
Functional Improvement in β -Islet Cells, Hepatocytes and Cardiomyocytes with Decreasing Deuterium from Low Carbohydrate Intake in a Type-II Diabetic

Edwin C. Jones^{1*} and Cortney L. Jardet²

Recent Developments in Medicine and Medical Research Vol. 7, 28 October 2021, pp 147-162.

DOI: <https://doi.org/10.9734/bpi/rdmmr/v7/4920F>

ABSTRACT

A 59-year-old patient with an 18-year history of type II diabetes showed remarkable improvements in glucose tolerance tests and improved fasting hepatic glucose production with systemic deuterium depletion. Deuterium, which is known to reduce the effectiveness of ATP synthesis nanomotors, is most likely to blame for systemic variations in insulin and hepatic glucose production in the pancreas and liver, respectively. Low carbohydrate (keto) diets with deuterium-depleted water can cause systemic deuterium depletion.

Keywords: *ATP; ATPase nanomotor; β -islet cell, deuterium; deuterium-depletion; deuterium-depleted water; glucose tolerance; HB_{a1c}; type-II diabetes.*

ABBREVIATIONS

CBC: complete blood count; CHO: carbohydrates; CMP: comprehensive metabolic panel; D: deuterium; DDW: deuterium-depleted water; DM: diabetes mellitus; DM-II: type-II diabetes mellitus; ¹H: protium hydrogen isotope; ²H: deuterium hydrogen isotope; HB_{a1c}: hemoglobin a1c; SNP: single-nucleotide polymorphism; $\tau_{1/2}$: half-life.

1. INTRODUCTION

Deuterium ²H is a naturally occurring heavy hydrogen isotope, with one ²H deuterium atom for every 6400 ¹H protium atoms on the earth. The efficiency of cellular ATP generation is reduced when these deuterium atoms interact with the ATP synthase in live organisms [1-3]. Deuterium-depletion is the process of lowering the deuterium:protium ratio below 1:6400. Data are presented that suggest deuterium-depletion via the consumption of a low carbohydrate diet was the mechanism responsible for the elimination for the need for 130 units of exogenous insulin in a type-II diabetic patient previously published [4]. During this period, the patient's c-peptide improved, indicating that the dysfunctional β -islet cells were being regenerated [4]. During this period of improvement, the patient was said to have used a cyclical ketogenic diet, a strenuous exercise programme, and oral GABA/probiotic supplementation. Over the past three years, further research was conducted to elucidate the mechanism leading to these dramatic improvements to glycemic control. A study from Ackermann et al. was published shortly after the original report showing that GABA does not appear to induce pancreatic α - to β -islet cell differentiation [5]. Another study showed that diabetic patients who choose low carbohydrate diets over low calorie diets have better glycemic control over their

¹Department of Veterans Affairs, Knoxville Outpatient Clinic, 8033 Ray Mears Blvd., Knoxville, TN 37919, USA.

²Endocrinology Consultants of East Tennessee, 1450 Dowell Springs Blvd., Suite 300, Knoxville, TN 37909, USA.

*Corresponding author: E-mail: Edwin.Jones2@va.gov;

counterparts [6] and this is believed to be due to lower deuterium ²H exposure. This is because plants store the deuterium in their storage sugars and starches [7-8].

Recently, animal studies have been published showing improvements to diabetes in rats with deuterium depletion [9-11]. Numerous publications over the last 20 years have been devoted to the study of the role of deuterium in natural (150 ppm) or reduced content in the human body. It has been shown that deuterium-depleted water (DDW) exhibits antidotal properties with individual and combined effects on the dosage of pharmaceutical substances and auxiliary substances [10,12-14]. Studies in humans are more limited; however, one recent study in 30 volunteers who consumed 1.5L of 104 ppm deuterium-depleted water for 90 days showed improvement to the peripheral glucose disposal in 15 of those individuals [15]. No toxic effects from the deuterium depletion process were observed in any of the CBC or CMP lab values [15].

In this case report, glucose tolerance improvements, hepatic glucose production rate changes, and Hb_{A1c} improvements are presented that reveal systematic metabolic changes with deuterium depletion utilizing deuterium-depleted water (DDW) after the initial improvements seen from the introduction of a low carbohydrate diet.

2. RESULTS

2.1 Genetic Risk Factors for DM-II

Diabetes mellitus is a metabolic disorder effecting over 100 million people worldwide. This metabolic disorder has both genetic and environmental risk factors. In this case report, the patient took a 23andme DNA test (<https://www.23andme.com/>) in September 2016 which tested for 960,614 SNP markers. Using the NIH Genome Data Viewer (<https://www.ncbi.nlm.nih.gov/genome/gdv/>), three SNP markers that increase the risk for the development of Diabetes Mellitus, Type II were identified from this list of markers. These are summarized in Table 1. The patient's genotype, odds of developing DM-II, and description of each gene are included in the table. These genes predict decreased insulin secretion and increased hepatic insulin production. Furthermore, one gene predicts functional hypoglycemia early in life followed by an increase risk in DM-II later in life.

Table 1. Genetic markers identified in the patient that are known to increase the risk of developing Type II Diabetes Mellitus

Gene	SNP	Chromosome	Patient Genotype	DM-II Odds	Description
TCF7L2	rs7903146	10q25.2-q25.3	TT	1.59x	Transcription factor 7-like 2 (92% predictor for DM-II)
IGF2BP2	rs4402960	3q27.2	TT	1.2x	Insulin like growth factor 2 mRNA binding protein 2
KCNJ11	rs5219	11p15.1	TT	1.17x	Potassium voltage-gated channel subfamily J member 11 found on β -islet cells.

TCF7L2 genotype TT and IGF2BP2 genotype TT are both strong predictors for decreased insulin secretion and increased hepatic glucose production. KCNJ11 genotype TT is known to increase the risk of hypoglycemia early in life and DM-II later in life.

2.2 Improved Glycemic Control with a Low Carbohydrate Diet

The patient was treated with insulin between the ages of 52 and 55 during which time he started recording detailed food intake logs. Fig. 1 illustrates daily carbohydrate (CHO) intakes in grams per 24 hours. In these data, one-half the fiber intakes were subtracted from the total carbohydrates which is standard practice in predicting exogenous insulin requirements. The solid curve indicates the three-week running average of daily carbohydrate intakes. These data were needed to maintain optimal control of his glucose values especially during the time he required short acting insulin aspart.

Shortly after initiating a low carbohydrate diet with weekly ketogenic cycling, described elsewhere, [4] the patient's need for exogenous insulin slowly decreased disappearing completely by age of 55.29 years. The patient's c-peptide had increased by 350% during this same time period indicating a regeneration in his β -islet cell functioning [4]. In 2002 it was shown that pancreatic ductal cells could differentiate into β -cell in response to glucagon-like peptide-1 [16]. An important question that now arose was whether or not the lower carbohydrate diet induced β -islet cell differentiation by virtue of a deuterium depletion process [7-8]. A lower deuterium:protium ratio would be expected to increase cellular ATP production efficiency [1-3] which in turn could induce the improvements to internal biochemical processes needed for the β -islet cell differentiation.

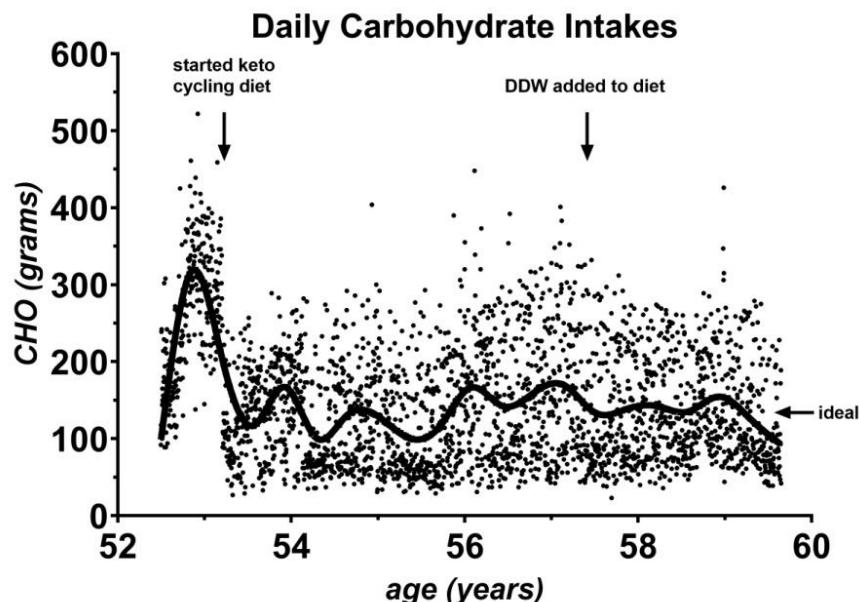


Fig. 1. Daily carbohydrate consumption as a function of age dating back to age 52 when the patient was initially started on short acting insulin aspart. By age 55.29 years, the patient no longer required any insulin therapy. The solid curve is a three-week running average carbohydrate intakes. The ideal carbohydrate intake based on lean body appearance was estimated to be around 130 grams per day. The age where the keto cycling diet (low CHO) and deuterium-depleted water (DDW) were started are indicated

2.3 Glucose Tolerance Improvement with Deuterium Depletion

To investigate this hypothesis, deuterium depleted water (DDW) was added to the low carbohydrate diet of the patient at the age of 57.5. Further improvements to his glucose tolerance tests were immediately observed as shown in Fig. 2. A hair sample that was originally collected for trace mineral analysis was later tested for deuterium content which estimated his systemic deuterium to be 143 ppm at the age of 55.3 before the possible link between deuterium and β -islet cell function was suspected. Three additional glucose tolerance tests were collected at the ages of 57.4, 57.6 and 57.9 years immediately after collecting breath deuterium levels. All of the hair and breath deuterium tests were analyzed by the Center of Deuterium Depletion (<https://www.ddcenters.com>) using mass spectroscopy. Tap water was the primary water consumed before age 57.5 years and deuterium-depleted water of various deuterium contents after age of 57.5 years. The deuterium level in the tap water at the time of these deuterium studies was also measured with mass spectroscopy to be 149.8 ppm.

These data indicate the most significant improvement to the β -islet cell functioning occurred between age of 51 and 55 when the patient transitioned between insulin dependent DM-II and non-insulin dependent DM-II [4]. Further β -islet cell improvements occurred after deuterium-depletion water was

added to the low carbohydrate diet lowering the breath deuterium to a low of 119.9 ppm. Breath deuterium is believed to be a very close estimate of the blood plasma deuterium level [17] which is already known to decrease the efficiency of ATP production in animals [1-3].

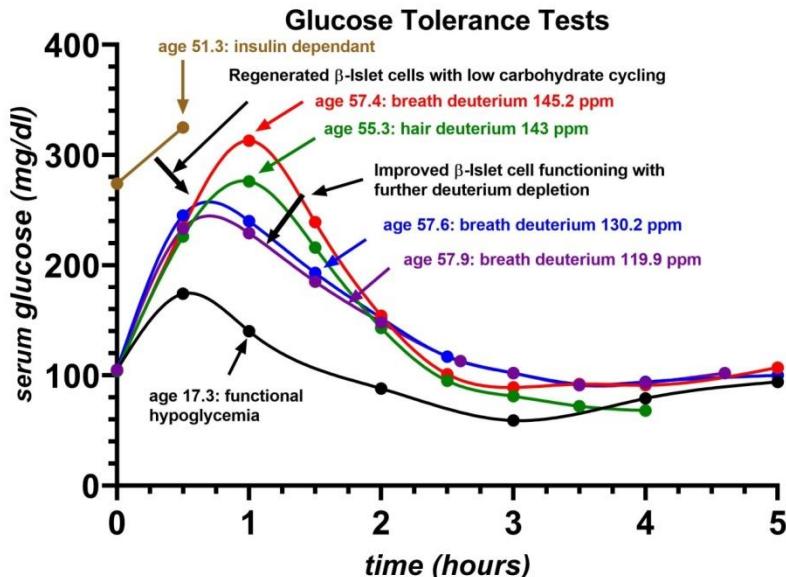


Fig. 2. Glucose tolerance tests following the administration of 50 grams dextrose (d-glucose) at the ages of 17.3, 51.3, 55.3, 57.4, 57.6, and 57.9 years. The patient was diagnosed with functional hypoglycemia at age 17, insulin dependent DM-II at age 51, and non-insulin dependent DM-II at age 55. After age 55, the glucose tolerance tests show a gradual improvement to β-islet cell functioning in response to decreasing systemic deuterium ^2H levels

2.4 Skeletal Fat Changes with Sleep

The patient is physically active with him hiking in the mountains nearly every weekend and spending an hour of weight lifting five days during the week to reduce his skeletal fat. At the age of 53, he began recording his total time slept using a timer to determine if there was an ideal amount of sleep needed to further reduce skeletal fat. The skeletal fat was measured daily using a full body electronic Omron HBF-514c scale described in more detail below. A decrease in skeletal fat not only improves overall physical appearance but also helps in optimizing glycemic control. Previous researchers did report a decrease in insulin sensitivity in type-1 diabetics with partial sleep restriction [18].

Skeletal fat measurements were made immediately after awakening from sleep when the water distribution is more evenly distributed throughout the body [19]. Fig. 3 plots the skeletal fat readings every morning over a five-year period plotted against the total time recorded for sleep. The data do show clear decreases in skeletal fat with longer sleep durations but optimal sleep times are difficult to achieve due to career/family obligations. These recorded sleep times would later prove useful in determining the hepatic rate of glucose production.

2.5 Change in Hepatic Glucose Production with Deuterium Depletion

Hepatic glucose production rates were estimated for each of the breath deuterium levels recorded at ages 57.4, 57.6, and 57.9 years. The deuterium depletion level in the water consumed was held constant for 6 weeks following each of the glucose tolerance tests shown in Fig. 2. Over a period of 6 weeks the patient's fasting glucose upon awakening was plotted as a function of total recorded sleep duration. The patient's TCF7L2 genotype TT and IGF2BP2 genotype TT both predict increased hepatic glucose production which are reflected as positive slopes in the best linear fits shown in Fig. 4. As the breath deuterium levels decrease, the slopes were found to increase indicating an increased

rate of hepatic glucose production strongly suggesting a more efficient metabolism within the hepatocytes with decreasing deuterium level.

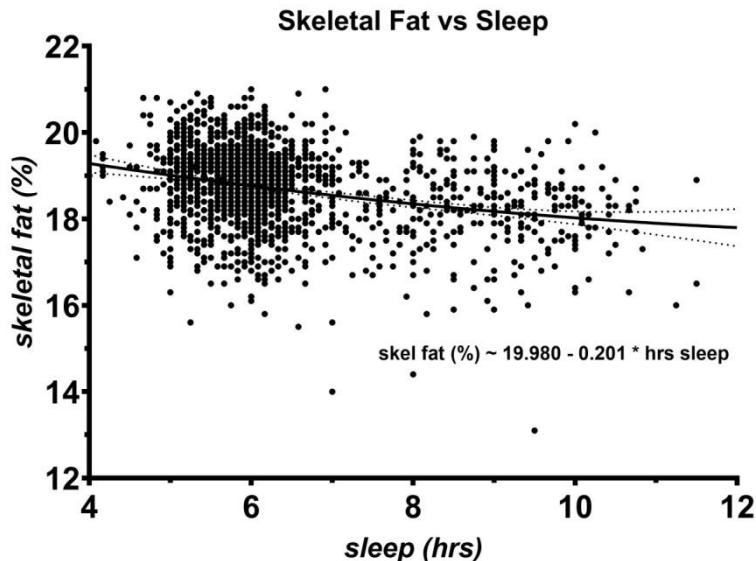


Fig. 3. Skeletal fat (%) immediately upon awakening from sleep plotted as a function of hours of total sleep duration. These data were recorded over a period of five full years (ages 53-58). The curve shows the trend decreasing by roughly 0.201% skeletal fat per hour of sleep. The dotted curves are the 95% confidence intervals. The upper confidence interval suggests an optimal sleep period of 10 hours per night

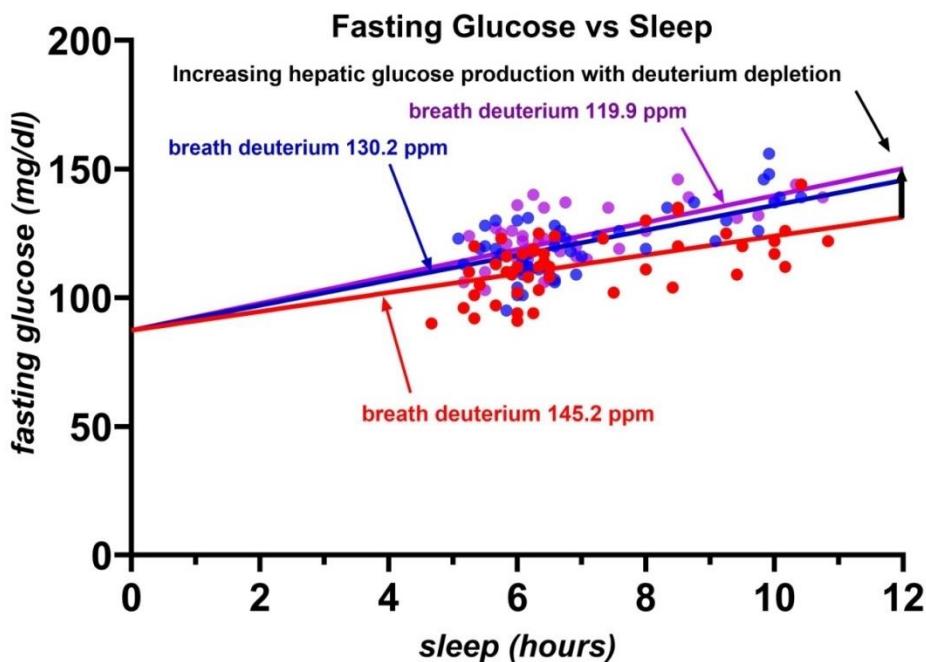


Fig. 4. Fasting glucose values immediately after awakening vs total sleep duration. These were recorded for 6 weeks for each breath deuterium level and color coded according to the breath deuterium level. The slopes in the trend lines extrapolated to the y-axis yield the hepatic glucose production rates. These slopes increased with the lowering of systemic breath deuterium levels

3. DISCUSSION

3.1 ATP Production Efficiency Estimated from Fasting Glucose Data

At this time there is no known method for directly measuring the deuterium level inside the mitochondria matrix where the majority of our ATP production occurs. Fortunately, deuterium levels can be measured in other body fluids including the liquid condensation of exhaled air which is believed to be close to our blood plasma deuterium level [17]. Saliva deuterium level testing is also available which is believed to be the best estimate of the deuterium level inside our cellular cytoplasm [17]. All of these deuterium levels are influenced by the deuterium levels that we are exposed to from both food and water consumption.

Glycolysis is a sequence of ten enzyme catalyzed reactions that occurs in the cytoplasm where deuterium rich hydrogens in glucose are stripped to produce pyruvate which then moves into the mitochondria. There deuterium depleted “metabolic” water molecules are added back into the structure via nine enzymatic steps called the Krebs Cycle. These “metabolic” water molecules are produced inside the mitochondria from the oxidation of fatty acids that are believed to be depleted of deuterium relative to glucose [17,20]. In sum, there is a total of 6 NADH and 2 FADH₂ that are produced inside the mitochondria matrix and these provide the deuterium depleted hydrogens needed to efficiently drive the ATPase nanomotors [20]. Any contamination of the mitochondria matrix by deuterium isotopes seriously reduce the efficiency of the ATPase nanomotors in producing cellular ATP [1-3].

An estimate of hepatic ATP production efficiency in our patient can be estimated from the slopes in the fasting glucoses vs total sleep duration trends taken from Fig. 4. As the patient lowered his breath deuterium by consuming low deuterium content water, hepatic glucose production during sleep increased. These data are shown in Fig. 5 which also shows ocean deuterium level and typical breath deuterium levels seen in North America before deuterium depleted water is consumed [17]. Improvements in his overall glycemic control occurred with these hepatic glucose outputs due to simultaneously improvements to his β -islet cell functioning (Fig. 2).

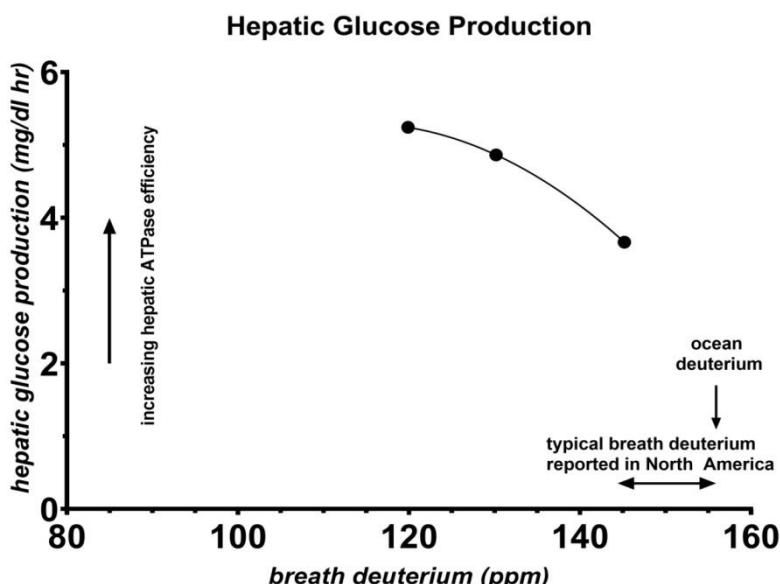


Fig. 5. The hepatic glucose production rates derived from the slopes in fasting glucose vs total sleep taken from Fig. 4. Higher hepatic glucose production was seen with lower deuterium levels suggesting higher ATPase efficiency. Vienna Standard Mean Ocean Water, 155.76 ppm, and typical breath deuterium levels reported before deuterium depletion in North American diets are labelled

3.2 Skeletal Fat Turnover with Hiking

The patient is physically active averaging 19.3km of mountainous hiking on the weekends and five hours of weight lifting during the week. Following each hike, it was previously reported that he would remain in a post-exercise ketosis state for 2-3 days [4]. Changes in skeletal fat for each hike taken from a five-year period, ages 53-58, are plotted in Fig. 6. A linear regression to these data reveals an average drop of 0.045% skeletal fat per each km hiked. Following each repetitive hike, the patient would maintain a low carbohydrate diet (Fig. 1) with a diet high in grass-fed animal or wild caught fish protein. It is believed this repeated skeletal fat turnover over time allowed for the replacement of skeletal fat with a reduced deuterium content. This low deuterium content skeletal fat is necessary for the production of low deuterium “metabolic” water found in the mitochondria matrix [20].

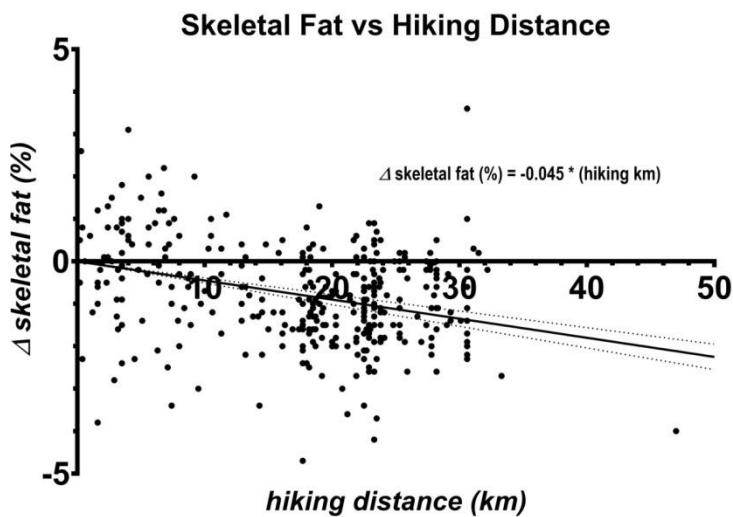


Fig. 6. Change in the patient's skeletal fat over a 24-hour period on hiking days. The patient's average hiking distance was 19.3 km and these data collected over a five-year period (age 53–58 years). The trend line in these data reveal a loss of 0.045% skeletal fat for each km hiked in mountains. The dotted lines represent the 95% confidence intervals. The one point at 47km was from a two-day trip with a loss of 4% skeletal fat over a 48-hour period. These data were recorded in the mornings of the hikes and the morning after the hikes when water distribution is more uniform [19]

3.3 HB_{a1c} versus Age and Environmental Deuterium Exposure

The hallmark lab for assessing glycemic control is the Hemoglobin a1c. The Hemoglobin a1c values dating back to the original diagnosis of Diabetes Mellitus II are shown in Fig. 7. These data have been color coded depending on the deuterium level recently tested from the water supplies from each location where the patient lived. These drinking water deuterium levels ranged from a low of 143.0 ppm at 2,700 meter elevation at a western US mountain range to a high of 149.8 ppm in the southeastern US. Once he added deuterium depleted water to his diet, his average water intake is estimated to have dropped to around 130 ppm after age 58.

These data reveal that the most significant reduction in HB_{a1c} occurred after the low carbohydrate diet was incorporated into the patient's lifestyle. The initiation of deuterium depleted water led to additional improvements to these already improved HB_{a1c}'s suggesting that the importance in deuterium depletion is governed by the following hierarchy.

²H sources in the body: CHO Intake > Drinking Water > Fat/Protein Intake

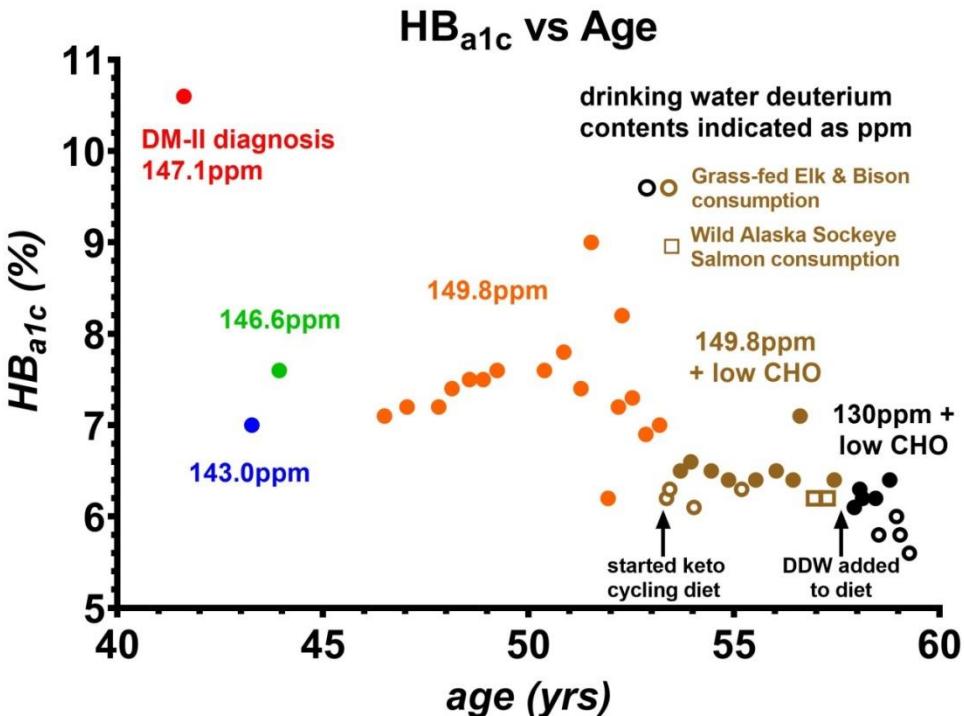


Fig. 7. Hemoglobin a1c levels as a function of age. The colors indicate the deuterium ^2H levels measured from the local water at the patient's residence - green and blue from a western US mountain range and the other colors from the southeastern US. The 130 ppm is the estimated deuterium level after the patient began consuming deuterium-depleted water (DDW) after age 58. The brown and black symbols represent the time period where the patient consumed a low carbohydrate (CHO) diet. The open circles indicate a high consumption of grass-fed Elk and Bison from the northern plain states (>50 grams of daily protein) and open squares indicate consumption of wild caught Alaska Sockeye Salmon (>50 grams of daily protein). Both are reported to be low-deuterium containing foods [7-8]. The lowest HB_{a1c} measured at 5.6% occurred with the regular consumption of grass-fed Elk and Bison plus the 130 ppm deuterium-depleted water.

3.4 Resting Heart Rates versus Age and Environmental Deuterium Exposure

Recorded resting heart rates, Fig. 8, taken from old electrocardiograms recorded prior to age 53 and recorded vital signs recorded monthly after age 53 show a significant decrease in resting heart rate (BR) after the low carbohydrate (keto) diet was adopted into the patient's lifestyle. These data further support this deuterium depletion hierarchy. Heart rates decreased by approximately 20 bpm with the initiation of the low carbohydrate diet. The later addition of deuterium depleted water (DDW) at age 57.5 lowered the resting heart rate by 4 bpm. These data clearly show the effect of keto cycling is more pronounced than the addition of DDW. It is important to point out that no medication changes were made at the time the keto cycling diet was adopted when these heart rates decreased. Furthermore, there are also no relationships between the patient's weight and these corresponding decreases in pulse. These heart rate data are very important and suggest that changes in heart contraction strength are significantly changed by the lowering of systemic deuterium levels in the body. Lower resting heart rates are also observed in above average longevity [21]. Systolic (SBP) and diastolic (DBP) blood pressures are also indicated in Fig. 8 but no overt relationships are identified between blood pressure and changes in systemic deuterium.

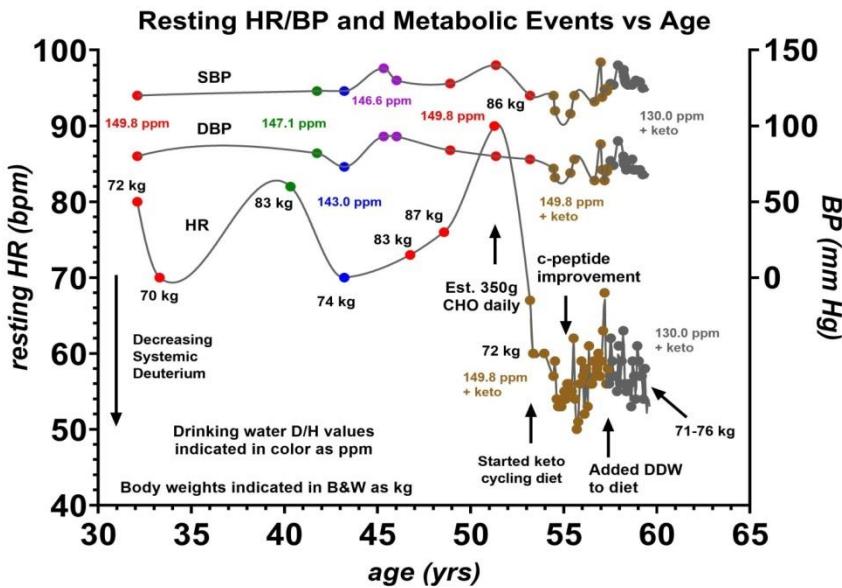


Fig. 8. Resting heart rate (HR) and systolic/diastolic blood pressures (SBP/DBP) versus age.

The patient had a resting heart rate between 70 and 90 beats per minute (bpm) prior to adopting the keto cycling diet. This heart rate dropped to 50 to 68 bpm after the keto cycling diet was initiated. A 74% ejection fraction (EF) measured with gated SPECT at age 57 indicates good contractility of the cardiac muscle which is consistent with no significant drop in blood pressure following the drop in heart rate. The addition of deuterium depleted water (DDW) at age 57.5 years appears to have lowered the resting pulse by an additional 4 bpm indicating that the keto diet had the most influence on the resting heart rate. The patient's weight in kg are indicated and these show that the decreasing heart rates are not due to changes in weight since the patient weighed more in the cluster of data beyond age 53 than prior to age 35. Furthermore, there were no changes in medications near the time the keto cycling diet was initiated. The data are also color coded according to the level of deuterium in the patient's drinking water

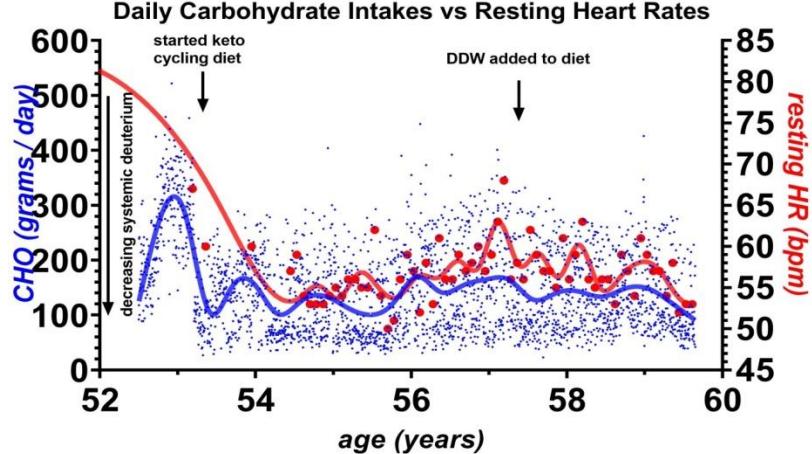


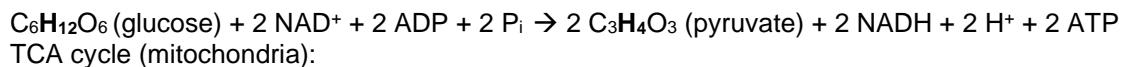
Fig. 9. Resting heart rate (HR) averaged over 30 day intervals (red) are compared to the daily carbohydrate intakes (blue). These data are fit to LOWESS smoothing splines and are shown as red/blue solid curves. The similarities of the peaks reinforce that food intake do contribute to the changes seen in the resting heart rates. The ages where the keto cycling diet was initiated and the deuterium depleted water (DDW) was added to the diet are indicated

Finally, the resting heart rates can be plotted against the daily carbohydrate data from Fig. 1. The averaged monthly resting heart rates (red) are compared to the daily carbohydrate consumption (blue) to reveal some similarity. These data are shown in Fig. 9. These findings again indicate that diet plays a significant role in the resting heart rates likely due to the efficiency of rapidly producing ATP with decreasing deuterium [1-3].

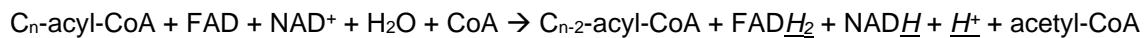
3.5 Cellular Energy Production

The deuterium:protium ratio in foods determined with mass spectroscopy at the Center of Deuterium Depletion are measurably higher in plant storage sugars than fats [7,17]. The center has measured wheat flour deuterium level at 150 ppm, sucrose (table sugar) at 146 ppm, butter at 124 ppm, and pork (bacon) at 118 ppm [7,17]. To allow for better visualization on how these different deuterium levels impact the cellular ATP production inside the mitochondria, the basic equations of cellular energy metabolism are summarized below where the hydrogens that contain higher levels of deuterium are bolded, i.e. **H**, and those with lower levels of deuterium are underlined and italicized, i.e. H.

Glycolysis (cytoplasm):

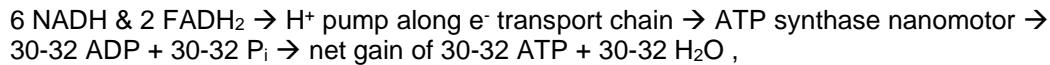


One cycle of β -oxidation of fatty acids (mitochondria):



The deuterium:protium ratio of the hydrogens that drive the ATP synthetase nanomotors are governed by the ratio of deuterium obtained by the relative contribution of the glycolysis of glucose to the β -oxidation from fatty acids. If the ATP synthetase nanomotors run near 100% efficiency, the total production 30-32 of ATP per glucose molecule is widely published in biochemistry textbooks.

Oxidative phosphorylation (inner mitochondria membrane):



where ADP = adenosine diphosphate, ATP = adenosine triphosphate, P_i = phosphate, FAD = flavin adenine dinucleotide, and NAD = nicotinamide adenine dinucleotide.

Finally, it is also useful to point out that the entry of deuterium depleted water into the mitochondria is likely occurring with the hydrolysis of ATP during various cellular processes as shown.

Hydrolysis of ATP (cellular energy supply):



The patient's saliva tested 0.5% to 2.8% above the measured breath deuterium levels strongly suggesting that the low carbohydrate diet had already decreased the cytoplasm to plasma deuterium level ratio by the time these deuterium tests were conducted. By the time the patient did any deuterium testing he had already been on a low carbohydrate intake to two years when the hair sample was collected and for four full years when the breath/saliva samples were collected. According to the Center of Deuterium Depletion, saliva deuterium levels typically run between 4.5% to 7.5% higher than breath deuterium levels in most individuals [17].

An interesting find from the patient's food logs was a high intake of grass-fed Bison and Elk during the time his β -islet cell function improved eliminating his need for exogenous insulin. The c-peptide used

in making this assessment were previously reported elsewhere [4]. These meats were obtained from Elk Marketing Council (<https://www.healthyelkmeat.com>) who obtained these grass-fed meats from the Northern Plains of North America. His food logs indicated an average protein intake of 57 grams a day from these sources between the ages of 53 - 54 years and 58 - 59 years. Between the age of 57 and 58, his food logs revealed a high protein (>50 grams daily) from wild caught Alaska Sockeye Salmon. The HB_{a1c}'s that correspond to these high intakes of grass-fed Bison and Elk and Alaska Sockeye Salmon are shown as open symbols in Fig. 7. These are clearly lower than the surrounding HB_{a1c} values and in the same range as the HB_{a1c}'s recorded after the addition of deuterium-depleted water to his diet. Furthermore, this grass-fed Bison and Elk were later added back to the diet at age 58.3 years after this connection was uncovered. Since the patient has consumed both deuterium-depleted water (1.0L of 25ppm daily) along with these grass-fed meats, his HB_{a1c} has dropped to the lowest value of 5.6% which is the lowest ever recorded for this patient since the diagnosis of DM-II.

4. MATERIALS AND METHODS

4.1 Deuterium Depletion

Once it was realized that deuterium might be playing a significant role in the environmental contribution to Type-II diabetes, a deuterium depletion case study was designed utilizing the consumption of deuterium-depleted water (DDW) to lower the patient's systemic deuterium level while assessing glycemic control. Deuterium-depleted water was obtained in advance from two sources: 1. Preventa America (<https://www.preventa.us>) and 2. ELW (<https://ExtraLightWater.com>). The 65ppm±5ppm water used in the case report was obtained from the first source while the 25ppm±5ppm water used in the case report was obtained from the second source. Ample supplies were obtained in advance to avoid any disruptions during the data acquisition. The rated deuterium levels by these suppliers were also independently confirmed by the Center for Deuterium Depletion (<https://www.ddcenters.com>) using mass spectroscopy.

Table 2. Average daily carbohydrate (CHO) consumption, water source deuterium level ²H, and systemic deuterium ²H (if known) at the time of each glucose tolerance test. The source of systemic deuterium determination is noted

Age (years)	Diagnosis	Avg Daily CHO	Water Source ² H !!	Systemic ² H
17.3	Functional hypoglycemia	~ 300 grams	Tap (149.8 ppm)	unknown
51.3	Insulin Dependent DM-II	~ 350 grams	Tap (149.8 ppm)	unknown
55.3	Non-Insulin Dependent DM-II	120 grams †	Tap (149.8 ppm)	143 ppm (hair)
57.4	Non-Insulin Dependent DM-II	140 grams	Tap (149.8 ppm) ‡	145.2 ppm (breath) 146.8 ppm (saliva)
57.6	Non-Insulin Dependent DM-II	140 grams	1.3 L 65ppm DDW daily x 50 days ‡	130.2 ppm (breath) 130.7 ppm (saliva)
57.9	Non-Insulin Dependent DM-II	140 grams	1.5 L 25ppm DDW daily x 50 days ‡	119.9 ppm (breath) 123.4 ppm (saliva)

†, Food logs revealed the patient was eating an average of 57 grams of protein from grass fed Elk and Bison sources from the Northern Plains. These meats are considered a low deuterium food source [7,8]

‡, These daily DDW intakes were continued for an additional 6 weeks following each glucose tolerance test during which time the fasting glucose vs sleep correlations were recorded.

!!, The patient is estimated to consume 6.0 L of water daily based on the drop in breath deuterium with the amount of deuterium-depleted water consumed for each test.

Tap water from all the locations where the patient resided from childhood to adulthood was also collected and deuterium levels measured by the Center for Deuterium Depletion (<https://www.ddcenters.com>) using mass spectroscopy. Furthermore, a hair sample remaining from an earlier collection for trace mineral analysis at age 55.3 was also analyzed by the Center for Deuterium Depletion to obtain an additional estimate of the systemic deuterium level at a date two years earlier. Breath deuterium levels were run on three occasions after the age of 57 just prior to three separate glucose tolerance tests. A summary of these systemic deuterium levels vs age when glucose

tolerance tests were made is shown in Table 2. This table also gives the patient's age, diagnosis, average daily carbohydrate (CHO) consumption, water source deuterium ^2H level, and measured systemic deuterium ^2H level if known.

Deuterium depletion by the consumption of deuterium-depleted water (DDW) was carried out for five half-lives prior to each glucose tolerance test. Since the half-life $\tau_{1/2}$ of deuterium in the human body was previously determined by Harvard researchers to be 10 days, [22] the steady state deuterium level was estimated to be reached by 50 days. Following the test, the level of deuterium depletion was maintained for an additional 6 weeks while the morning fasting glucose readings were recorded against the total time slept. These data were later used to calculate the rate of glucose production by the liver as shown in this article.

All glucose tolerance tests were run in the mornings immediately after awakening from sleep while the patient was resting quietly. The patient was also physically active during the ages of these glucose tolerance tests with him hiking an average of 19.3 km per week for each test. At the age of 55 and 57 he was also engaged in a 5 hour per week of weight lifting in addition to this hiking. Consistent activity levels were maintained during these tests to minimize variability in the glucose tolerance tests as a result of changes in physical activity.

4.2 Skeletal Fat Measurements

Skeletal fat was determined with a full body electronic Omron HBF-514c scale. This system determines the skeletal fat with a bioelectrical impedance method by applying a 50 kHz 500 μA rf current between the feet and hands. The technique is generally considered to be accurate to within 5% [19]. Readings are also made immediately after awakening when water distribution is more uniform [19].

5. CONCLUSIONS

The metabolic effects of deuterium depletion have recently been studied in lung [23], rare childhood [24], renal cell [25] and colorectal cancers [26]. Human based deuterium depletion studies in Diabetes Mellitus are very limited with one recent study showing improvement to the glycemic control in 50% of the subjects; however, the diets in these subjects were not controlled [15]. The current case report showed systematic improvements in the glucose tolerance response to dextrose challenges with deuterium depletion in a well-controlled and well characterized DM-II patient. The underlying medical biochemistry on how deuterium hampers ATP production within the mitochondria promoting the development of disease are described in detail elsewhere [27,28]. This new field in medicine, called Deutenomics, has recently expanded to include deuterium metabolic imaging (DMI) of glioblastoma multiforme brain tumors in rats and humans [29].

As Type II Diabetes Mellitus is a common metabolic disorder affecting millions worldwide, simple, metabolically well positioned and well tolerated treatments are desired. This disorder is directly influenced by both genetic and environmental components. This article presents a well-controlled case that reveals deuterium level as an important factor to the environmental component of glycemic control. As systemic deuterium levels rise the efficiency of ATPase within the mitochondria matrix decreases leading to corresponding decreases in insulin production in the β -islet cells and changes in glucose production by the liver. These metabolic changes likely occur in all tissues. Ideally, a double-blind placebo-controlled trial in a large group of patients could prove useful in confirming these findings. Finally, it does appear that deuterium depletion does play an important adjunctive role in the improvement of glycemic control; however, it is not a complete cure since genetics continues to play a role in these metabolic disorders. Fortunately, this patient is now managing his diabetes with HbA1c in the normal range.

CONSENT

A written informed consent was obtained from the patient for publication of this report.

AUTHOR'S CONTRIBUTIONS

Analysis of the deuterium depletion data, ECJ; endocrinology guidance, CLJ. Both authors have read and agreed to the published version of the manuscript.

FUNDING

There are no financial interests to disclose regarding any aspect of this case report nor was the research done using Department of Veterans Affairs time or resources.

ACKNOWLEDGEMENTS

Research began on this subject while employed by Vanderbilt University Medical Center and completed while employed by the Department of Veterans Affairs, and was a privately funded research separate from these organizations funding and time. The authors thank László Boros, Gábor Somlyai, Stephen K. Souther, James E. Phelps, David K. Christen, Curtis Sexton, Andrew Sexton, and Robert Hierholzer for informative discussions.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

REFERENCES

1. Dorgan LJ, Schuster SM. The effect of nitration and D₂O on the kinetics of beef heart mitochondrial adenosine triphosphatase. *J. Biol. Chem.* 1981;256(8):3910-3916.
2. Urbauer JL, Dorgan LJ, Schuster SM. Effects of deuterium on the kinetics of beef heart mitochondrial ATPase," *Arch. Biochem. and Biophysics.* 1984;231(2):498-502.
Available:[https://doi.org/10.1016/0003-9861\(84\)90413-2](https://doi.org/10.1016/0003-9861(84)90413-2).
3. Dorgan LJ, Urbauer JL, Schuster SM. Metal dependence and thermodynamic characteristics of the beef heart mitochondria adenosine triphosphatase. *J. Biol. Chem.* 1984;259(5):2816-2821.
Available:<https://pubmed.ncbi.nlm.nih.gov/6230351/>
4. Jones EC, Rylands JC, Jardet CL. Regeneration of Pancreatic β -Islet Cells in a Type-II Diabetic. Case Reports in Endocrinology. 2018;Article ID 6147349:6.
Available:<https://doi.org/10.1155/2018/6147349>.
5. Ackermann AM, Moss NG, Kaestner KH. GABA and artesunate do not induce pancreatic α -to- β cell transdifferentiation in vivo. *Cell Metab.* 2018;28(5):787-792.
Available:<https://doi.org/10.1016/j.cmet.2018.07.002>.
6. Hussain TA, Mathew TC, Dashti AA, Asfar S, Al-Zaid N, Dashti HM. Effect of low-calorie versus low-carbohydrate ketogenic diet in type 2 diabetes. *Nutrition.* 2012;28(10):1016-1021.
Available:<https://doi.org/10.1016/j.nut.2012.01.016>.
7. Available:<https://www.cignaturehealth.com/about-deuterium-food-facts/>
8. Available:<https://extralightwater.com/what-foods-are-low-and-high-in-deuterium/>
9. Lisitsyn AB, Bogatyrev AN, Dydykin AS, Derevitskaya OK, Soldatova NE, Fedulova LV. Influence of meat semiprepared foods produced with an addition of water having a reduced deuterium content on the indicators of the laboratory animals with the model of alloxan diabetes. *Vopr. Pitan.* 2017;86(1):64-71.
PMID: 30645892.
10. Halenova T, Zlatskiy I, Syroeshkin A, Maximova T, Pleteneva T. Deuterium-depleted water as adjuvant therapeutic agent for treatment of diet-induced obesity in rats. *Molecules.* 2020;25(1):23.
Available:<https://doi.org/10.3390/molecules25010023>.

11. Molnár M, Horváth K, Dankó T, Somlyai G. Effect of deuterium oxide (D₂O) content of drinking water on glucose metabolism on STZ-induced diabetic rats. Proceedings of the 7th International Conference Functional Foods in the Prevention and Management of Metabolic Syndrome; 2010.
12. Strekalova T, Evans M, Chernopiatko A, Couch Y, Costa-Nunes J, Cesuglio R, Chesson L, Vignisse J, Steinbusch HW, Anthony DC, Pomytkin I. Deuterium content of water increases depression susceptibility: The potential role of a serotonin-related mechanism. *Behavioural Brain Research*. 2015;277:237-44.
13. Cărpinişan L, Petcu MD, Petrovici S, Chiş C, Ghişe A, Zehan R. The Influence of deuterium depleted water on the hematocrit and the leukocyte formula in rats intoxicated with chromium. *Scientific Papers Animal Science and Biotechnologies*. 2010;43(1):464-8.
14. Basov A, Fedulova L, Baryshev M, Dzhimak S. Deuterium-depleted water influence on the isotope 2H/1H regulation in body and individual adaptation. *Nutrients*. 2019;11(8):1903.
15. Somlyai G, Somlyai I, Fórízs I, Czuppon G, Papp A, Molnár M. Effect of systemic subnormal deuterium level on metabolic syndrome related and other blood parameters in humans: A preliminary study. *Molecules*. 2020;25(6):1376.
Available:<https://doi.org/10.3390/molecules25061376>.
16. Bulotta A, Hui H, Anastasi E, Bertolotto C, Boros LG, Di Mario U, Perfetti R. Cultured pancreatic ductal cells undergo cell cycle re-distribution and beta-cell-like differentiation in response to glucagon-like peptide-1. *J. Mol. Endocrinol.* 2002;29(3):347-360.
Available:<https://doi.org/10.1677/jme.0.0290347>.
17. The Center for Deuterium Depletion.
Available:<https://www.ddcenters.com/>.
18. Donga E, van Dijk M, van Dijk JG, Biermasz NR, Lammers GJ, van Kralingen K, Hoogma RPLM, Corssmit EPM, Romijn JA. Partial Sleep Restriction Decreases Insulin Sensitivity in Type 1 Diabetes." *Diabetes Care*. 2010;33(7):1573-1577.
Available:<https://doi.org/10.2337/dc09-2317>.
19. Pieribone D. Bio-electrical Impedance Analysis. TheBody; 1998.
Available:<https://www.thebody.com/article/bio-electrical-impedance-analysis>.
20. Boros L. Biological nanomechanics: ATP synthesis and deuterium depletion. 2016 presentation.
Available:<https://youtu.be/6P8gqB4zLGQ>
21. Jensen MT. Resting heart rate and relation to disease and longevity: Past, present and future. *Scand J Clin Lab Invest*. 2019;79(1-2):108-116.
Available:<https://doi.org/10.1080/00365513.2019.1566567>
22. Schloerb PR, Friis-Hansen BJ, Edelman IS, Solomon AK, Moore FD. The measurement of total body water in the human subject by deuterium oxide dilution with a consideration of the dynamics of deuterium distribution. *J. Clin. Invest.* 1950;29(10):1296-1310.
Available:<https://doi.org/10.1172/JCI102366>.
23. Hao D, Sarfaraz MO, Farshidfar F, Bebb DG, Lee CY, Card CM, David M, Weljie AM. Temporal characterization of serum metabolite signatures in lung cancer patients undergoing treatment. *Metabolomics*. 2016;12:58.
Available:<https://doi.org/10.1007/s11306-016-0961-5>.
24. Gros SJ, Holland-Cunz SG, Supuran CT, Braissant O. Personalized treatment response assessment for rare childhood tumors using microcalorimetry-exemplified by use of carbonic anhydrase IX and Aquaporin 1 Inhibitors. *Int. J. Mol. Sci.* 2019;20:4984.
Available:<https://doi.org/10.3390/ijms20204984>.
25. Pandey N, Lanke V, Vinod PK. Network-based metabolic characterization of renal cell carcinoma," *Scientific Reports*. 2020;10:5955.
Available:<https://doi.org/10.1038/s41598-020-62853-8>.
26. Arima K, Lau MC, Zhao M, et al. Metabolic profiling of formalin-fixed paraffin-embedded tissues discriminates normal colon from colorectal cancer. *Mol. Cancer Res.* 2020;18:883-90.
Available:<https://doi.org/10.1158/1541-7786.MCR-19-1091>.

27. Boros LG, D'Agostino DP, Katz HE, Roth JP, Meuillet EJ, Somlyai G. Submolecular regulation of cell transformation by deuterium depleting water exchange reactions in the tricarboxylic acid substrate cycle. *Med. Hypothesis.* 2016;87:69-74.
Available:<https://doi.org/10.1016/j.mehy.2015.11.016>.
28. Boros LG, Collins TQ, Somlyai G. What to eat or what not to eat – that is still the question. *Neuro-Onc.* 2017;19(4):595-596.
Available:<https://doi.org/10.1093/neuonc/now284>
29. De Feyter HM, Behar KL, Corbin ZA, Fulbright RK, Brown PB, McIntyre S. Deuterium metabolic imaging (DMI) for MRI-based 3D mapping of metabolism in vivo. *Science Advances.* 2018;4(8):7314.
Available:<https://doi.org/10.1126/sciadv.aat7314>

Biography of author(s)



Edwin C. Jones

Department of Veterans Affairs, Knoxville Outpatient Clinic, 8033 Ray Mears Blvd., Knoxville, TN 37919, USA.

Research and Academic Experience:

University of Tennessee- Knoxville, Tennessee Ph.D., Physics, Dec 1992
Research Associate at the Oak Ridge National Laboratory, Oak Ridge, Tennessee, Jan 1993-Aug 1996. Conducted research in high-temperature superconductivity, cryogenic engineering and fusion energy.
Meharry Medical College- Nashville, Tennessee M.D., May 2000
Vanderbilt University Medical Center-Nashville, Tennessee Completed residency training June 2004.
Private Medical Practice in California 2004-2005
Physician at the Dept of Veteran's Affairs, 2005-present

Research Area: Investigating the beneficial effects of ketogenic diets and deuterium depletion on the human body. Currently studying the effect of deuterium on cardiac functioning.

Number of Published papers: 33

Special Award: Thirteen papers in physics ranked as high impact (top 2% of literature citations).

© Copyright (2021): Author(s). The licensee is the publisher (B P International).

DISCLAIMER

This chapter is an extended version of the article published by the same author(s) in the following journal.
Medical Research Archives, 9(6): 2-19, 2021.