SAFE HEALTH REPORT

Scientific Data … Real Value … Actionable …Worth Every Dollar

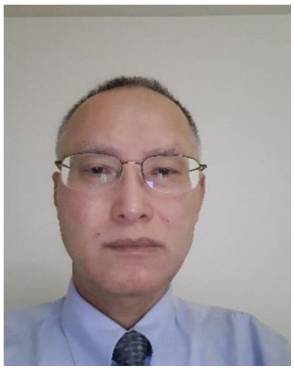
September 2022 *Official Newsletter for MrGineaPig* *Issue 2*

Please repeat once before proceeding: He Can Do It, SHe Can Do It, I Can Do It.

Inside …

Epigenetics and Disease

Avoiding Pitfalls for Premature Death Next 5 Years



Ike Kim, Editor

Epigenetics is the study of how environment influences gene expressions. Genes are turned off or on temporarily often in a reversible manner in epigenetic regulation versus permanent DNA changes that occur in gene mutation. A good example is a fresh water tropical Mexican fish known as Astyanax mexicanus that completely lost its eyesight due to silencing of 2 dozen genes due a cave environment. Further, epigenetic biomarker (DNA) changes have been shown to occur even in very-short-term exposure to hepato-toxic agent, (i.e., clofibrate).

Finally, dose-response relationship of many drugs is affected by epigenetic patterns. Epigenetic changes may be brought about in human body via air we breathe, food we eat and through skin exposure.

One of the major routes of toxin exposure is by food we eat. The surface area of gastro-intestinal tract in the body ranges from 322 square feet to 430 square feet for average person with average about 376 square feet. That is 19 times of average body surface area. There is even larger surface area inside the lungs of about 1000 square feet. The toxins we introduce 3 times a day via intestines is 19 times that of being smeared topically on the entire human body. Put it another way, we introduce environmental toxins far more easily through the air we breathe continuously and through the food we eat. These two activities have far-reaching effect in certain genes being off and on. Identical twin studies have already shown physical aging difference in the terms of telomere length. Even the speed of aging is not the same for everyone and is related to what we breathe

in, what we eat and drink, and other lifestyle choices we make. While disease will get us sooner or later, we can potentially optimize the time allotted to us by Lord Crono.

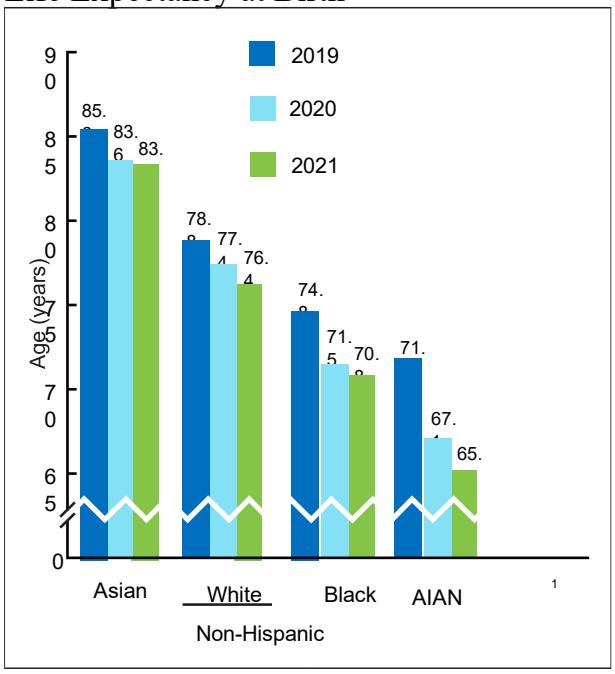
Conjoined Mice Experiment Proves That Certain Gene Expression of Younger Mice Makes Old Mouse Behave Like the Young

How can we use epigenetics and intentionally use such knowledge to our advantage beyond traditional dose-response relationship of receptor-substrate drug model? By intentionally providing certain food exposure to intestinal surface area of nearly 400 square feet, can you cause certain genes to turn on and off? The answer appears to be yes. We do not get immediately noticeable effect but may provide beneficial changes over much longer period. We know our genes make too much of group of harmful proteins or no longer make certain beneficial proteins.

We get glimpse of this in the conjoined mice experiment. Irina Convoy and her colleagues in 2005 at the University of California, Berkeley, discovered that making conjoined twins out of young and old mice – such that they share blood – can make old mice behave like young mice with signs of tissue rejuvenation and regeneration. The same research team in 2020 showed that simply diluting the blood of old mice without the blood from young mice achieved similar age-reversing effects. Simple dilution of old blood caused the dilution of harmful proinflammatory proteins that is elevated with aging and increased concentration of beneficial proteins via molecular reset.

The main take home point here is we can increase beneficial proteins that decline with age or even decrease harmful substances. That may partly explain the life span differences recently released by the Center for Disease Control. Average life expectancy in the US is just 76 years. While Covid-19 was responsible for the decline in the expected average US lifespan, opioid epidemic also played a key role.

Life Expectancy at Birth



*Adapted from CDC report August 2022, Report No.23

Looking at the table, one cannot wonder but question why the wide differences. One hypothesis is the food exposure differences and food over-exposures. With current Covid-19, the access to medical care probably played even larger role and contributed bigger weight in the life expectancy calculation as compared before the pandemic. Getting latest bivalent Covid-19 vaccine would be a common-sense approach to avoiding premature death.

Tsimane Indians of Bolivia demonstrate the effect of food on BPH prevalence

Tsimane Indians of Bolivian jungle is a case in point. Tsimane diet consists of

rice and plantain (2/3 of diet), fish (16%), and wild meat (6%). Trumble et al in their 2015 observational study reported Tsimane males have less than half of the BPH prevalence experienced by U.S. men, and prostate volumes 62.6% smaller than American males. Tsimane males with high testosterone and high glycosylated hemoglobin (aka A1C) were more likely to experience BPH. Not only do Tsimane males have lower incidence of BPH, but heart disease is non-existent. Perhaps the food we ingest – an epigenetic environment in 400 square feet of GI exposure area - are causing not only abnormally high testosterone levels in the US males but also high blood sugar levels, which in turn, causes higher release of insulin. Insulin in response to excess carbohydrate ingestion and insulin-like growth factor (IGF-1) in response to excess meat intake are the growth hormones likely to play important roles in prostate hyperplasia in addition to elevated estrogen production in the older US males.

Thus, it appears that epigenetic changes brought about by the excess consumption of unnatural food, unnatural to human body in the setting of sedentary lifestyle from evolutionary standpoint plays a very large role in human health. This single summary appears to be too simplistic an explanation for human ills but often answer is right in front us. Safe Health Report will use Occam's razor to delineate trifecta of competing explanations for human diseases.

Dietary overexposure of unhealthy food causes the enlargement of prostate

In preparation for this month's case discussion, factors influencing enlarged prostate will be discussed. One consequence of over exposure of carbohydrates and protein is increased secretion of insulin and increased-like growth hormone respectively. These two hormones are no longer needed as we pass over the age of forty – when our children label us as 'old farts' – where growth is no longer needed. These two hormones are responsible for obesity and enlargement of organs including prostate. O Obesity in turn causes excessive secretion of estrogen in males with its adverse effects on the prostate.

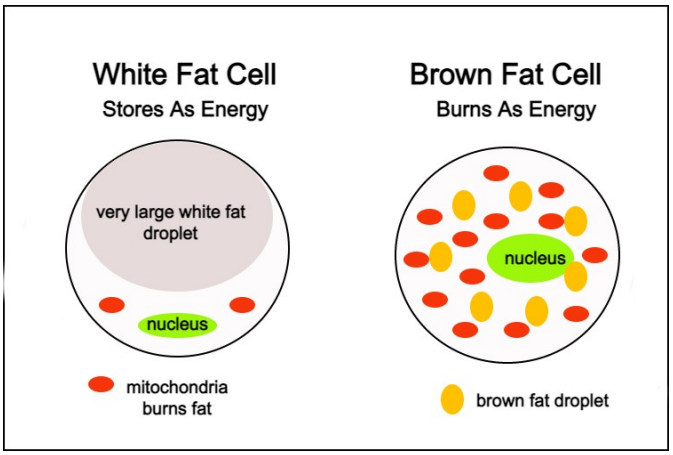
One key component of long-term treatment of benign prostate hypertrophy (BPH) is lowering dihydrotestosterone and estrogen since each contribute to the enlargement of prostate via androgen receptor (AR) and estrogen receptor β (ERβ) respectively. The conversion of testosterone to dihydrotestosterone can be blocked by taking one of the 5-alpha reductase inhibitors including finasteride, dutasteride and saw palmetto. More importantly, one should not be fixated on taking supplements to increase testosterone boosters. Abnormally high male hormone will cause priapism or continuous erection which causes bladder neck constriction. Bladder neck is constricted during sex to prevent retrograde ejaculation into bladder. Taking these testosterone boosters is over-hyped and over-rated. In fact, Tsimane males have been shown to have lower testosterone levels (182.9 picograms per milliliter vs 266.8 picograms per milliliter in US males) in a study by Trumble et al where 88 16- to 59-year-old men were compared via age-matched and body-adjusted statistics.

Lowering estrogen really involves eating balanced diet so that there is not so much excess calories in the form of various sugars and proteins. Many diets can be considered for this endeavor as well as routine exercise.

Will taking supplements change epigenetic parameters?

Epigenetic changes brought about by 450 square feet of intestinal exposure to higher dose of pantothenic acid may have consequences fatty acid metabolism. Pantothenic acid is a key precursor for the coenzyme A (CoA) biosynthesis. In other words, we need it to make CoA. CoA is ubiquitous throughout the body and essential cofactor involved in many essential metabolic reactions, including the synthesis and degradation of fatty acids, synthesis of phospholipids, and is involved in Krebs cycle or citric acid cycle. One of the most important functions of CoA is its involvement in fatty acid metabolism

Zhou et al published important findings on the effects of pantothenate on obesity in July 2022 edition of American Journal of Physiology-Endocrinology and Metabolism. Specifically, pantothenate appears to protect against obesity. The vitamin B5 stimulated production of brown fat in cell cultures and in mice. The importance of this finding cannot be overstated since brown fat is used up in mitochondrial metabolism to



produce heat unlike that of white fat. Brown fat is much smaller than white counter part but also packed with energy generating mitochondria along with iron that gives the brown coloration.

While calorie restriction and exercise are important as well as avoiding excess sugar and proteins, taking pantothenic acid or pantethine may aid in maintaining healthy weight. For this reason, pantothenic acid is on long-term trial on MrGineaPig's long-term trial. Will taking pantothenic acid keep the prostate from getter fatter?

Case Number 2. Can BPH symptoms resolved for 60-year-old male with urinary symptoms? Case of Michael Verde.

We discussed prostate and metabolic syndrome in preparation of our case discussion of Michael Verde male (fictious name) with relatively good 'health'.

Michael is a sixty-year-old African American with right hip issues and high cholesterol issues. He is relatively fit except central obesity. He had played college football with Wyoming Cowboys in his youth, had been in the US Navy for six years, worked as mechanical engineer for 20 years prior settling to a desk job as a patient care coordinator. It is said anything placed in mouth was digestible within minutes at his peak, and that he was so potent his urine landed 20 feet away when he answered the call of the nature while camping. This is how a legend is born. He now leads a sedentary lifestyle both at work and at home.

Michael really needs a right hip replacement for which he's been delaying a few years. Some days, he needs cane to walk, but most of days he can walk normally with monthly cortisone injections. Now, here is another kicker. He has benign prostate hypertrophy like most of fellow Americans of his age. Michael makes 5-6 bathroom trips a night and is managed with alpha-blocker, tamsulosin 0.4 mg capsule once a day. To make matters even difficult, he is also sexually active and has been taking testosterone boosting supplements.

As I discussed earlier, boosting testosterone level is not necessarily good when one has BPH since higher level is likely to result in longer period of penile tumescence during which bladder neck is likely to be more constricted. Other than stopping hormone boosters, we will now look at Michael's five-year outlook.

Michael Verde with Central Obesity

Age: 60
Sex: .....Male
Weight: .....175 pounds
Height: .....6 feet 1 inches

Activities of Daily Living (ADL) components: transfer, bed mobility, toileting, and eating

- **0 – Independent: If the resient completed the activity with no help or oversight every time during the 7-day prior period.**
- **1 – Supervision: If oversight, encouragement, or cueing was provided three or more times during prior 7 days.**
- **2 – Limited Assistance: If resident was highly involved in the activity and received physical help in guided maneuvering of limb(s) or other non-weight-nearing assistance three or more times during the last seven days.**
- **3 – Extensive Assistance: If resident performed part of the activity over the prior 7 days, help of the following type(s) was provided three or more times: ▪ Weight-bearing support provided three or more times. ▪ Full staff performance of activity during part, but not all, of the prior 7 days.**
- **4 – Total Dependence: If there was full staff performance of an activity with no participation by the resident for any aspect of the ADL activity. The resident must be unwilling or unable to perform any part of the activity over the entire prior 7-day period. ▪ 7 – Activity occurred only once or twice: If the activity occurred but not 3 times or more. ▪**

8 – Activity did not occur: If, over the prior 7-day period, the ADL (or any part of the ADL) was not performed by the resident or staff at all. ADL support measures the most support provided by staff over the prior 7 days.

*Adapted from Minnesota Department of Health Guideline

Michael Verde's ADL Score 0

What do you think is Michael 5-year outlook? He is clearly independent on the ADL chart and Managing Ok category on the frailty score. But he is at transitioning from Managing Ok category to Very Mild Frailty category as he is using cane once every few months to get around. Looking at average expected life expectancy of 66.7 years for a baby born in 2021 for African American male, ADL score of zero (independent status) and Frailty Score of 3, his chance of living next five years looks good. The mortality rate after hip replacement is zero percent in 30 days, and 10-year survival is >89% for 65 years or younger should he pursue surgical option for hip-related issues.

Is there something he could do to shift his odds? While he has ideal body weight for his height, he has central obesity commonly found in the US. More than anything else, he will need surgical procedures to fix his right hip problem. At the same time, he will need a routine physician visit for hyperlipidemia. He will likely need to change his diet with some help from dietician or physician for his metabolic syndrome. Finally, he could potentially supplement with pantothenic acid for better fat metabolism. While it has

Michael Verde

Clinical Frailty Score

- **1 – Very Fit: Very fit for their age with no disease symptoms, very active and exercise regularly- 5 days a week**
- **2 – Fit: Still no active disease as in 1 but exercise only occasionally – three times a week or only seasonally**
- **3 – Managing Ok: Disease symptoms are well managed. Not able to exercise at all other than walking.**
- **4 – Very Mild Frailty: Symptomatic disease. Not dependent on others for daily activities but disease symptoms slow down their activities. May need cane for walking occasionally for example**
- **5 – Mild Frailty: Symptomatic disease limit daily activities. Needs walkers. Needs help with walking and shopping.**
- **6 – Moderate Frailty: Needs helps with walking, shopping, climbing stairs, bathing with disease progression.**
- **7 – Severe Frailty: Completely dependent for personal care and daily activities but seem stable and at risk of death within the next 6 months.**
- **8 – Very Severe Frailty: Same as 7 but unstable and even mild illness is likely to cause death.**
- **9 – Terminally Ill: As in 8 but not likely to live next 3-6 month.**

*Adapted from Rockwood & Theou 2020

Michael Verde's Frailty Score 4

not been proven in large clinical trial, it seems reasonable.

Bonus Coverage: Water Supply Contamination with Stainless Steel Braided Flexible Hose

For ease of installation of new or replacement hot water heaters, braided flexible hoses are often used. Inner tube is made with EPDM rubber (ethylene propylene diene monomer rubber) – the same stuff used in rubber roofing membrane and automotive door and window seals- is used make rubber hose. It is then encased with stainless steel braids. EPDM contains harmful chemicals as well as containing carbon black. The issue with EPDM is both acute and chronic toxicity are not known. As I

was turning on bathtub, I noticed black water was pouring out. After several gallons later, I decided to collect a sample. First black particles started pouring out. Then interlinked sticky black membrane is what is shown in the wash basin. After years of use, the inner EPDM hose starts to wear out. The Material Safety Data Sheet for EPDM states it is a "Possible Cancer Hazard" and can be an irritant to lungs, eyes, and skin. The International Agency for Research on Cancer (IARC) states carbon black contained in EPDM is possible carcinogen to humans, and that short-term exposure to high concentration of carbon black dust is a respiratory irritant. At any rate, EPDM is not something you want to ingest or be exposed to in short- or long-term basis.

Safe Health Report Recommendation:

- ✓ **Do not use braided flexible hose shown on the left**

- ✓ **Use corrugated stainless steel or corrugated copper installation kit shown on the right**

MrGineaPig's Core Long-Term Trial

LONG-TERM TRIAL	SUPPLEMENT	START DATE	
Muscle Weakness	Hyaloronic Acid 50 mg	07/01/2019	1 capsule daily
Back Pain	Pantothenic acid 500 mg	09/01/2021	1 capsule daily
	Pantethine 450 mg	09/01/20211	1 capsule daily

Purpose of Safe Health Report

If you feel you are used by someone or somebody or institution or institutionalized philosophy or even by your parents or siblings or your coworkers or even your boss, you are a GineaPig. This newsletter is designed to empower GineaPigs in the area human health.

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