# INTERNATIONAL HEALTH NEWS

*William R. Ware, PhD - Editor*

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Familial hypercholesterolemia (FH) is an inherited disorder. The genetic mutations make the liver ineffective in metabolizing (or removing) excess LDL-cholesterol and this results in highly abnormal levels and thus also high total cholesterol, starting generally in early childhood. The prevalence of FH cited in the literature is around 1/500 individuals although both somewhat higher and lower estimates are seen. This low prevalence may cause readers to wonder why it is an appropriate topic for IHN. FH cannot be prevented and treatments are somewhat controversial but generally emphasize statins. However, individuals with FH from an early childhood have their arteries exposed to high levels of LDL, the so-called bad cholesterol. Thus conventional wisdom suggests that FH should be a potent risk factor for atherosclerosis including coronary artery plaque. This was consistent with premature coronary heart disease assumed related to coronary atherosclerosis.

In the early 1990s a method was develop based on a non-invasive CT scan of the heart which allowed quantification of the plaque burden, i.e. coronary artery disease. Since the scan focused on calcified plaque which represented the majority of lesions, the results were quantified in a calcium score or more properly a coronary artery calcium score (CACS). It turns out that if the score is zero, even though there is some unobserved, i.e. non-calcified plaque, the risk of an acute coronary atherosclerosis related event such as a heart attack is both very small and independent of traditional risk factors. A simple view is that if there are almost no plaques to rapture, there will be almost no heart attacks. The determination of the calcium score is not at present considered justified for risk-screening by mainstream medicine. There of course is some radiation exposure and probably at least an hour devoted to the visit to the scanning lab and frequently the procedure is not covered by insurance.

Nevertheless, before the last US presidential election, the health reports including CACS of both contenders were published. One had a score of zero the other 100. There is also probably a strong correlation between getting the scan and income. One argument for more extensive use of this prognostic tool is that even if one has a risk of greater than 7.5% for an acute atherosclerosis related event based on a risk calculator, the new magic number as of 2013, and is thus a candidate for statin treatment, if the CACS is zero, this may indeed be over-treatment with undesirable side effects for what is in fact a very low risk individual after adjustment for CACS = 0.

A recent study found that for a large cohort of FH individuals (age 31—59), the prevalence of CACS = 0 surprisingly was about 50%. It is interesting that population studies of various groups have also found high prevalence of CACS = 0, up to about 70% of the group studied and even among older individuals. However, the FH group is special since as mentioned, they have had very high arterial exposure of LDL cholesterol, many from childhood on. Thus the 50% with CACS = 0 appears anomalous to say the least and raises questions regarding the conventional wisdom.

Consider individuals with CACS = 0. What is unique about them? There is a similarity between this question and the question of what is responsible for unique small and frequently isolated populations with great longevity and the absence of chronic diseases. This latter question was studied by Dr. Weston Price in the 1930s and later by Dan Buettner in the famous Blue Zone studies. The results are available today in two books and provide considerable insight into the decline of health in the modern world since the abnormal populations studied failed to share many lifestyle and dietary practices common to modern civilization. Given that many with CACS = 0 have elevated traditional risk factors for heart disease (it is almost automatic as one ages), attention needs to be focused on diet, lifestyle, and environmental factors without the burden of discredited notions such as dietary fat is bad.

Such a study exists and is based on the Multiethnic Atherosclerosis Study (MESA) population. The major lifestyle factors associated with low (including zero) CACS were regular exercise, adherence to a Mediterranean diet, smoking avoidance and maintaining of normal weight (Body Mass Index ≥ 18.5 to ≤ 24.9). Calculators are available online. It is interesting that just having a high healthy lifestyle score based on these four factors also favorably impacted all-cause mortality (Am J Epidemiol 178:12). The authors cited other studies consistent with their results. Both Price and Buettner also observed that favorable psychosocial factors were a common characteristic of the populations they studied in the context of healthy longevity and absence of chronic disease into old age. Strong family ties and a wide circle of close friends appeared important. One of the most impressive observations of both Price and Buettner was that when members of these isolated and remarkably healthy micro populations left to join the more civilized world, they rapidly developed the health problems common in their new location.

*Wishing you and your family a healthy and Happy Holiday Season,*

***William R. Ware, PhD, Editor***

**Highlights**



## ARE E-CIGARETTES SAFE FOR CHILDREN AND ADOLESCENTS?

In recent years the prevalence of cigarette smoking has declined and this has been accompanied by the presence of compelling evidence of the association between smoking and both cancer, heart disease and other lesser syndromes. As many readers have probably observed, cigarettes are being replaced by artificial devices called E-Cigarettes or so called vap pens. Statements both by US government agencies like the CDC and the NIH, but also published in the scientific literature frequently use the term Electronic Nicotine Delivery System (ENDS) which is actually quite descriptive of these cigarette replacements. The devices have a capsule of liquid containing nicotine and generally a flavoring agent dissolved in a solvent generally consisting of propylene glycol, glycerol or both. A wick heated by a battery-driven heating coil vaporizes a small portion of the liquid to generate an aerosol (very small liquid droplets similar to fog) and this aerosol is then inhaled to produce the sensation of inhaling smoke and allow the mouth and lungs to absorb the nicotine along with whatever else is in the vapor. One company (Juul Labs) now produces a model that looks like a USB flash drive stick but simply a bit longer. This effectively disguises its real nature, a convenience appreciated by schoolchildren wishing to conceal their “vaping” as this artificial smoking is called. With care, vaping can be done with low risk of detection. Incidentally, it is illegal in the US to sell these devices to anyone under 18, but as everyone knows, it is child’s play to circumvent such restrictions. The under 18 years of age group have no trouble acquiring alcoholic drinks, cigarettes and street drugs. All that is required are friends and money.

Red flags are being waved in the media and the medical literature. Nicotine is an addictive substance! The US FDA is suggesting we have an epidemic of vaping among adolescents and younger. This widespread use and the known and especially unknown health risks are raising alarm. The FDA is even considering actively preventing companies from marketing products that are attractive to children and adolescents. In fact, the FDA is now reconsidering its decision to delay regulatory decisions until 2022. All this seems to ignore the obvious failure of the war on drugs on all fronts. If one wants alcoholic drinks, addictive drugs whether it is nicotine from E-Cigarettes or from street drugs or from for example ADHD drugs identical with the street drug methamphetamine, they can get them, even by selling their own prescription drugs.

The Juul E-Cigarettes introduced in 2015 have skyrocketed in popularity among teens and college students across the US according to widespread reports. Smoking E-cigarettes has also become known as Juuling. An alarming increase in use has been

reported among middle and high school students. Juul appears to deliver nicotine more efficiently and more quickly than competitive brands. Each cartridge contains as much nicotine as a pack of cigarettes. However products that do not contain nicotine are also available. In the 2011-2015 National Youth Tobacco Survey, which used 'past 30-day use' as a metric, the use of E-cigarettes went from 5.7% to 64%. Ages ranged from 9 to 17[1]. Prevalence of used data varies considerably due to a number of different measures of use. However, the trend definitely appears to be strongly up.

As will be discussed below, for recent vaping devices and traditional E-Cigarettes, the issues are complex, but foremost is the potential for nicotine addiction and the potential to encourage cigarette smoking, the reverse of what these devices are supposed to accomplish. Young vapers are attracted by the flavorings, the compelling hype provided by the industry, pressure from their vaping peers and to be "cool." Not only regulators and public health officials but also parents are now forced to deal with an activity among children and adolescents where the long-term risks are of necessity unknown, and this includes the risks to the fetus and its postnatal development from the various chemicals in the artificial smoke. Foreign chemicals can influence brain development all the way to the adolescent-adult transition and even early adulthood. Brain development is not more or less complete until the mid-20s. We will briefly review various aspects of this risk problem.

**NICOTINE ADDICTION**

There is general agreement that nicotine is addictive. In addition, there is the potential to switch to or include cigarette smoking due to nicotine addiction acquired from E-cigarettes. The addiction is even obvious to anyone witnessing withdrawal problems so common in cigarette smokers. In a publication by the US NIH available on line, the following points are made. Nicotine causes a transient surge of endorphins associated in the brains with reward and a brief "high" and like other drugs of abuse, nicotine increases the levels of the neurotransmitter dopamine which reinforces the behavior of taking the drug. Repeated exposure leads to changes in brain circuits involving learning, stress, and self-control. Long-term use results in true addiction with associated withdrawal symptoms and difficulty to adhere to the resolution to quit. Since E-cigarettes provide considerable nicotine exposure, it seems clear that this is a major downside to vaping. A study revealed that use of E-cigarettes with higher concentrations of nicotine by youths increase subsequent frequency and intensity of vaping and in addition, smoking cigarettes.[2] Aside from addiction, health problems associated with cigarette smoking are clearly associated with vaping if it leads to subsequent tobacco use.

Nicotine has also been implicated as causing cancer (oral, esophageal and pancreatic and in women cervical) but the evidence is merely suggestive of a possible link. There may also be links to vascular disease, inflammatory bowel disease and kidney disease, but again the links are merely hypothesis generating.[3]

The US FDA now views the addiction problem serious enough that action is being taken to prohibit sale of E-cigarettes in convenience stores, gas stations and vending machines to those under 18 years.

## FORMALDEHYDE EXPOSURE

Formaldehyde is an extremely toxic chemical. When humans are exposed, toxic damage occurs rapidly near the site of exposure. It is also a metabolite of methanol metabolism and when this alcohol encounters the enzyme that converts it to formaldehyde, damage to tissue and individual cells occurs close to the site of the enzyme activity. It is implicated in many chronic diseases with the main sources being canned fruits, tobacco smoke and the artificial sweetener aspartame.[4] The production of formaldehyde from methanol can be prevented by high doses of ethyl alcohol, the alcohol in alcoholic beverages. If enough is consumed, it blocks the enzyme by overwhelming it with a high concentration of this competitive substrate. This appears to be the only example where the emergency response to an accidental or intentional poisoning is treated by making the patient extremely drunk until the methanol itself is eliminated naturally.

Formaldehyde is a known thermal degradation product of propylene glycol and reacts with both this glycol and glycerol to form addition compounds called hemiacetals. These molecules can then release formaldehyde at some location distant from the site of the reaction. The production of formaldehyde in E-cigarettes occurs with increasing yield at higher filament temperatures, but in normal vaping may be only at low concentration. Ideally, the desired level is zero which may not be the case even in normal vaping. This is a controversial area currently under investigation.[5]

## OTHER RISKS

In an extensive report from The National Academies of Science, Engineering and Medicine and reported in Medical News Today (January 29, 2018), the conclusions regarding other risks are as follows. There is no evidence available regarding whether or not E-cigarettes cause respiratory diseases in humans. In addition, no available evidence indicates an association with pregnancy outcomes or fetal development. There is also no evidence concerning an association with cancer. This sounds more reassuring than it is. This is not a popular field of research, industry studies should be viewed with extreme caution, and we are here concerned with the need for long-term (a decade or decades) exposure to the inhaled chemicals, particulate matter and known toxins such as cadmium. There are no studies that are long-term and one must recognize the potential of dose relationships.

What can be concluded? Note that the above discussion applies to adolescents and children but one can imagine extrapolation to adults. It would seem wise to take potential addiction seriously, recognize the poorly understood risk vs. benefit and venture into the unknown with caution if at all. After all, for many years the general public was told that cigarette smoking was safe, even healthy, and major medical journals accepted cigarette advertising. It turned out to even worse than the most vocal critics proclaimed. It is highly likely that the use of E-cigarettes is much safer but the risk of it leading to tobacco use appears significant.

# OVER 75 YEARS OF AGE AND HEALTHY, WHY ARE YOU TAKING A STATIN DRUG FOR PRIMARY PREVENTION OF ATHEROSCLEROSIS?

This was the title of a commentary in the New York Times January 5, 2018. According to the Centers for disease Control, for adults 75 and older, almost half are on statins. The percentage in 2001-2003 was already 30%.[6] This is for primary prevention, i.e. in the absence of a history of an atherosclerosis-related acute cardiovascular event such as a heart attack or stroke or angina. The prevalence of statin use increases almost linearly with age, and the high percentages are a principal reason for the frequent discussions of this drug in IHN since many older readers must be on statins or have parents that are. Part of the reason for this heavy use of statins is the large influence of age when common calculators used to determine the risk of atherosclerotic associated major events and the low thresholds of risk indicate statin need according to guidelines that are in general use.

Another reason is the large overestimation of the risk calculator introduced in 2013 by the American College of Cardiology and the American Heart Association (ACC/AHA) and the significant lowering of the 10-year event rate risk threshold for recommending statins for primary prevention to 7.5%[7] As discussed in the October 2018 IHN, there is now a new ACC/AHA calculator which has considerably less overestimation, but it has probably yet to impact statin recommendations (see October 2018 IHN). Both the US preventive Services Task Force and the American College of Cardiology currently claim there are no data to provide guidance for those over 75 for primary prevention. However, as will be discussed later, the most recent version of the calculator from the Multi-Ethnic Atherosclerosis Study (MESA) accepts up to 85 years of age and continues to give significantly lower 10-year risks than the new ACC/AHA calculator **https://sanjaybasu.shinyapps.io/ascvd** which also accepts age 85[8].

There are in fact two trials containing pure primary prevention results for the age group in question if one ignores small trials and a trial where an elevated level of inflammation was required at baseline. The trial called PROSPER was a 3.5 year study of statin efficacy and had an age range of 70-82. **No statistically significant benefit was found in primary prevention of CHD death, non-fatal heart attack, or fatal or non-fatal stroke**.[9] The ALHAT-LLT trial examined two age groups, 65-74 and 75 or older. The primary endpoint was all-cause mortality and secondary endpoints were coronary heart disease events and stroke. The trial was of 5-year duration and compared a statin to usual care. **No significant benefits were found** in a recent post hoc secondary data analysis.[10]

A study report just published reopens the question of statins for primary prevention of cardiovascular events in old and very old adults age over 75 with a mean age of 79 for the group 75-86 and 89 for those ≥ 85.[11] Not only did it include older individuals, it stratified by the presence or absence of type 2 diabetes and included more endpoints than the two above trials. It was a cohort study with a duration of 5.6 years and included almost 50,000 participants but was retrospective and used a database of a Spanish

primary care system**. For those free of diabetes, no benefit was found**. For the diabetic group, absolute benefit over the 7.7 years for the prevention of coronary heart disease was 2.2%, and for all-cause mortality and stroke each 2.5%. All three of these studies included a range of cardiovascular event risks. Thus if one is over 65, it appears that statins can be rejected for primary prevention without even considering the calculated 10-year risk of acute events, and this includes rejecting argument for statin preventive therapy based on elevated total cholesterol (which implies elevated LDL), low HDL or family history.

This should settle the matter of statins for this age group free of diabetes as it appears to be an ineffective treatment. However, for diabetics free of heart disease, the small benefit probably justifies the automatic prescription to diabetics with risk above the threshold. However, the results which are consistent with other studies highlight the inability to standard therapy to reduce the cardiovascular risks associated with diabetes in a clinically significant manner where for example only 50% instead of > 95% do not benefit.

Age is a strong determinant when the 10-year risk of acute cardiovascular events is calculated by any of the common algorithms used in online calculators, and this has a profound effect on the recommendation for statins. In the 2012-2013 period, the latest for which there appears to be data, the percent in the US using statins was 19%, 47.8% and 48.6% for the age categories 40-64, 65-74 and ≥ 75. How consistent this is with estimated risk is interesting. The 2015 version of the Multi-Ethnic Atherosclerosis Study (MESA} calculator appears to be a good choice if one is trying to minimize overestimation. In the table below are results for nondiabetic Caucasian men and women, age 65 to 85, total cholesterol of 180 mg/dL, HDL 55 mg/dL, systolic blood pressure of 140 mm mercury, non-smoker with no history of family or personal heart disease, and not on either cholesterol lowering or anti-hypertensive drugs. The table includes input of zero coronary calcium score, the results when coronary calcium was not known (NK), and for this latter circumstance, the level of coronary calcium score (CASC) that can be estimated (by trial and error) by the calculator with everything else the same that would have given the same results as when no score was used in the input). Calculators such as the ACC/AHA do not allow input of calcium scores and thus the NK column is what one use for comparison. Risks are for acute coronary heart disease events over 10 years.

| AGE | 65 YEARS | | | 75 YEARS | | | 85 YEARS | | |
|---|---|---|---|---|---|---|---|---|---|
| | CAC=0 | NK | CACS | CAC=0 | NK | CACS | CAC=0 | NK | CACS |
| M | 2.2% | 5.8% | 35 | 2.6% | 9.0% | 100 | 3.1% | 13.8% | 270 |
| F | 1.5% | 2.8% | 10 | 1.8% | 4.4% | 30 | 2.1% | 6.8% | 80 |

For men, at age 75 and greater, the 7.5% threshold for statin recommendation is crossed whereas for women, it is never crossed. Since a very significant percentage of any population will have zero coronary calcification, it is noteworthy that for both men and women not only is this threshold never crossed if CACS = 0, and the risks remain so low as to be relatively insignificant. Measurement of coronary calcification is rare but

it obviously is a powerful tool for determining risk. It can be calculated that for the 75 year old man, the risk of 9% is reduced to 7.5% at a CACS of 50 rather than 100. The table implies that increasing plaque burden is also a major factor in the increase in risk with age, simply because coronary calcification progresses with age. Note also the very large changes in risk caused by going from zero to the study population average of the CACS, all other risk factors remaining the same. If a graph is made of the results in the table, it is seen that for men, over this age range, the risk when the CACS score is not used increases with age much faster than linear and is in fact close to exponential. For both men and women, if CACS = 0, the increases are very slow and linear. Finally, if the older threshold for concern, a 10-year event risk of 10% is used, then this is crossed only at age 85 by men.

Since the new ACC/AHA calculator is now online, it is possible to calculate the degree of overestimation when compared the 2015 MESA calculator. For men at 65, 75 and 85 years of age, the overestimation by ACC/AHA was by a factor of 1.4, 1.7 and 1.8 whereas for women, it was factors of 1.4, 1.9 and 2.6 respectively This is significantly lower than what would have been obtained with the 2013 version, but still large enough to skew recommendations for statin use from unnecessary to recommended. This of course depends on the other parameters used, but the set used reflect low risk conventional risk factors. In the ACC/AHA calculators CACS is not used since it was of necessity never considered in the construction of the so-called Pooled Equations. Of course there is a huge population variation over which the calculator averages.

Finally, if one's physician expresses concern over cholesterol or recommends statins, it might be a good idea to delay the decision, ask for a copy of the lab report, and use the MESA calculator to evaluate heart disease risk. Compare with the new and old ACC/AHA calculators. The old one was probably used to judge the blood results. In addition, all that is needed is systolic blood pressure and a knowledge of family history of heart disease and answers to simple questions. Google will provide access to the old (2013) ACC/AHA and MESA calculators and the latter should have 2018 at the bottom of the fill-in screen. This also allows the examination of the effect or risk of family history of heart attack which is not insignificant but has been set at "no" in this discussion to keep it simple.

The MESA calculator probably gives the best estimate of risk available today. When interpreting this "do at home" assessment, some may want to question the 7.5% threshold and regard 10% over 10 years as more realistic. After all it was used for decades until 2013. If the result is that one decides that statin therapy should be considered, then it boils down to absolute benefit vs. absolute risk of serious side effects as has been discussed in IHN repeatedly over the last few years. If one already has cardiovascular disease, then these calculators do not apply and anyway, the case for statins is then much stronger and has few critics, even though the absolute benefit is still rather small (generally rarely more than 95% fail to benefit. If one has diabetes, the benefits are also small but appear to be real, and the side effect of diabetes is obviously not an issue, although it is a big issue in the absence of this disease.

What happens if we include diabetes or family history of heart disease and leave out CACS? The MESA calculator indicates that the risk for both males and females increases by about a factor of 1.5 – 1.6, independent of age from 65 to 85. If we do the same for family history the factor is similar and again independent of age. However, if we specify CAC = 0, either additional risk factor produces an almost negligible increase in risk which is already very low. This is in sharp contrast to when the CACS is left unspecified and indirectly turns up because it is present and increasing dramatically with age in the population in which the algorithm is based. Obviously, preventing coronary artery plaque build-up should be a high priority challenge for cardiovascular researchers and the large percentage in for example the US population with CACS = 0 merits further study. What are the large number with ACS = 0 doing right? As will be discussed in a future issue of IHN, the interpretation of the result CACS = 0 is more complex than implied above because there can be unclarified lesions and even significant obstruction, but this does not invalidate the conclusions presented. CACS remains a very strong indicator of future acute atherosclerosis related events. Also, note the editorial in this issue where it is discussed that in those with familial hypercholesterolemia approximately 50% have CACS = 0 in spite of *lifelong* exposure to elevated arterial LDL.

## NEW STUDY HELPS DETERMINE NEED FOR CHEMO IN EARLY STAGE BREAST CANCER. VIEWED AS "PRACTICE CHANGING"

At a plenary session of the meeting of the American Society of Oncology (ASCO 2018) the long awaited results of the TAILORx study (Trial Assigning Individualized Options for Treatment) were presented and simultaneously published in the *New England Journal of Medicine*.[12] The study involved the question of when, after breast cancer surgery, should hormone therapy be combined with chemotherapy or just hormone therapy used alone. A proposed way of making this decision was examined for a large number of patients for which there had been no clear answer—sort of an intermediate group. The total group studied (approximately 10,000 patients) were hormone receptor positive, HER2 negative and axillary node (lymph node) negative.

Early stage breast cancer is generally defined as cancer which has not spread beyond the breast or the axillary (arm-pit) lymph nodes. This includes ductal carcinoma in situ and stages I, IIA, IIB and IIIA. After surgery the need for and type of additional treatment is based on the estimated risk of recurrence. Recent guidelines in the US and Europe make use of an *Oncotype DX Recurrence–Score Assay,* a commercial test that includes determination of the expression of 21 genes in a tumor sample after it has been removed by surgery or by biopsy. The assay also takes into account the individual tumor pathology and generates a score of 0-100. Patients with high scores indicating high risk of recurrence are generally recommended to have both chemotherapy and hormone (endocrine) therapy whereas those with low scores are viewed as needing only hormone therapy.

The TAILORx study was organized because there was uncertainty as to the criteria best suited for those who were neither of high or low risk and to further segregate this group for just a single therapy, hormone, or chemotherapy using an evidence-based tool. This is a serious issue given the side effects of chemotherapy. Those with an intermediate range score (11-25) were randomly assigned to receive either hormone or chemotherapy alone with the endpoint of invasive disease-free survival (freedom from invasive disease recurrence, second primary cancer or death). Those with high or low risk scores were treated according to the guidelines and were given chemotherapy plus hormone therapy or just hormone therapy, respectively.

At the end of the follow-up of 9 years of this intermediate cohort, both treatment groups had similar outcomes for invasive disease-free survival, freedom from disease recurrence at a distant site or at a distant or local-regional site and overall survival. When further analyzed these results suggested that the 21-gene assay and the associated recurrence score may identify up to 85% of women with early breast cancer who can be spared chemotherapy, especially those 50 years of age or older and having a recurrence score of 25 or less and as well women 50 or younger who have a recurrence score of 15 or less. While the title of the study suggests this is just a gene-based test, the recurrence score has significant additional clinical and pathological input.

In this study, sponsored by the US National Cancer Institute, about 6700 participants were in the questionable treatment group. The remainder was about equally divided between those where the indication was clear that hormone therapy alone or hormone therapy plus chemotherapy were indicated. The recurrence score allowed about 5700 to avoid chemotherapy simply because hormone therapy had very similar outcomes. This would seem to be a highly worthwhile outcome based on a relatively simple test protocol which included a commercially available genetic test. Women scheduled to undergo surgery for early stage breast cancer followed by post-surgery therapy should ask their oncologist if the issue examined in the above study was going to be considered. Some oncologists may not have heard about these very recent results although the medical news services quoted prominent oncologists as saying this was predicted to be a practice-altering study.

## HOLIDAY READING SUGGESTIONS

- ***Sapiens. A brief history of humankind*.** Y. N. Harari, McClelland & Stewart, 2014. While published about 4 years ago, in the past few months it has reappeared on the New York Times best seller list. The book traces the history of *Homo Sapiens* throughout its history with emphasis on how our species succeeded in the battle for dominance, the advent of cognitive power, agriculture, religion, nations, money, laws and the ultimate results of bureaucracy, consumerism and the search for happiness. The book has been described as bold, challenging and provocative.

- ***How to Change Your Mind. What the new science of psychedelics teaches about consciousness, dying, addiction, depression and transcendence.*** Michael Pollan, Penguin Press, New York, 2018. Michael Pollan is a well-known author of books on health, food and medical matters, and a long time contributor to the *New York Times Magazine*. This book appears to have been inspired by the remarkable resurgence starting in the 1990s of interest in medical and psychology circles in psychedelics after a hiatus of over 20 years following the outlawing of such drugs as LSD due to bad experiences of some on psychedelic "trips." New research led by groups at New York University and Johns Hopkins University and has resulted in a recognition of the potential of such trips in the context of informing regarding psychological problems and even dramatically influencing the coping with inevitable death, especially from terminal cancer. The book contains interviews with researchers, patients, and the author informed himself by experiencing a number of trips, described in the Travelogue chapter, starting with one that involved only unusual breathing (holotropic breathwork). If nothing else, the book cannot fail to impress the reader of the complexity and innate subconscious control of our brain functions.

- ***The End of Alzheimer's. The first program to prevent and reverse cognitive decline.*** Dale E. Bredesen, MD. Penguin—Random House, New York, 2017 Dr. Bredesen is professor and founding president of the Buck Institute, and a professor at the University of California, Los Angeles. This has been described as a scientific rigorous paradigm-shifting book that brings hope to Alzheimer's patients with a new understanding of the disease and a new program that they can put into effect themselves. It is based primarily on the results from his research group which have been published in major journals. The book suggests a recognition of the problem of bringing a protocol to the attention of the general public which involves diet and supplementation based on the classification of Alzheimer's disease types, and also applies to mild cognitive impairment. A must read for anyone with family, loved ones, and friends with this terrible disease or its early stages. Since it is not a pharmaceutical approach but nevertheless evidence-based, don't expect to hear about this from mainstream medicine.

- ***Why We Sleep.*** Matthew Walker, Ph.D. Scribner, New York, 2017. Dr. Walker is director the University of California at Berkeley Sleep and Neuroimaging Laboratory. The book has been described as a ground-breaking exploration of how we can harness the transformative power of sleep to change our lives for the better. This is an important book because most take sleep for granted with no appreciation of its great importance in our lifelong health and the amazing things that occur while we sleep.

- ***Unsavory Truth.*** How food companies skew the science of what we eat. Marion Nestle, Ph.D. Basic Books, 2018. Dr. Nestle is Paulette Goddard Professor Emeritus of Nutrition, Food Studies and Public Health New York University and visiting professor of Nutritional Sciences at Cornell University. This book exposes the horror story of the extent to which what we are told about food and many tend to believe is intentionally misleading, incorrect, deceptive beyond forgiveness, and a threat to public health. It also informs on the problems and difficulties associated with nutritional research, current and past. In the age of junk food and ultra-prepared food, it is wake-up call concerning a danger that permeates all developed countries and is infiltrating those that are not. This is a good companion book to Larry Olmsted's book ***Fake Food/Real Food. Why you don't know what you are eating and what you can do about.***

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