

THE REWARD DEFICIENCY SYNDROME: AN EXPLORATION  
*Demystifying the Dopaminergic System*

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General Psychology

Research Essay

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4 May 2010

Abstract

This essay is an intensive inquiry into/regarding scientific research and findings regarding the age-old riddled nature of the disease of alcoholism, drug, and other behavioral addictions cause or source ranging from Dr. William Silkworth, M.D.'s findings regarding alcoholism and his documented contribution of such, circa his 1930's book entitled, *Alcoholics Anonymous*, to present day 2010. It spans through significant scientific research, confirmed statistics, and other findings until Dr. Kenneth Blum, M.D.'s most recent coining of his extensive research and discoveries regarding addiction and genetics, *The Reward Deficiency Syndrome*—his exceptional extensively supported claim regarding the D2 dopamine receptor gene as being a definite determinant of the reward deficiency syndrome at the *University of Texas Health Science Center* in San Antonio, Texas in 1996. As thoroughly as at all possible, this essay's aim is to attempt to find, gather, and tether together the established findings of this otherwise enigmatic life-altering, so-called *incurable*, most troubling condition of its afflicted and the people who love them.

The Reward Deficiency Syndrome: An Exploration

*Demystifying the Dopaminergic System*

Herbert Spencer once said, “There is a principle which is a bar against all information, which is proof against all arguments and which cannot fail to keep a man in everlasting ignorance—that principle is contempt prior to investigation” (Wilson & Silkworth, 2001, p. 568).

It is 2,010 years after the death of a great man who was known to have turned water into wine. These days, it is most likely a positive thing that the process of making alcohol is a bit more difficult to achieve, as the human consumption of it still is not. Due to many somber sobering facts and statistics found everywhere via the click of a button today, people have become more and more aware of the ubiquitousness of this problem.

The indubitable question of how to go about treating or curing alcohol addiction has skyrocketed above many other pressing health topics in the past decade and today, it looms larger than ever. Will there ever be a cure? After years of scratching our heads, it is time we roll-up our sleeves, adopt an eager disposition, and dive straight into the depths of valid current findings.

*“Alcohol is both a food and a drug; as a food it has caloric value. In moderate quantities it serves as a tonic and stimulant. In larger amounts it acts as a depressant. Alcohol has certain useful effects when moderately taken such as a sedative action [an emotional pain-killer] and it is known that it benefits persons suffering from angina pectoris, as it dilates the coronary arteries. Alcohol should not be a bugaboo about which to frighten ourselves. Moderate convivial drinking has its right place. There is no primitive tribe in this world that is not without its fermented potion of some sort. However, excessive drinking proves harmful to the very condition one is trying to relieve. It should be handled so that it breaks the ice at parties, not so that it breaks down every human*

*reserve and leads to serious complications (Caprio, 1965, pp. 117-118)."*

If simply ceasing to drink alcohol were the true answer to alcohol addiction, then success rates pertaining to a plethora of forms of available treatments would be drastically higher and more consistent. The fact is that one must consider and try to implement *all* factors known to date with regards to regaining one's physical, mental, and spiritual health in order to have the best chance at a true recovery from alcoholism.

Simply ceasing to drink alcohol is far from a complete answer which might equate to enjoying a genuinely robust state of health. If any part of an engine is damaged that is responsible for making a car operate, repairing that engine involves much more than to simply stop driving the vehicle. The road ahead is long in repairing one's brain chemistry, other illnesses that may be discovered while experiencing abstinence, human relationships, and a sense of well-being in daily living.

Dr. Robert R. Perkinson, Clinical director of Keystone Treatment Center in Canton, South Dakota has specialized in alcohol and drug addiction for 26 years. He has this to say:

*"The brain of someone addicted to alcohol is a changed brain. The chronic use of any mood-altering chemical first chemically changes the brain as the cells respond to the poison by producing counteracting chemical compounds that reduce the effects on the cell. If the use continues, the brain changes in structure and, finally, it changes in genetics. In chronic alcohol abuse, the body produces chemical, structural, and genetic changes that do the opposite of what the drug is doing. Alcohol is a depressant so the body produces chemicals, structures and, finally, genetics to stimulate the brain. The alcohol is depressing the central nervous system, the brain picks this up as being abnormal, so the brain changes*

*to counteract the drinking. Alcoholics lose brain cells; using MRIs professionals can see the loss of brain tissue by the widening of the spaces in the sulci and ventricles of the brain; the alcoholic's brain is thus smaller. Evidence says that 68% of people who come to a trauma center have an alcohol or drug problem. Alcoholism is a medical emergency; this is the only way to think about alcoholism accurately. You are dealing with a person who is dying" (Perkinson, 2010).*

Can an individual suffering from alcohol addiction who has a desperate desire for sustained sobriety find a legitimate wholesale answer which may prove to fully utilize all dependable knowledge to confidently entrust one's body, mind, and soul? Today, with the great advances of science, technology, and accumulated human experiences to be gleaned from, might some synergistic approach be on the more promising horizon?

Again, Herbert Spencer once said, "There is a principle which is a bar against all information, which is proof against all arguments and which cannot fail to keep a man in everlasting ignorance—that principle is contempt prior to investigation" (Wilson & Silkworth, 2001, p. 568).

Firstly, in order to properly "investigate," it is helpful to situate the mind in the most productive position possible to be capable of contemplating knowledge when in regards to such a socially stigmatized subject such as *alcoholism*; it is imperative to shun any reticence or bias either way.

In this way, it would be wise to mentally categorize the *alcoholic* in a similar way that one may apply to the *diabetic*. A person who has contracted diabetes is not stereotyped with such immediate disdain in our society. In the way of the human body's functioning or malfunctioning, a diabetic may in fact be a closer cousin to an alcoholic body type than some

may imagine. Sure, a diabetic who just wolfed down a *Snickers* bar and whistled happily up a hill may not wind up slapped in hand-cuffs like an alcoholic who just guzzled down a few *Budweisers* and drove a vehicle, but for the sake of this exploration, alcoholism is known to be a medical *disease*—a definite malady of the body and mind.

Some of our society is unaware that there exist some people who suffer from alcoholism who may have never even had a drink of it... yet. One may never do so, yet he/she remains in a state of discontentedness and is prone to display other incoherent “signs” of “alcoholism” if even never tasting a sip of “it.” This is why the issue has remained an enigmatic one over the many eye-opening and excruciatingly devastating years. In order to openly explore remedies or current findings which may shed more light, in this particular case it is most helpful if we do not “separate” the *mind* from the *body*. After all, the mind crowns the body and is utterly responsible for its body to be able to perform all things. Each must be regarded as *one* when constructively dealing with the complex nature of *alcoholism*.

Secondly, it is important to define what afflicts a person before being able to explore what to do about it. The origin of the word *addiction* dates back to the mid- 16th century; its Latin root, *addict*, from the verb, *addicere*, then meaning, “*assigned to*” (Jewell, Lindberg, Thompson, McKinzey, & Costa, eds., 2001). At present, the word *addiction* for this purpose refers to a person who is physically or mentally dependent on a particular substance, who is unable to stop taking it without incurring adverse effects. These “adverse effects” are vast and numerous due to a substance people take in the form of drink called *ethyl alcohol* aka *alcohol*—“a colorless volatile flammable liquid that is the intoxicating constituent of wine, beer, spirits, and other drinks, and is also used as an industrial solvent and as fuel” (Jewell et al., 2001).

Adverse effects? Grim research statistics in America are spilled all over the web like a drunk map. Averages can be helpful when providing the basic scope or magnitude of this subject in question, however, much bias comes into play with “numbers” when offered by drug rehabilitation centers’ who have additional financial aims or Alcoholics Anonymous [AA] World Services, Inc, in which there is no accurate log-keeping of exactly how many people attend its meetings.

It is of no benefit to perpetuate any such “guesstimate” regarding AA recovery statistics due to many factors including people who claim to be *recovered* using the Twelve Steps and principles practiced in AA who may not even attend its nearest meetings if they were ever to be counted as a *member* by which to deduct reliable statistics which may point to some truth.

Additionally, accurate statistics may naturally be more difficult to achieve in this area, in the way of “honest” numbers from which to derive averages, partially due to the social stigma that causes discomfort which still blankets our society with the outmoded, “Shh!” and in part due to the dubiousness of asking heavy drinkers to be honest about how often they attend AA meetings or how much or how often they drink. This may not be as trusty of a gathering-hunt as surveying people about which flavor of ice cream they prefer.

After extensive perusal, it may be true that considering “alcoholic statistics” is much like contemplating “unfrozen ice” due to the impossible variables involved in arriving at such with accuracy. However, there do exist some glaring noteworthy statistics about alcohol use that may convey the pervasiveness of this issue for any reader who may not yet grasp the gravity of the seriousness of this disease. One may wish to peruse them with a piece of unfrozen ice, but nevertheless, Bedford, Ohio’s *Alcohol Information* website published these research statistics (“The National Center,” 2005):

- ⇒ Alcohol dependence and alcohol abuse cost the United States an estimated \$220 billion in 2005. This dollar amount was more than the cost associated with cancer [\$196 billion] and obesity [\$133 billion].
- ⇒ American youth who drink before the of age 15 are four times more likely to become alcoholics than young people who do not drink before the age of 21. Every day in the U.S. more than 13,000 teens take their first drink.
- ⇒ Every year, 1,400 American college students between the ages of 18 and 24 die from alcohol-related inadvertent injuries including motor vehicle accidents. More than 150,000 college students develop alcohol-related health problems.
- ⇒ In the United States, almost three times as many men [9.8 million] as women [3.9 million] abuse alcohol or are alcohol-dependent.
- ⇒ Alcoholism and alcohol abuse are the third leading cause of the preventable deaths in the United States in the way of car accidents.
- ⇒ 95% of alcoholics die from their disease and die approximately 26 years earlier than their normal life expectancy.
- ⇒ There are approximately 14 million people in the U.S. addicted to alcohol and millions more who display symptoms of abuse, including binge drinking; of these, it is estimated that 1 in every 13 American adults abuse alcohol or are alcoholic.

“Using data from the 1992 National Longitudinal Alcohol Epidemiological Survey [NIAAA], the authors found that 15% of all U.S. children were currently exposed to alcohol abuse and/or dependence in the family—which includes any adults living in the household—and 43% of all children were exposed to someone who, during their lifetime, satisfied a diagnosis of alcohol abuse or dependence. Assuming that the best estimate lies between these two extremes, it was determined that approximately 1 in 4 children in the US is exposed to alcohol abuse and/or dependence in the family at some point before age 18” (“American Journal,” 2000).

As a healthily functioning nation, we have an alarmingly grave problem on our hands. Have our men and women in the fields of science, health, technology, spirituality or religion found some clues worthy of hope? The answer is yes. The question now is why has valid scientific research not been enmeshed and implemented in with older methods that are still practiced today which admittedly claim in print that they “know only a little” (Wilson & Silkworth, 2001, p. 164) when far more about the roots of alcoholism has indeed been revealed?



Today, due to new discoveries in the fields of science, medicine, and technology, there exist several methods to handle the “not drinking” part of alcoholism. Recently, an indubitable biochemistry-based path to a clinical cure has become available and is unfortunately buzzing below the social radar as of yet. Genetic findings are also promising in the way of soon having approved clinical value once all of the dots are connected.

Alcohol, drug, and tobacco companies are sure to be a beastly impediment to an otherwise more natural course in the way of the implementation of valid new findings that are aimed toward our fullest health. Sadly, this is why we do not “hear” about the positive aims as much. Well-intentioned individuals with no financial aims rarely “scream” of their “findings” loudly. One must search. I attempt herein.

Many alcoholics and addicts have found relief through the recovery meeting society called Alcoholics Anonymous [AA], named after 164 pages of a book (Wilson & Silkworth, 2001), which was originally printed in 1939. These initial pages have been kept in tact over the years due to many finding its message and prayer to a “higher power” enough to achieve or maintain sobriety. In the words of the late 1700’s philosopher, David Hume,

*“Let me emphatically state at the outset, that I do not criticize anyone for praying for themselves or anyone else if they choose to; nor do I deny that there may be benefits to some individuals that stem from prayer. These activities might stimulate subtle mechanisms of psychology and physiology which, when understood more fully, may add to the established benefits of medication and surgery, as they obviously do in psychiatric illnesses. Along with placebo effects, the alleged benefits of prayer may be the result of feelings of well-being, optimism and confidence that result from praying and similar practices like meditation or*

*relaxation. I agree, all of this may exist, and could, perhaps should, be a subject of legitimate scientific inquiry” (Hume, Millican, & Gaudia, 2007, sec. 3-4).*

Some alcoholics, however, do not believe in “God” and find AA’s abstinence and prayer to a “higher power” of their “choice” to be an unfitting *answer* to their personal beliefs. Some alcoholics get a jump-start at rehabilitation treatment centers—most of which practice AA’s Twelve Step program along with consistent group therapy sessions, meal, and sleep regimes in order to establish a practice of new healthy habits. AA and treatment facilities that are AA-based (“Foundations,” 2009) suggest complete abstinence from alcohol in order to get sober.

In recent years, a newer method hit the scene by which alcoholics or heavy drinkers can “drink their way to sobriety” in the way of the brain learning *extinction*. This practice was coined as *The Sinclair Method*. It utilizes a new form of medical technology developed by Dr. David Sinclair over the course of 20 years of research in the Biomedical Research Laboratories in Finland (Sinclair & Neuro-Assisted Recovery, Inc., eds., 2010).

This method arose from the mentality that effective treatment comes from understanding *why* the brain is craving. Dr. Sinclair employs this reasoning in his *solution to*: “The enjoyment derived from using alcohol involves the opiate system in the brain. Neurons in the brain release endorphins when alcohol is present. Certain prescription medications known as opioid inhibitors block the reinforcement from endorphins. By following the specific *Naltrexone* oral medication protocol, drinking and craving are extinguished” (Sinclair & Neuro-Assisted Recovery, Inc., eds., 2010) over an approximate six-month period of time. The brain simply learns by *extinction* to not wish for alcohol anymore because the medicine blocks the “high” (adrenalin rush) one experiences when drinking by replacement of the opioid inhibitor.

AA’ members may wish to try it. I’m sure Bill Wilson would have. He would have lost

his wife if she had not been such a sick untreated *Alanon*. Bill was quite the brilliant entrepreneur, husband, and businessman, if/when not for the doomed drink. He lost his money, and almost lost his wife. If he could have trained his brain to stop yearning for alcohol, he may have been a very different man who was able to enjoy a very different lifestyle...aka: a “rich” lifestyle that he quickly lost when the quicksand of drinking alcohol drained his resources and worldly accomplishments.

Bill and his wife slept on the sofas of many miscellaneous drunks. *Naltrexone* could have been handy as hell (see below *reward deficiency syndrome* explanation and abstracts)...minus the stubbornness factor of alcoholics who would rather die than implement change—that relentless corroding “fear factor” constitutes the very fiber of these reticent mentally ill people.

The Sinclair Method claims, “a statistical analysis of the data obtained from clinics in Finland shows highly significant reductions in alcohol drinking: more than 78%; in Florida, the results since 2002 have been more than 85%. Furthermore, more than 80% of all clients in the Method were successful in long-term control of their alcohol consumption to abstinence or acceptable *social* levels” (2010).

Back in 1939, while finding his medical approaches to be unpromising in his attempt to treat desperate alcoholics, a well-known doctor and chief physician at a nationally prominent hospital who specialized in alcohol and drug addiction, endorsed the recovery society, AA, as an encouraging form of treatment in this letter (“The Doctor's Opinion,” 2001, pp. XXV-XXVI):

*To Whom It May Concern:*

*I have specialized in the treatment of alcoholism for many years. In late 1934 I attended a patient who, though he had been a competent businessman of*

*good earning capacity, was an alcoholic of a type I had come to regard as hopeless. In the course of his third treatment he acquired certain ideas concerning a possible means of recovery. As part of his rehabilitation he commenced to present his conceptions to other alcoholics, impressing upon them that they must do likewise with still others. This has become the basis of a rapidly growing fellowship of these men and their families. This man and over one hundred others appear to have recovered. I personally know scores of cases who were of the type with whom other methods had failed completely. These facts appear to be of extreme medical importance; because of the extraordinary possibilities of rapid growth inherent in this group they may mark a new epoch in the annals of alcoholism. These men may well have a remedy for thousands of such situations. You may rely absolutely on anything they say about themselves.*

*Very Truly Yours,*

*William D. Silkworth, M.D.*

AA maintains the belief that a *spiritual* answer is the only real answer that may lead to any kind of quality and/or long-term sobriety. In those earliest days of people coming together to try to find a common solution as a group, the aforementioned medical benefactor and dear friend of AA, Dr. Silkworth, also noted, “We doctors have realized for a long time that some form of moral psychology was of urgent importance to alcoholics, but its application presented difficulties beyond our conception” (“The Doctor's Opinion,” 2001, p. XXVII).

Since approximately 1935, some practicing alcoholics noted that when even just one *spoke* about his/her experience to just one other, s/he did not find it as *necessary* to take a drink that day or night. This kind of Christian-based principal [the Twelve Steps were borrowed as a

spiritual practice from an early Christian church called The Oxford Group] of “one man helping another” continues to provide relief for desperate alcoholics in rooms across the world. Again, however, AA World Services does not readily offer firm recovery statistics due to their decided traditional lack of record-keeping of its “members” or their recovery updates.

Silkworth also claimed, “We believe, and so suggested a few years ago, that the action of alcohol on these chronic alcoholics is a manifestation of *an allergy*; that the phenomenon of craving is limited to this class and never occurs in the average temperate drinker. These allergic types can never safely use alcohol in any form at all; and once having formed the habit and found they cannot break it, once having lost their self-confidence, their reliance upon things human, their problems pile up on them and become astonishingly difficult to solve” (“The Doctor's Opinion,” 2001, p. XXVIII). He also mysteriously added, “unless this person can experience an entire *psychic change* their is very little hope of recovery” (“The Doctor's Opinion,” 2001, p. XXIX).

Referring to the drugs that radically changed the treatment of depression, Dr. Mark Willenbring said, “Today, in treating alcohol abuse and alcoholism, we haven’t yet reached the *Prozac* moment” (Brody, 2009). Dr. Willenbring, an expert on treating alcohol addiction, predicts, “the day is not far off when giving a pill and five minutes of advice to an alcohol abuser will be all that is needed to keep drinking under control” (Brody, 2009).

A *phenomenon* is a fact or situation that is observed to exist or happen, especially one whose cause or explanation is in question (Jewell et al., 2001). Today, with advancements that have evolved, the explanation of alcoholism would best not be tagged as a *phenomenon*, as many causes have since been identified thanks to the painstaking research of professionals. An *allergy* is defined as a damaging immune response by the body to a substance to which it has become

hypersensitive (Jewell et al., 2001). A *psychic change* is noted to be, “a personality change sufficient to bring about recovery from alcoholism” (Wilson & Silkworth, 2001, p. 567, par. 1).

Particular genes and their variants have been located that may soon be the bottom line of Silkworth’s intuitively predictive termination in referring to it as an *allergy*. Less mysteriously today, the *psychic change* he suggested may quite practically be hastened in an alcoholic by taking particular care to replenish the body with certain long-starved nutrients, namely vitamin B6 [pyridoxine] when combined with certain amino acids, namely L-threonine [glycine], that is “a pharmaceutical composition having an anti-alcoholic and nootropic affect” (Komissarova, Gudkova, Soldatenkova, Kondrashova, & Burbenskaya., 1998).

According to a technological invention pertaining to medicine which was patented by the United States on August 25, 1998, hope is alive in the way of restoring the body and mind appropriately in order that one may have a fighting chance for a *sustained* sobriety. AA offers lots of *coffee* while hosting no helpful chapter or appendix most recent addition regarding how pertinent it is to rebuild one’s physical health—after confessing that they have fried so many necessary neurons and their neurotransmitters. This is incomplete and could account for AA’s approximate “10%” consistent “sobriety success rate.”

Coffee/caffeine continues to stimulate and feed the *reward deficiency syndrome* at its genetic level, and therefore is antagonistic—yet another challenge—to a shaking desperate alcoholic’s assured *recovery* (Blum et al., 1996, pp. 396-400). An entire journal could be written regarding nicotine’s prolongation of cravings on the gene(s) (Blum et al., 1996, pp. 396-400).

Why are there candy dishes at AA meetings? Can one go to *jail* for consuming coffee, caramels, peppermints, or cigarettes? Drilled down AA members proclaim a 1935 educated *no*. I propose that this kind of *prolonging* of the refusal to educate oneself of his/her bodily health

simply *prolongs* a fated jail booking. So what, then, becomes the point of shaky candy/caffeine-laden shaky “sobriety” at the end? Temporary “solutions” are malarkey to the real alcoholic.

A health professional [more updated since 1939 when “they believed” that “sugar-water” cured most things] should be summoned and forever branded into the stubborn alcoholic text of the “forever unchanging pages” (Wilson & Silkworth, 2001, pp. 1-164) of the semi-successful (as per AA World Services quiet 10% statistics) society’s book, *Alcoholics Anonymous*.

If social sharing of jonesing for alcohol or missing it are to save one life, then rock on, but I am seriously and proposing earnestly that there is much more to the quagmire of mystery that was beautifully inspired in those first 164 pages of Wilson’s text. That was “only a beginning,” as Wilson put it, and any “good” AA member should responsibly continue to dedicate oneself to *keeping the torch lit* and passing it on by continuing to invite solid research findings and allow room for the newest proof to be adopted into its initial pages since Bill is now dead. It is wise to remain open minded, willing, and honest. Bill’s *Big Book* suggests to do so. Bill would have done so, as the maverick he was in this field, I am quite certain.

This [just one of many new resources and findings] may prove to be of help: “The invention is based on the task of development of a new medicinal composition endowed simultaneously with an anti-alcoholic and nootropic effect, high activity, lacking toxicity and inducing no side-effects” (Komissarova et al., 1998). The patent’s description section expounds:

*“At the present time, a reduction in the use of alcohol is relatively easily achieved with preparations which to some degree produce an alcohol-like effect [tranquilizers, barbiturates, GOBA, antihistamine drugs with the tranquilizing effect]. Such therapy, however, is known to lead to the development of toxicomanias significantly complicating the course of alcoholism, as well as reducing*

*mental capacity. In treatment of alcoholism, the use of different psychotropic drugs and sensitizing drugs does not achieve the desired effect either, and, more than that, forms a markedly negative attitude to therapeutic measures. In this connection, of special importance is the search for and development of new anti-alcoholic drugs having none of the above-mentioned shortcomings, reducing the pathological attraction and at the same time endowed with nootropic properties [increasing attention, improving memory, mental activity]. There are known preparations SAAVE™ and tropamine™ produced by Matrix Technologies, Inc. SAAVE™ is a combination of amino acids DL-phenylalanine, L-tryptophan, L-glutamine and pyridoxal-5-phosphate and is recommended as a dietary supplement to the therapy for the subjects suffering from alcoholism and drug addiction [heroin, opiates, etc.]. As compared with SAAVE, tropamine contains more additional substances and includes such amino acids as DL-phenylalanine, L-tyrosine, L-tryptophan, L-glutamine as well as pyridoxal-5-phosphate. It is also a dietary supplement in therapy for drug addicts. Thus, both preparations are dietary supplements, that is, are used alongside with other therapeutic means and contain L-tryptophan the use of which in drugs and dietary supplements was forbidden by the FDA in 1989. Besides, these drugs have no nootropic effect. The amino acid-containing mixtures are used for subjects abusing alcohol and suffering from alcoholism or in the form of dietary supplements [international application WO 89/04165] or in the form of compositions [FR application No. 2607391] which comprise a full set of substitutable or non-substitutable amino acids and additionally an abundance of most variable chemical compounds*



*[sugars, polymeric carbohydrates, organic acids, fatty acids, phenol acids, phenol aldehydes, aspirin]*” (Komissarova et al., 1998).

According to another alcohol-metabolism model, “the oxidized alcohol product, or aldehyde, interacts with neurotransmitters to create tetrahydroisoquinolines, or TIQs, which are thought to create the intense craving for alcohol that alcoholics demonstrate” (Peele, 1990, p.53).

*Dopamine* is a subject which alcoholics would do best to thoroughly understand about their disease. It is one of a number of neurotransmitters, or chemicals, produced in the body that convey information throughout the nervous system. “Neurotransmitters communicate by attaching to receptors on nerve cells which are tailored specifically to them” (Peele, 1990, p.52). Also, when alcohol is taken into any system, the GABA receptors in the brain are paralyzed, causing problems and delays with vision, speech, and physical coordination.

Dr. Silkworth’s self-proclaimed *belief* of the 1930’s proved to be a seedling of truth in the way of far more that has now come to be revealed. Fast-forward to August 1990 when Kenneth Blum, a pharmacologist at the University of Texas Health Science Center in San Antonio, and Ernest Noble, a psychiatrist and biochemist at the UCLA Alcohol Research Center and a former director of the National Institute of Alcohol Abuse and Alcoholism, performed an extensive study (Blum et al., 1996, pp. 396-400) that led them to conclude that, “A1 "allele," or variant, of the dopamine D2 receptor gene was associated with alcoholism” (Peele, 1990, p.52).

The *Journal of the Royal Society of Medicine* published Dr. Blum and six other doctors’ extensive and painstaking findings from 66 cumulative genetic clinical studies in a fascinating article (Blum et al., 1996, pp. 396-400). This published article partially states:

*“The dopaminergic system, and in particular the dopamine D2 receptor, has been profoundly implicated in reward mechanisms in the brain. Dysfunction of the D2*

*dopamine receptors leads to aberrant substance-seeking behaviour [alcohol, drug, tobacco, and food] and other related behaviours [pathological gambling, Tourette's syndrome, and attention deficit hyperactivity disorder]. We propose that variants of the D2 dopamine receptor gene are important common genetic determinants of the reward deficiency syndrome" (p. 396, sec. intro.). "Here we review the evidence that the D2 dopamine receptor gene [DRD2] is associated not only with alcoholism but also with a group of impulsive—addictive—compulsive disorders (396, par. 2). Deficits in dopamine function result in abnormal drug and alcohol seeking behaviour. DA receptors are profoundly involved. The D2 dopamine receptor gene, localized in the q22-q23 segment of chromosome 11, has multiple allelic forms. A strong correlation between variants of the dopamine D2 receptor gene and alcoholism and polysubstance abuse [including crack/cocaine] has been reported by several investigators (p. 396, par. 3). In brain tissue obtained from patients carrying the A1, B1, and intron-exon haplotypes of the DRD2 gene dopamine D2 receptor densities are low. Similarly, DRD2 densities have been found lower in alcohol-preferring rodents than in alcohol-non-preferring animals. Moreover, D2 receptor agonists reduce, and D2 receptor antagonists increase, alcohol intake in alcohol-preferring rats (p. 396, par. 4). A meta-analysis on all published exant studies related to alcoholism showed an odds ratio of 2.18 with a p-value of 10<sup>-7</sup> indicating strong correlation of the DRD2 gene with this disease. Variants of the DRD2 gene have been correlated with increased risk of severe alcoholism, crack/cocaine dependence, carbohydrate bingeing, obesity, attention deficit hyperactivity*

*disorder, Tourette's syndrome, pathological gambling, and smoking" (p. 396, par. 6). In all reports chemical dependent subjects were identified who did not have the DRD2 allele or other variants, together with the healthy non-drug-abusing individuals who had the A1 allele. Uhl and coworkers reported that the A1 and B1 alleles of the DRD2 gene account for 27% of the variance of drug dependence, independent of the environment or other gene defects, and data from twin studies indicate that genes influence up to 60% of the vulnerability to severe substance abuse. If these two findings are taken together, the DRD2 variants could represent one of the most important single-gene determinants of susceptibility to severe substance abuse" (p. 397, par. 1).*

It is important to note that these scientists and doctors performed sixty-six different intensive research projects/intricate tests in order to arrive at what they coined the *reward deficiency syndrome*. As importantly, it is convincing to learn that “in order to calculate the sensitivity of genotyping, the doctors employed the mathematical method called *Bayes Theorem*—which is widely used in medicine to predict the likelihood that a particular event [defect] will result in another event [disease]” (Blum et al., 1996, p. 397, pars. 1-4).

“Moreover, to calculate the sensitivity of genotyping, we took data from studies where the probands were characterized for chronicity or severity of disease” (Blum et al., 1996, p. 397, par. 3). The same report continues in making mention of hopeful potentialities of Dr. Blum and others’ findings (1996, pp. 398-399):

*“The concept of a ‘reward deficiency syndrome’ unites addictive, impulsive, and compulsive behaviours and may explain how simple genetic anomalies give rise to complex aberrant behaviour. What are the possible therapeutic implications?”*

*Nishimura has reported that bromocriptine shortens the latency of the N200 wave in persons with long latency. Such N200 wave abnormalities occur in 'reward deficiency syndrome', and if bromocriptine and other D2 agonists can stabilize or shorten wave latency, they could have clinical value. In a double-blind study bromocriptine or a placebo was administered to alcoholics with either the A1 [A1/A1 and A1/A2 genotypes] or only the A2 [A2/A2] genotype allele of the DRD2 gene. The greatest improvement in craving and anxiety occurred in the bromocriptine-treated A1 alcoholics and attrition was highest in the placebo group A1 alcoholics. These findings raise the possibility of selection in treatment of alcoholics" (p. 398, par. 8). One important obstacle to treatment or rehabilitation in substance use disorders is denial, and we believe that a positive result of the 'reward deficiency syndrome' concept will be its aid in countering this reaction (p. 398, par. 9). A time will come when we have identified all the gene variants and we shall have a stronger DNA test for reward deficiency syndrome" (p. 399, par. 1).*

Four years later, a determined Blum and his team of eight other doctors and scientists from the Department of Biological Sciences at the University of North Texas in Denton put these findings in layman's terms in a new abstract that was condoned by the U.S. National Library of Medicine and is published at PubMed online today. This abstract (Blum et al., 2000) states:

*"The dopaminergic system, and in particular the dopamine D2 receptor, has been implicated in reward mechanisms. The net effect of neurotransmitter interaction at the mesolimbic brain region induces "reward" when dopamine [DA] is released from the neuron at the nucleus accumbens and interacts with a dopamine*

*D2 receptor. "The reward cascade" involves the release of serotonin, which in turn at the hypothalamus stimulates enkephalin, which in turn inhibits GABA at the substantia nigra, which in turn fine tunes the amount of DA released at the nucleus accumbens or "reward site." It is well known that under normal conditions in the reward site DA works to maintain our normal drives. In fact, DA has become to be known as the "pleasure molecule" and/or the "anti-stress molecule." When DA is released into the synapse, it stimulates a number a DA receptors [D1-D5] which results in increased feelings of well-being and stress reduction. A consensus of the literature suggests that when there is a dysfunction in the brain reward cascade, which could be caused by certain genetic variants [polygenic], especially in the DA system causing a hypodopaminergic trait, the brain of that person requires a DA fix to feel good. This trait leads to multiple drug-seeking behavior. This is so because alcohol, cocaine, heroin, marijuana, nicotine, and glucose all cause activation and neuronal release of brain DA, which could heal the abnormal cravings. Certainly after ten years of study we could say with confidence that carriers of the DAD2 receptor A1 allele have compromised D2 receptors. Therefore lack of D2 receptors causes individuals to have a high risk for multiple addictive, impulsive and compulsive behavioral propensities, such as severe alcoholism, cocaine, heroin, marijuana and nicotine use, glucose bingeing, pathological gambling, sex addiction, ADHD, Tourette's Syndrome, autism, chronic violence, posttraumatic stress disorder, schizoid/avoidant cluster, conduct disorder and antisocial behavior. In order to explain the breakdown of the reward cascade due to both multiple genes and*

*environmental stimuli [pleiotropism] and resultant aberrant behaviors, Blum united this hypodopaminergic trait under the rubric of a reward deficiency syndrome.”*

On May 26, 2004, WebMD published an article regarding how researchers have identified an alcoholism gene:

*“A new study links a gene to alcohol addiction -- backing up a long-recognized pattern showing that alcoholism runs in families. The finding also provides evidence that an inborn high level of anxiety is part of this picture. Research has shown that alcohol addiction is a complex disease, with both genetics and a tendency toward anxiety playing "crucial roles," writes researcher Subhash C. Pandey, PhD, a psychiatrist with the University of Illinois at Chicago. "Some 30% to 70% of alcoholics are reported to suffer from anxiety and depression," Pandey said in a news release. "Drinking is a way for these individuals to self-medicate." Pandey's research focuses on the CREB gene, so-named because it produces a protein called CREB—cyclic AMP responsive element binding protein. The CREB gene regulates brain function during development and learning. The gene is also involved in the process of alcohol tolerance, dependence, and withdrawal symptoms, writes Pandey. A section of the brain—called the central amygdala—is another piece of this puzzle. Both the CREB gene and the central amygdala have been linked with withdrawal and anxiety. When there is less CREB in the central amygdala, rats show increased anxiety-like behaviors and preference for alcohol. Pandey's newest study puts it all together: It is "the first direct evidence that a deficiency in the CREB gene is associated*

*with anxiety and alcohol-drinking behavior," Pandey writes. In this study where mice were bred for alcohol addiction, Pandey and colleagues worked with rats specially bred to be deficient in the CREB "alcoholism" gene. In a series of experiments, he found that: Rats deficient in the CREB protein drank about 50% more alcohol than normal rats. They also showed more anxiety-like behavior in a maze test. These rats also showed a higher preference for alcohol over water compared with normal rats; yet they had similar preferences for sugar water—indicating that the alcohol consumption was not related to taste preferences. These rats also displayed more anxiety than normal mice, which decreased when drinking alcohol. The anxiety-reducing effect of alcohol was not as great in the normal rats (Ichihara, Kamei, Okumura, Mizukoshi, & Nagasaka, 1998). Alcoholic rats had higher levels of the CREB protein in the central amygdala. These results indicate that the CREB or alcoholism gene is "crucial" to the anxiety relief that triggers alcohol addiction" (Davis, 2004).*

More recently, the rigorous and passionate Dr. Blum wrote of future implications: "By the beginning of 1989, scientists were generally agreed that genetic anomalies were the primary causative factor in at least some forms of alcoholism; there were those who disagreed, but genetic predisposition toward craving for alcohol was firmly established in both the scientific and treatment communities. The presence of the A1 allele of the dopamine D2 receptor gene in 39 children who had not been exposed to alcohol. This indicates that this polymorphism is genetically transmitted, not the result of alcohol intake. If our findings are correct, they constitute a powerful argument in favor of the disease concept of

*alcoholism and the importance of the genetic factor. This controversy is still raging, and in many quarters alcoholism is still considered a product of weak moral character and lack of will power. Even the U.S. Supreme Court seemed to side with this viewpoint in a much-publicized 1988 decision. We hope that our findings will remove much of the stigma, enable more individuals to accept their craving as a symptom of an illness, and make it easier for them to seek treatment and affiliation with self-help Twelve Step programs. For the future, the first step we can envision is the development of a diagnostic tool—a blood test, for example—that will identify children at risk in alcoholic families. We used brain tissues for our experiments, but using DNA derived from lymphocytes will enable us to test living subjects and large pedigrees. As more is learned about genetic anomalies and their effect on the brain's neurochemistry, we may be able to design more effective adjuncts to treatment; fine-tune our pharmacological intervention in terms of genotype as well as phenotype” (Blum, 2008).*

The chromosome 15 cluster was also recently tested by a team of seven scientists for genetic association with alcoholism using a family-based association test, followed by case-control replication; results indicated that “the CHRNA5-CHRNA3-CHRN4 locus is involved in susceptibility to alcohol dependence” (White et al., 2008).

Though helpful, very soon alcoholics will not have to rely *solely* on prayer, pills, or meetings to hope to achieve and maintain a dependable sobriety. It may come to be possible to preclude them from the enslaved fate of having to endure the sheer unnecessary hell that practicing alcoholics have had to endure from decades past to present day.

Bill Wilson—a New York stock-broker and co-founder of AA—liked doctors. After all,



it was a doctor by the name of “Bob” who joined him in starting AA. If Bill or Bob were alive today, it would be a fine thing indeed to witness their eager delight in shaking hands and meeting minds with our very-much-alive, dedicated, and passionate Dr. Blum of San Antonio, Texas, to see if they could pool their diverse knowledge of alcoholism to further help alcoholics in an even more devoted, comprehensively endowed, promise for recovery from this once utterly mysterious disease.

If the north and south do begin to shake hands in cooperation of shared knowledge then grave alcoholic statistics around the globe are sure to lessen dramatically. Moreover, this kind of synergy may better the mind, body, and spirit of alcoholics in the way of a more comprehensive “cure.”

Unfortunately, a well known personality trait of alcoholics is a certain rigidity, reticence, or stubbornness to be open to some things which are new or unfamiliar. Alcoholics are “driven by a hundred forms of fear” (Wilson & Silkworth, 2001, p. 62). When dealing holistically with a system which simply could not function without one of its parts [mind, body, spirit], it is truly wise to attempt to expand our understanding to encompass all of this complex system, as this pertinent knowledge may harmoniously boost discoveries for a cure to those suffering from the disease of alcoholism.

AA’s are drilled to be of the mind that “there is no cure,” but the humble writer of their trusted book did warn, “Our book is meant to be suggestive only. We realize we know only a little” (Wilson & Silkworth, 2001, p. 164) and they welcomed the discoveries of the people of science, medicine, and religion. “Logic is great stuff. We liked it. We still like it. It is not by chance we were given the power to reason, to examine the evidence of our senses, and to draw conclusions” (Wilson & Silkworth, 2001, p. 53).

“Faith without works is dead” (Wilson & Silkworth, 2001, p. 88). The long-revered author and recovered alcoholic, Bill Wilson, also stressed the imperative nature of certain recovering alcoholic perspectives: “Willingness, honesty and open-mindedness are the essentials of recovery. But these are indispensable” (2001, p. 568). I ask for each/all.

There used to be no rocket dreamed of, let alone built, in order for one to successfully travel to the moon and back. In this burgeoning new day we live and learn in, one can hope that alcoholics might gratefully make room for a long-awaited and much needed “rocket” by way of aiding to hasten its arrival by promoting the supported disposition of an open mind.

AA’s current *welcome prayer* [known to be *The Prayer of St. Francis of Assisi* and also sung by artist, Sinead O’Connor] may be a lovely way of introducing alcoholics’ present exploration of the powerlessness of their disease. Knowledge changes things. We must implement knowledge as best we can accordingly. Results in doing so might potentially rocket them to the moon, far from the dregs of the still-accepted 1930’s enigma.

A healthy, curious hunger to learn all about the newest sound findings of many cutting edge dedicated researchers and scientists might open the door. Today, addiction facts are friendly in the way that some *firm ones now exist* today regarding their formerly baffling, mysterious disease. Since prayer is the bedrock of most self-help groups of this day, a longer, less outmoded version of *The Prayer of St. Francis of Assisi* (when said in recovery rooms), may serve to bring recovering alcoholics and addicts up to a more current speed if perhaps beginning to sound just a little something more like this, for instance:

*God, grant me the serenity to accept the things I can not change: my DNA dictates that I indeed possess what is now being coined as **The Reward Deficiency Syndrome**.  
The courage to change the things I can: that I may learn about my body, mind, and soul,*

*and that I may vow to keep a quenchless thirst about the valid possibility of a cure for my syndrome.*

*...and the wisdom to know the difference: Most of all, please help me to know the difference between persisting in my fear or denial of positive change and the promising possibility of becoming open and willing to indeed allow more to be revealed; if only my knowing may ever prove to help to serve in the saving of but one single human life.”*

In the words of one of the medical mavericks of AA, [when advising fearful alcoholics to adopt an open mind regarding educating themselves about the 1930’s newest findings in the way of a found solution], “I earnestly advise every alcoholic to read this book through, and though perhaps he came to scoff, he may remain to pray” (“The Doctor's Opinion,” 2001, p. XXXII).

A “God” who reveals this kind of real hope for change is surely a God worth believing in.

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End Notes

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Diseases, and director of the Laboratory of Pharmacogenetics at the University of Texas Health Science Center at San Antonio. An internationally recognized authority in the field of psychopharmacology and substance abuse, Blum has published more than 225 scientific articles in major journals and contributed dozens of chapters in books. He is the author of *Handbook of Abusable Drugs*, editor of several research books, and founder, with Dr. Ernest Noble, of the journal, *Substance and Alcohol Actions/Misuse*. Blum and Noble have co-chaired two Gordon Research Conferences on alcohol. Blum is responsible for developing the "link" hypothesis for isoquinolins in the actions of alcohol and opiates, and for suggesting that opioid peptides are mediators in alcohol predisposition in animals and humans. He has coined *the reward deficiency syndrome*. He is principal inventor of the amino acid supplements SAAVE and TROPAMINE used as adjuncts to facilitate recovery of chemically dependent individuals. He is the lead author with Dr. Noble and associates on discovering that one form of the dopamine D2 receptor gene is linked to alcoholism. His most recent book, *Alcohol and the Addictive Brain: New Hope for Alcoholics From Biogenetic Research*, was released by McMillan (N.Y.) and is available in print today.

\*\*Dr. Frank S. Caprio is a member of the American Medical Association [AMA], Society for the Advancement of Psychotherapy, and the American Association for the Advancement of Science.

\*\*\*Gil Gaudia, PhD, Professor Emeritus, State University of New York at Fredonia; Disclosure: Gil Gaudia, PhD, has disclosed no relevant financial relationships.

\*\*\*\*Pharmaceutical composition endowed with an antialcoholic and nootropic effect. This application is a 371 of PCT/RU96/00006 was filed by inventors on Jan. 4, 1996. Patent 5798371 was issued by the United States of America on August 25, 1998. Its estimated expiration date: September 6, 2016. doi:  
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\*\*\*\*\*Dr. Robert R. Perkinson, Clinical director of Keystone Treatment Center in Canton, South Dakota has specialized in alcohol and drug addiction for 26 years.

\*\*\*\*\*Originally written in 1939 by Dr. William D. Silkworth, the A.A. society's great medical benefactor.

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