What is Bartter’s Syndrome?

Bartter’s Syndrome is an inherited defect in the renal tubules that causes low potassium levels, low chloride levels, which in turn causes metabolic alkalosis. Bartter Syndrome, is not a single disorder but rather a set of closely related disorders. These Bartter-like syndromes share many of the same physiologic derangements, but differ with regard to the age of onset, the presenting symptoms, the magnitude of urinary potassium (K) and prostaglandin excretion, and the extent of urinary calcium excretion.

At least three clinical phenotypes have been distinguished:

- **Classic Bartter Syndrome**
- **The Gitelman Variant**
- **The Antenatal Variant** (also termed Hyperprostaglandin E Syndrome).

There are also many patients who have other variant that they believe may be variants of Bartter’s that has not yet been identified. Whatever type of electrolyte problems you are having will determine what type of Bartter’s syndrome you have. There are many patients who have characteristics of Classic Bartter’s and Gitelman’s combined. From the research I have done it appears that many of the patients that have Classic Bartter’s initially seem to change as they get older and start having problems with magnesium which is more characteristic of Gitelman’s. This is one thing that has baffled many nephrologist’s and researchers. These patients fall into that category of having both or many of them have their diagnoses switched from Classic Bartter’s to Gitelman’s. No one knows why this occurs.

**Classic Bartter Syndrome**

Bartter’s Syndrome was first discovered in 1962 by Frederic Bartter. Bartter described this syndrome in two African-American patients: a 5 year old boy and a 25 year old man with a long history of slow growth, weakness and fatigue. On high sodium diets, both patients had normal blood pressure and high urinary aldosterone excretion, resulting in metabolic alkalosis. This syndrome is a disorder of the renal tubules in the kidneys that causes a higher than normal Aldosterone level and low serum potassium levels which lead to metabolic alkalosis. Patients with this syndrome share a myriad of clinical symptoms and laboratory abnormalities. Most notable are:

- Profound hypokalemia (Very low serum potassium levels)
- Increased urinary excretion of potassium (K) and prostaglandins.
- Normal blood pressure despite elevated plasma renin and aldosterone levels. (High renin and aldosterone causes hypertension in a normal healthy person. In Bartter’s the Renin and Aldosterone are elevated but the patients do not have hypertension)
- Hypochloremic (Low serum chloride) metabolic alkalosis.
- A relative vascular resistance to the pressor effects of exogenous angiotensin II
- Hyperplasia of the juxtaglomerular apparatus

Bartter described this combination of juxtaglomerular hyperplasia, hyperaldosteronism and hypokalemic alkalosis in two African-American subjects: a 5yr old boy and a 25yr old man with a long history of slow growth, weakness and fatigue. On high sodium diets, both subjects had normal blood pressure and high urinary aldosterone excretion, resulting in hyperbicarbonatemia.

Initially, it was considered a vascular disease. In the 1970’s, when prostaglandins were discovered, it was found that Bartter’s Syndrome patients overproduced prostaglandins. If treated with a prostaglandin inhibitor, aldosterone levels returned to normal. Plasma potassium levels did not. Subsequently, experimental potassium deficiency induced prostaglandin production and many of the symptoms of Bartter’s Syndrome. The suggested problem was not intravascular, but a renal tubular problem.

**Frequency In the US**

There are both familial (Inherited) and sporadic forms of Bartter’s and Gitelman’s syndromes. The prevalence of this disorder is not precisely known, but one study cites an estimate of 1.2 per million. Although many cases appear to be sporadic, Bartter’s syndrome is well described in siblings as well as in children of consanguineous marriages. This
pattern of transmission suggests an autosomal recessive* mode of inheritance. However, in a few kindreds, the inheritance pattern is more consistent with autosomal dominant** transmission.

*Autosomal Recessive – Both parents carry the gene which is passed on to the child.

**Autosomal Dominant – One parent carries the gene which is passed on to the child.

Frequency Internationally

Estimates of incidences vary from country to country.

In Costa Rica, incidence of neonatal Bartter’s from live births is estimated at 1.2/100,000, higher if all preterm births are considered. No evidence of consanguinity was found in the Costa Rican cohort.

In Kuwait, the incidence of consanguineous marriages or related families in Bartter’s syndrome patients is higher than 50% and the incidence is 1.7/100,000.

In Sweden, the incidence has been calculated as 1.2/1,000,000. Of the twenty-eight patients reported by Rudin, seven cases came from three families. The others were unrelated.

Sex

Bartter’s syndrome is inherited as an autosomal recessive trait, there is no gender preference.

Race

There is no racial predisposition for Bartter’s Syndrome.

Age

Classic Bartter’s syndrome is usually diagnosed in childhood or adolescence.

Symptoms

- Fatigue
- Polyuria (Increased urination)
- Polydipsia (Increased Thirst)
- Nocturia (Waking up at night to urinate)
- Generalized weakness
- Salt Cravings
- Dehydration
- Mental confusion
- Vomiting
- Muscle weakness
- Muscle spasms
- Tetany
- Failure to thrive
- Short stature (If untreated)

Lab and Physical findings

- Low serum potassium levels
- Low-normal magnesium levels
- Increased renin
- Increased aldosterone
- Metabolic Alkalosis
- Increased Prostaglandin E2 excretion
- Normal-high urinary calcium excretion
- Normal-high urinary Mg excretion
- Normal-low serum Mg levels (20% have decreased Mg levels)
- Normal – Low Blood Pressure
- Increased urinary potassium excretion
- Increased plasma angiotensin II
- Nephrocalcinosis
- Tetany, muscle spasms, Chvostek’s sign and Trousseau’s sign may be seen in hypokalemia, hypocalcemia, and hypomagnesemia patients. In the older literature rickets was also occasionally reported.
- In 1997, Madrigal described a type of this syndrome in Costa Rica in sixteen of the twenty patients with a “peculiar facies, distinguished by a triangularly shaped face, large eyes, and protruding ears”.
- Another eight had sensorineural hearing loss determined by audiography.
In addition to these biochemical perturbations, a small subset of patients have developed progressive renal insufficiency due to severe tubulo-interstitial nephritis. It is not clear whether the loss of renal function in these patients was a direct consequence of their primary molecular defect or secondary phenomenon related to their chronic hypokalemia.

**What Causes this Syndrome?**

The most accepted explanation for Classic Bartter Syndrome involves a primary defect in Cl transport in the TAL. This is a part of one of the tubules in the kidneys where electrolytes are absorbed into the bloodstream.

**Treatments**

There is no cure for Bartter's syndrome. The treatments consist of supplements to replace what is lost and medications to prevent urinary wasting of potassium and magnesium. In younger children growth hormone may be used to prevent the short stature and prostaglandin inhibitors to decrease the elevated prostaglandin levels.

- Potassium Chloride Supplements
- Magnesium Supplements
- Spironolactone
- Amiloride
- Triamterene
- Indomethacin
- Captopril
- Growth Hormone

**Prognosis**

The limited prognostic information available suggests that early diagnosis and appropriate treatment of infants and young children with Classic Bartter Syndrome may improve growth and perhaps neurointellectual development. On the other hand, sustained hypokalemia and hyperreninemia can cause progressive tubulointerstitial nephritis, resulting in end-stage renal disease (Kidney failure). With early treatment of the electrolyte imbalances the prognosis for patients with Classic Bartter Syndrome is good.