Health Risk Assessment Test
For Alzheimer’s Disease
Alz-ID™ Test

A simple blood test that identifies patients at elevated risk for developing Alzheimer’s disease (AD).

Plasmalogens (PlsEtn) are key structural membrane components in the brain and sufficient levels are critical for normal synaptic function, amyloid processing, and cholesterol homeostasis. The Alz-ID™ is a blood test that measures the levels of docosahexaneonic acid (DHA) containing ethanolamine plasmalogens.

The quantitative Plasmalogen Biosynthesis Value (PBV) is reported as follows:

<table>
<thead>
<tr>
<th>PBV Level</th>
<th>Risk Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Below Normal PBV</td>
<td>Increased risk of developing Alzheimer’s disease</td>
</tr>
<tr>
<td>Normal PBV</td>
<td>Average risk of developing Alzheimer’s disease</td>
</tr>
<tr>
<td>Above Normal PBV</td>
<td>Decreased risk of developing Alzheimer’s disease</td>
</tr>
</tbody>
</table>

Plasmalogens: Biological Background

- Reduced cholinergic nerve transmission is the primary biochemical mechanism responsible for the reduced cognition observed in dementia. Current drug therapies work by either reducing acetylcholine degradation in the synapse (Aricept) or by enhancing post-synaptic function (Memantine). Neither of these drugs address the underlying causal mechanisms leading to reduced cholinergic transmission and therefore only work temporarily.

- Nerve transmission occurs when an action potential causes pre-synaptic neurotransmitter vesicles to move to the synaptic membrane, fuse to the membrane and release neurotransmitters into the synapse. (Figures 1,2)

- This vesicular fusion process is affected by the phospholipid composition of both the vesicle and synaptic membrane. Specifically, a special type of phospholipid: an ethanolamine plasmalogen (PlsEtn) with a polyunsaturated fatty acid (like DHA) must be present in sufficient quantities for this process to occur.
• Braak stage is used to classify the degree of pathology in Alzheimer’s disease. It ranges from stages I - VI with increasing severity.

• Plasmalogen levels were measured in 100 brain samples of subjects with varying levels of pathology and cognitive impairment to determine the association between plasmalogens and cognition.

Table 1. PlsEtn and Cognition (output)

<table>
<thead>
<tr>
<th>PlsEtn</th>
<th>R-Squared</th>
<th>Coeff.</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>22:6 (DHA)</td>
<td>0.300</td>
<td>9.16</td>
<td>&lt;0.00001</td>
</tr>
</tbody>
</table>

Table 1: corrected for age, gender, and education, n=100

• Increasing brain levels of DHA-PlsEtn are strongly correlated with increased cognition

Figure 3. Serum levels are normalized to PtdEtn 16:0/18:0. * p<0.05. Braak 0-I (n=11, age 82.9+/−2.6, MMSE=28+/−0.5, 4F); Braak II (n=8, age 86.0+/−1.9, MMSE=25.4+/−3.6, 3F); Braak III (n=23, age 88.2+/−1.0, MMSE 23.9+/−1.2, 14F); Braak IV (n=23, age 91.1+/−0.8, MMSE 22.4+/−1.7, 9F); Braak V-VI (n=21, age 89.1+/−1.0, MMSE 12.5+/−2.1, 14F).

• Figure 3 outlines the effect of Braak stage on pre-mortem Mini-mental state examination (MMSE) and Serum DHA-PlsEtn, and post-mortem temporal cortex DHA PlsEtn levels.

• DHA-PlsEtn levels decrease in both post-mortem brain and pre-mortem serum samples with increasing Braak stage.

Table 2. PlsEtn and Pathology (output)

<table>
<thead>
<tr>
<th>PlsEtn</th>
<th>R-Squared</th>
<th>Coeff.</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>22:6 (DHA)</td>
<td>0.205</td>
<td>-2.986</td>
<td>&lt;0.00001</td>
</tr>
</tbody>
</table>

Table 2: corrected for age, gender, and education, n=100

• Increasing brain levels of DHA-PlsEtn are strongly correlated with decreased AD pathology
Plasmalogens: Biological Background Summary

• Brain DHA-PlsEtn levels are correlated with blood levels.

• PlsEtn are synthesized in the liver within peroxisome organelles and constitute close to 50% of the ethanolamine phospholipids in the brain.¹

• As we age, we become at increased risk of reduced liver function and as a result peroxisomal biosynthesis of PlsEtn can become less than that needed to maintain healthy brain function, which puts us at increased risk of Alzheimer’s disease.

PBV and Cognition

Serum Changes in PlsEtn Subjects

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Age</th>
<th>Gender</th>
<th>MMSE</th>
<th>ADAS-cog</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive Normal (CN)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADAS 5-19 (Low)</td>
<td></td>
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<td></td>
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<tr>
<td>ADAS 20-39 (Moderate)</td>
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<tr>
<td>ADAS 40-70 (Severe)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAT (All)</td>
<td></td>
<td></td>
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</tbody>
</table>

Table 3. ADAS (AD Assessment Scale), DAT (Dementia of Alzheimer’s type)

- Serum DHA-PlsEtn levels were observed to decrease with increasing dementia in 256 living subjects (Figure 4). Subjects at time of diagnosis who were later confirmed at autopsy to have AD, in Japanese demented subjects as well as in subjects with post-mortem AD pathology (Goodenowe et al., 2007).⁵

- As cognitive impairment increases from normal (CN) to severe, PlsEtn levels decrease (Table 3).

Cognitive Status of Alz-ID Cohorts

PBV values were determined in 862 subjects aged 58-104 (average age 84.8) and correlated with their cognitive status. An above normal PBV was associated with higher cognition (p<0.001, models corrected for age, education, gender and ApoE genotype).

Persons with a below normal PBV had lower cognition and persons with an above normal PBV had higher cognition versus those with a normal PBV value. (Figure 5)
Other than age...Who develops AD?

**Apolipoprotein E (ApoE) genetic risk factor**

- ApoE ε4 carriers: risk gene in Alzheimer’s
  - ApoE is considered a “non-modifiable” risk factor

- Percent of people with AD
  - ε2: 2%
  - ε3: 9%
  - ε4: 16%

- People with a below normal PBV
  - Decreased Risk (Above Normal PBV): 3%
  - Average Risk (Normal PBV): 9%
  - Increased Risk (Below Normal PBV): 19%

**ApoE – Genotype and Its Role**

- High Plasmalogen Biosynthesis capacity is shown to be protective against genetic (ApoE) risk factors.

- Above Normal PBV decreases risk in each of the the ApoE genotypes.

- The Alz-ID result can override the genetic risk for developing AD.
Healthy Body, Healthy Brain

Healthy lifestyle choices will help keep the brain as healthy as possible. Some risk factors cannot be controlled, such as genetic makeup and growing older, but there is a lot that can be done that may help decrease the risk of developing Alzheimer’s disease.

✓ Challenge the Brain
✓ Be Physically Active
✓ Be Socially Active
✓ Maintain a Healthy Diet
✓ Protect the Head

A recent study conducted on cognitive and motor function in patients institutionalized for dementia showed the following: 

“A combination of aerobic and strength training is more effective than aerobic-only training in slowing cognitive and motor decline in patients with dementia.”

Key Points

• Use Alz-ID results in conjunction with other methods to assess a patient’s overall risk of Alzheimer’s disease.

• Alz-ID is a simple blood test that does not require any fasting or dietary restrictions prior to the test.
When & Why To Get Tested?

• At 60 years of age. Typically, testing about 10 years prior to the average onset of Alzheimer’s disease is recommended.

• Motivate the patient to adjust lifestyle:
  - ✔️ Diet
  - ✔️ Exercise
  - ✔️ Cognitive Stimulation

• If a patient is pre-disease but at risk, Alz-ID can help motivate the patient or the family to get the patient active.

• It’s never too soon, or too late to make changes that will maintain or improve brain health, changes that may also help decrease the risk of developing Alzheimer’s disease.

References


Ordering Information

BC LifeLabs 1-800-431-7206
Ontario LifeLabs 1-877-849-3637
Ontario CML HealthCare 1-800-263-0801
Kit Ordering Service 1-877-990-1575
contactus@lifelabs.com
www.lifelabs.com