Optimizing Health for Individuals with Down Syndrome

Dr. Erica Peirson
Testimonial

Just wanted to give you an update on (our daughter). In 1 month of being on (treatment):

1. Reflux (used to spit up half of whatever she ate) gone the first day.
2. First 2 teeth came in the first week, another 2 the 2nd week
3. Pulled herself to a standing position first day
4. Stood up without support 2nd week
5. Tongue is in her mouth 80% of the time rather than 20% of the time
6. Crawling (had just begun to bear crawl in August maybe 50 meters a day.) now up to on average 300 meters a day of proper crawling
7. Curious (before just sat there) - dumps out the dog bowl once a day and pulls all books of the shelves - she's a royal pain :) we love it.
8. Was eating 3 x 6 oz. bottles plus 8 oz of baby food per day. In one month - eating 3 bottles +28 oz of baby food, but is slimmer

THANK YOU for understanding what she needed. You are an invaluable resource and we are so happy to have found you. Thank you!
Why Treat Down Syndrome?

Treating patients is different than curing patients.
Why Treat Down Syndrome?

Treating and researching the biochemical causes of DS has been largely ignored by the medical community for years.
Down Syndrome is the most common congenital anomaly worldwide but the least funded for research.
Why Treat Down Syndrome?

Their symptoms are treated as “normal” for the condition.
Why Treat Down Syndrome?

Our genes are not the end-all-be-all of our health
Overview

• Genetic Over-expression
• Oxidative Stress
• Methylation
• Hypothyroidism
Genetic Overexpression

- Decoding of human genome in 2003 made new research possible
- We know what proteins are coded for on chromosome 21, but don’t know what all of those proteins do.
- They’ve been able to narrow the area of chromosome 21 to the genes that are involved in DS. The DS critical region (DSCR - 21q21-22.3)
Genetic Overexpression

• DS is caused by over-expression of genetic material
  – The role of genes is to make proteins.
  – What proteins are being over produced?
• Most important one: SOD (superoxide dismutase)¹
  – A free radical scavenger
  – Converts free radicals to hydrogen peroxide
  – Hydrogen peroxide is then converted to water by catalase and glutathione
  – Problem: gene for enzyme that makes glutathione is on chromosome 20.
  – This creates an imbalance and build up of hydrogen peroxide that is damaging to all cells.

¹Annerén G, Edman B. Down syndrome—a gene dosage disease caused by trisomy of genes within a small segment of the long arm of chromosome 21, exemplified by the study of effects from the superoxide-dismutase type 1 (SOD-1) gene. APMIS Suppl. 1993;40:71-9.
Genetic Overexpression

\[
\begin{align*}
O_2^- &\xrightarrow{\text{SUPEROXIDE DISMUTASE}} H_2O_2 \\
&\xrightarrow{\text{GLUTATHIONE PEROXIDASE}} H_2O \\
&\xrightarrow{\text{GLUTATHIONE REDUCTASE}} GSGS \\
GSH &\xrightarrow{\text{GLUTATHIONE REDUCTASE}} GSSG
\end{align*}
\]
Genetic Overexpression

Superoxide dismutase (SOD)

\[
\cdot O_2 + \cdot O_2 \rightarrow H_2O_2
\]

\[
2 H^+ + \cdot O_2 \rightarrow H_2O + O_2
\]

\[
H_2O_2 + \cdot O_2 \rightarrow \cdot OH + H_2O
\]

\[
2H_2O_2 \rightarrow 2OH^- + H_2O
\]

Catalase

Glutathione peroxidase (GSHPx)

Damage DNA

Damaged mitochondria

Cellular death

Lipid peroxidation (MDA)

Protein Carboxyl Content (PCC)
Oxidative Stress

a disturbance in the balance between the production of reactive oxygen species (free radicals) and antioxidant defenses
Oxidative Stress

Oxidation = lose of electrons (because oxygen is the biggest electron "thief" in the body)

Reduction = gain of electrons (because the charge is reduced, i.e. made more negative)
Oxidative Stress

• Atoms are most stable when they have a complete set of electrons in their outer orbit.

• Atoms losing electrons is a normal consequence of chemical reactions in the body.

• Atoms that have lost an electron are called free radicals, are very unstable and seek out electrons to complete their outer orbit.

• Antioxidants are compounds that have extra electrons in their out shell and satisfy the free radicals need for electrons, making them less reactive.
Oxidative Stress
Oxidative Stress

Reactive Oxygen Species (ROS)

- $\bullet =$ unpaired electrons

- $O_2$
- Peroxide $O_2^-$
- Superoxide anion $O_2^-$
- Hydroxyl radical $\cdot OH$
- Hydroxyl ion $OH^-$
Oxidative Stress

DNA

Deoxyguanosine

Oxidation site

8-OHdG
Oxidative Stress
Oxidative Stress

The gene for SOD is on chromosome 21 and overproduced in all cells of those with Ds. The production of oxygen free radicals is increased due to more SOD enzyme that makes it.

Hydroxyl free radicals are produced from H2O2 that did not get converted to water. These free radicals are the most reactive free radicals in the body.

Oxygen free radicals are produced as a byproduct of normal cell metabolism. Neutralizing oxygen free radicals (ROS) in the first place is accomplished with antioxidants like vitamin C and vitamin E.

Production of Catalase and Glutathione peroxidase need to be supported in order to keep up with higher activity by SOD.
Oxidative Stress

Three steps to lowering oxidative stress

1. Prevent free radicals in the first place from forming with antioxidants
2. Support SOD/glutathione system by optimizing glutathione levels
3. Provide building blocks for repair should damage from free radicals occur