. It will clearly show if a continent or country has changed its shape.

Microarray analysis allows scientists to scan the chromosomes, looking more closely at the genes. Different types of microarrays are able to detect different things, for example if there are insertions or deletions of genetic material or compare the expression of genes (remember, this means whether the gene is 'turned on' or not) in a healthy sample versus a diseased one. Think now of a more powerful satellite image that gives you the ability to see cities.

Targeted gene sequencing allows scientists to look very closely at our DNA (about 25,000 genes) to detect small changes in the sequence, or 'letters' in the DNA. Think now of a satellite so powerful that is able to see single homes.

Most individuals with Kabuki will have normal chromosomal study test results. The 'error' is in a letter – a home, not a continent. Even though the change is 'small', that is not to be misunderstood as being a minor error – just a difficult one to see until recently. Increased ability to see smaller and smaller elements of our body and increased understanding of what those elements do, make it possible to more accurately diagnose conditions. But science is a continuous process - one discovery and level of understanding leads to another. Much still needs to be understood, which may even lead to prevention in the future. These are exciting times in the genetic world!

In the case of Kabuki, mutations of the MLL2 gene has been found to occur in 75% of individuals who have been subjectively diagnosed with Kabuki. They were found to be due to either nonsense or frame-shift mutation which resulted in a shortened, nonfunctional protein. A nonsense mutation *(Fig 4*) is a change in one DNA base pair. The altered DNA sequence prematurely signals the cell to stop building a protein. This type of mutation results in a shortened protein that may function improperly or not at all. In the example below, you can see how the insertion of the base thymine (T) is now read as TAG instead of the intended CAG. Since TAG is read as a STOP, the resulting protein is shortened. Refer back to the DNA Decoder Wheel to see how this happens. A frameshift mutation (*Fig 5*) occurs when the addition or loss of DNA bases changes a gene's reading frame. A reading frame consists of groups of 3 bases that each code for one amino acid. A frameshift mutation shifts the grouping of these bases and changes the code for amino acids. The resulting protein is usually nonfunctional. Insertions, deletions, and duplications can all be frameshift mutations. In the example below you can see how the shift of the first DNA base means that the succeeding bases are all read incorrectly.

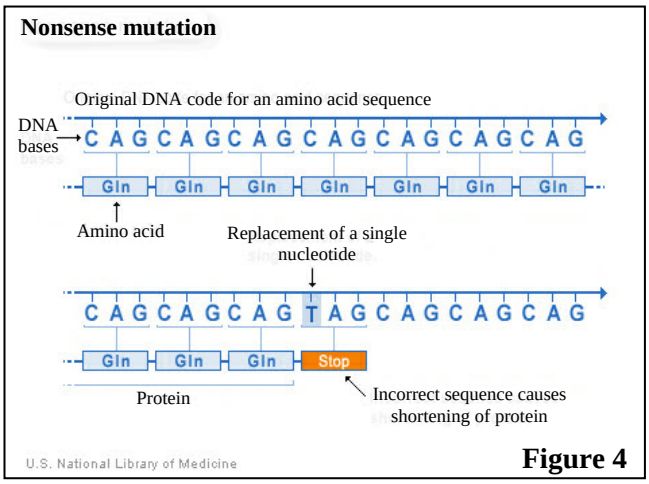

Figure 4

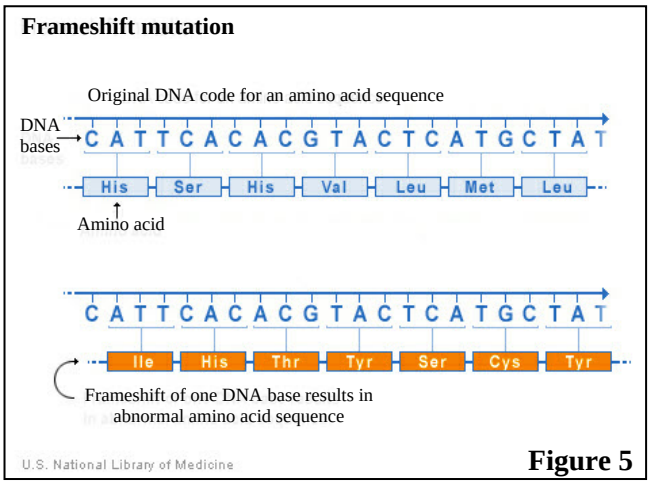

Figure 5

More specifically in the case of Kabuki

Addition by Maggie McMillin

A genome is an individual's entire genetic code. The Human Genome Project was the first time scientists had completely looked at every base (letter) of the genome. There are about 4 billion bases in the entire genome. It is still very difficult and very expensive to sequence an entire genome.
Only about 1% of the genome contains genes. There are about 20,000 genes in the genome. An exome is a newly made-up word to describe targeted sequencing of all the genes. Remember that genes are the part of the genome that code for proteins, and proteins are the things that perform functions in the body. If something does not function or develop properly, a gene is the first place to look to find a change that might cause the disease or dysfunction. So exome sequencing is a way to focus on looking at the most important part of the genome. And because there is much less sequencing than looking at the *entire* genome, the cost is much less.

Recently researchers studying Kabuki syndrome at the University of Washington and Seattle Children's Hospital used exome sequencing to identify the gene causing the syndrome. In the study, researchers sequenced the exomes (all the genes) of 10 individuals with Kabuki Syndrome. Then they compared the information between all 10 individuals to find a gene that contained a change that would be predicted to cause dysfunction of the protein. They found a gene (MLL2 gene*) that had changes, or mutations, in 9 out of the 10 individuals. Then researchers used targeted sequencing to look at the same gene in more individuals with Kabuki and about 75% of individuals had a change in the gene.

The gene provides the instructions, (like a recipe) to make a type of protein called a histone methyltransferase. Histones are proteins that the DNA is tightly wound around, like a spool of thread. This helps to package all the DNA so that it can fit inside the cell nucleus. When a cell needs to "read" the DNA to make a protein and perform a function, it unwinds whatever little part needs to be read. Histone methyltransferase is type of protein, called an enzyme that helps to unwind the DNA from the histone.

There are two clues as to why this gene is a causative agent of Kabuki:

1. The individuals without Kabuki (control individuals) do not have the same types of changes in this particular gene.
2. The parents do not have the change (unless they also have Kabuki). So most of the time the change in an individual with Kabuki is a new, "sporadic" change. This is just something that happens by chance.

This means that researchers have identified a gene that explains a large number of cases of Kabuki syndrome, and now a clinical test can be developed. For individuals with Kabuki that do not have mutations, there is likely another gene that causes the syndrome. The researchers are still conducting the study to look for other genes.

It's not yet known how the changes to the gene change the function of protein or why it causes the features of Kabuki syndrome. It's also not known if different changes within the gene can lead to more or less severe clinical features. But now that the gene has been identified, scientists have the next step in moving forward to try to answer these questions.

* Inserted following Aug 15, 2010 publication release.

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Please see *Inheritance* on page 2 for updated information on testing. It's important to note, that with continual new information, the websites are where you will find the most current information available!

Facial Characteristics

Facial characteristics typically include:

- long palpebral fissures
- lower palpebral eversion
- arched eyebrows with sparse outer lateral half
- long eyelashes
- blue sclerae
- ptosis (drooping of upper eye lid)
- depressed nasal tip
- cleft lip/palate or arched palate
- dysmorphic ears
- preauricular pits (dimples in front of ears)
- abnormal dentition

Children with Kabuki have similar facial features, most notably the large eyes, long and thick eyelashes, arched eyebrows, flat nasal tip and prominent ears. Eyebrows can be interrupted in some. Outer lower lid eversion can contribute to sleeping with eyes partially open. Ocular conditions that occur more commonly in KS than the general population are blue sclerae, strabismus, coloboma and ptosis. Less common conditions can include nystagmus, Peters' anomaly, Marcus Gunn phenomenon, and numerous others. Ears are frequently large, cupped, low-set, and incompletely formed. Hearing loss has usually been attributed to both repeated ear infections and sensorineural problems. Cleft palate/lip or high arched palates are commonly found. A thin upper lip has also been noted. Teeth are often wide spaced, irregularly shaped and misaligned. Hypodontia is common, in particular the upper incisors.

Dr. Takuya Iida

Kabuki Syndrome and Cleft Palate

By Takuya Iida, M.D.[1)], Susam Park, M.D[2)] , Eri Iida, M.D.[3)]

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What is a "Cleft Palate"?

The term "cleft" refers to a condition where the two sides of structure did not fuse or join together, and the word "palate" means the roof of the mouth. Thus "cleft palate" means a condition where there is an opening in the roof of the mouth (Fig.1). Cleft palate is a congenital defect, or birth defect, and it is often associated with cleft lip, which means a splitting in the lip.

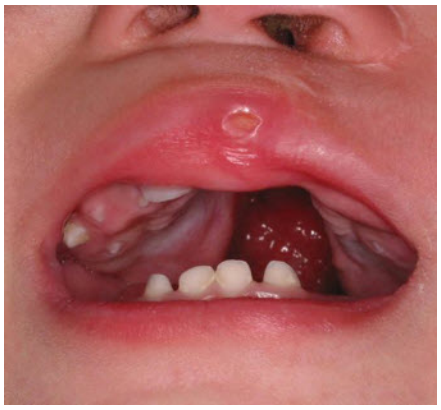

Figure 1

Kabuki syndrome and cleft palate

In general, cleft lips or palates are reported to occur in about 500-700 births worldwide. It is reported that children with Kabuki syndrome have cleft lip/palate at a higher incidence (33-50%).

The chief symptoms of cleft palate are as follows:
Feeding problem: Babies with cleft palate are not able to suck and swallow normally because the opening in the roof of the mouth directly connects the mouth to the nasal cavity, resulting in milk and air escaping from the nose.
Speech and language problems: Children with cleft palates may develop their speech later and have difficulty in pronouncing several kinds of sounds such as "p," "t," and "k" because they cannot raise air pressure in the mouth due to the air leakage through the nose.
Dental problems: Teeth may not erupt normally; some teeth might be absent, malformed, or malpositioned.
Ear infections and hearing difficulties: The function of the auditory tube that connects the middle ear and the throat is often impaired and therefore ear infections can occur easier.

Cleft palate is a treatable condition by multidiciplinary approach. The "Cleft team" will take care of your kids and can help improve not only the function but also the appearance of the child.

Submucous Cleft Plate

Cleft palate is usually diagnosed shortly after birth because it is easy to find the cleft if you look into the baby's mouth. However, there is a special type of cleft palate called submucous cleft palate (SMCP). The term "submucous" means that the cleft is covered by the thin layer of mucosa at the center of the roof of the mouth, although the underlying muscles do not join together. Since there is no apparent opening in the roof of the mouth, SMCP is sometimes difficult to find in infancy (Fig. 2) and might remain undiagnosed until they become older. One of our findings is that SMCP is observed at a much higher rate than has previously been reported. We treated six patients with cleft palate associated with Kabuki Syndrome at Shizuoka Children's Hospital. Three of them had an overt cleft palate and the other three had a submucous cleft palate.

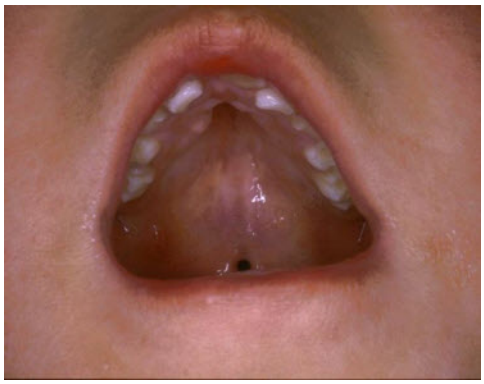

Figure 2

The most important presenting symptom indicating that a child is suspected of having SMCP is abnormal and nasal speech. Another symptom of SMCP is a uvula bifida, which means a splitting "uvula," a small, soft piece of flesh that hangs down at the back of your mouth. If your child has these symptoms, we recommend you consult with a cleft palate specialist.

Treatment

Many medical professionals in different fields are involved in the treatment for your children because the skills of many different areas are necessary to solve the problems caused by cleft palate. A Cleft team, which usually includes a plastic surgeon, a dental surgeon, an ear-nose-throat (ENT) surgeon, a pediatrician, a speech-language pathologist, and a nurse, will take care of your child. Treatments include mainly surgery, speech therapy, and dental therapy.

Surgery

Surgery for cleft palate repair is usually performed between 10 and 18 months after birth. The surgery, which is called " palatoplasty," consists of reconstruction of the splitting palate, including not only the mucosa but also the underlying muscle, which is most important for the speech and swallowing. There are several methods of palatoplasty. One of the most common procedures, "push-back" palatoplasty, is shown in Figure 3. In this procedure, incisions are made on both sides of the palate. Then the palatal tissues, including mucosa and muscle, are moved from each side to the center back, and then sutured. With this procedure, the separated muscles are joined together and the palate can be reconstructed and elongated.

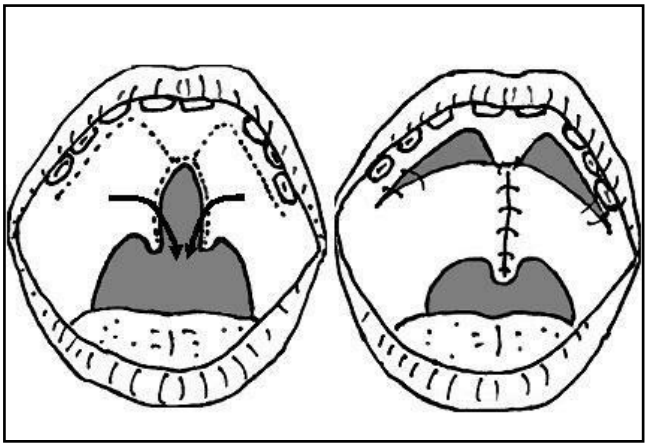

Figure 3

Speech therapy

After palatoplasty, children with cleft palate usually have speech therapy to learn how to use the reconstructed palate properly and acquire the correct pronunciation of sounds and words. The speech-language pathologist will evaluate your child's speech production and language development. The goal of speech therapy is to help them acquire correct sound and good speech habits.

Dental Care and orthodontic treatment

Children with a cleft palate often need dental and orthodontic treatment. Since the growth of the upper jaw is slower and less than the lower jaw, a child's upper teeth may not fit together properly with the lower teeth. In such cases, the orthodontist will help correct the alignment of the teeth and the relationship of the upper jaw to the lower jaw. If the tooth alignments cannot be made normal by orthodontics alone, they may need orthognathic surgery, which is called an osteotomy, to reposition the upper jaw both forward and down.

Ear treatment

Children with a cleft palate are susceptible to ear infections, so it is important to have an regular examination by an ENT doctor for your child's ears. Since Children with severe ear infections are not able to hear language normally due to fluid collection in the middle ear, there is a risk for language delays and speech problems To obtain proper drainage of the fluid in the middle ear, a small plastic tube is often inserted into the eardrum by an ENT surgeon.

Figures:
1 Appearance of cleft palate
2 Appearance of a submucous cleft palate (cited from The Cleft Palate-Craniofacial Journal, Allen Press Publishing Services. 2006, Iida T et. al. Cleft palate in Kabuki syndrome: a report of six cases)
3 Schematic illustration of "push-back" palatoplasty

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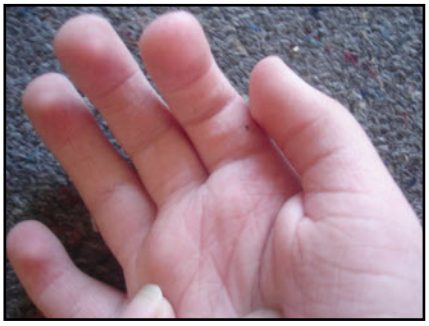
Musculoskeletal Characteristics

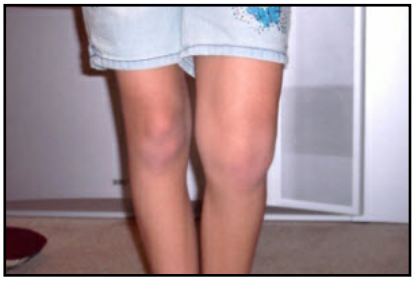
Musculoskeletal characteristics typically include:

- short fingers
- short middle phalanx of fifth finger
- syndactyly - mild webbing between fingers
- cranial abnormalities
- vertebral abnormalities
- rib anomalies
- scoliosis
- Hypotonia
- joint laxity
- dislocations of hip, patella and shoulders

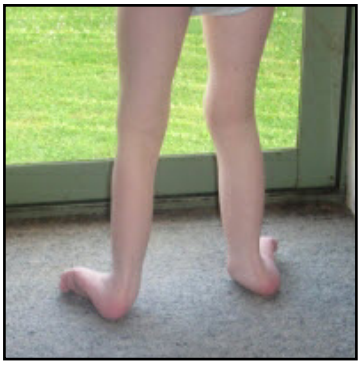
Vertebral anomalies can include butterfly vertebra, sagittal cleft, narrow intervertebral disc space, spina bifida occulta, and scoliosis.
Joint hypermobility is very common, in particular in the younger child. The hypermobility, exacerbated by hypotonia, can lead to dislocation of joints, in particular the hip, knees and shoulders. It is yet unclear whether joint laxity is neurogenic or due to a connective tissue disorder.
Short fingers, in particular the fifth finger, is common. Webbing between the fingers is less commonly seen.



Fetal pads and short fifth finger



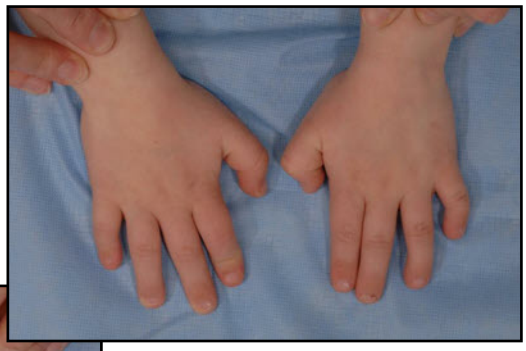
Dislocated Left Knee Cap

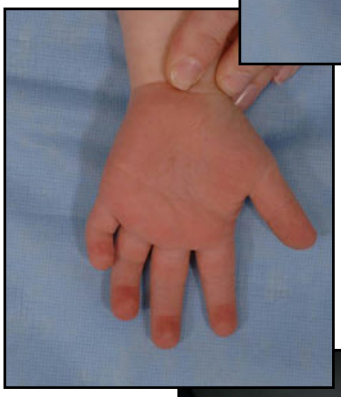


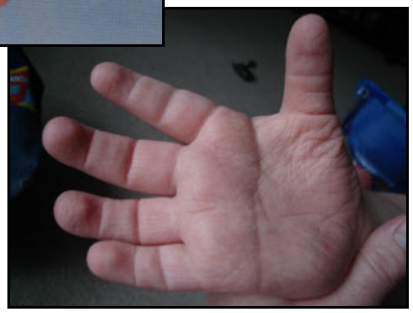
Severe pronation with active overuse of the foot everters in attempt to aquire stability

Dermatoglyphic Characteristics

With the recent genetic discovery for Kabuki, there will be less need to use dermatoglyphics for diagnosis. However, as one of the five cardinal characteristics, it may still be used as a contributing factor for diagnosis.







Dermatoglyphics and Kabuki Syndrome

By Dr. Albert Chudley

About Author:
Dr. Chudley is a medical geneticist and pediatrician. He is a professor at the University of Manitoba , at Winnipeg Children's Hospital.

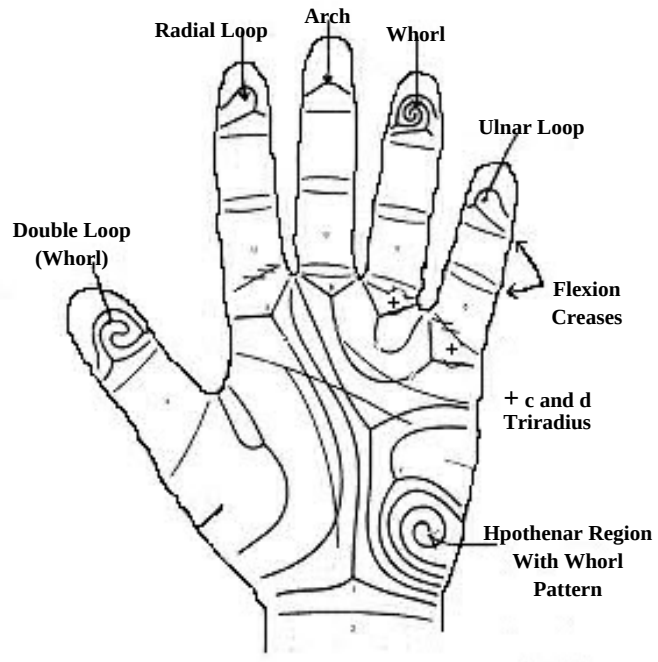
Dermatoglyphics (writing on the skin in Greek) is the study of epidermal ridges. Epidermal ridges form early in fetal life, and are unique to each individual. They consist of patterns of ridges on the finger pads, palms and soles of all individuals. They form different patterns, and are unique to individuals. This means they can be used for personal identification in criminal investigations. In genetics and medicine, they are useful in diagnosis, since recurring abnormal patterns are often seen in a variety of genetic syndromes. In addition, creases are formed on palms and soles that are also altered in syndromes. Although creases are not part of epidermal ridges, which require a magnifying glass or an ink impression to examine thoroughly, creases are part of what a geneticist looks at during his or her dermatoglyphic analysis and examination.

In Down syndrome, the creases are frequently abnormal on the palms with two of the three large creases forming what appears to be a single palmar crease (31% compared to 2% of controls). Also, individuals with Down syndrome have tibial arch patterns on the soles near the base of the great toes (60% compared to 0.5% of controls) and they tend to have 10 ulnar loops on their finger pads (30% compared to 7% of controls).

For Down syndrome, there is a diagnostic test, the chromosome analysis, that confirms the presence of 3 chromosome # 21's, instead of the usual 2. Therefore, dermatoglyphic analysis has become less important for the diagnosis of Down syndrome than for syndromes in which the genetic alteration has not been identified, such as for Kabuki syndrome (KS).

In many children with KS (over 75%), there are prominent fetal fingerpads. Usually these fingerpads become flat by the time of delivery, but in KS individuals, they remain prominent. This is not specific for KS, as they have been described in other syndromes, and can also be present in individuals without a genetic syndrome. Dr. Niikawa and co-authors brought our attention to the fact that in most people with KS, there are dermatoglyphic findings that separate affected individuals from unaffected. His findings showed that there was an increase in ulnar loops (63%); absence of digital triradius c (48%); absence of digital triradius d (30%); increase of hypothenar loops; and a single flexion crease of the 5th finger. Overall, in his study of dozens of KS individuals, about 93% showed some unusual dermatoglyphic findings. (See illustration).

Geneticists use dermatoglyphic analysis to help support the diagnosis of KS. However, as in Down syndrome, eventually the genetic cause of KS will be established, and the use of dermatoglyphic analysis will become less important



This illustration shows the various landmarks related to dermatoglyphics and some common patterns or formations. In Kabuki syndrome, there are at least five commonly seen changes: (1) increase in ulnar loops (2) absent of the digital c or d triradius –region highlighted with asterix (3) increase in hypothenar patterns (4) single flexion crease in 5th digit (5) prominent fingerpads (not shown).

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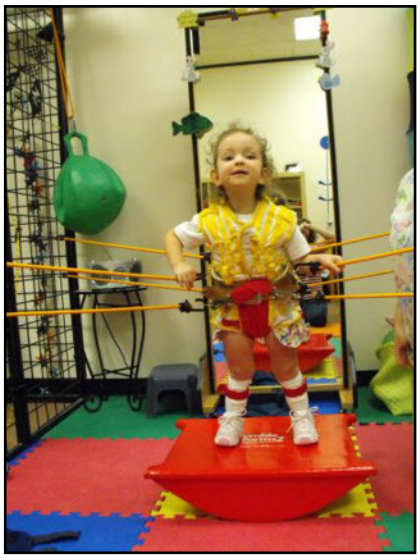
Intellectual, Sensory and Behavioral

Many individuals with Kabuki syndrome have sensory processing disorder. This inability to accurately organize sensory information can lead to behavior problems.

Some of the more commonly reported sensory issues include need for oral stimulation (chewing on non-food items), tactile defensiveness towards various sensations and stimuli, panic-like reactions to certain noises, and aversion to textures and/or smells of select foods. Anxiety, obsessive/compulsive traits and autistic-type behaviors are commonly observed. Individuals with Kabuki syndrome often have an obsessive need for routine. Mild depression has been reported in young adults.

Parents frequently report an excellent memory for face recognition, song lyrics, dates of events, etc.



Margot Schmiedge

Kabuki and Autistic Behaviors

By Margot Schmiedge and Jen Morton

The spectrum of characteristics associated with Kabuki syndrome is extremely varied. As with any newly described syndrome it is initially difficult to know if certain presenting characteristics are typical of the syndrome or simply typical for that individual. However, it has become increasingly evident that many individuals with Kabuki display autistic-type behaviors. Although few children have been officially diagnosed with autism, virtually all children have some degree of sensory processing disorder.

What is autism?

Autism is a spectrum disorder. This means the symptoms and characteristics can present themselves in a wide range of combinations and from mild to severe. In other words, two children with the same diagnosis can be very different from each other and have varying abilities/disabilities. Autism is a combination of several developmental challenges.

According to the Autism Society of America, the following areas are among those that may be affected:

Communication

- language develops slowly or not at all
- uses words without attaching the usual meaning to them
- communicates with gestures instead of words
- short attention span

Social Interaction

- spends time alone rather than with others
- shows little interest in making friends
- less responsive to social cues such as eye contact or smiles

Sensory Impairment

- may have sensitivities in the areas of sight, hearing, touch, smell, and taste to a greater or lesser degree

Play

- lack of spontaneous or imaginative play
- does not imitate others' actions
- does not initiate pretend games

Behaviors

- may be overactive or very passive
- throws tantrums for no apparent reason
- perseverates (shows an obsessive interest in a single item, idea, activity or person)
- apparent lack of common sense
- may show aggression to others or self
- often has difficulty with changes in routine

Behaviors often associated with children with Kabuki

Communication

- almost all families report language delays

Social Interaction

- some families report their child as being very social, others report their child as having little interest in friendships, preferring to play alone, often able to speak more freely with adults than peers
- poor eye contact (50% according to survey done by KSN)
- poor at understanding the unspoken "rules" of socialization
- poor at understand the give-and-take of a conversation or how to end one
- very literal thinkers, have difficulty thinking abstractly
- unable to 'read between the lines'

Sensory Impairment

- hypersensitive to touch (such as play dough, walking barefoot, etc)
- aversion to loud noises
- aversion to particular smells (cooking smells, etc)
- hypersensitive to visual stimuli
- aversion to particular food tastes and textures (often causing gagging)
- self-stimulatory behaviors such as hand flapping, head shaking, rocking, repeating phrases over and over (over 50% according to survey done by KSN)
- self injurious behaviors such as biting self and head banging
- very oral, many chew on non-food items (over 60% according to survey done by KSN)

Play

- some do not seek out friendships, preferring to play alone or with adults
- others seek friendships but prefer younger children
- many like to play the same thing or watch the same videos over and over

Behaviors

- extreme need to know what to expect throughout the day and exact schedule of events (about 60% according to survey done by KSN)
- repeating of questions over and over
- difficulty waiting
- interrupting often
- talking to self (about 60% according to survey done by KSN)

What does this mean for the child with Kabuki?

It is important to know that developmental delay in general can be accompanied by several types of symptoms and behaviors that one sees with autism (speech and language delay, self-stimulatory behaviors, social impairment, inappropriate behavior). It is true that autism is more easily recognized today and if a child fits into a set of criterion, a diagnosis of autism may come about. This is not to say that the autistic diagnosis is permanent or that it conflicts with the Kabuki diagnosis. With skill development and ongoing intervention, a child may mature and gain ground in an area so that they no longer 'fit' into the autism heading. The fact that our children have Kabuki syndrome is the reason they are demonstrating autistic-like tendencies in the first place. Autism is not necessarily a separate label. More than likely, ALL of our children at some point or other are demonstrating behaviors that could be considered autistic-like. Whether our children have been given an autism label or not, the types of therapy and intervention that we would seek to assist with their areas of need are the same. Many autism treatment approaches are very beneficial for all children facing issues in any of these functional areas.

Growth

Twins Hannah and Zachary on 10th Birthday

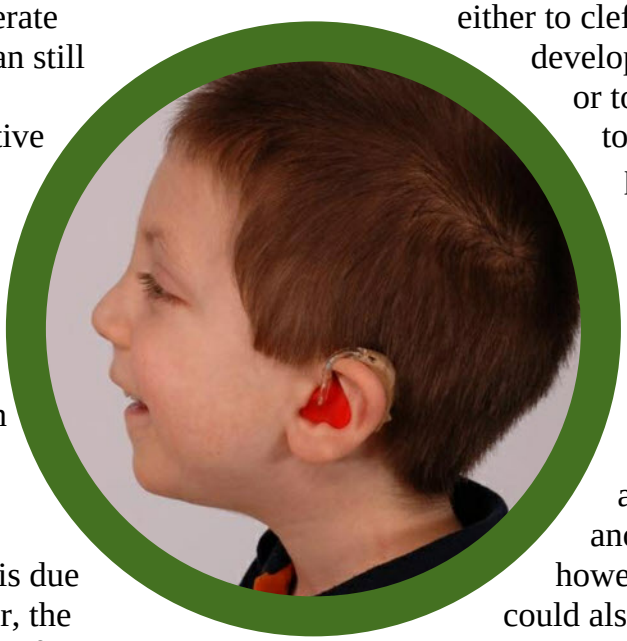
Postnatal short stature is one of the cardinal features of Kabuki Syndrome. It is still unclear as to what extent growth hormone deficiency contributes to this characteristic.

Although birth weight and length are generally normal, growth delay often starts during the first year of life. Poorly coordinated sucking & swallowing, reflux, recurrent infections, cardiac defects, and hypotonia may all be contributing factors. Although growth hormone levels are in the normal range for most children, a significant number have a partial or complete deficiency. Obesity seems to be a common problem during puberty years. The adult with Kabuki will be shorter than the norm – two or more standard deviations below the mean.

Hearing

Hearing loss is a common finding in Kabuki syndrome and can be of three basic types: conductive, sensorineural or mixed.

Conductive hearing loss occurs when sound is not conducted properly through the outer ear, middle ear, or both, such as in ear canal obstruction or in acute otitis media (ear infection). It is generally a mild to moderate impairment because sound can still be detected by the inner ear. Generally, with pure conductive hearing loss, the quality of hearing (speech discrimination) is good, as long as the sound is amplified loud enough to be easily heard. This type of hearing impairment can often be medically or surgically treated.



Sensorineural hearing loss is due to the damage of the inner ear, the cochlea, or to the impairment of the auditory nerve. It can be mild, moderate, severe, or profound, to the point of total deafness. It is a permanent loss and it doesn't only affect sound intensity such as the ability to hear faint sounds but also makes it more difficult for you to recognize complex sounds, to understand speech and to hear clearly.

Mixed hearing loss - In some cases, such as in complication of recurrent/chronic otitis media, a conductive hearing loss occurs in combination with damage of the inner ear or of the auditory nerve. When this occurs the hearing loss is referred to as a mixed hearing loss.

Conductive hearing loss, mainly due to recurrent otitis media, is reported with a frequency ranging from 24% to 82%. In fact chronic otitis media is extremely frequent in individuals with Kabuki syndrome during childhood. It is probably related either to cleft palate and abnormal development of the Eustachian tube or to immune deficiency. It has to be cured in order to limit permanent hearing loss sequelae (mixed hearing loss).

Sensorineural hearing loss is very rare in Kabuki syndrome. Only a few cases are reported in the literature and are mainly caused by anomalies of the inner ear, however this low prevalence could also be due to incomplete neuro-radiological investigations (CT brain) reported up to now in the medical literature.

Some children may utilize a personal or classroom soundfield FM system, either in conjunction with aids or without. The FM system enhances the distance to noise ratio, in the typical classroom, so that environmental/background noise is decreased while the voice of the speaker is amplified.

Dr. Stefania Barozzi

Dr. Di Berardino

Audiological and Vestibular Findings in Kabuki Syndrome

By S. Barozzi [1], F. Di Berardino [1], A. Selicorni [2]

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Note: *For complete study results see: Audiological and vestibular findings in the Kabuki syndrome - Am J Med Genet A Jan15;149A(2):171-6 2009 Author: Barozzi S, Di Berardino F, Atzeri F, Filipponi E, Cerutti M, Selicorni A, Cesarani A*

In Kabuki syndrome there is a high prevalence of otolaryngologic problems such as ear diseases (92%), hearing loss (82%) and airways problems (58%) only partially due to the prevalence of cleft palate. *See Fig. 1*

Concerning the external ear, which consists of pinna and external auditory meatus, minor anomalies are typical of this syndrome and have been described by most authors. Prominent large and cup-shaped ears are the most common findings (85-100%) and one of the diagnostic criteria of the Kabuki facies. However aural atresia (absence of the pinna), small external ears or preauricular fistula can also be present along with accessory auricular appendages (preauricular pits).

Hearing loss is also a common finding in Kabuki syndrome and can be of three basic types: conductive, sensorineural or mixed.

- *Conductive hearing loss* occurs when sound is not conducted properly through the outer ear, middle ear, or both, such as in ear canal obstruction or in acute otitis media. It is generally a mild to moderate impairment because sound can still be detected by the inner ear. Generally, with pure conductive hearing loss, the quality of hearing (speech discrimination) is good, as long as the sound is amplified loud enough to be easily heard. This type of hearing impairment can often be medically or surgically treated.

- *Sensorineural hearing loss* is due to the damage of the inner ear, the cochlea, or to the impairment of the auditory nerve. It can be mild, moderate, severe, or profound, to the point of total deafness. It is a permanent loss and it doesn't only affect sound intensity such as the ability to hear faint sounds but also makes it more difficult for you to recognise complex sounds, to understand speech and to hear clearly.

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Conductive hearing loss, mainly due to recurrent otitis media, is reported with a frequency ranging from 24% to 82%. In fact chronic otitis media is extremely frequent in patients with Kabuki syndrome during childhood. It is probably related either to cleft palate and abnormal development of the Eustachian tube or to immune deficiency. It has to be cured in order to limit permanent hearing loss sequelae (mixed hearing loss).

Sensorineural hearing loss is very rare in Kabuki syndrome. Only a few cases are reported in the literature and are mainly caused by anomalies of the inner ear, such as bilateral absence of cochlea with dilated dysplastic vestibule and unilateral enlarged vestibule. This low prevalence could also be due to incomplete neuro-radiological investigations (CT brain) reported up to now in the medical literature.

In our study of ten patients affected by Kabuki syndrome, seven males and three females, with ages ranging from 10 to 25 years, only three showed normal hearing. We found that a slight mild or moderate hearing loss was extremely frequent since it was evident in 70% of the affected ears.

In this group of ten subjects, all hearing losses were conductive or mixed. We didn't find any sensorineural hearing loss, thus confirming that it is a rare disorder in Kabuki patients.

Otomicroscopy was mandatory to study the condition of tympanic membrane and chronic otitis media complications. Pure tone audiometry was easily performed in seven patients, while three non-cooperative individuals required behavioural audiometry (audiometry used in young children).

In the ears with hearing loss the most frequent finding was otitis media and its consequences (otitis media with effusion, serous adhesive otitis media, antroatticotomy and tympanomastoidectomy).

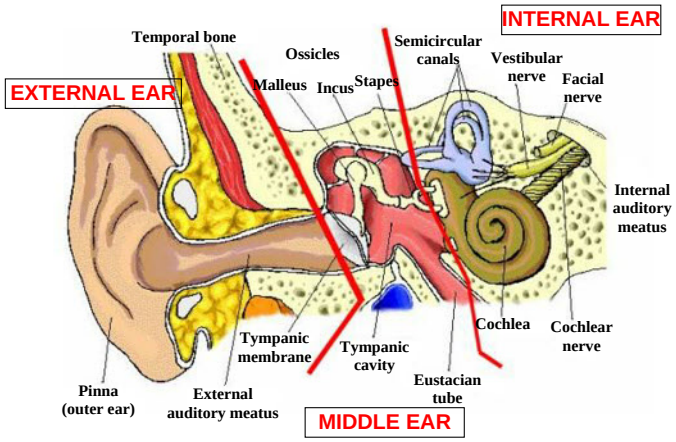

Fig 1

In Kabuki patients, the frequency of otitis media is likely related both to the high incidence of infections and to the Eustachian tube impairment. In our study, none of the seven patients affected by otitis media and its complications had had a cleft palate. These findings support Peterson-Falzone et al. (1977) who indicated that the prevalence of ear disease in Kabuki syndrome cannot be explained solely on cleft palate and suggested that hearing loss in Kabuki syndrome requires the diagnosis and treatment expertise of audiologist and otolaryngologists.

The hearing loss in the other impaired ears was related to aural atresia in one ear and, in 5 ears, it was associated with a normal otomicroscopy and, in immittance audiometry tympanometry, with the absence of stapedial reflexes suggesting a possible ossicular fixation. As reported in literature, the skeletal anomalies frequently observed in Kabuki patients might also involve the middle ear ossicles with a fixation of the joints. Therefore we suggest to always perform a complete hearing test that includes pure tone and immittance (tympanometry and stapedial reflex determination) audiometry.

In our experience the vestibular evaluation was difficult in the Kabuki subjects since they cannot offer the cooperation needed for caloric examination. Caloric test is used to evaluate the peripheral vestibular function through the irrigation of cold and warm water into the external auditory canal. This test can be carried out exclusively in cooperative patients with no anomalies of the external ears, tympanic membrane perforation, or oto-surgical outcomes. In our patients, caloric tests have been possible only in six subjects.

In the restricted group of patients examined for the vestibular function, 92% showed normal results. In particular, all the ears studied with caloric tests were normoreflective. As the vestibular caloric stimulation was impossible in the patient with aural atresia, the implementation of bone VEMPs was useful, revealing a saccular impairment on the side of the abnormal ear. Vestibular Evoked Myogenic potentials can be used to investigate saccular function, measured from the tonically contracted sternocleidomastoid muscles in response to bone conducted sound stimuli at 70 dB SPL. The saccule is a small labyrinthic sac situated between the cochlea and the semicircular canals. Also this test requires patient cooperation to keep the head elevated in order to contract the sternocleidomastoid muscles.

In view of these findings, it would be advisable to study each patient affected by Kabuki syndrome through audiological examinations and reserve the vestibular assessment for selected patients with vestibular symptoms, with sensorineural hearing loss or inner ear abnormalities.

In conclusion we recommend audiological evaluation in all patients with Kabuki syndrome and vestibular assessment in selected individuals.

Speech

Delay in speech and language acquisition is very common, exacerbated by craniofacial anomalies, hypotonia, and poor coordination.

Articulation errors are common and are likely due to oral-motor hypotonia and general poor coordination. It is not felt that structural abnormalities such as velopharyngeal insufficiency, dental malocclusion and cleft palate are major contributors.

Also common is abnormal oral resonance, again likely due to oral-motor hypotonia and not structural abnormalities. Resonance is the quality of the voice as the result of sound vibrations in the pharnyx (throat), oral cavity (mouth) and nasal cavity (nose).

Abnormal prosody, defined as the the rhythm, stress and intonation of speech, is evident in many children. One study showed that the prosody and articulation errors became more pronounced when spontaneous speech increased in length and complexity. It also found that pitch, loudness and prosody did not mature significantly over time, despite ongoing speech services, resulting in inappropriate and difficult to understand speech production by adolescence. More long term follow-up studies of the distinctive speech patterns of Kabuki Syndrome are needed. This will hopefully lead to better tailoring of speech-language therapies, specific for Kabuki.

Theresa Cinotti

Kim Tillery

The CAPD Model and Kabuki Syndrome

By Theresa Cinotti, M.A., CCC-SLP & Kim Tillery, Ph.D., CCC-A

What is Central Auditory Processing Disorder (CAPD)?

CAPD is not how one hears, but rather "what one does with what they hear". Clients with a CAPD display a wide range of functional behavioral limitations: difficulty understanding or remembering auditory information, weak phonemic skills, intolerance to noise, difficulty understanding speech in background noise, frequently require directions to be repeated, substitute improper speech sounds, display weak reading, spelling, organization and comprehension skills, and often act as if they have a hearing loss.

There are different types of CAPD that dictate specific therapy regimens. Decoding type of CAPD involves a breakdown at the phonemic level where the client struggles in understanding each sound, displays weak reading and spelling skills and requires a long time to respond. A second type of CAPD is known as Tolerance-Fading Memory (TFM) which involves weak short-term memory resulting in poor reading comprehension and weak expressive language skills. Often those with TFM forget the first set of information verses the final set. A third type of CAPD is known as Organization, as weak sequencing and organization abilities are characteristic of this type. A fourth CAPD subtype is Integration, involving poor language and phonemic ability and severe reading and spelling delays.

While an audiologist is the professional who diagnosis the types of CAPD, it is usually the speech-language pathologist who provides therapy and who also evaluates language skills. Most individuals with a CAPD exhibit normal hearing. The etiology is unknown although it is speculated that a history of ear infections and genetic links may be related.

LIZ

Liz was first diagnosed at 14 years of age with Kabuki Syndrome. Currently at age 22 years, she presents with several characteristics related to the syndrome, such as a submucous cleft of the palate, hypotonia, visual perceptual difficulty and mild-to-moderate cognitive challenges. Hearing problems include sensorineural (inner ear) and conductive (middle ear) hearing impairment with recurrent bouts of ear infections. In addition she exhibits speech-language delays and increased nasality of speech.

Liz was first referred for a CAPD evaluation at 16 years of age by a reading specialist as Liz could write the grapheme (letters), but was unable to make the sound-symbol relationship. For example, Liz was able to write her name, but did not understand the relationship of the sounds to the letters, an essential precursor to reading, rhyming and spelling. The reading teacher reported a lack of understanding of left to right scanning of words across the page and also noted that Liz was unable to perform on preschool literacy testing.

The CAPD evaluation indicated two subtypes of CAPD: TFM and Decoding and Liz was referred for CAPD therapy. She received two 50-minute therapy sessions, per week for one and half years, targeting the Decoding CAPD subtype. Therapy consisted of Phonemic Synthesis Training Program (Katz and Fletcher, 1982), Visual-Rhyming Therapy, and general auditory training exercises.

Phonemic Synthesis Training Program consists of 15 lessons to expose the client to the concept of sounds in words by auditorily presenting one sound at a time for which the client is instructed to properly blend the sounds into the target word. For example, the client hears: "b-oa-t" and should respond "boat" without any form of delay or struggle. The goal of this program is to enhance the client's ability to properly perceive sounds in words and utilize that skill in higher level of comprehension, reading and spelling tasks.

Visual-Rhyming Therapy is a technique derived from Soundabet, a training activity in the Processing Power program (Ferre, 1997), which assists the client to recognize sounds and sound patterns represented by all graphemes (letters), thus enhancing rhyming skill. For example the

client is presented a target pattern such as “at” and must rhyme this provided word or nonsense word using all probable consonant sounds. The client would respond with, “bat, dat, fat, gat, hat, jat, kat, lat, mat”, etc. with the visual cue provided in left-to-right format.

b d f g h j k l m

n p r s t v w y z

Upon the success of accurately blending the above consonants with the target pattern, the chart is expanded to include consonant blends, such as br, bl, dr, fl, fr, and st, etc.
This therapy enhances knowledge of left-to-right reading, phonemic and phonological awareness, rhyming, and sound-symbol awareness, again all skills needed for comprehension, reading and spelling. General auditory training exercises were used to supplement the above therapies. Therapies utilized would be considered aural rehabilitation (AR) therapies, although the impact is often seen in language and written language development.

After completing the above therapies, Liz demonstrated progress in the areas of focus. On the Phonemic Synthesis Test (Katz and Fletcher, 1981), a measure of Liz’s sound blending skills, Liz’s progress was follows:

Pre Therapy:
4 accurate responses
1 year later:
19 accurate responses

Lesson 12 of the Phonemic Synthesis Training Program was administered as a baseline measure prior to beginning the entire Phonemic Synthesis Program (lessons 1 through 15). On Lesson 12 Liz performed as follows:

Pre Therapy:
2 accurate responses
3 months later:
21 proper responses
1 year later:
39 proper responses

In August of 2002, at 19 years of age, Liz entered a therapy program which focused on further enhancing auditory decoding and phonological awareness skills while concurrently fostering language abilities, in essence combining aural rehabilitation and language therapy techniques for functional generalization of skills learned.

With this new therapy program, sound blending was a continued focus with sound segmentation added to the challenge. Sound segmenting tasks involve an individual hearing a word, perceiving the sounds in the word, and then being able to identify the sounds individually and in sequence, the inverse of a blending task. For example, if asked to segment the word “tent” the individual would be verbally presented with the word and then required to say the sounds “t-e-n-t”.

Being able to perceive the sounds in a word is a precursor to actual spelling abilities and an aid to fluent reading. As segmenting skills develop, an individual is then challenged to represent sounds with symbols. At first arbitrary symbols such as blocks may be used and, later, the actual graphemes (letters) will be added. As an example, when segmenting the word “ten” an individual may verbally respond “t-e-n” and place three different colored blocks on the table, representing the three different sounds heard. They then could assign letters to correspond to the blocks to actually spell the word. As segmenting skills and sound symbol association skills increase, an individual’s spelling as well as reading skills should subsequently improve. The aforementioned methodology is similar to that advocated in programs such as the Lindamood Phoneme Sequencing Program (Lindamood and Lindamood, 1998), the Phonological Awareness Kit (Robertson and Salter, 1997), and the Ortan Gillingham Program (Institute for Multi-sensory Education), to name a few.

When Liz first began attempting segmenting tasks she required maximal support to separate the sounds in two phoneme (sound) words (ie. no = n-o). As therapy progressed, she was able to consistently identify the sounds in two sound words and also represent the number of sounds heard using arbitrary symbols (colored blocks). Liz continued to progress in segmenting and is currently able to segment four phoneme words using colored blocks and match blocks to appropriate letters with some consistency. Liz is able to match sounds to corresponding consonants approximately 90% of the time with less consistency with matching vowel sounds to letters. However, using this structured system with a speech-language pathologist to guide her through the process, Liz is able to spell two, three, and four sound words with minimal error. Some carryover is seen in spontaneous spelling of words outside of the clinic setting, however, Liz has not fully generalized her skills and continues to work toward independence in this area.

Given that the development of decoding and phonological awareness skills begins in infancy and continues through a child’s school years, LS has made remarkable progress in “catching up” over the last six years of her life to reach a level of phonological processing consistent with early readers. Her most recent testing, using the Phonological Awareness Test (Roberson and Salter, 1997) revealed rhyming skills to be at a 5 year 2 month level and segmentation skills to be at a 5 year, 4 month level. Liz’s ability to isolate sounds in words (determining what sound

was heard at the beginning, middle, or end of the word) was found to be at a 6 year, 0 month level, and her deletion skills(ability to determine what the remaining sounds in a word are when a sound or set of sounds are deleted – say "bat", say "bat" again without the "b") were found to be at a 5 year, 10 month level.

As Liz continues on her journey toward enhanced skills it is a goal to have her consistently make sound symbol associations for functional vocabulary that she will encounter in her environment or during her daily routine. In addition to using decoding therapies to enhance spelling and reading ability, sight word reading is also a focus to enhance comprehension and use of written words pertinent to Liz's vocational, academic, and personal life. Visualization, association, and first letter cuing strategies are currently utilized to develop Liz's recognition of words. Although Liz requires several weeks for the establishment of each new set of sight word vocabulary, this practice has allowed Liz to use, recognize, and read words too complex at this point in her development to sound out independently. Recently, in addition to sight word recognition, common phrases have been targeted for recognition. The goal is to have Liz recognize common phrases from a list of phrases that she will use as a cue to independently create appropriate written language, particularly targeting e-mail communication with friends and relatives.

(L to R)Theresa Cinotti, Liz S, and Dr. Kim Tillery

In addition to written language (spelling, reading, and writing), Liz's understanding and use of language has been targeted through the years. Particularly, Liz has made outstanding progress in compensating for auditory comprehension issues resulting from language delay and hearing loss and compounded by her auditory recall difficulty and perception related to her auditory processing disorder. Liz has developed and frequently utilizes strategies such as attending to visual cues (body language and lip reading), recognizing comprehension breakdowns, and repairing breakdowns through asking for repetition or clarification.

Liz's expressive language has continued to blossom with therapy targeting expansion of simple utterances to form complex. In addition, pragmatic skills, which are interaction abilities have flourished as Liz's practice and maturity have resulted in improved conversational abilities. As language and auditory processing skills have developed, Liz has been able partake in functional activities geared to enhance daily living through improved organization and problem solving. For example, medication recognition and organization, calendar planning, event planning, and situational problem solving and role-playing have contributed to enhancement of Liz's overall independence. Liz has made outstanding progress through the years in all aspects of her communication and overall development. Liz's successes are likely a function of her positive attitude and the outstanding support that she receives from each of her family members. Liz consistently attends and participates in scheduled sessions, and carryover of skills is facilitated by family as her mother regularly attends sessions and continually communicates with Liz's speech-pathologist, audiologist, and ENT to optimize care. Continued success is projected for Liz's future. Liz's story has been shared at numerous conferences and serves as an inspiration to professionals, conveying the message that those with multiple challenges can achieve amazing feats with the appropriate therapies and supports. Central auditory processing therapies have been integral in Liz's skill development, particularly related to her comprehension skills and her reading, writing, and spelling development. The first step in proper treatment planning is appropriate evaluation. Those suspecting an auditory processing disorder, should consult a qualified audiologist with verbal and written language skills assessed by a speech-language pathologist. It has been an honor to work with Liz and her family. They are truly an inspiration to all.

About The Authors

Theresa M. Cinotti, M.A., CCC-SLP
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Theresa is currently the Speech-Language Coordinator and one of the clinical supervisors at the University at Buffalo Speech-Language and Hearing Clinic, a training clinic for graduate students pursuing their master's degree in speech-

language pathology. Theresa runs the Intensive Language and Auditory Processing Program at the University, an intensive summer program which addresses the language and auditory processing needs of children ages 5 years and older. In addition, Theresa coordinates the adult language and auditory processing program at the University, a program which focuses on optimizing processing skills and functional communication for adults with auditory processing and related issues.

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Dr. Kim Tillery has authored one chapter and co-authored four chapters and several peer-reviewed journal publications regarding Auditory Processing Disorders (APDs) and it's relationship with Attention Deficit Hyperactivity Disorders (ADHD). Invited international, national and state presentations include her research of 1) Ritalin's effects on APD, 2) therapeutic measures for Decoding and Integration types of ADP, 3) the co-morbidity of attention, learning and auditory processing deficits, and 4) how reliable differential diagnosis improves effective management of ADHD, LD and APD. Besides her teaching and research Dr. Tillery maintains a private practice, has served as the Co-President of the Speech-Language and Hearing Association of Western NY (SHAWNY) for two-years, received the 2003 SHAWNY Award for her dedication and service to the communicatively disabled of WNY, and serves on other Professional Advisory Boards and Committees.