



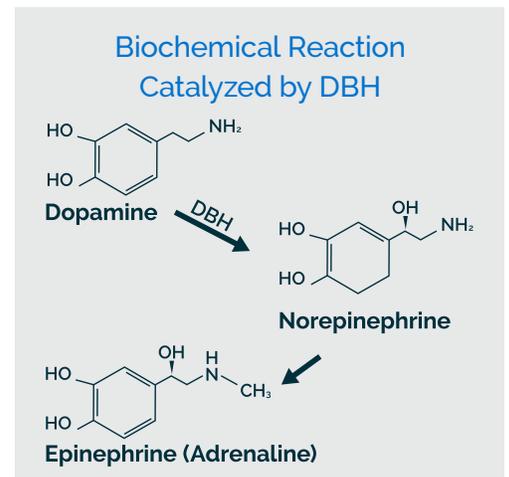
The Great Plains Laboratory, Inc.



Abnormal Dopamine Beta Hydroxylase (DBH) Enzyme Activity:

The Missing Link in POTS, Dysautonomia, Autism, ADHD, Infertility, Impaired Immunity, and Many Other Diseases

Dopamine beta-hydroxylase (DBH) is a key enzyme in the conversion of dopamine to norepinephrine in the central nervous system and is the enzyme needed for the conversion of dopamine to norepinephrine in the sympathetic nervous system of the autonomic nervous system. Dopamine beta-hydroxylase can be readily measured in serum and correlates highly with the amount of the same enzyme in the cerebral spinal fluid. The DBH gene has been mapped to chromosome 9 at the q34 position. Seventy-one polymorphisms of the DBH gene have been identified in just 80 subjects: 68 single nucleotide polymorphisms (SNPs), two insertion/deletions, and one repeat. Because of the large number of SNPs, there are a very large number of possible combinations of variants for DBH (4,970 combinations).



Abnormalities of DBH result in severe postural hypotension (POTS) and are also associated with the following symptoms and disorders:

- ADD/ADHD
- Parkinson's Disease
- Depression
- Tourette's Syndrome
- Hyperflexible Joints
- Fainting Spells
- Schizophrenia
- Low Muscle Tone
- Autism Spectrum Disorders
- Huntington's Chorea
- Bipolar Depression
- Low Blood Pressure
- Hypoglycemia
- Psychosis
- Impaired Ejaculation
- Spontaneous Abortion
- Alzheimer's Disease
- Hypertension
- Cardiac Heart Failure
- Bed Wetting (Enuresis)
- Exercise Intolerance
- PTSD
- Seizures
- Alcoholism

Women with DBH deficiency are much more likely to have children with autism. In animals, DBH deficiency is associated with severe immune deficiency, impaired response to immunization, and lack of maternal care. It might be expected that similar abnormalities occur in humans. Because of the very large number of possible combinations of variants for DBH and the fact that the amount of enzyme activity associated with each variant is unknown or reports on such SNPs are contradictory, assessment of DBH enzyme in serum or plasma is an excellent substitute for DNA testing.

DBH and Autism

Abnormalities in the metabolism of dopamine in autism consistent with DBH deficiency have been reported in the research literature for more than 40 years (Lelord 1978). DBH deficiency greatly increases the concentration of dopamine and its metabolite homovanillic acid in the cerebrospinal fluid, blood, and urine because of the accumulation of dopamine when the DBH enzyme is less active.

Lelord, Callaway, Muh, Sauvage, and Arlot (1978) and Garreau et al. (1980) reported that urinary levels of the dopamine metabolite, homovanillic acid (HVA) were higher in autistic than in normal children, and that the clinical improvement of these young autistic patients under vitamin B6 was associated with a decrease of their urinary HVA excretion (Lelord, Muh, Barthelemy, Martineau, Garreau, & Callaway, 1981). Abnormalities also included elevated concentrations of HVA in cerebrospinal fluid (Cohen, Caparulo, Shaywitz, & Bower, 1977, Gillberg). In addition, the degree of elevation of HVA in urine was correlated with the increased severity of autistic symptoms (Garreau 1980).

The mean serum DBH was 30% lower in mothers of children with autism compared to mean values of those without a child with autism, indicating a likely genetic involvement of DBH as a cause of autism. In the same study, it was found that mothers of sons with autism had a higher incidence of a 19 base pair deletion polymorphism (DBH-) in the DBH gene. The epidemiological term "attributable risk" for this gene was 42%, interpreted as meaning that the risk of having a son with autism was 42% higher for the mothers with this genetic variant than without it. DBH genotypes also differed significantly among mothers and controls, with 37% of mothers with two affected sons having two DBH- alleles, compared to 19% of controls. The DBH- allele was associated with nearly a 50% lower mean serum DBH enzyme activity (nondeletion homozygotes: 41.02 ± 24.34 IU/liter; heterozygotes: 32.07 ± 18.10 IU/liter; and deletion homozygotes: 22.31 ± 13.48 IU/liter in a pooled sample of mothers and controls. These researchers suggest that lowered maternal serum DBH activity results in a suboptimal uterine environment (decreased norepinephrine relative to dopamine), which, in conjunction with genotypic susceptibility of the fetus, results in autism spectrum disorder in some families.

Unfortunately, the children with autism of these mothers with low DBH were not tested for low DBH. However, a high incidence of hyperflexible joints and postural hypotension has been reported in autism, implicating a potential role of DBH deficiency as a cause of autism.

Dysautonomia and its Connection to DBH

Dysautonomia is an encompassing term used to describe several different medical conditions that cause a malfunction of the autonomic nervous system, the system that controls the automatic functions of the body that we do not consciously think about, such as heart rate, blood pressure, digestion, dilation and constriction of the pupils of the eye, kidney function, and temperature control. The autonomic nervous system consists of two main divisions: the sympathetic nervous system and the parasympathetic nervous system. The sympathetic nervous system is often considered the "fight or flight" system, while the parasympathetic nervous system is often considered the "rest and digest" or "feed and breed" system. In many cases, both of these systems have "opposite" actions where one system activates a physiological response and the other inhibits it. At the effector organs, sympathetic ganglionic neurons release noradrenaline (norepinephrine) while parasympathetic postganglionic neurons release acetylcholine as the main neurotransmitter. If DBH is deficient in the sympathetic nervous system, the substrate of the enzyme dopamine accumulates while the products of the enzyme, norepinephrine and epinephrine, decrease.

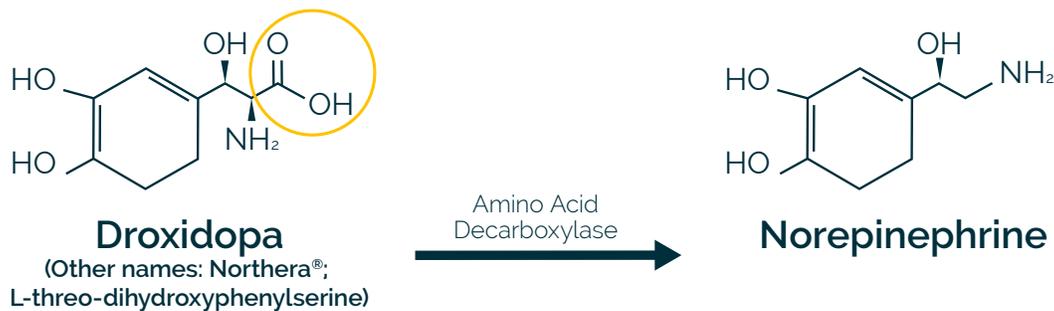
DBH and Infertility

Thomas and his colleagues (1995, 1997) found that in pregnant female mice that lacked DBH virtually all progeny died and that there were many deaths of progeny even in pregnant mice with only a single copy of the DBH gene. By providing additional norepinephrine from the Droxidopa drug to the pregnant mice with the genetic deficiency, the excess mortality of the offspring was prevented. Although not yet reported in humans, DBH deficiency may also be a cause of infertility in humans.

Help For a Patient with Severe Hypotension (Low Blood Pressure)

The following is a typical story of a patient dealing with severe hypotension written by the health writer Amanda Gardner on www.health.com:

A patient, Megan, first experienced troubling symptoms as a child. Whenever she stood up for more than two minutes, she collapsed. She had similar problems whenever she stood up in church or school. She suffered from bed wetting when she was older and also had droopy eye lids, excessive bladder infections, and hypoglycemic (low blood sugar) episodes that left her shaky. As she became a teenager she suffered from severe exercise intolerance and was unable to walk a block or climb a flight of stairs without resting. She consulted many physicians with no answers. Her standing blood pressure was extremely low (50/30). All of Megan's symptoms were due to a deficiency of DBH. After finally finding a physician who diagnosed her with dopamine beta hydroxylase deficiency, she was put on the drug Northera® which was able to form norepinephrine by circumventing the impaired DBH pathway as illustrated below:



In 2010, after taking Northera®, Megan completed an Olympic-length triathlon: a 1,500-meter swim, 40-kilometer bike ride, and 10K run. "For me it was like checking this off the list," Megan says. "I was so grateful for my new physicality."

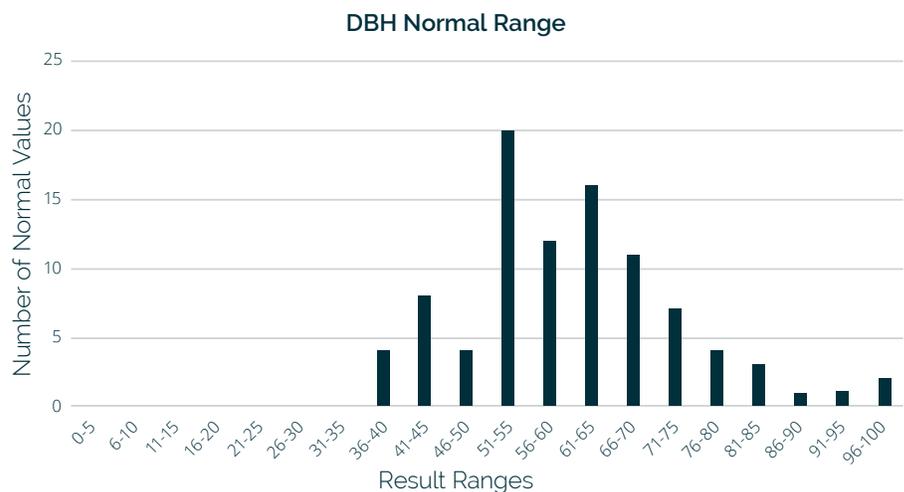
Droxidopa (Northera®) has been used as a replacement for norepinephrine and has been effective in treating other disorders besides POTS and hypotension, such as autism and Parkinson's disease.

Postural Orthostatic Tachycardia Syndrome (POTS)

Dysautonomia is not rare. Over 70 million people worldwide live with various forms of dysautonomia. People of any age, gender or race can be impacted. POTS is estimated to impact a total of 1,000,000 to 3,000,000 Americans. The condition can cause lightheadness, fainting, tachycardia, chest pains, shortness of breath, GI upset, shaking, exercise intolerance, temperature sensitivity and more. While POTS predominantly impacts young women who look healthy on the outside, researchers compare the disability seen in POTS to the disability seen in conditions like COPD and congestive heart failure.

Normal Values for DBH

A normal range study at The Great Plains Laboratory of both adult males and females found no difference between adult males and females, so data were combined into a single normal range shown below.



Sample Report



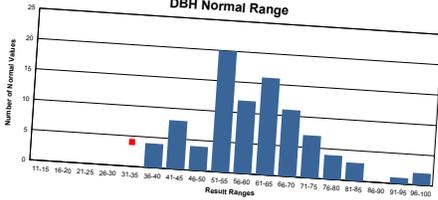
The Great Plains Laboratory, Inc.

William Shaw, Ph.D. Director | 11813 W. 77th Street, Lenexa, KS 66214 | (913) 341-8949 | Fax (913) 341-6207

Requisition #: 888888 | Physician Name: WILLIAM SHAW
 Patient Name: Test Test | Date of Collection: Mar 24, 2019
 Date of Birth: Mar 30, 1978 | Time of Collection: 08:00 AM
 Gender: F | Print Date: Mar 29, 2019

DBH-Dopamine Beta-Hydroxylase Test

Test	Reference Range	Patient Value	Deviation from the Mean %
DBH-Dopamine Beta-Hydroxylase	35.2 - 86.1	34.00 L	-43.9 %



DBH Normal Range
Population Mean = 60.6

Interpretations

Low values of DBH are associated with all of the conditions in the table below. The mean value of DBH for women who had children with autism was 30% below the mean value of DBH for women who did not have a child with autism.

Reference ranges have been established for adults 20 and older but not yet for children under 13. All children's values should be interpreted with great caution.



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Dopamine Beta-Hydroxylase Test

Conditions associated with low DBH

Attention deficit disorder	Autism	Alzheimer's disease
Parkinson's	Huntington's chorea	Hypoglycemia
Depression	Bipolar depression	Cardiac heart failure
Tourette's syndrome	Low blood pressure	Bed wetting (enuresis)
Hyperflexible joints	Arsenic toxicity	Exercise intolerance
Fainting spells	Psychosis	PTSD
Schizophrenia	Impaired ejaculation	Seizures
Low muscle tone	Spontaneous abortion	Alcoholism
POTS	Severe postural hypotension	Small brain size
Immune deficiency		

Low values have been associated with hypertension.

Effect of Age and Sex on DBH Results

Previous studies have found no significant differences between male and female results. We do not have normal ranges for children but previous studies have found significantly lower values of DBH for children. We will test children since a complete absence of DBH would be significant even in the absence of children's reference ranges but all children's results will have the message:

"Reference ranges have been established for adults but not yet for children under 13 years old. All children's values should be interpreted with great caution."

Possible Interferences

The following substances may interfere in the test and cause lower results:

- Clostridia metabolites
- Phenols
- Fusaric acid from Fusarium mold species
- Antabuse®
- Nutrasweet® (aspartame)

Sample Collection

This test requires a serum sample. The sample is stable for one week at room temperature and three weeks at -20 degrees C. Dried blood spot (DBS) samples are not currently acceptable.

Discounts

Discounts for the DBH test are available when ordered on the same sample as the IgG Food Allergy Test (serum only). This discount is not available for the dried blood spot (DBS) IgG Food Allergy Test.

Contact Us
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