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# **Kabuki Syndrome: A Challenge for the Primary Care Provider**

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**Abstract**

This is a case study of a pediatric patient with a genetic disorder called Kabuki syndrome. The patient's medical history and pathophysiology are examined. In addition, a discussion of current advanced medical research and treatment in the area of genetics relating to Kabuki syndrome is explored. Ethical, social issues and disease prevention are included along with the financial impact this disorder can have on the family unit as a whole. Finally, the theoretical framework created by Merle Mishel with her Uncertainty in Illness Theory is utilized to help expand on the role of the advance practice nurse (APN) as a primary care provider who is treating a patient with Kabuki Syndrome.

## **Kabuki Syndrome: A Challenge for the Primary Care Provider**

### **Introduction**

This is a case study of a 2.5 year old Hispanic male, E.R., who was born with Kabuki syndrome. The initial meeting with this child took place during a clinical rotation at a local pediatric ambulatory care center. His unusual diagnosis and the extraordinary relationship that was observed between the office staff and this patient's family greatly intrigued the observer. This created an interest in this syndrome and its pathophysiology. There was also curiosity as to how the family was coping with the tremendous burden of caring for a child with a syndrome that requires special needs. It is a disorder that is so uncommon that much of the research has only been conducted in the last thirty years. This paper examines the pathophysiology, ethical, social, financial and family dynamics associated with this rare genetic condition.

Kabuki Make-up or Niikawa Kuroki Syndrome was first described in 1981 by two doctors, Dr Niikawa and Dr.Kuroki who were working independently in Japan studying this disease. The name "Kabuki make-up" was selected because of the facial resemblance to the makeup of actors in Kabuki, a traditional Japanese theatre form. The term "make-up" was later dropped from the name (Schmiedge, 2009). It is now described as a multiple congenital anomaly mental retardation syndrome characterized by distinguishing facial features. These include arched eyebrows, thick eyelashes, eversion of the lateral lower lid, and long palpebral fissures which all contribute to this resemblance, especially in children of Asian descent (Schmiedge, 2009). The cause is still yet unknown and there are only 350 known cases worldwide (Morris, 2007). This syndrome occurs in approximately 1 out of 32,000 births (Schmiedge, 2009). The proportion of male to female occurrence is equal and no correlation with birth order has been found (Morris,

(Morris, 2007). For the great majority of children, chromosomal studies yield normal results (Schmiedge, 2009). Microscopic deletions or duplications do not presently exhibit themselves in the chromosomal studies (Schmiedge, 2009). There is no prenatal screening, genetic test or consensual diagnostic criteria to confirm this condition. The patients are diagnosed according to the recognizable facial features (Lung & Rennie, 2006).

The children are of normal size at birth but have postnatal growth deficiency where 80% of these patients have a short stature. The typical facial features are present from an early age aiding the clinical diagnosis. Clinical recognition of the syndrome in the neonate is difficult as the phenotype appears to evolve with time (Morris, 2007). The diagnosis is, on average, made by the age of two years (Lung & Rennie, 2006). The mean IQ of children with Kabuki Syndrome is 62 which are consistent with mild retardation. Expressive language is delayed and visual-spatial abilities are impaired. Math skills tend to be a relative strength (Morris, 2007). Autism spectrum disorder has been reported in approximately 16% of patients (Adam & Hudgins, L. 2004). Most individuals with Kabuki have mild to moderate intellectual disability. Delay in speech and language acquisition is very common, exacerbated by craniofacial anomalies, hypotonia, and poor coordination. Sensory issues include need for oral stimulation, tactile defensiveness towards various sensations and stimuli, panic-like reactions to certain noises, and aversion to textures and/or smells of select foods. Individuals with KS have a need for routine. They have a tendency to fixate on certain activities or thoughts. It appears they have excellent memories for face recognition, song lyrics, and dates of events. Anxiety, obsessive/compulsive traits and autistic-type behaviors are commonly observed (Schmiedge, 2009).

A cleft or high arched palate has been observed in 80% of the patient's with this condition (Morris, 2007). Other less frequent craniofacial abnormalities can include epicanthal folds,

ptosis, strabismus, malformed ears, and micrognathia, abnormal or absent teeth, widely spaced teeth, and a low posterior hairline. The ears are large and prominent in 85% of individuals with this syndrome (Morris, 2007). Hearing loss is common. Other dysmorphic features include skeletal abnormalities. The most common is a short incurved 5<sup>th</sup> finger (Schmiedge, 2009). Vertebral anomalies can include butterfly vertebra, sagittal cleft, narrow intervertebral disc space, spina bifida occulta, and scoliosis (Schmiedge, 2009).

Congenital heart disease occurs in 30-50% of individuals (Morris, 2007). The most common heart defects are ventricular septal defect (VSD), atrial septal defect, (ASD), and bicuspid aortic valves (Morris, 2007). Other abnormalities include undescended testes in males and urinary tract malformations. A characteristic feature is prominent fingertip pads in all fingers (Upton, Stadler, Landis, et al, 2003).

Medical complications reported in Kabuki Syndrome include recurrent otitis media in 50%, hearing loss in 24%, early breast development in 25% of females, obesity with onset at puberty in 20%, and seizures in 15% (Morris, 2007). Infants are hypotonic and poor feeders (Morris, 2007). Chronic otitis media is a significant problem. IgA and IgG may be decreased, and autoimmune diseases, such as ITP, occur more frequently (Morris, 2007). Endocrine problems reported in some patients include diabetes, hypothyroidism, growth hormone deficiency, and precocious puberty. For an individual with Kabuki Syndrome, the recurrence risk is presumed to be 50% with each pregnancy (Morris, 2007). The prognosis of survival to adulthood is relatively good as Kabuki Syndrome is not typically associated with severe medical complications (Lung & Rennie, 2006).

There is too wide a range of abilities to make a general prediction as to the future of these patients as they reach adulthood. The answers to whether or not these patients will be able to live on their own are dependent on the individual capabilities and their support systems.

A study done in 2004, which included long-term follow-up of three individuals with Kabuki, found that although all three adults achieved independent daily living skills and were able to hold part-time jobs, they all needed to live in sheltered environments. As a result, appropriate long-term planning is needed (Schmiedge, 2009).

Kabuki is not a progressive condition and is not typically associated with severe medical complications (Schmiedge, 2009). It is presumed the prognosis for survival into adulthood is good, particularly if congenital anomalies, such as congenital heart defects, and infections are properly managed in childhood (Adam, & Hudgins, 2004). However, new conditions can arise later in life due to having this disorder. Most of those conditions will be ongoing issues experienced in childhood; increased susceptibility to infections, dental issues, or cardiac problems (Schmiedge, 2009). Furthermore, there are some conditions that may only appear for the first time when these patients become older (Schmiedge, 2009). Some children will develop seizures as late as middle childhood (Schmiedge, 2009). Loose ligaments and hypotonia may cause joint or patella dislocations in teen or adult years (Schmiedge, 2009). The adult with Kabuki will be shorter than the norm; two or more standard deviations below the mean (Schmiedge). Hemolytic anemia, hypogammaglobulinemia, and low IgA levels have all been reported (Morris, 2007). Obesity can lead to associated health problems such as diabetes mellitus, high blood pressure and joint problems. There is still little evidence regarding the long-term follow up of individuals with Kabuki (Schmiedge, 2009).

## The Patient

### *History of Present Illness*

E.R. came to the clinic in March of 2009 during an acute care visit. He was 2.5 years of age at the time and had chief complaints of fever and cough for over one week. His mother took him to the emergency room five days prior to this appointment because of a fever over 104°F and chest congestion. He was diagnosed with pneumonia. The patient received a dose of IV antibiotics and was placed on a course of oral antibiotics for ten days. He also was receiving Albuterol nebulizer treatments every four hours and Pulmicort twice a day for his cough and wheezing. His mother stated he had vomited a few times from the coughing spasms, but was still able to tolerate an intake of fluids such as Pedialyte.

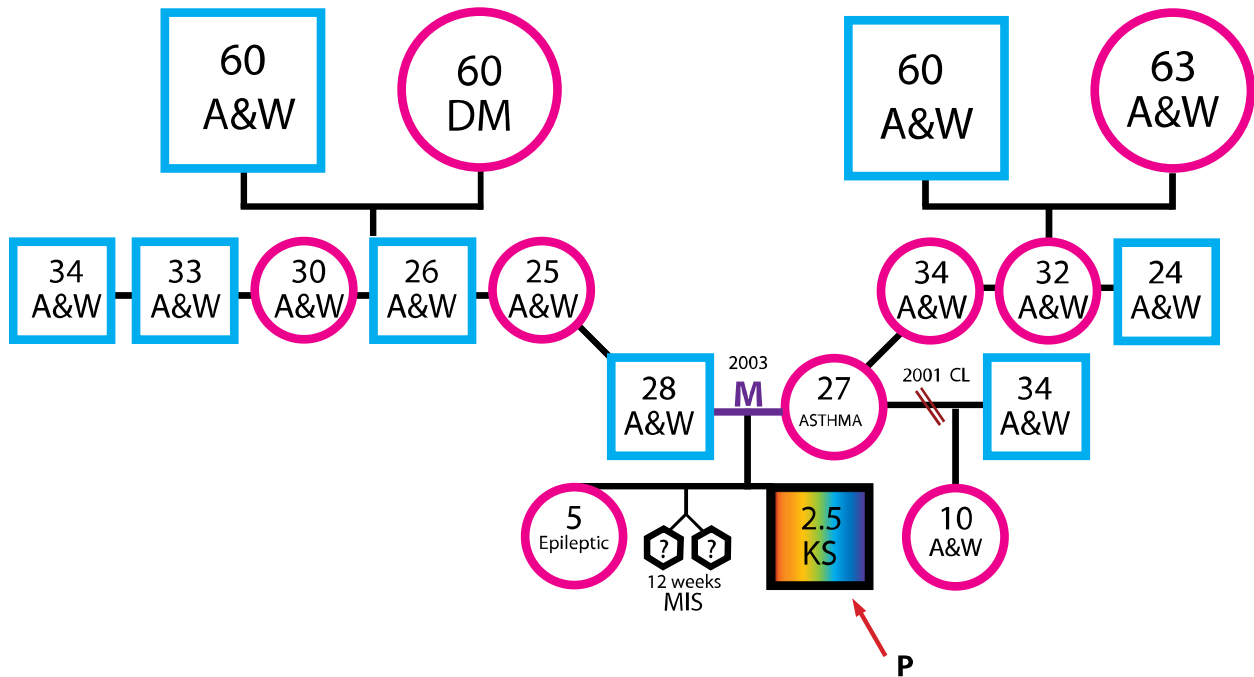
E.R. visited the clinic on May 29, 2009. The chief complaints were coughing and a fever of 103°F which occurred intermittently for two weeks. His mother was administering oral antibiotic therapy with Amoxicillin, Albuterol treatments every four hours along with the Pulmicort twice a day without relief of his cough. His most current chest X-ray showed no infiltrates to his lungs. At this time he was eating well and drinking fluids. It was decided by the attending physician to stop the antibiotics because she felt the fevers were most likely secondary to a viral etiology. If the fever continued over the weekend, the patient would return to the clinic for a blood work-up and urinalysis. The mother was instructed to use the Albuterol only if the child was wheezing and not as a prophylaxis.






*Prenatal and Family History*

E.R. was first seen at the age of five months by Dr M., a geneticist. An extensive medical genetics evaluation was completed in 2007 when the patient was 11 months old by Dr. M. and is in his current medical record. It is a detailed assessment based on the family history and patient's own medical history. According to the information in the medical record, the parents of E.R. were in good health. The father's height is 5 feet and 7 inches. The mother's height is 5 feet and 6 inches. The mother has a history of asthma. The paternal grandmother has diabetes. There is no history in the family of mental retardation, birth defects or known consanguinity. The mother has a nine year old daughter from a previous union who is in good health. The couple has a four year old daughter who is epileptic. The mother had a miscarriage of a twin pregnancy while at home when she was at 12 week's gestation.

E.R. was the product of the mother's fourth pregnancy. She was 24 and the father 26 at the time of the patient's birth. Both parents had no known exposures to human teratogens such as cigarette smoke, illicit drugs or alcohol. The mother did have some fever during the second trimester of pregnancy but was unable to obtain regular prenatal care due to lack of insurance. She was admitted to the hospital during this pregnancy because of episodes of vaginal bleeding and signs of miscarriage. A maternal serum alpha-fetoprotein (AFP) was performed during her second trimester and revealed an elevated risk for Down syndrome. The mother declined to have an amniocentesis.

# FAMILY GENOGRAM



-  = Male
-  = Female
-  = Male Subject
-  = Twins Unknown Sex
-  = Breakup

- A&W = Alive & Well
- DM = Diabetes
- KS = Kabuki Syndrome
- M = Marriage
- CL = Common Law
- MIS = Miscarriage
- P = Proband

### *Birth History*

E.R. was delivered at 37 weeks gestation by repeat cesarean section at a local hospital. A heart murmur was detected at birth along with some dysmorphic features. His birth weight was 6 pounds and 13 ounces which graphs in the 25th percentile on the growth chart; his birth length was 18.5 inches and in the 10th percentile. There was no documentation of his head circumference or APGAR scores in the record. A cardiologist evaluated the infant and found the echocardiogram and electrocardiogram to be normal. He was discharged home with his mother after passing a newborn hearing screen and receiving the Hepatitis B vaccine.

### *Current Health*

The patient has visited his current pediatric clinic since January, 2008 for well child checks along with acute care visits. His immunizations are up to date. He has no known allergies and currently takes Zantac 75 mg p.o twice a day; Keppra 250mg twice a day; Pulmicort 0.5mg twice a day; Albuterol 2.5mg per unit every 4 to 6 hours as needed; and Auralgan ear drops to both ears twice a day as his medications.

### *Diet and Nutrition*

E.R. eats an age appropriate diet such as fruits, vegetables, and meats. His mother reports that he does not appear to chew and typically will swallow foods. Therefore, she has to cut the food into small pieces. He drinks four cans of Pediasure (237 calories) a day which equals approximately 1000 calories. The total caloric intake for a child this age should be approximately 1300 calories. His weight has been consistently in the 25 percentile on previous exams.

### *Personal and Social History*

E.R. lives with his mother and five year old sister in a house in North Las Vegas. He has an

works in California due to the current economic conditions here in Las Vegas. He has been married to the child's mother since 2003 and visits his family once a month. E.R.'s mother does not smoke or work outside the home. The family does not have any pets. E.R.'s maternal grandparents, aunts and uncles live nearby to help with child care.

#### *Past Medical History*

E.R. was admitted to the hospital at one month of age in order to repair bilateral inguinal hernias and have a circumcision performed. He was also noted to have an umbilical hernia but did not have surgical intervention at the time. At age three months he turned blue at home and was admitted to the hospital for a work-up of febrile seizures. They were described as convulsive type seizures lasting less than five minutes in duration. He was having two to four of these seizures during any febrile illness. He developed non-convulsive seizures without fever at approximately two years of age. His mother reported he would stop in the middle of his activity and stare off unresponsively for two to three minutes. He would try to sit down or lean over something and would occasionally fall down. After the seizure, E.R. would be very lethargic. The seizures occurred about twice per month. He was evaluated by a neurologist and is currently on anticonvulsant treatment with the oral medication Keppra 250mg twice a day for seizures consistent with complex partial epilepsy. The latest EEG findings were not available in the patient's medical record for review.

E.R. was also diagnosed with gastroesophageal reflux as an infant and was on Zantac 75mg twice a day. During infancy he was spitting up and vomiting. However as a toddler, he was exhibiting regurgitation symptoms that were audible. An esophagogastroduodenoscopy was performed in September, 2008 and revealed active eosinophilic esophagitis which continues to be treated with the medication, Zantac.

A sleep study performed in February, 2008 was non-conclusive. E.R.'s mother stated the test was performed on a night her son was having difficulty falling asleep. He did not have stretches of sleep that were more than one hour in length. E.R. and his mother were sent home from the lab at 4:00 a.m. prior to the test being completed. Therefore, his mother does not trust the results of the sleep study. Currently, the patient still has a very poor quality of sleep.

He cries at night and has difficulty breathing due to choking. This causes him to wake up frequently. His mother wants to have this problem further investigated. He was scheduled to have a second sleep study completed in August of this year.

Other surgeries performed on E.R. were bilateral myringotomies in June, 2008, an umbilical hernia repair and exploration of his nasolacrimal ducts in September of 2008. His mother reports that E.R. has a hearing loss in his right ear. The doctors told her it was due to the unusual anatomy of his ear structures and his ear canals are arched "down" towards his throat. Since his ear tubes were placed the patient has had a slight improvement in hearing. However, his mother states E.R. continues to have recurrent ear drainage. The drainage is happening approximately three to four times a month and is brownish in color. E.R. has periodic fevers that seem to coincide when the drainage reoccurs. An ENT specialist recently prescribed Auralgan drops twice a day for the ear drainage. The physician informed his mother if the otorrhea continues the patient may require bilateral tympanostomy tube removal. He also recommended the child have an updated audiogram.

E.R. was hospitalized numerous times for respiratory infections including pneumonia. Because of his frequent emergency room visits, (over five just in the month of February, 2009) the patient is being worked up for a possible immunodeficiency and is presently being followed by a hematology specialist.

Past evaluations have included chromosome studies that were normal (46, XY). A CT scan of the head and MRI were also both normal along with an EEG. He has been seen twice by a cardiologist; once in September, 2006 and again in March, 2007. His echocardiogram was essentially normal and initially showed mild peripheral pulmonary artery stenosis which has since resolved. Currently, his cardiac findings remain normal. A retroperitoneal ultrasound was completed in September, 2007. His kidneys did show some asymmetry and were noted to be at the upper limits of normal for his age. An X-ray of his spine indicated there are no vertebral abnormalities (from patient's current medical record).

Developmentally, E.R. smiled at three months, rolled over at four months, and was able to tripod sit at five months. At ten months he began pulling to a stand and cruising. This patient was evaluated by the State of Nevada's Early Intervention Services (NEIS) when he was twenty-five months old. At that time he was repeating less than thirty words and signing less than five words. He was unable to remove any of his clothing or assist with dressing. He did not recognize any of his body parts. E.R. was able to make great eye contact with the examiner from NEIS and smiled several times. He was also able to follow simple commands but did not speak any words. He consistently responded to his name. E.R. did not point to items of interest but tried to get things independently. During the interview he appeared to have absence of fear. His mother reported her son often rocked himself and had some imitative behavior. He also liked to head bang and sit in the closet. He was not able to sleep very long at night and had difficulty transitioning to sleep. It was also documented in this report that the child was very cooperative throughout the examination.

The final impressions and recommendations from Nevada Early Intervention Services were that his physical exam was significant for dysmorphology and speech delay. He demonstrated

some peculiar behaviors but did not fit the criteria for Autism disorder although he did have some autistic-like features. Early intervention services recommended behavior modification strategies targeting his head banging in addition to a neurology referral for his irregular sleeping pattern. A pediatric dental evaluation, speech and sign therapy were recommended in addition to a follow up with the geneticist. It was also suggested that the entire family would benefit from respite care and counseling (Clemons, 2008). Currently, his mother reports E.R. has speech therapy sessions once a week by Nevada Early Intervention Services and has a vocabulary of approximately thirty words.

### *Review of Systems*

His mother reports E.R. is an active child who is developmentally delayed. His verbal abilities are delayed but he is happy to speak and is very engaging. He has not had any problems with rashes and occasionally has dry skin. His black hair is long and kept in a pony-tail with an elastic band. He does have staring spells and his right eye turns inward. Presently, he still has occasional ear drainage and has a right-sided hearing loss. He has all of his deciduous teeth but has dental malocclusion. E.R. has no known heart problem but does have problems with frequent respiratory infections. He currently wears diapers but is still being potty-trained. The patient has not had any problems with urinating but does get occasional diarrhea when he is taking oral antibiotics. E.R. is able to move all his extremities and is very active and playful. During the exam he interacts well with his mother and five year old sister.

### *Current Medications*

E.R. is currently on Ranitidine (Zantac) one teaspoon (15mg/ml) or 75mg by mouth twice a day; Levetiracetam (Keppra) 250 mg by mouth twice a day; Budesonide (Pulmicort) 0.5mg per nebulizer treatment twice a day; Albuterol nebulizer 2.5 mg unit every 4 to 6 hours as needed

for wheezing. He was recently prescribed Auralgan ear drops twice a day for his ear drainage by the ENT specialist. He also receives Acetaminophen (Tylenol) 160mg by mouth every four to six hours as needed for fever.

The Ranitidine was prescribed for the patient's active esophagitis that was confirmed as eosinophilic esophagitis by an esophagogastroduodenoscopy performed in September, 2008. Eosinophilic esophagitis can occur at any age.

In infants and young children, eosinophilic esophagitis presents with symptoms similar to those of GERD but fails to respond to conventional acid blockade therapy. Dysphagia and food impaction can occur in older children and adolescents. Eosinophilic esophagitis is often seen in patients with atopy who have asthma, eczema, or chronic rhinitis or in those who have a family history of atopic disease. Endoscopy may reveal a ringed appearance or linear furrows. Standard biopsy findings reveal severe eosinophilic infiltration; more than 15-20 eosinophils per high-magnification microscopic field are necessary for diagnosis. The biopsy results for E.R. showed scattered occasional eosinophils in the specimen. There was no evidence of Celiac Sprue disease or H. Pylori identified. In contrast to GERD, eosinophilic esophagitis involves the mucosa, submucosa, and, possibly, the muscularis. Multiple food antigens (e.g., eggs, nuts, beef, wheat, fish, shellfish, corn, soy) can induce eosinophilic esophagitis; cow's milk protein is the most common precipitant. Eosinophilic esophagitis is currently diagnosed based solely on endoscopy findings. The exact pathophysiology of eosinophilic esophagitis is unknown, but contact of the allergen with the esophageal or intestinal mucosa is thought to be the initiating event (Wen, Chu, Mascarenhas, et al, 2005).

E.R. has a history of febrile seizures and presently has recurrent complex partial epilepsy seizures. These are being controlled by the medication, Levetiracetam (Keppra).

Central nervous system involvement is frequently reported in Kabuki syndrome. Together with mental retardation, epilepsy can be a primary feature of this disorder. The incidence of seizures in Kabuki syndrome is 10 to 40%. (Ogawa, Yasumoto, Tomoda, et al, 2003).

A febrile seizure occurs when a child contracts an illness such as an ear infection, cold, or chickenpox accompanied by fever. Febrile seizures are the most common type of seizure seen in children. Two to five percent of children have a febrile seizure at some point during their childhood (Baumann, 2008). Why some children have seizures with fevers is not known, but several risk factors have been identified. These include children with relatives, especially brothers and sisters, who have had febrile seizures, are more likely to have a similar episode. In this instance E.R's sister had seizures between the ages of four months and three years which required pharmacological intervention. Children who are developmentally delayed or who have spent more than 28 days in a neonatal intensive care unit are also more likely to have a febrile seizure. One of four children who have a febrile seizure will have another, usually within a year; children who have had a febrile seizure in the past are also more likely to have a second episode (Baumann, 2008). The setting is fever in a child aged 6 months to 5 years whereas the single seizure is generalized and lasts less than 15 minutes (Baumann 2008).

Complex partial seizures cause impaired consciousness and arise from a single brain region. Impaired consciousness implies decreased responsiveness and awareness of self and surroundings. During a complex partial seizure, the patient may not communicate, respond to commands, or remember events that occurred. Consciousness might not be impaired completely. During a complex partial seizure, some patients may make simple verbal responses, follow simple commands, or continue to perform simple or, less commonly, complex motor behaviors. Complex partial seizures typically arise from the temporal lobe but may arise from any cortical region. Complex partial seizures of the temporal lobe often begin with a motionless stare followed by simple oral or motor automatisms. They often last from thirty seconds to two minutes in length. Longer seizures may occur when the seizures become generalized convulsions (Murro, 2006).

E.R. has had a history of seizures described as staring episodes by his mother that last several minutes. He averages four to five per month. During his post-ictal state he is tired and confused for up to thirty minutes. His mother has called the paramedics twice for his high fever and seizure activity but he has not become apneic during any recent episodes other than his first initial febrile seizure when he was three months of age.

E.R. was also on Budesonide (Pulmicort) and Albuterol nebulizer treatments for numerous respiratory infections including bronchiolitis and pneumonia since the age of eight months. Presently, there is no other documentation in the record at the clinic that includes all his hospitalizations and emergency room visits during his first year of life. He routinely takes the Budesonide twice a day and the Albuterol every four to six hours when there is an exacerbation of his symptoms. He has not yet been seen by a pulmonologist.

#### *Physical Examination*

#### Vital Signs for May 29, 2009

TEMP	HR	RR	BP	PaO2	HEIGHT	WEIGHT	OFC	BMI
98.2 F	98 bpm	22	104/55	98% RA	93 cm 50 <sup>th</sup> percentile	13.2 kg 25 <sup>th</sup> percentile	45cm <3 <sup>rd</sup> percentile	48 <sup>th</sup> percentile

E.R. is well developed, well nourished Hispanic male, who is active, smiling and is in no acute distress. His head is microcephalic, (< 3<sup>rd</sup> percentile), and atraumatic. His facial features are course. He has eyelashes that are quite long. His eyes' conjunctivae and sclerae are clear, external ocular movements are intact; pupils are equal, round, and reactive to light direct and

consensual with accommodation. He has mild ptosis of the right eye. His lateral palpebrals are upslanted. His ears are posteriorly rotated. There is no tenderness to the tragus or mastoid region. The auricles and external canals are not deformed. The tympanic membranes are dry. There are bilateral myringotomy tubes in place and patent. He is not cooperative for the voice test. His nose is symmetric and midline. The nares are patent without drainage. The turbinates are pale pink in color and moist. No septal deviation or perforation. No tenderness to the maxillary or frontal sinuses. His mouth is very wide. The philtrum is well developed. The lips are moist and dark pink without cracking or lesions. No missing or loose teeth. There are twenty deciduous teeth present with malocclusion. Gums are pink. They are free of food and decay. He has high arched palates which are intact. There is no erythema or exudate noted on the tonsils which are +2 bilaterally. The uvula is midline. E.R.'s neck is supple without masses or lymphadenopathy. The trachea is midline. His lungs are clear with good aeration bilaterally per auscultation. There is no wheezing or other adventitious sound. E.R.'s heart has a regular rhythm and rate with audible S1 and S2 identified. There are no murmurs or extra heart sounds noted on exam. Nail beds are pink. There is no lesion, edema or clubbing. Capillary refill is less than two seconds. Brachial, femoral and dorsalis pedis pulses are +2 bilaterally. Inguinal nodes are not palpable. There are well-healed bilateral inguinal herniorrhaphy scars. His abdomen is flat and symmetrical. There is no bulging or masses noted. An umbilical scar is well healed. Bowel sounds are present and normoactive in all four quadrants. There is no tenderness or masses felt with palpation. He is circumcised with both testes descended and is in Tanner Stage 1. Neurologically, E.R. is developmentally delayed and has a history of seizures. He has brachydactyly and deep palmar flexion creases to both hands. On his feet he has deep creases

and prominent toe pads. His muscle strength is equal bilaterally to upper and lower extremities. There is no muscle atrophy noted. His back is straight.

E.R's Mean Platelet Volume (MPV) is elevated. The MPV is the average size of platelets in a volume of blood. In healthy patients there is an inverse relationship between the platelet count and size (Turgeon, 2004). The volume increases as the platelet count decreases. Because of this inverse relationship, the MPV and platelet count must be considered together. No single normal range exists. The MPV often increases in patients with idiopathic thrombocytopenia and sickle cell anemia (Turgeon, 2004). E.R's platelet count is normal so his increased MPV may not be significant. The MPV normal values can range from 7.8 to 8.9 or from 9.9 to 13.0 fl depending on the laboratory which conducts the test (Turgeon, 2004).

Monocytes are the second line of defense against infection and foreign substances (Jakubik, Cockerham, & Altmann, 2003). They are macrophages capable of phagocytosis that respond to bacterial infection, viral infection, some chronic inflammatory diseases, and other chronic conditions. Monocytes respond late during the acute phase of an infection or inflammatory process, they are stronger, can ingest larger particles, and live longer, allowing them to continue to function during the chronic phase of infection. Their normal range is 4%-7% (Jakubik, et al, 2003). Elevated monocytes (monocytosis) are present in a variety of conditions including: monocytic leukemia, ulcerative colitis, viral diseases such as mononucleosis and herpes zoster, and parasitic diseases such as Rocky Mountain spotted fever. A decreased monocyte count (monopenia) occurs in some forms of leukemia and in bone marrow failure or suppression (Jakubik, et al, 2003).

Lymphocytes are divided into two categories: B cells and T cells. They are responsible for regulation of the immune system through both humoral (B cells) and cell-mediated (T cells) immunity. The normal range for lymphocytes is 35%-61%. An increase in the presence of lymphocytes

(lymphocytosis) is most commonly seen in response to a viral infection but can also be seen in bacterial infection and allergic conditions. A decrease in the lymphocyte count is seen with an increase in adrenal steroids either as a result of corticosteroid therapy, conditions which stimulate the adrenal gland (stress, shock, etc.), or adrenocortical hyperfunction (Jakubik et al, 2003)

### **Pathophysiology**

#### *Bronchiolitis*

E.R. had bronchiolitis as an infant numerous times according to his mother and his medical record. Bronchiolitis is an acute infectious disease of the lower respiratory tract that occurs primarily in young infants, most often in those aged 2-24 months. This illness is usually due to a viral infection of the small airways. Infection of bronchiolar respiratory and ciliated epithelial cells produces increased mucus secretion, cell death, and sloughing, followed by a peribronchiolar lymphocytic infiltrate and submucosal edema (Krillov, 2009).

The combination of debris and edema produces critical narrowing and obstruction of small airways. Decreased ventilation of portions of the lung causes ventilation/perfusion mismatching, resulting in hypoxia. During the expiratory phase of respiration, further dynamic narrowing of the airways produces disproportionate airflow decrease and resultant air trapping. Work of breathing is increased due to increased end-expiratory lung volume and decreased lung compliance. Recovery of pulmonary epithelial cells occurs after 3-4 days, but cilia do not regenerate for about 2 weeks. The debris is cleared by macrophages. Infection is spread by direct contact with respiratory secretions. Previous infection with the common etiologic viruses does not confer immunity. Reinfection is common. In children aged 2 years, approximately 95% have serologic evidence of past infection with the predominant causative agent, respiratory syncytial virus (RSV) and presence of antibodies to RSV does not confer immunity (Krillov, 2009).

*Pneumonia*

E.R.'s mother reports he was hospitalized for pneumonia three times. According to an article published by Nicholas, 2009 in *emedicine*:

Pneumonia is characterized by inflammation of the alveoli and terminal airspaces in response to invasion by an infectious agent introduced into the lungs through hematogenous spread or inhalation. The inflammatory cascade triggers the leakage of plasma and the loss of surfactant, resulting in air loss and consolidation. An inhaled infectious organism must bypass the host's normal nonimmune and immune defense mechanisms in order to cause pneumonia. The nonimmune mechanisms include aerodynamic filtering of inhaled particles based on size, shape, and electrostatic charges; the cough reflex; mucociliary clearance; and several secreted substances. Macrophages, neutrophils, lymphocytes, and eosinophils carry out the immune-mediated host defense.

Conditions that allow pneumonia-causing infectious organisms to circumvent the upper airway defense mechanisms include intubation, tracheostomy, impaired cough reflex, and aspiration. These conditions provide infectious organisms with easier access to the alveoli and terminal airspaces. Ciliary dyskinesia, bronchial obstruction, viral infection, cigarette smoke, and certain chemical agents create disruption in the mucociliary blanket (Nicholas, 2009). Anatomic abnormalities, gastric fluid aspiration or other causes of noninfectious inflammation, altered pulmonary blood flow, and pulmonary edema also increase the predisposition for pneumonia along with immunodeficiency and immunosuppression (Nicholas, Domachowske, & Virella-Lowell, 2009)

Inoculation of the respiratory tract by infectious organisms leads to an acute inflammatory response in the host that typically lasts 1-2 weeks (Burns, 2009). This inflammatory response differs according to the type of infectious agent. Viral infections often involve both the conducting airways and the alveoli. The lung defenses are affected by altering normal secretions, inhibiting phagocytosis, modifying the normal bacterial flora, and disrupting the epithelial layer. Children with immunologic problems or chronic illnesses are prone to primary bacterial pneumonia and experience recurrent pneumonias or fail to clear the initial infection completely as in E.R.'s situation (Burns, 2009). A patient with these infections presents with wheezing and crackles.

Bacterial infections occur when the alveoli fill with proteinaceous fluid, which triggers a brisk influx of RBCs and polymorphonuclear cells followed by the deposition of fibrin and the degradation of inflammatory cells. During resolution, intra-alveolar debris is ingested and removed by the alveolar macrophages. This consolidation leads to decreased air entry and dullness to percussion. Inflammation in the small airways leads to crackles. Wheezing is less common than in viral infections. The inflammation and pulmonary edema that result from these infections cause the lungs to become stiff and less distensible, thereby decreasing tidal volume. The patient must increase his or her respiratory rate to maintain adequate ventilation. Poorly ventilated areas of the lung may remain well perfused, resulting in ventilation/perfusion (V/Q) mismatch and hypoxemia. Tachypnea and hypoxia are common. (Nicholas et al 2009).

Kabuki syndrome (KS) is associated with multiple organ system involvement. An increased incidence of infection has been reported in KS, and a few patients have been noted to have immune defects. However, the frequency and severity of the immune deficiency has not been

clearly defined. Studies suggest that hypogammaglobulinemia is a frequent finding in children with KS (Hoffman, Ciprero, & Sullivan, et al, 2005).

The pattern of antibody abnormalities seen in children with KS resembles common variable immune deficiency (CVID). Due to this increased susceptibility to infection, children with KS should have immunologic evaluations at the time of diagnosis in order to reduce preventable morbidity and mortality. A consultation from the hematology specialist has not yet been received in the medical record for evaluation of a possible immunodeficiency disorder. This would provide additional information as to the incidence of recurrent acute illness in this patient (Hoffman, Ciprero, Sullivan et al, 2005).

Recurrent infections, principally otitis media, as well as upper respiratory tract infections and pneumonia occur in patients with Kabuki Syndrome (Dahms, 2004). Recurrent pneumonia may be related to immune dysfunction as opposed to true airway abnormalities (Adam & Hudgins, 2004). E.R. had frequent ear infections and bronchiolitis at least three times according to the medical record. He has a history of gastroesophageal reflux and eosinophilic esophagitis. Aspiration of gastric content into the airway might result in reactive airway disease, aspiration pneumonia, recurrent pneumonia, chronic cough, and laryngospasm. Respiratory symptoms can be initiated by the presence of acid in the lumen of the distal esophagus without any aspiration into the airway or lung (Dahms, 2004).

### *Seizures*

As previously mentioned, E.R had a history of seizures since the age of three months old. He initially had febrile seizures but was later diagnosed with complex partial epilepsy which is controlled with Levetiracetam (Keppra) 250 mg by mouth twice a day. He continues to have

staring episodes four to five times a month and has not had any clonic-tonic type activity since February, 2009.

Central nervous system involvement is frequently reported in Kabuki syndrome. Mental retardation is one of the cardinal manifestations of this syndrome, being observed in most patients. The other features of Kabuki syndrome are neurologic abnormalities such as neonatal hypotonia, feeding problems, microcephaly, brain atrophy, subarachnoid cyst, hydrocephaly, autistic features, growth hormone deficiency, precocious puberty, delayed sexual development, and diabetes insipidus. These neurologic abnormalities appear to be more common in non-Japanese patients compared with Japanese patients. Seizures are one of the most important neurologic complications. Epilepsy together with mental retardation can be a primary feature of Kabuki syndrome. It is mainly localization related epilepsy with a favorable seizure outcome (Ogawa, 2003).

A seizure or convulsion is a paroxysmal, time-limited change in motor activity and/or behavior resulting from abnormal electrical activity in the brain (Kliegman, Behrman, Jenson & Stanton, 2007). This abnormal neuronal firing is manifest clinically by changes in motor control, sensory perception, behavior, and/or autonomic function. The aberrant electrical activity that underlies epilepsy is the result of biochemical processes at the cellular level promoting neuronal hyperexcitability and neuronal hypersynchrony ( Stafstrom & Rho, 2009) The neuronal hyperexcitability is characterized by cellular depolarization secondary to massive influx of sodium and calcium (Nickel & Desch, 2000)

When the permeability of the membrane's ionic channels for sodium and potassium are varied sequentially, a fluctuation in the membrane voltage occurs, which is termed the action potential. As the sodium attempts to enter the nerve cell, the potassium permeability increases as the potassium channels open, and the membrane begins to repolarize to the "resting" membrane potential. The nerve cell

repolarizes and is ready for the next action potential to come along. These action potentials are also modified by the flux of chloride ions and the presence or absence of GABA activity in the membrane of the axon (Minczak 2007).

Gamma-Aminobutyric acid (GABA), the principal inhibitory neurotransmitter in the cerebral cortex, maintains the inhibitory tone that counterbalances neuronal excitation. When this balance is perturbed, seizures may ensue. GABA is formed within GABAergic axon terminals and released into the synapse, where it acts at one of two types of receptor: GABAA, which controls chloride entry into the cell, and GABAB, which increases potassium conductance, decreases calcium entry, and inhibits the presynaptic release of other transmitters (Minczak, 2007).

A neuron or group of neurons in the brain can become hyperexcitable or irritable due to hypoxia, ischemia, hypoglycemia, or electrolyte abnormalities that affect the action potential and cause these nerve cells to discharge action potentials irregularly without adequate suppression and attenuation of the abnormal activity. Depending on where the focus of this aberrant discharge is in a particular region of the brain, the corresponding motor or sensory area will be affected, leading to either motor symptoms such as tonic-clonic contractions or sensory manifestations of seizure-like activity, such as paresthesias, déjà vu, or hallucinations (auditory, visual, or olfactory). These foci of aberrant electrical activity (the seizure) may be isolated, or the focus may spread and involve various areas of the brain, leading to chaotic, uninhibited discharge of electrical activity of various neurons in the brain. Control of the seizure can be accomplished by suppressing the action potential via manipulation of sodium and potassium ion permeabilities, rendering the axon refractory to the action potential, or blocking transmission of impulses at the synapse by blocking the neurotransmitter from binding to its receptor site, or preventing its release and/or synthesis (Minczak, 2007).

The EEG provides important information about background EEG and epileptiform discharges and is required for the diagnosis of specific electroclinical syndromes (Sheth, 2008).

Epileptiform discharges help separate generalized from focal seizures (Sarco & Masanori, 2009).

They refer to spike waves, sharp waves, spike and wave activity, or other rhythmic waveforms that imply epilepsy or may be associated with epilepsy. However, epileptiform activity alone does not confirm a diagnosis of epilepsy (Sarco & Masanori, 2009).

### *Gastroesophageal Reflux*

E.R. has been on Raniditine since he was an infant for gastroesophageal reflux. The dose was increased to one teaspoon twice a day. He did have an esophagogastroduodenoscopy performed in 2008 which showed eosinophilic esophagitis.

During the last decade, clinical practice saw a rapid increase of patients with esophageal eosinophilia who were thought to have gastroesophageal reflux disease (GERD) nonresponsive to medical and/or surgical GERD management. Subsequent studies demonstrated these patients had a “new” disease termed eosinophilic esophagitis (EE) or “allergic esophagitis”.

Eosinophilic esophagitis (EE) is a disease of the esophagus that has become increasingly recognized in children and adults in recent years. It is a clinicopathologic disorder characterized by a dense esophageal eosinophilia with severe squamous epithelial hyperplasia generally occurring in association with upper gastrointestinal symptoms, primarily esophageal. Food allergy is suspected to be the etiology of EE but is not a universally accepted idea. Most cases of EE present in children beyond infancy with symptoms similar to those of GERD: pain, vomiting, dysphagia, and chronic respiratory complaints (Dahms, 2004).

In EE, the gastric and duodenal mucosae are normal. The esophageal abnormalities do not respond to treatment with high-dose proton pump inhibitor (PPI) therapy. EE should be considered in young children with GERD-like symptoms, including feeding problems, and in older children and adults with

GERD-like symptoms, especially in those with dysphagia or esophageal food impaction. When the primary diagnosis is EE, symptoms are unresponsive or only partially responsive to acid blockade. They do improve with an elimination diet or corticosteroid treatment. Skin prick testing and patch testing can help identify which foods might contribute to this disease. The foods most commonly associated with EE are cow's milk, soy, egg and wheat. Airborne allergens may also be a contributing factor. Many children with this disorder have more than one allergy problem (Furuta, Liacouras, Collins et al, 2007).

The esophageal mucosa accumulates eosinophils in disease states. In patients who are previously sensitized, IgE interacts with a food allergen or aeroallergen leading to resident mast degranulation. Chemokines, histamine, and eosinophilic chemotactic factors are released from the mast cells. These factors induce eosinophil migration and degranulation. Among the products released by eosinophil granules are major basic protein, eosinophil peroxidase, eosinophil cationic protein, and eosinophil-derived neurotoxin (Swoger, Weiler, & Arora).

Eosinophils have proinflammatory effects that release cytokines, chemokines, and lipid mediators. They also induce smooth muscle contraction in the esophagus which leads to the sensation of dysphagia and episodes of food impaction. The released proteins cause tissue damage and dysfunction. It ultimately results in fibrosis and further mast cell degranulation continuing the cycle of inflammation and tissue damage (Swoger, Weiler, & Arora, 2007).

## **Interventions**

### *Advanced Pharmacology*

Pharmacologic interventions for ER were made according to his diagnoses of frequent respiratory infections and recurrent ear drainage; partial complex seizures; gastroesophageal reflux (GERD), eosinophilic esophagitis; and recurrent ear drainage.

Budesonide (Pulmicort) is an anti-inflammatory, corticosteroid agent that controls the rate of protein synthesis; depresses the migration of polymorphonuclear leukocytes and fibroblasts; reverses capillary permeability; and stabilizes lysosomal membranes at the cellular level to prevent or control inflammation (Takemoto, Hodding, & Kraus, 2007). Pulmicort decreases the number and activity of cells involved in airway inflammation such as macrophages, eosinophils, and T lymphocytes. Prolonged inhalation of this steroid medication reduces the hyperresponsiveness of the airway smooth muscle to bronchoconstrictor stimuli such as allergens, cold air, and irritants. This medication has no direct effect on the airway smooth muscle (Howland & Mycek, 2006). E.R. is receiving Pulmicort 0.5 mg twice a day by nebulization treatment to help prevent exacerbation of his reactive airway disease caused by recurrent episodes of bronchiolitis and pneumonia. The maximum recommended dose is 1mg/day (Takemoto, 2007). Adverse reactions may include facial edema, nervousness, migraines, insomnia, fatigue, headache, fever, rashes, pruritis, hypokalemia, Cushingoid state, nausea, vomiting, diarrhea, leukocytosis, purpura, nasal irritation, pharyngitis, growth of *Candida* in the mouth, throat, or nares. Other reactions are growth suppression, decreased bone mineral density, conjunctivitis, otitis media, cough, and wheezing, decreased sense of smell hoarseness, rhinitis, and sinusitis (Takemoto, et al, 2007). The patient should have his mouth rinsed after each inhalation to decrease the chance of oral candidiasis (Takemoto et al, 2007).

Albuterol is a short-acting beta 2 agonist used primarily as a bronchodilator for symptomatic treatment of bronchospasm and as a “rescue agent” to combat acute bronchoconstriction. Beta 2 agonists like Albuterol relax airway smooth muscle. This medication is administered by a nebulization treatment and has a rapid onset (Howland & Mycek, 2006). E.R. is given Albuterol 2.5 mg every four to six hours as needed for wheezing. The maximum dosage is 5mg every four

to six hours (Takemoto, 2007). Adverse reactions include tachycardia, palpitations, nervousness, CNS stimulation, hyperactivity and insomnia, urticaria, hypokalemia, vomiting, diarrhea, hoarseness, dysuria, tremor, irritation of the oropharynx, coughing, diaphoresis (Takemoto, 2007).

Levetiracetam (Keppra) is used in the treatment of refractory partial onset seizures. The exact mechanism of the anticonvulsant action is unknown. Several studies suggest one or more of the following central pharmacologic effects: Inhibition of voltage-dependent N-type calcium channels; blockade of GABA-ergic inhibitory transmission through displacement of negative modulators; reversal of the inhibition of glycine currents; reduction of delayed potassium current; and binding to synaptic proteins which modulate neurotransmitter release (Takemoto et al, 2007). Levetiracetam is free of pharmacokinetic drug interactions which makes it a good choice for adjunctive therapy (Howland & Mycek, 2006). The half-life is approximately five hours and the maximum dosage is 60mg/kg/day (Takemoto, 2007). Currently, E.R. is on 250 mg twice a day which calculates to 38mg/kg/day. This is well below the recommended maximum dose. Adverse reactions may include somnolence, accidental injury, hostility, nervousness, and loss of strength (Takemoto, 2007).

Ranitidine (Zantac) is used in the long term prophylaxis of gastroesophageal reflux (GERD). It is a histamine H<sub>2</sub>-receptor antagonist which main function is to inhibit gastric acid secretion by blocking the binding of histamine to H<sub>2</sub> receptors (Takemoto, 2007). This reduces the intracellular concentrations of cyclic adenosine monophosphate (cAMP) and the secretion of gastric acid. Ranitidine inhibits basal, food-stimulated, and nocturnal secretion of gastric acid after a single dose (Howland & Mycek, 2006). E.R is on 75mg twice a day which calculates to

11.5 mg/kg/day. The maximum recommended dosage for GERD is 300mg/day (Takemoto, 2007). Adverse reactions may include bradycardia, sedation, malaise, anxiety, rash, constipation, nausea, vomiting, abdominal discomfort, thrombocytopenia, leukopenia, hepatitis, and pneumonia (Takemoto, et al, 2007).

Antipyrine and Benzocaine (Auralgan) ear drops were prescribed to E.R. by his ENT specialist to be used twice a day as needed for ear drainage. It is used for the temporary relief of pain and reduction of inflammation associated with acute congestive and serous otitis media. It is not intended for prolonged use as it may mask symptoms of a fulminating middle ear infection. Adverse reactions for this medication include burning, stinging, tenderness, edema, and hypersensitivity reactions. The usual dosage is fill the ear canal; moisten cotton pledget, place in external ear, repeated every one to two hours until the pain and congestion is relieved (Takemoto et al, 2007).

#### *Theoretical Foundation of Nursing Practice*

Merle Mishel developed the middle range theory called the Uncertainty in Illness Theory which grew out of her dissertation research with hospitalized patients. Uncertainty is defined as the cognitive state in which individuals are unable to determine the meaning of illness-related events (Tomey & Alligood, 2006). Mishel's main concepts provide a comprehensive framework within which to view the experiences of acute and chronic illness and to organize nursing interventions to promote optimal adjustment (Tomey & Alligood, 2006). The theory helps to explain the stresses associated with the diagnosis and treatment of a major illness or chronic condition; the processes by which the individuals assess and respond to the uncertainty inherent in an illness experience; and the importance of professional caregivers in providing information

and supporting individuals in understanding and managing uncertainty (Tomey & Alligood, 2006).

Three major themes construct Mishel's framework. These are antecedents of uncertainty; the process of uncertainty appraisal; and coping with uncertainty. The antecedents include the stimuli frame, cognitive capacities, and structure providers. Uncertainty is seen as a neutral state until it has been appraised by an individual. This appraisal includes inference and illusion. Inference is constructed from the individual's personality and includes learned resourcefulness, mastery, and control. The individual believes they have the ability to handle life's events. Illusion is a belief constructed from uncertainty that considers the favorable aspects of a situation. Uncertainty is viewed as either a danger or an opportunity. Coping is the third theme and occurs in two forms with the end result of adaptation. If uncertainty is seen as a danger then coping includes direct action, vigilance, seeking information in order to mobilize strategies, disengagement, and cognitive support. If it is appraised as an opportunity the coping offers a buffer to maintain the uncertainty (Tomey & Alligood, 2006).

#### *The Role of the Advanced Practice Nurse (APN)*

E.R. and his family present quite a challenge to the advanced practice nurse involved in this case. He has significant pathophysiology affecting several major body systems which the APN, acting as his primary care provider, must take into consideration. She must develop and implement a plan of care utilizing many different roles including expert clinician, collaborator, educator, researcher, as well as the overall coordinator of care.

Mishel's Uncertainty in Illness Theory can be applied to the lived experiences of E.R. and his family since they are dealing with a genetic disorder which is extremely rare. It was discovered in 1981 and there is limited information available in the literature concerning this multi-system anomaly. Support groups have formed internationally by families affected with Kabuki

Syndrome (KS) via the Internet; however, E.R.'s mother was not aware of these groups. By utilizing Mishel's Uncertainty in Illness Theory as a theoretical framework, the advanced practice nurse must first research Kabuki Syndrome (KS) extensively in order to help guide her nursing practice. Each patient born with Kabuki Syndrome is unique therefore not all individuals have the same characteristics. Ultimately, the goal is to share new information about this rare genetic disorder with E.R. and his family in order to help provide appropriate interventions. As an expert clinician, the APN must utilize the latest information to effectively manage this patient's chronic infection and inflammation; provide suitable pharmacological management and evaluate its effectiveness; review steps to be taken to provide the appropriate long term care that fit the patient's and family's needs.

#### *Non-Pharmacological Interventions and Health Promotion*

E.R. has a history of several health problems that affect three of his major physiological systems. These include the respiratory, neurological, and gastrointestinal systems. In addition he has a genetic anomaly with distinguishing facial features and musculoskeletal abnormalities that provide a great challenge to the advanced practitioner.

As a collaborator and educator, the APN can implement several interventions for health promotion with this patient. The non-pharmacological management would include the instruction of basic hand hygiene to all members of the family in order to help prevent the spread of infection along with explaining the benefits of a yearly influenza vaccine because E.R. is susceptible to illness. Education about providing humidification in the home environment would also be encouraged due to his recurrent reactive airway disease. Recording a complete 24 hour diet history to assess the child's caloric intake and evaluate his nutrition to ensure adequate

growth would be an additional step in health promotion because he has been in the 25<sup>th</sup> percentile for his weight. It would also be important for the APN to collaborate with the pediatric gastroenterologist on the management of the patient's history of GERD and eosinophilic esophagitis.

Furthermore, obtaining results of a second sleep study would help with the diagnosis of sleep apnea or other respiratory ailment which is affecting the child's ability to sleep at night. Other steps in promoting health and preventing illness would be involving other health care professionals such as a pulmonologist who would review the child's past medical record and possibly offer new solutions; evaluation by a pediatric dentist to assess his dentition and malocclusion; and continued follow-up by the ENT specialist for his ear problems. Assessment by the hematologist regarding his immunological status would be a priority along with allergy testing to help determine the cause of his eosinophilic esophagitis.

The American Academy of Pediatrics (AAP) recommends monitoring of a child's developmental progress as part of preventive health care (AAP, 2003). Early identification of developmental problems with early intervention is an important factor in caring for children with disabilities and chronic conditions (Nickel & Desch, 2000). The advanced practice nurse's management of E.R. would include follow-up appointments with Nevada Early Intervention Services (NEIS) for assessment of his progress with language and motor development which include speech, sign therapy, occupational and physical therapy. Other services would include a feeding evaluation taking place ideally after a pediatric dental assessment, and behavior modification strategies for any autistic-like mannerisms.

Families are taught how to carry out the medical treatment and developmental care of their children but are not prepared for the daily and long-term effects that living with children who

have disabilities may have on family members individually or on the family's life together (Nickel & Desch, 2000). Caring for children with significant, long-term problems confers enormous responsibilities on the provider, family, community, and society. Primary care providers assume a variety of roles related to the care of children with genetic disorders. One of these roles is being the overall coordinator of care. This includes promoting health of persons with genetic conditions and supporting children and families to reduce risk for medical problems by assisting parents to use specialized services; teaching health principles, monitoring and evaluating clients with genetic diseases; working with families under the stress of caregiving (Burns, et al 2009). Mothers of children with disabilities and chronic illness experience more depression, psychosocial problems, physical illness, and isolation than mothers of healthy children. These women are tired, overwhelmed, and their physical health is often ignored by health professionals. Mothers handle the day-to-day care of their children by mastering the technical and medical details. Health professionals have focused on teaching the specific therapies children with disabilities and chronic conditions require; however, little attention has been given on how to handle these children's daily care along with family life (Nickel & Desch, 2000).

Respite care is the temporary care of a child with a disability or chronic condition for the purpose of providing relief to family caregivers. Families need various types of respite care services to promote overall family health (Nickel & Desch, 2000). Presently, Mrs. R. uses members of her immediate family to assist and provide the needed breaks from E.R's care so she can have some time to herself and her daughters.

Some available resources for E.R. and his family are the National Information Center for Children and Youth with Disabilities; National Organization for Rare Disorders, Inc., and the Federation for Children with Special Needs. Another agency available to assist E.R.'s family is the Sibling Support Project. This is a national effort dedicated to the life-long concerns of brothers and sisters of people who have special health, developmental, or mental health concerns. It is based in Seattle and has trained service providers in all 50 states, England, Ireland, New Zealand, and Japan. The Kabuki Syndrome network is another resource that would benefit this family. Introducing E.R.'s mother to the Kabuki Syndrome network would connect her with parents of children who have similar situations and offer a strong support system. Furthermore, continued follow-up with the local geneticist on a regular basis would enable Mrs. R. to have access to the latest research and treatments recommended for her son's hereditary disorder.

The National Association of Pediatric Nurse Practitioners (NAPNAP) and the AAP all emphasize the importance of the family within a child's life (Burns, et al, 2009). It is important for the advanced practice nurse (APN) to follow the principles of family-centered care whenever possible. This involves collaboration among families, health professionals and others who deliver care to patients. E.R.'s family members are the constant in his life while the personnel in the health care system constantly fluctuate. It is imperative that partnerships between the caretakers and health professionals are formed to help with decision making. The APN will also act as a coordinator by sharing information about all treatments, ethical concerns, and uncertainties with regard to E.R.'s health care (Nickel & Desch, 2000). The APN must recognize and build on the strengths of each child and family even in difficult and challenging situations.

The role of the researcher is an important part of the advanced practice nurse's core competency. Preparation for conducting evidence based practice is inherent of the APN graduate

programs (Hamric, Spross, & Hanson 2005). The APN must identify research topics and questions in practice as part of the blended roles of clinician and problem solver in order to help investigate complex patient issues and promote continuity of care (Hamric, et al, 2005). Future research topics to be studied in this regard might be the correlation between reactive airway disease and eosinophilic esophagitis in the patient with Kabuki Syndrome; how prevalent is Kabuki Syndrome in the local vicinity where E.R. resides; what effect does E.R's Hispanic culture play on his growth and development compared to other children with Kabuki Syndrome.

### *Human Diversity*

Human diversity involves being culturally competent and remaining sensitive to the racial, ethnic, cultural, and socioeconomic differences of families and their effects on the family's experience and perception of care (Narayan, 2003). Culture affects family decision making, use of alternative medicines and therapy; acceptance of a plan of care; beliefs about illness and major medical procedures and health care decisions. It also influences whether or not people are respectful of healthcare providers or mistrust authority (Narayan, 2003). Each family's cultural values, learning styles, health beliefs and practices must be respected (Burns, et al, 2009).

One of the fastest growing and largest populations in the United States are the people of Hispanic culture which increased by 13.2 % in the last decade of the 20<sup>th</sup> century (Galanti, 2003). They represent a diverse group of cultures and national origins. Members of the Hispanic American community have their origins in Cuba, Central and South America, Mexico, Puerto Rico, and other Spanish speaking countries. Mexican Americans are the largest of these groups comprising 58% (Galanti, 2003). The family is the primary unit within

Hispanic culture and a strong cultural value. Many of these families frequently live in the same neighborhood or general vicinity of their relatives (Galanti, 2003).

E.R. and his family are of Mexican American descent and are very close-knit. They are at the lower end of the socioeconomic spectrum. E.R.'s healthcare is provided by Medicaid. His mother has a very strong support system that includes her parents, siblings, and husband's family. Her husband is temporarily living and working in California but travels home each month to be with his wife and children. E.R. is close with both of his siblings. His ten year old sister resides mainly in California with her biological father but visits her mother often. Mrs. R. also keeps in contact with her older daughter's extended family members who also reside in California.

The family has a strong belief system and attends church services on a semi-regular basis. Mrs. R. does not work and stays at home to care for E.R. and his five year old sister. She only allows members of her family to take care of E.R. when she has to be away from home and reports she is fiercely protective of her only son.

E.R. had numerous visits to the clinic this year for a variety of health issues. Several members of the nursing staff at the clinic are also of Mexican American descent. E.R. and his family have developed a close rapport with them and are not hesitant about contacting the office whenever a medical problem arises. Some of the nurses have attended social events at E.R.'s residence and are considered part of his "La Familia."

### *Ethics*

The Human Genome Project (HGP) was begun in 1990 to accomplish certain goals. These include identifying genes and their function; expanding the database and data analysis

capabilities; sequencing the entire genome; studying the ethical, legal, and social implications of current and anticipated information. The completion of this project promises to usher in a new era in biomedical research and clinical medicine. Knowledge about genetics for delivery of primary care clinical services is increasingly important. Primary care providers must meet the core competencies developed by a coalition of member organizations representing nursing, medicine, psychology, genetic counseling, and others (National Coalition for Health Professional Education in Genetics). These competencies are to appreciate the limitations of one's own genetic expertise; understand the social and psychological implications of genetic services; and know how and when to make a referral to a genetics professional (Burns, et al, 2009). Genetic information is linked to concepts of privacy and confidentiality and the availability of this information is increasing. Because of this, the advanced practice nurse will encounter legal issues and ethical dilemmas related to the use of genetic data (Hamric et al, 2005).

Other ethical considerations include issues involving follow-up care. There is only one local geneticist who has a lengthy waiting list for referrals. Families are forced to wait a period of several months to one year for an appointment to be seen or otherwise elect to travel out of town to consult another physician for an evaluation. Most insurance companies will not pick up the costs for these out of state referrals. Furthermore, a majority of the health practitioners in Las Vegas are not familiar with Kabuki syndrome and, therefore, have limited knowledge in the treatment of patients affected by this genetic condition.

One of the other ethical dilemmas noted was E.R's mother did not have routine prenatal care due to lack of insurance and developed complications of fever and vaginal bleeding with signs of miscarriage. She declined to have an amniocentesis. Another ethical issue deals with what little management is provided by health professionals to children with chronic conditions on how to

handle the burden of their daily care and family life. More attention tends to be focused on teaching what specific therapies are involved with the condition itself.

Additional ethical concerns involve the financial costs and how far the advanced practitioner can go when making referrals in E.R.'s care. Currently, he has a number of serious health care issues that need constant monitoring. His family has no health insurance and is covered by Medicaid. It will be important to prioritize what services are potentially needed as this child matures. Fortunately, at this time, his pediatrician and the other health care professionals involved in his care accept Medicaid so E.R. can continue to be followed for any ongoing concerns. Ultimately, it will be interesting to see if the advanced practice nurse will be the person coordinating the majority of care for patients like E.R. at many health clinics throughout the United States.

Finally there are the ethical principles of beneficence, nonmaleficence, respect for persons and justice. Beneficence refers to securing a patient's well-being by balancing the benefits and burdens of treatment options. This applies to all children since they lack the capacity to make informed, independent decisions (Allen, Vessey, & Schapiro, 2010). According to Allen

Burdens for children with chronic conditions include repeated pain and suffering associated with invasive procedures, symptoms, or disability, as well as emotional distress caused by fear, immobilization, prolonged hospitalization, or isolation from family and friends (Allen, et al 2010).

It is important to help the patient, like E.R., and his family members create a meaningful life by balancing the burdens of his genetic disorder and its many chronic conditions with the positive aspects of life (Allen, et al, 2010).

Nonmaleficence means that it is the duty of the health care professional to prevent harm or burden to an individual with pain, new therapies, or maltreatment. This includes the prevention of medication errors; assessment of the patient's discomfort; providing safe treatments;

recognition and early intervention of any maltreatment to reduce the incidence (Allen, et al, 2010). Finally there are the principles of respect for persons and justice. Respect for persons means recognizing another person as sharing a common human destiny (Allen, et al, 2010). Justice pertains to the fair and equal treatment of others (Allen, et al, 2010). E.R. cannot make his own autonomous decisions, therefore relies on his parents and health care professionals to work together in his best interest without judgmental attitudes and behaviors. E.R's treatment should also not be influenced by his gender, socioeconomic status, nature of his illness, or religious beliefs (Allen, et al, 2010).

### *Financial Impact*

Today, Medicaid helps to finance health and long-term care for more than 55 million low-income children and parents, people with severe disabilities, and elderly Americans, at an annual cost of nearly \$300 billion to the federal and state governments (Rowland, 2005). The program currently provides health coverage to 1 in 4 U.S. children, covers half of all spending on nursing home care, and supplements Medicare for 7 million elderly and disabled persons (Rowland, 2005). Children account for half the enrollees, but the elderly and people with disabilities account for 70 percent of the spending (Rowland, 2005). Medicaid is the nation's health safety net, but its growing role and increasing costs in the face of state budgetary pressures and the federal deficit have made it a target for reform that could fundamentally reshape the program (Rowland, 2005).

The caring for a child with disabilities places not only financial costs on the family, but psychological and emotional costs as well. The impact of having a child with a disability together with social and financial implications increases the psychological and emotional burdens. These burdens may be depicted as sleep deprivation, stress and depression (Warner,

2006). Families of children with special needs experience life differently than other families. The family's identity and the parents' employment may be altered radically. Holidays and vacations are affected as it is difficult to plan activities. Mothers appear to carry the larger burden of care although fathers are not unaffected. Although these parents may feel trapped, isolated, and experience a loss of freedom, their need to survive as a family usually continues to motivate them (Kyle, 2007).

### **Conclusion**

Kabuki syndrome (KS) is a complex disorder that provides a great challenge for the advanced practice nurse because there is still little evidence-based research concerning this rare genetic condition. The mode of inheritance and etiology is currently unknown and it has only recently been recognized as a genetic syndrome over the course of the last thirty years. Given that the number of medical professionals who are familiar with KS is still growing, it is believed that this hereditary disorder is under-diagnosed. Diagnosis is further complicated by the fact that Kabuki syndrome is a multiple malformation and mental retardation syndrome characterized by distinctive facial features, skeletal anomalies, dermatoglyphic abnormalities, mild to moderate retardation, and post-natal growth deficiency. There are also a number of visceral, endocrinologic, and immunologic/hematologic abnormalities associated with this condition (Adam & Hudgins, 2004). However, these characteristics tend to vary among patients with KS and there are no specific pre-natal or post-natal screening tests to detect this syndrome. A genetic consult is needed to help confirm the diagnosis.

The APN must recognize that children like E.R. with chronic conditions such as Kabuki syndrome are entitled to all of the preventive health care needs as those of other children. This

time; identification of the need for subspecialty consultation and referrals; interaction with school and community agencies; and maintenance of a central record and database containing all pertinent medical information (Nickel& Desch, 2000). The care of these children also requires a commitment by the APN to gain further knowledge of the disability or genetic condition in order to better serve these patients.

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**Lab Results from 3/9/09**

TEST	IN RANGE	OUT OF RANGE	REFERENCE RANGE
WBC	11.6		5.0-15.0 k/cmm
RBC	4.31		3.90-5.20 m/cmm
Hemoglobin	12.1		11.5.0-13.5 0 %
Hematocrit	35.5		34.0-40.0 %
MCV	82.2		70.0-86.0 fl
MCH	28.1		
Red Cell Distribution	13.6		7.0-16.0 %
Platelet Count	208		135-450 k/cmm
Mean Platelet Volume		13.7	6.9-10.9 fl
Segmented Neutrophils	37.9		18.0-40.0 %
Lymphocytes		40.4	44.0-74.0 %
Monocytes		21.0	3.0-10.0 %
Eosinophils	0.2		0.0-3.0 %
Basophils	0.5		0.0-2.0 %
IgA		123	24-121 mg/dl
IgG	719		533-1078 mg/dl
IgM	124		26-218 mg/dl
IgE	8		0-93 IU/ml