Lesch-Nyhan Syndrome (LNS)

Cause/etiology and prevalence

- **X-chromosome.** Lesch-Nyhan Syndrome (LNS) is a rare condition that is caused by a defective gene called hypoxanthine phosphoribosyl transferase (hprt) on the X-chromosome. It is usually inherited from the mother who is a silent carrier of the gene (i.e., a recessive gene). However, it can occur from a spontaneous mutation of the gene, which occurs early in the child’s development.

- **Prevalence.** The prevalence of LNS is 1 in 380,000. It is evenly distributed across races and geographic locations. It is generally a condition that is pronounced in males. However, research by Yukawa et al. (1992) documented an incident in a female. Males are more susceptible to contracting the syndrome because they only have one X-chromosome, whereas females have a second X-chromosome to protect them.

- **Expression.** Symptoms of LNS are expressed when there is an almost complete absence of an enzyme called hypoxanthine guanine phosphoribosyl transferase (HGPRT) enzyme. This enzyme is responsible for the recycling of purines in the body. The lack of purine recycling causes a build up and the purines are wasted. Wasted purines turn into uric acid, which clump together to form crystals and stones. Correction of this metabolic defect unfortunately does not change the physical and psychological characteristics of these children.

- **Basil ganglia.** Abnormal functioning in a small area of the brain known as the basil ganglia is responsible for most neurological and behavioural problems. MRI and CT scans indicate shrinkage in two areas of the basil ganglia, the caudate and the putamen. Studies have also shown there is a shortage of dopamine, which is a neurotransmitter (a chemical in the brain) responsible for sending signals between cells in the brain.

- **Lesch-Nyhan variants (LNV).** Some individuals do not have all three problems (overproduction of uric acid, developmental delays with a neuro-motor disability, and problem behaviour) typical of LNS. These individuals have less severe symptoms.

Distinctive physical characteristics

- **Developmental milestones.** Children with LNS appear normal at birth and develop typically for the first 6-8 months. Symptoms progress from a lack of muscle tone to muscle rigidity and then to uncontrolled movements of arms and the body. The development of involuntary muscle movements occurs between 8-12 months. Individuals with LNS may have sudden spasms where their head is thrown back suddenly and forcefully. Their motor development is so severely disturbed that they are unable to stand and sit without support and none of them learn to walk. All individuals with LNS have cerebral palsy.

- **Physical growth.** Individuals with LNS are typically underweight, short in stature, and develop excessive muscle tone with the development of involuntary movement.

- **Early indicator.** An orange crystalline material may appear in the child’s diaper as a result of having high levels of uric acid.

- **Body mutilation.** Individuals with LNS engage in self-injurious behaviour (SIB) that results in body mutilation. These mutilations include partial self-amputation of fingers and toes, tissue loss of lips and tongue due to biting self, injury to eyes, and cutting self with sharp objects.

- **Teeth.** Their teeth are sometimes extracted to prevent self-harm and harm to others by biting.
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Health issues

- **Hyperuricemia.** Hyperuricemia is characterized by an overproduction of uric acid. If there is a high level of uric acid in the body it sticks together in clumps known as crystals and stones. These crystals and stones form in three areas of the body.
  1. It forms between joints and bones usually in the toes and fingers. This is commonly known as Gout and is characterized by swelling, redness, and pain.
  2. It forms under the skin. This is known as Tophi. It commonly demonstrates as bumps in the tissue around the ear.
  3. It forms in the kidneys. If a stone gets stuck, it can prevent a kidney from functioning and can result in kidney failure. This is the most common cause of early death in individuals with LNS.
- **Arthritis.** Acute arthritis may develop after a number of years of untreated hyperuricemia.
- **Life expectancy.** The life expectancy of an individual with LNS is 20-25 years.

Cognitive abilities/challenges

- **IQ.** Recent research indicates that individuals with LNS are less severely cognitively delayed than previously thought (Anderson, Ernest, & Davis, 1992). Some individuals have below average cognitive functioning (i.e., IQ between 60-70, which indicates a mild to moderate cognitive impairment) while others are able to reach an average range.
- **Attentional difficulties.** Individuals with LNS have relatively good memories and language, however they have low attention spans. Due to deficits in attention, combined with motor impairments and SIB, standardized assessments are not accurate indicators of the cognitive abilities of individuals with LNS.
- **Planning and predicting.** Individuals with LNS have difficulties with complex planning and predicting consequences.

Language/communication abilities/challenges

- **Receptive language.** Individuals with LNS have normal receptive communication and are able to comprehend well.
- **Expressive language.** Their speech is characterized by poor articulation.

Sensory and/or motor abilities/challenges

- **Spastic cerebral palsy and choreoathetosis.** Rapid, jerky, involuntary muscle movement accompanied by slow sinuous writhing movements characterizes these conditions. It usually is noticeable in the hands.
- **Neuro-motor disability.** Individuals with LNS have difficulties controlling their muscles. The muscles appear to be stiff when in use. This is known as dystonia. Dystonia is severe enough to prevent standing, walking, and sitting independently. It can also inhibit the use of hands for self-feeding.

Social emotional/behavioural abilities/challenges

- **Self-injurious behaviour (SIB).** Individuals with LNS can engage in aggressive, self-mutilating behaviours that continue throughout their lifespan. Some of these behaviours include biting and hitting self, poking own eyes, cutting self on sharp objects, and banging their heads. The biting can be severe enough to cause self-amputation of fingers and toes and tissue damage/loss of the lips and tongue. Individuals with LNS are sensitive to pain (i.e., they scream when they injure themselves) and are often fearful at the anticipation of self-injury.
- **Aggression towards others.** Aggression can be directed towards others in the form of biting, kicking, hitting, spitting, or using foul language. However, their motor deficits limit their ability to cause physical harm to others. With the onset of puberty, sexually oriented grabbing, pinching, or touching
may develop. These acts of aggression are impulsive and often uncontrollable. Individuals with LNS are often apologetic after successful attempts.

- **Restraints.** When restrained, individuals with LNS appear happy and content; they are good-natured and laugh easily. When their restraints are removed they quickly become anxious or terrified of engaging in aggressive behaviour. Some individuals will scream, some will call for help, and others who are older may try to put the restraints back on themselves.

### Other unique abilities/challenges/issues

- **Recurrent vomiting.** Severe vomiting can affect nutrition and growth. Individuals with LNS are usually under weight and short in stature. In cases where the vomiting is severe, a feeding tube is inserted into the stomach.

- **Anemia.** Anemia is characterized by very large red cells in the blood. It is usually caused by dietary deficiency of vitamin B12 or folic acid. Individuals with LNS do not have these particular deficiencies and supplements are not beneficial. Fortunately, symptoms are not severe and there is no need to treat.

### Implications for education and learning

- **Environment.** Individuals with LNS are confined to wheelchairs; therefore the educational setting should be wheelchair accessible. To prevent injuries, all sharp objects should be safely stored in an out of reach area and sharp edges of tables, cabinets, counters, wheelchair, etc. should also be padded. Soft mats should be available, if the child is to be taken out of his/her wheelchair. However, it is preferable to keep the student in his/her wheelchair most of the day. Staff should not stand directly behind the student with LNS due to the potential of the student having a sudden spasm that causes the student to throw his/her head back forcefully and suddenly.

- **Teachers/educational assistants/interventionists.** Individuals with LNS have very specific needs and staff should be trained to appropriately attend to them. For example, staff should be trained on how to use physical and manual restraints appropriately/effectively to ensure student safety, yet allowing maximal participation in activities (i.e., allowing some movement of hands). One-on-one staffing may be required depending on how severe the individual’s needs are. Children with LNS are unable to sit, stand, and sometimes feed themselves independently. Two staff members are required for bathing and toileting. Staff also need to be aware if the student is taking medication to counteract the over production of uric acid or to reduce muscle stiffness. Staff members need to ensure that the student is well hydrated (after vomiting and to keep the uric acid flowing).

- **Pharmaceutical treatments.** Allopurinol may be prescribed to slow the production of uric acid. Frequently used medications to help alleviate neurological symptoms such as muscle stiffness and immobility include baclofen, diazepam, and clonazepam. Medications that may reduce but not eliminate SIB include gabapentin, carbamazepine, and diazepam. Risperdal causes sleepiness and can make neuro-motor problems worse. If it is being used, ensure that improvements in SIB are not being traded for sedation or worsening of neuro-motor functioning.

- **Instructional Strategies.** Testing and educational opportunities need to be tailored to the individual’s strengths and weaknesses. Individuals with LNS enjoy social interactions and have a short attention span. Therefore, learning activities need to be short in nature, allow for different ways of showing concept comprehension (e.g., verbal responses instead of written responses), and socially interactive. Individuals with LNS typically do not do well on standardized IQ tests. This is due to the length of time required to focus to complete the tasks and to their motor impairments. Therefore, if students do not perform well on their IQ tests, it is important to realize that this may not be due to cognitive delays. Students with LNS can be of average intelligence and are capable of learning many things in the right environment. An IEP should be developed with the team, implemented, and reviewed throughout the school year.
• **Problem behaviour.** It is important to complete a functional assessment of problem behaviour before creating a PBS plan and implementing any interventions for problem behaviour. Research has shown that aversive techniques such as electric shock and verbal reprimands are ineffective in reducing or eliminating SIB in individuals with LNS (Anderson et al., 1978; Bergen et al., 2002). These aversive techniques may even worsen problem behaviour. Both studies found that positive reinforcement of non-SIB in the form of social attention and time out from social reinforcement were consistently and rapidly effective in treating SIB in individuals with SIB. These finding suggest that there is an environmental component in addition to the genetic component of SIB. Since there is a genetic component, it is not safe to assume that all problem behaviour can be eliminated.

• **Related services.** Services from a physical therapist and/or occupational therapist may be helpful in reducing muscle stiffness and increasing mobility. A speech language pathologist can help create and implement programs to improve expressive language skills.

**Images**

An infant with LNS who has bitten off his finger tip.

An individual with LNS who has tissue damage/loss of the lips.

An Individual with LNS in a padded wheel chair with arm restraints. He also has his teeth removed.

**References**


