How Do I Get a Diagnosis?
"HIT THEM BETWEEN THE EYES WITH THE FACTS!"

By
Susan Q. Knittle-Hunter

We met with a technician for medical equipment when we were trying to get oxygen because I was having trouble breathing. She told us the best way to get the help we needed and a diagnosis was to, "Hit them (doctors) between the eyes with the facts". That is just what we did!! Based on that idea I have created the following plan for others to use to gain a diagnosis. I am presenting it in an outline format to make it easy to follow and to use as a checklist. The story of my own diagnosis is on page 7.

1. You must **gather all the facts**:
    - **a.** It is important for **everything else to be ruled out**. These are done by your PCP and a neurologist, because most of the symptoms resemble a neuromuscular disorder. The tests ruling everything else out might include but are not limited to:
        - **i.** Lab work of all types,
            - **1.** blood
            - **2.** urine,
        - **ii.** MRI's,
            - **1.** brain
            - **2.** spine
        - **iii.** Spinal Taps,
        - **iv.** X-rays,
        - **v.** EEGs
        - **vi.** EMGs,
        - vii. EKGs
        - viii. CMAPs
        - ix. Muscle Biopsy
    - b. Some of the tests above may show changes that can be markers for PP.

2. Most doctors diagnosing PP want **lab work** showing either:
    - a. paralysis during shifting in normal ranges
    - b. paralysis during shifting in low potassium and/or,
    - c. paralysis during shifting high potassium
        - i. This is done by obtaining serum potassium levels
            1. May need to be done several times until a baseline is established
            2. Then during episodes every 5 to 10 minutes...not just one blood draw...there is no way to see the shifting otherwise.
            3. It may be necessary for hospitalization in order to do this while in the paralysis.
            4. May need to be done for more than 24 hours until each is documented, during the episodes.

5. If the shifting is in the normal ranges, it may never show up during tests, unless it is done every few minutes.
    a. 50% of PP patients may not have potassium shifting out of normal ranges'
    b. ATS patients may shift all three ways.

d. However, the latest information for diagnosing PP based on potassium levels in blood serum is as follows:

i. During an attack, there is usually, **but not always**, a measurable fall in levels of serum potassium, but in some patients the K+ level may never fall below normal. Johnsen's series of provocative studies recorded an episode of weakness of 11 hours duration provoked by a 0.3 mmol/l fall in the serum K+, and an episode of total paralysis of 19 hours duration provoked by a one point drop. During the attack there is urinary retention of sodium, potassium, chloride and water. Base your decisions on your patient's strength and cardiac signs, not on serum potassium levels alone.

http://www.hkpp.org/physicians/hypokpp_er.html

ii. "It becomes evident to those who read the entire body of literature that while some patients with HypoKPP exhibit serum potassium readings of 2.0 and below during episodes, others may experience paralysis and arrhythmias with K+ readings which are still within normal limits. The determining factor is not the level of the serum potassium written on the lab slip but the condition and response of the patient."

http://hkpp.org/physicians/dxing_hypokpp.html

iii. In primary HypoPP the K level is low during attacks. HyperPP, K levels may be elevated; however, the K level remains within the normal range in up to 50% of cases (Plassart et al., 1994; Chinnery et al., 2002).

http://brain.oxfordjournals.org/content/129/1/8.full.pdf

*******The information above needs to be shared with your doctors…most do not understand this and won't diagnose without # 2 a. and b. Too many people are not getting diagnosed due to this misconception.*********

3. There needs to be periods of paralysis, either total or partial, which can be documented.
    a. #3 video taping is the best way to do this.
    b. It may be necessary for hospitalization in order for doctors to see one while in the paralysis.

4. ECGs or EKGs consistent with "ion channelopathy" especially if ATS is suspected).

a. Needs to be done while in the paralysis so it may need to be done for more than 24 hours until each is documented, during the episodes.
    i. Holter Heart Monitors are the best method.

5. Oximitry (oxygen) recordings
   a. Indicating, levels dropping during paralysis.
   b. If in an advanced case of PP, it may show hypoventilation.

6. Genetic testing is available
   a. Not necessary, but helpful for treatment and prognosis
   b. See below for Specifics for Genetic Diagnosing of PP page 4
      i. 30% of all people with PP do not have identified mutations.
   c. See below for Specifics for Genetic Diagnosing of ATS page 5
      i. 30% - 40 % of all people with ATS do not have identified mutations.

7. Gather all previous medical records.
   a. Be sure to ask for all doctors' records from each appointment you attend.
   b. Get all lab records, xrays, hospitalizations, etc.

8. Chart the triggers for the episodes.
   a. See "What are the Periodic Paralysis Triggers" and "How Do I Discover My Triggers" at http://www.periodicparalysisnetwork.com/
   b. Documenting an increase of episodes after eating carbs or red meat, after exercising or after taking certain medications is important for being able to control the episodes and letting the doctor see what the triggers are for a diagnosis.

9. Documenting a reduction of episodes when using potassium is good. This can indicate the loss of potassium after shifting and may indicate low potassium levels.

10. Gather a team of doctors. (Knowledgeable about PP or willing to learn)
    a. PCP
    b. Neurologist
    c. Electrocardiologist
    d. Nephrologist
    e. Endocrinologist
    f. Counselor or therapist
    g. Others as needed for symptoms
    h. MDA doctors if possible

11. Gather as much medical information as possible from family members who may have symptoms similar to PP. It has a hereditary component.
    a. If one suspects Andersen-Tawil Syndrome, gather as much medical information as possible from family members and note the

characteristics/symptoms. Create a family flowchart with this information. Adding pictures can be helpful in demonstrating the characteristics.

i. See example of a family flowchart on page 12 and 13

#2,4,5 need to be done while in the paralysis so may need to be done for more than 24 hours until each is documented, during the episodes.

(# 1-5 above can give one a "clinical diagnosis")

Specifics for Genetic Diagnosing of Periodic Paralysis

"Genetic testing is being used for research, but it is not yet reliable enough to be entirely relied upon for diagnostic purposes. While a positive genetic test can prove your patient has HypoKPP, a negative result does NOT rule out the possibility of HypoKPP. While **eleven** mutations have been identified the commercial genetic labs currently only offer tests for the **three** most common mutations. There are also other mutations yet to be identified. So far genetic tests can identify about 30-70 out of 100 of positively diagnosed patients, which means that a substantial number of patients have genetic variants which have yet to be identified."

http://hkpp.org/physicians/dxing_hypokpp.html

"The most definitive way to make the diagnosis is to identify one of the calcium channel gene mutations or sodium channel gene mutations known to cause the disease. However, known mutations are found in only 70% of people with hypokalemic periodic paralysis (60% have known calcium channel mutations and 10% have known sodium channel mutations). This situation will improve as further mutations are identified. In the meantime, if potassium helps relieve or prevent episodes, this fits with hypokalemic periodic paralysis."

"Among the 30% of people who appear to have hypokalemic periodic paralysis but don't have mutations in the two genes known to cause hypokalemic periodic paralysis the following are often noted:

- Migraines
- Heart rhythm abnormalities

- Attention deficit disorder (ADD, ADHD)
- Relative insensitivity to the local anesthetic lidocaine and "dental anxiety"
- Severe premenstrual syndrome (PMS)"

http://simulconsult.com/resources/hypopp.html

Specifics for Genetic Diagnosing of Andersen-Tawil Syndrome

I have sited a few articles below, which explain this.

How Common Is It?

Andersen-Tawil syndrome is a rare genetic disorder; its incidence is unknown. About 100 people with this condition have been reported worldwide.
Type 1 accounts for about 70% of all cases of Andersen-Tawil syndrome.
Type 2 accounts for the remaining 30% of cases of Andersen-Tawil syndrome.

Genetics & Inheritance

Andersen-Tawil syndrome type 1 is caused by mutations in the KCNJ2 gene. The cause of cases of Anderson-Tawil syndrome type 2 is unknown.

http://www.inheritedhealth.com/condition/Andersen-Tawil_Syndrome/37

ATS is caused by missense mutations or small deletions (Plaster *et al*., 2001; Tristani-Firouzi *et al*., 2002; Ai *et al*., 2002; Andelfinger *et al*., 2002; Donaldson *et al*., 2003; Hosaka *et al*., 2003) in *KCNJ2*, encoding the inwardly rectifying K channel, Kir 2.1 (Plaster *et al*., 2001), in approximately two-thirds of the affected individuals (ATS1) (Plaster *et al*., 2001; Tristani-Firouzi *et al*., 2002; Donaldson *et al*., 2003). The molecular lesion(s) have not been identified in ~ 30% of subjects including kindreds not linked to *KCNJ2*.

http://brain.oxfordjournals.org/content/129/1/8.full

The following is the criteria for making a clinical diagnosis:

Table 3 Diagnostic criteria for ATS

(1) A clinically definite diagnosis requires two of the following three features:

a. PP

b. Prolonged QTc interval or ventricular ectopy (identified on ECG or Holter)
c. The typical ATS facies including:
Low set ears, ocular hypertelorism, small mandible, fifth digit clinodactyly, syndactyly

(2) Alternatively, a diagnosis may be made with one of the three features above and an affected family member meeting two of three.

http://brain.oxfordjournals.org/content/129/1/8.full.pdf

Based on the above criteria, I was diagnosed by meeting a, b and c. Therefore, my relatives could be diagnosed based on a, b or c and my diagnosis.

In a paper written by and just updated by Dr Rabi Tawil himself, it is stated that Type 1 and Type 2 are indistinguishable in how they are manifested. They can't find any difference in people with Type 1 or Type 2. The cause is the difference; in Type 1 the cause is known, in Type 2 the cause has not yet been found.

Here is the research:

Periodic Paralysis: Andersen-Tawil Syndrome Type 2

Type 1 and Type 2

Two types of Andersen–Tawil syndrome are distinguished by their genetic causes.

- Type 1, which accounts for about 60 percent of all cases of the disorder, is caused by mutations in the *KCNJ2* gene.[1][2]
- The remaining 40 percent of cases are designated as type 2; the cause of the condition in these cases is unknown.

The protein made by the *KCNJ2* gene forms a channel that transports potassium ions into muscle cells. The movement of potassium ions through these channels is critical for maintaining the normal functions of skeletal muscles which are used for movement and cardiac muscle. Mutations in the *KCNJ2* gene alter the usual structure and function of potassium channels or prevent the channels from being inserted correctly into the cell membrane. Many mutations prevent a molecule called PIP2 from binding to the channels and effectively regulating their activity. These changes disrupt the flow of potassium ions in skeletal and cardiac muscle, leading to the periodic paralysis and irregular heart rhythm characteristic of Andersen–Tawil syndrome.
Researchers have not yet determined the role of the KCNJ2 gene in bone development, and it is not known how mutations in the gene lead to the developmental abnormalities often found in Andersen–Tawil syndrome.
http://en.wikipedia.org/wiki/Andersen-Tawil_syndrome#Type_1_and_type_2

Molecular Genetic Testing (Written by Dr Tawil himself)

Andersen-Tawil Syndrome

LQT7, Long QT Syndrome 7, Andersen Syndrome. Includes: Andersen Syndrome Type 1, Andersen Syndrome Type 2
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Initial Posting: November 22, 2004; Last Update: May 13, 2010.

"**Gene. *KCNJ2*, encoding the inward rectifier potassium channel 2 protein (Kir2.1), is the only gene known to be associated with Andersen-Tawil syndrome type 1 (ATS1).**

Other loci. To date, no other loci have been identified to account for ATS (termed Andersen-Tawil syndrome type 2, or ATS2) in the 40% of kindreds not linked to *KCNJ2*."

Genotype-Phenotype Correlations

Individuals with clinically defined ATS are phenotypically indistinguishable, regardless of the presence of a *KCNJ2* mutation (ATS1) or absence of a *KCNJ2* mutation (ATS2) [Tristani-Firouzi et al 2002, Donaldson et al 2003].

In a single large kindred with the *KCNJ2* Arg67Trp mutation, periodic paralysis was observed only in men, cardiac symptoms only in women, and congenital anomalies in both [Andelfinger et al 2002]. However, this apparent sex-limited bias in clinical presentation has not been confirmed [Donaldson et al 2003, Davies et al 2005]. "

http://www.ncbi.nlm.nih.gov/books/NBK1264/

A link to a good article about diagnosing Periodic Paralysis:

http://emedicine.medscape.com/article/1171678-diagnosis

How I got my diagnosis

I am 62 years old and was newly, clinically diagnosed with Periodic Paralysis (PP) on February 7, 2011. The type I have is Andersen-Tawil Syndrome Type 2. I have had episodes of partial and total paralysis for many years. During the episodes, my potassium shifts are low (hypokalemia), high (hyperkalemia) and within the normal ranges (normokalemia). Due to several misdiagnoses and a lack of proper diagnosis and treatment for over 50 years, I have become totally and permanently disabled with weak muscles throughout my body including those involved with my vision, digestion, breathing and my heart. I must be on oxygen constantly and cannot exert myself in any way. The electrical workings of my heart are defective. I have had a heart loop monitor inserted in my chest to monitor the tachycardia and arrythmias, that include long QT interval beats. I now spend my days in a recliner, unable to walk farther than across a room. I must use a motorized wheelchair for anything farther. If I did not have the help of my husband, I would have to live in an assisted living program. I was misdiagnosed for many years.

Through the past years of my physical decline, I have had to give up my career as a special education teacher, my hobbies to include hiking, walking, swimming, exercising, fishing, camping, traveling, shopping, cooking and baking. I had to sell, and move away from, a beautiful home in the mountains of Utah. I can no longer drive. I have lost many friends, because I could not keep up with them or entertain any longer. I have lost contact with family members who did not understand or did not want to watch my decline or who thought I was a hypochondriac. I have lost the connection I once had with my grandchildren because I can no longer keep up with them or continue a meaningful relationship with them. The relationship with my husband has changed from husband and wife to caregiver and patient. Most of the over 30 doctors I have seen in the past 6 years have treated me poorly and like I was mentally ill.

I have spent the past several years working diligently to get a diagnosis and treatment for the ailment that cruelly stole the quality of my life. The most difficult part of this, for me, is knowing that I may not have became this seriously ill if just one of the over 30 doctors I have seen in the last 6 years in Oregon and the many years before, would have taken me seriously.

Once I realized what I actually had, the struggle became even more difficult trying to convince my doctors. By this point, everything else had been ruled out, but no one wanted to diagnose me. I heard I was "too old" to have it. I was ignored. I was dismissed and told to go have a "good time" as long as I was in Portland, after driving 250 miles for the results of a muscle biopsy (The test did show myopathy, change in shape and size of muscle fiber but I was told it was normal). I was given lidocaine after telling my primary care physician (PCP) I could not have it during a mole biopsy…it caused an episode of paralysis but I was treated as if I were a naughty child behaving badly. I was left alone in the room in paralysis. I was in metabolic acidosis, twice in front of my PCP and sent home rather than to the hospital. My heart was in tachycardia and I could not breathe. After discovering that I was having long QT interval heatbeats on a holter monitor (a marker for ATS), this was dismissed by my PCP, even after being told it meant I could go into cardiac arrest at any given moment. After two months, I had to request a referral to an electrocariologist. The referral took two more weeks to get from my PCP and the insurance company.

All during this time, I continued to decline as I had more and more severe total paralytic episodes. I had tachycardia and palpitations of my heart and I was having difficulty breathing. Sometimes my breathing would actually stop for a few seconds at a time. It felt like an elephant sitting on my chest. It was very frightening. Soon the difficulty of taking breaths in and out began to happen when I was not in paralysis. I found it more and more difficult to breathe. Every time I stood up, ate a meal or exerted myself in anyway, the breathing got worse and my heart would speed up until it was beating 130 to 140 beats per minute, even while I was eating.

My husband became so concerned with the lack of caring being displayed by my PCP and our insurance company, that he walked into a medical supply company and told them

what was happening and asked if they could help me to get oxygen because I could not breath. After speaking with him for a few minutes, the manager told my husband that she would give all of the information he had carried in with him, to one of the technicians and that they would see what they could do for us. She told my husband that they find it is best to get all the information together and then, “Hit them (doctors) between the eyes with the facts”.

They came out and hooked me up with a recording oximeter. It was discovered that my oxygen saturation levels were dropping dangerously low during my episodes of paralysis and it was apparent that they were low every time I exerted myself in any way. The technician took the information to my PCP and she had no choice but to sign a referral for me to get oxygen. At that point, we began to look for another PCP and decided to change insurance companies to avoid the need for referrals.

A month or two before this point, I was in despair over trying to find a doctor who knew about Periodic Paralysis. Then on the evening news, I saw their weekly feature of offering direct calls to doctors with any medical question. I quickly picked up the phone. After a wait of only a few minutes, I was speaking with one of the physicians. I asked her if she had heard of PP or knew of any doctors who might know about it. As luck would have it, she herself had a patient with it. She gave me the name of the neurologist the patient sees.

I went to my PCP with this information and talked her into giving me yet another referral. The neurologist eventually diagnosed me with “probable” Periodic Paralysis. He wrote a letter telling my PCP that I needed to see an electrocardiologist right away. It was several months before I got the referral. He described my heart condition, by that point as serious with no treatment, but insisted I needed to have a heart monitor implanted. He also set up a renal specialist to help diagnose what he believed was Andersen-Tawil Syndrome based on all the information being presented to him by me, my pcp and the neurologist. I did get the diagnosis while in the hospital for the implant after going into paralysis and being observed by the doctors. The paralytic episode was caused by them giving me a saline drip and lidocaine during the procedure, by mistake. My diagnosis was actually based on an accident.

The following is the letter I wrote to my family about my final diagnosis:

> *Hello Family and Friends.....I made it through one of the toughest days of my life.....I had a heart loop recorder inserted in chest with only lidocaine to numb it, because I cannot tolerate any meds. I told them the lidocaine would send me into paralysis, so they used a type without epinephrine and felt assured it would not cause paralysis. As luck would have it (and I knew it) 1/2 way through the procedure, I went into paralysis. By that time the device was already implanted. The doctor and rest of the team were watching my heart doing it's thing (tachycardia, arrythmias) saying things like, "Look at the huge T-waves" and reading off numbers that I didn't understand and ohing and awing. He proceeded to explain my disease to them. Then when I*

was able to answer questions, they all began to ask me questions about it...remember.... what I have, Andersen-Tawil Syndrome..... only 100 other people, world-wide, have been diagnosed with.

As they were ready to take me to recovery, I noticed an IV drip in my arm. I got horribly upset and asked what it was. They told me "saline". I swore and told them I was not supposed to have that. They then removed it. What I did not know was that it had been on me the entire procedure. I thought they had just hooked it up and then took it off after I told them that.

I went back to recovery and was doing fairly well, except for slipping in and out of small paralysis episodes.

My heart doctor had put together a "team" for the rest of the procedures they were going to do for a confirmation of how my potassium shifts and how to treat it. The plan was to put me in ICU and have a kidney specialist direct the testing and an intensivist to monitor all signs and symptoms and be there to treat my symptoms which could include my heart stopping.

I called Shari to tell her how well I was doing and tell her the plan to pass on to everyone.

Just as the kidney specialist showed up to tell me the plan and ask me a few questions, I began to have trouble answering his first question. I slipped into the worst episode of paralysis to date. My heart began to beat at a sustained heart rate of 130 to 140 bpm for over the next hour. My blood pressure was at 168/80. I felt like an elephant was on my chest. I could feel and hear my heart racing and the horrible pain from it. I could not have any pain meds or any meds to slow my heart because it would have made it worse. Everyone was in astonishment watching the heart monitor and not knowing what to do. Calvin was so afraid and I thought I was dying. I could hear everything but was unable to open my eyes, or speak. I could not move, just hear everything and feel all the pain and pressure. The doctors kept saying they had never seen anything like it and the nurses kept touching my hands, arms and face, telling me they were sorry they couldn't help me.

(The saline drip caused this...if you have PP/ATS never let them put a saline or glucose IV in you)

My heart finally began to slow down over the next hour. I was finally able to open my eyes and could speak a little. Finally, I was doing very well. The doctors decided to proceed as planned and told us the plan to put me in ICU and load me with carbs to start the paralysis again and then test my potassium levels through the paralysis process, etc.

They got me upstairs and had me ready to begin the next phase. Calvin left to go home and get some much needed rest. The kidney specialist came in at that point and said, "We have decided not to proceed with the testing and are sending you home now." I asked why? His reply floored me....."We don't need to do anymore testing...there is no doubt you have Andersen-Tawil Syndrome (ATS). Everything we have read tells us that you could die if we do the testing we were going to do, if you have ATS. We are going to give you diamox to treat your paralysis symptoms, but because you have ATS it may not work for you....but we want to try". I thanked him and told him I already knew that but was taking the chance for the little hope I had that the meds might help me...otherwise there is not much else I can do for a better quality of life.

I already had the diagnosis of Periodic Paralysis (PP) from my neurologist, but now I had the diagnosis of the type of PP.

He told me how humbled he felt to be diagnosing me. He said he was just an ordinary MD..nephrologist...not like the big and powerful doctors who wrote all the info on PP and ATS back East. But after seeing what happened and going over all the facts and by the process of elimination and studying all of the latest research I had presented to them and the family flowchart I had put together with all of the family medical history and all of your input....including Kristen's toes!!!.....he felt he had no other choice. He told me I had done all the work and had done an excellent job of presenting it all to them. Without that, I might never have got the ATS diagnosis also. He had never heard of ATS before, none of them had, but they had been researching and studying it.

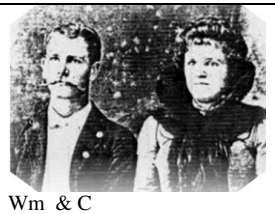
Thank you Family, for answering the little questionaires I sent out and all of your input and patience with me over the years.

He has dictated a report which each of you will get. You can then give it to your doctors. My children have a 50/50 chance of having it and of passing it on. All of you must get checked. The Long QT interval heartbeat is nothing to ignore.

Thank you all for your best wishes and kind words and thoughts.

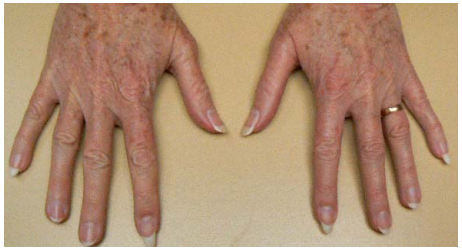
Andersen-Tawil Syndrome Flow Chart
Duggins-Critchfield & Alexander-Stevenson Family

Red= Family members who are symptomatic or have some characteristics.

		Alexander & Martha Died 38	 H & S	Sanderson & Harriet <<<<<<<		
			 Wm & C	William periods of paralysis Died 59-paralysis & heart & 1 Carrie <<<<<<<		William periods of paralysis Died 59-heart & 2 Mary
William (No children) Died heart	Russell Died heart	Alex (No children) Died heart	 Louis Duggins	Louis & Sudden death due to heart 1 Quentine <<<<<<<	Mary (No children) Periodic Paralysis symptoms	Edward (No children) Died 41-heart stopped during paralysis Periods of weakness and paralysis Heart palpatations
				Lahlee Barbara		
				Louis & 2 Geraldine		
				Jeannette		
				Louis & 3 Bernadine		
				Jackie Frances Nedra		

This is a modified version of the front page of my family flowchart. Members with symptoms are listed in red. The blue is the known symptoms.

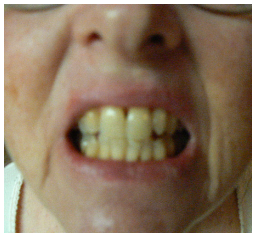
Susan's Curved little fingers



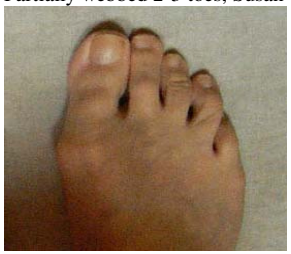
Susan

Susan:
periodic paralysis
long QT waves
6 teeth missing
(2 eye teeth 4 wisdom)
gradual muscle weakness
uses electric wheelchair
exercise intolerance
partial and total paralysis
disabled by age 50
partially webbed 2-3 toes
curved tiny finger
paralysis from anesthesia
diabetes II borderline
muscle cramps legs
fatigue
chronic pain, back, legs
fasciculations
severe reaction to meds
tachychardia
angina,
PVC's and PAC's
"nonspecific mild ST segment abnormalities of the inferior lead"
extra bone in left foot
resless leg syndrome

No eye teeth, Susan



Partially webbed 2-3 toes, Susan



This is another page listing the symptoms and showing some pictures of characteristics…some names and pictures have been removed due to privacy.