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TuftScope

The Interdisciplinary Journal of Health, Ethics, and Policy

Interview with Dr. Jim O'Connell

Sugar Tax Sugarcoats Problem of Obesity

Ethical Dilemma of Gender Selection

A Publication of TuftScope, the Student Bioethics Organization of Tufts University

TuftScope

THE INTERDISCIPLINARY JOURNAL OF
HEALTH, ETHICS, AND POLICY

JOURNAL HISTORY

Since 2001 *TuftScope: The Interdisciplinary Journal of Health, Ethics, & Policy*, has provided an academic forum for discussion of pertinent healthcare and biosocial issues in today's world. The journal addresses different aspects of healthcare, bioethics, public health, policy, and active citizenship. It is operated and edited by undergraduate students of Tufts University and is advised by an Editorial Board composed of Tufts undergraduates and faculty. Today the journal is one of the few peer reviewed undergraduate published journals in the country.

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Cover Image: In this issue, *TuftScope* discusses the new sugar tax and its efficacy.

LETTER FROM THE EDITORS

Growing Pains

Dear Reader,

This year marks a period of growth for Tuftscope. The TuftScope website, the journal's health news weblog (tuftscope.blogspot.com), and our presence on Twitter (@tuftscope) and Facebook have provided Tuftscope with a solid foundation to expand our printed publication's exposure to not only Tufts University but to the global community as well. This will not be easy, but it is necessary that Tuftscope incorporates our past achievements in obtaining well-written and well-researched articles and our future objectives to showcase these types of articles to a broader audience.

Some of these changes include the recruitment of a new generation of underclassman staff members, the appointment of a Research Highlights Editior, Ariel Lefland, and New Media Editors, Alejandra Garcia and Alison Pinkerton, and an increase in the number of issues this year from 2 to 4. These ambitious aims have pushed our staff to produce higher quality of work to measure up to the higher quantity of articles we have received.

To showcase local health care experts, Managing Editor Hallie Abelman spoke with the president of Boston Health Care for the Homeless, Dr. Jim O'Connell, who was recently awarded the Albert Schweitzer Prize for Humanitarianism. Over the course of his 27 year career with this organization, Dr. O'Connell has become a pioneer in the field of homeless health care.

On a global health scale, the original articles by Jonathan Lis and Alana Fruauff offer insight into the health care systems in places such as The Gambia and Nepal. Additionally, the fascinating article written by Alon Slutzky, a current Tufts undergraduate, explores the health effects of the long-term exposure to arsenic in Bangladesh.

Next semester, in junction with the Tufts course, EPIIC: Global Health and Security, we plan to publish an issue featuring reports by the students who are taking this class. This issue will be released during EPIIC's symposium (February 2013) and will hopefully demonstrate the captivating research conducted by these students this fall semester.

We are committed to publishing stimulating and informative articles that broaden the scope of our readers' knowledge on health-related topics. We feel that they have acheived this goal with our issue this semester. We thank the entire staff of writers, reviewers, editors, and layout editors, without whom there would certainly not be a journal of this caliber. We also thank our faculty advisers for their continued guidance and advice.

We hope you enjoy the issue!

Sincerely,

Eriene-Heidi Sidhom & Brian Wolf

A Bright Future For Organ Transplants

Parsa Shahbodaghi

Imagine printing an organ in less than an hour. Anthony Atala and others have implemented various techniques that allow them to accomplish this goal.[1] This represents a way to circumvent many of the moral questions and logistical problems associated with organ transplants. It may be a while until transplanting 3-D organs is the norm in medicine, but this development is still a promising one.

First, it is important to provide a little background as to why organ transplantation is an issue in society today. There is a scarcity of organs in the United States. Many individuals have died waiting for them. Some have argued that opening a market for organ transplants would be a reasonable solution. However, that market is considered to be a repugnant one. For one, many individuals view organs as something sacred and intrinsic to the human body. Merely trading them represents an affront to that notion.[2]

Secondly, there is an issue of coercion. In other words, markets can compel people to sell their organs. Hypothetically, a working-class individual could make $2000 a month. If this person were offered $5000 for one of his kidneys this would represent more than a month's wages. Even though $5000 seems like very little money for an organ it could be an enormous sum for a few people. Selling one of his organs could be even more appealing to him if the amount offered is higher. There's a chance that one's economic situation could be particularly dire and that person could be very needy. Therefore the presentation of a very large sum could essentially force one's hand into donating an organ when he or she wouldn't have done so.[2]

Regardless of whether or not organ transplants exist, there are huge logistical issues trying to coordinate donors. For example, Person A needs a kidney but his sister Person B isn't a match for him. Person C is in the same predicament as Person A. However, Person C's sibling, Person D, is a match for Person A and Person's A's sister is a match for Person C. An organ swap can be coordinated and both Persons A and B get the organs they need. Unfortunately, there are logistical issues to be dealt with when one has to deal with four surgeries.

The issues with current transplantation have been established, but how does 3D organ printing alleviate them. To answer these questions, it is necessary to understand how this technology works.

Dr. Anthony Atala of Wake Forest University has printed an organ by first taking CT scans of patients in need of an organ.[3] He then builds a scaffold in the shape of the organ. Using a modified inkjet printer, Dr. Atala adds layers of human cells to the scaffold. The cells then grow at human body temperature. Normally, it is difficult to maintain cells outside the body, but recent advancements in the field of cell culture have resulted in cells being maintained for a longer period of time.

How does this development address the ethical and logistical concerns associated with organ transplants? First, the organs are being generated from a patient's own cells, so they are not only a perfect match, but it completely sidesteps any issue of using biological materials from anyone else's body. Secondly, this technology is scalable, meaning that there hypothetically can be many 3D printers that generate organs. This means that the supply of organs has increased and that the price of printing those organs could foreseeably go down. It also means that the costs of performing transplantation surgeries could decrease as well, because doctors now would have the ability to perform many more surgeries. This means that they could become routine procedures and the risks associated with them could decrease as well.

The most exciting thing about this is that this medical revolution could very well be on the horizon. In 1998 Dr. Atala successfully treated Luke Massella, an individual who suffered from spina bifida. After undergoing many surgeries to treat his condition no treatment seemed to be working. Finally, it was agreed that undergoing this experimental procedure was best for Luke.[3]

Using Luke's own cells, Dr. Atala generated a new bladder for him. The organ then underwent transplantation. As of January 2010, Luke was a happy, healthy college student.

There is no question that these procedures can be successful, but when are they going to be used on a massive-scale? It's going to be a while until full organs can be printed. However, there are important advancements that suggest a promising future. Small-scale tissues are currently being used for drug discovery.[4] It's impossible to tell exactly when this technology will present itself as new organs. Hopefully, it will be sooner rather than later.

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Parsa Shahbodaghi is a staff writer for Tuftscope.

Selections From Our News Analysis Weblog

Creativity 'closely entwined with mental illness'

Jesse Starger

The Journal of Psychiatric Research reports, researchers at the Karolinska Institute in Sweden have begun to uncover the link between mental illness and creativity. Writers, being the most at risk for these mental illnesses, were almost twice as likely to kill themselves with other problems stemming from afflictions such as schizophrenia, unipolar depression, and substance abuse. Famous examples include Virginia Woolf who had depression and drowned herself and Ernest Hemingway who was affected by depression and later killed himself with a shotgun. Dr. Simon Kyaga, the lead researcher, suggests disorders be viewed in a new light so certain traits can be considered beneficial or desirable. Such as the concept of 'originality' proceeding from the disordered thoughts of a schizophrenic or 'genius' originating from the intense focus provided by autism. Dr. Kyaga states, "In psychiatry and medicine generally there has been a tradition to see the disease in black-and-white terms and to endeavor to treat the patient by removing everything regarded as morbid." Yet, "If one takes the view that certain phenomena associated with the patient's illness are beneficial, it opens the way for a new approach to treatment." Although, Beth Murphy, the head of information at Mind warns, "It is important that we do not romanticize people with mental health problems, who are too often portrayed as struggling creative geniuses."

Hospitals Ditch Formula Samples to Promote Breast-Feeding

Enshu Chawla

More hospitals are banning the distribution of formula samples, as about half of the hospitals surveyed by the CDC have done so. In contrast, only about a quarter of these hospitals had a ban on formula samples in 2007. States including Oklahoma, Massachusetts, and Rhode Island are seeing these changes in policy, and Mayor Bloomberg's "Latch on NYC" initiative has grown in popularity among hospitals. Breast-feeding is widely known to be much healthier than formula, as the companies who sell formula agree to this. Individuals in favor of breast-feeding argue that the samples should not be given out to all mothers and marketed, but instead to those mothers who choose to use formula. On the other hand, formula companies claim that the formula can give an option due to the difficulty and pain involved with breast-feeding. Some mothers felt that they used formula at times only because it was available to them, while others saw it as a valuable resource for certain situations. At Cooper University Hospital, seventy percent of mothers were using formula to feed their babies before formula was documented by nurses and stored away. Following these actions, seventy percent of mothers were breast-feeding. However, at Virtua Hospital, breast-feeding rates continue to increase with formula readily available to mothers. The argument over breast-feeding versus the allowance of formula giveaways has been seen in both lights throughout the politics of states such as Massachusetts and hospitals such as UMass Memorial. Formula companies are making it difficult for hospitals to distance themselves from the groups, because of free samples and gifts to hospital staff members. In general, the move that hospitals have made to ban formula samples has been very controversial due to opposing viewpoints among staff members, mothers, and formula companies.

Millennium Goal on Hunger Is Within Reach, But Food Instability Threatens Progress

Alice Chan

According to the U.N's State of Food Insecurity in the World 2012 report, published by the Food and Agriculture Organization and affiliated organizations, there is an estimated 870 million people who are starving or undernourished in the world. Data compiled and compared from the last twenty years show signs of decline in the number of malnourished people, as that number has dropped by 132 million people between 1990-2 and 2010-12. Although these results seem to hint success for the U.N. in accomplishing its millennium development goal of reducing the number of hungry people in the world by half by the year 2015, some critics remain alarmed and doubtful. Aid agencies argue that progress on reducing the number of malnourished people has decelerated, which may be influenced by the recent rise in food prices in September, after months of stability. As a result, according to the Global Hunger Index for 2012 report, twenty out of the 120 countries studied in the report face hunger at "alarming" or "extremely alarming" levels. Most of these countries are in sub-Saharan Africa and South Asia, however the report also addresses the entire world in its recommendation for immediate action: "To feed nine billion people – the projected world population in 2050 – it is clear that more food must be produced with fewer resources, and wasteful practices and policies must be eliminated."

US Supreme Court is asked to rule on validity of patents on BRCA1 and BRCA2 genes

Denali Rao

The University of Utah Research Foundation and a Utah company, Myriad Genetics, hold contentious patents on two human genes: BRCA1 and BRCA2. The fact that these genes are associated with breast and ovarian cancer is just one point used to argue that the patents must be overturned:

open research on these genes could save lives. Another argument deals with the legal aspect: under US law, patents cannot be made on "'laws of nature' [or] 'products of nature'". The ACLU and Public Patent Foundation argue that the human genome, whether certain genes are isolated or not, is a product of nature. The same groups, the ACLU and the Public Patent Foundation, are among groups asking the Supreme Court to review these patents. So far, the lower courts have gone back and forth about this issue. The patents have appeared in various courts three times. The Supreme Court "is expected to allow Myriad to respond" before deciding to take the case on.

What Your Breath Reveals About Your Health

Kristiina Yang

Breath testing, while not quite ready to be used in doctors' offices yet, presents a new and exciting frontier in preventative and diagnostic medicine. Researchers have found that each individual has a unique breath content consisting of volatile and nonvolatile materials, which can be analyzed for the presence and progression of various health problems. They hope to use individuals' unique breath content to develop noninvasive medical tests for diagnostic and monitoring purposes, amongst other possibilities. Studies, for example, have already shown that breath analysis can be used to indicate whether one has lung cancer.

Researchers' and scientists' efforts to develop breath analysis technologies are rooted in the many benefits that this noninvasive form of medical testing may present. Breath analysis, researchers hope, will enhance the efficiency of the medical field by taking a small sample with no pain to the patient, which can be processed quicker than blood tests or biopsies for a wide variety of inflictions, and at a potentially lesser cost. What remains to be done is for scientists to identify and catalogue thousands of chemicals in the breath, and to understand how their presence and changes indicate disease. While trials and studies still need to be undertaken to standardize and validate the process, the field of breath testing is expected to see great development and progress in the coming years.

Redefining Medicine With Apps and iPads

Prachi Sharma

New advances in digital technology have been critical in redefining patient-doctor roles. The plethora of new available gadgets, apps, and web-based information centers provide innovative ways to diagnose symptoms, treat patients, and share information. The ePocrates, for example, is an app that allows doctors to look up proper drug dosages and interactions. According to a study by the University of Chicago, residents with iPads entered orders in a timelier manner, and a majority of residents believed that utilizing iPads improved their work efficiency. Some doctors, however, worry that the personal connection between the patient and the doctor is being lost through the intricacies of the tech world, and that many younger physicians are becoming too dependent upon the new technology. Despite his belief, many prominent medical schools, such as University of Chicago and John Hopkins University, are keeping up with the trend by providing all internal-medicine residents with iPads. Thus, as digital technology further advances, physicians will need to discover the proper balance between utilizing traditional medical methodology and the innovative products of the tech boom.

Open Season on Salt: What the Science on Hypertension Really Shows

Evan Balmuth

On September 26th, Melinda Wenner Moyer of Scientific American published this important article questioning interpretations of a recent study in Pediatrics. The study in question, conducted by CDC researchers, has resulted in claims by newspapers including the Associated Press and USA Today that the 25 percent of American children who ingest the most sodium are two to three times likelier to develop hypertension than the 25 percent who take in the least sodium. However, the Scientific American article reveals that, as the lead author of this study and results from several other studies suggest, there is not enough statistically significant data to make this bold and causal claim. The primary reasons for this are that: this was a cross-sectional study, which cannot guarantee total control of confounding variables; and that two past studies found no significant correlation between urinary sodium levels and hypertension. In fact, Scientific American juxtaposes with a 2011 study in The Journal of the American Medical Association which found that – most likely due to adverse effects of a low-sodium diet – consumers of the least sodium had a 3.3 percent higher death rate over time than consumers of the most sodium.

Ultimately, this Scientific American article has shed some light on the dangerous phenomenon of media falsely interpreting study results. Instead of focusing on the less sensational yet true finding that high salt intake may correlate with high blood pressure in obese children, media outlets have skewed the results into a striking yet unjustifiable causality. This can sell papers, but it can also disseminate the misconception that salt is deadly, when in fact it has been shown that a low-sodium diet has deadly correlates as well. The end of this article is an example of how to properly interpret statistically significant findings, as it suggests the superiority of cutting weight over cutting salt due to much proven causality. Hopefully, for the sake of public health, Scientific American and other media publications will continue to blow the whistle on unjustified interpretations of scientific findings.

References for News Briefs may be found online at

Tuftscope.Blogspot.com

FEATURE INTERVIEW

A Discussion with Dr. Jim O'Connell

Hallie Abelman

PHOTO OF DR. JIM O'CONNELL

Dr. O'Connell is one of the founding members of he Boston Health Care for the Homeless Program (BHCHP) in 1985. As evident in his committment to this organization for the past 27 years, his compassion for delivering quality health care to one of Boston's most vulnerable populations has continued to grow. Currently, he is the president of the program and one of the head physicians working with a team to deliver primary and specialty care to homeless people around Boston day or night, rain or shine.

Could you tell me a bit about how you got involved with the Boston Health Care for the Homeless Program?

I was a resident in medicine at Mass General Hospital. I was interested and about to go do a fellowship in oncology. However, in my last year, the city of Boston got a grant from the Robert Wood Johnson Foundation to try to organize health care for homeless people around the city and integrate it into the mainstream. The coalition of people that put that together were very insistent that there be a full time, non volunteer doctor because they wanted the program to have a social justice approach rather than a charity approach. They didn't want volunteers; they wanted full time people. They could not find a doctor at the time. My chief of medicine at the time, who was Doctor John Potts, and Dr. Tom Durant, who had been one of my mentors, called me in and asked if I would mind doing this job for a year. You know when your chief of medicine calls you into his office you don't have much option of saying no. I ended up doing this thinking I would do it for one year before I would do my fellowship, similar to a gap year.

Though once I got dragged into it, it turned out it was really complicated stuff. The medicine was totally fascinating. The obstacles thrown in the way of health by all the social determinants of health were overwhelming. I went from thinking I could control most of what I was doing working in the hospital to this and I was totally fascinated by the challenge. I realized after the first year that it was way too complicated and I needed another year and delayed my fellowship. Then I just got hooked. It's been my full time job ever since. It's actually been my only job as a doctor. My mother keeps wondering when I'm going to get a job.

Obviously Boston has great resources that help its healthcare systems, from the universities to hospitals to research centers. What are some things that Boston might be lacking in helping to support and maintain this program?

Let me turn it around first and tell you some of the positive because the foundation of our program, which was really conceived by a community of stakeholders, had several principles that we were charged with. One is that we had to get out of our traditional clinics and to take care of people where they were in the shelters and on the streets. They wanted clinicians - the doctors, nurse practitioners, and physician's assistants working in a team. Their big concern was continuity of care. They didn't see how anyone could have good health care delivered if there wasn't continuity.

In the experience of most homeless people, their lives were already marked by loss and fragmentation and disjoint health care delivery. They would go to the emergency room and then they wouldn't have any primary care follow up. The next time they got sick they'd go to the ER and they'd see someone totally different. There was no continuity in that cycle. They wanted us to work in teams and I've always worked in a team with a nurse practitioner, physician assistant, social worker and the last fifteen years with a psychiatrist. This was all for continuity. They wanted to make sure that if I disappeared for two weeks, there was still a team that a homeless person knew where they felt comfortable.

The other thing they insisted was that we change our attitude. In the hospital you're used to seeing lots of people every hour. They always insisted that it's all about the relationship. You have to take time, to be present, to be consistent and earn the trust of the people who are outside and in the shelters. Only when you get that trust can you begin to think about a primary care, continuity of care relationship. Much of what we had to do was learn how to have cups of coffee with people. The van that we take out at night is Pine Street Inn's van but it brings soups, sandwiches and blankets. There was also a charge to us to make sure that the care we were giving was fully integrated into the mainstream. Getting horizontally integrated into the community was an interesting lesson for me because when you train in an academic medical setting you really don't get a chance to learn much about your surrounding neighborhoods. I was horrified that I knew so little. I thought Pine Street Inn was an inn, not a huge shelter with six or sever hundred people sleeping there. We also had to get vertically integrated within the mainstream, so they insisted that if I saw or treated someone on the street that got sicker and had to come to the hospital, I would still be the doctor treating them.

It was brilliant because they made us stay part of Boston City Hospital, which is now Boston Medical Center, where the vast majority of homeless people were getting their care. The other place we've always been part of is Mass General Hospital, who sees the second largest number of homeless people

Hallie Abelman is Managing Editor of TuftScope.

in the city because of the street population down there. Our program had to have clinics in those hospitals every day and when people got sicker and had to go to the emergency room we could be involved in their care.

The last thing they did was insist that we provide respite care for people, which is an interesting concept that I had never heard about in 1985. It was basically designed because the shelters were very nervous about people that were too sick to be walking the streets every day. The shelters kick everybody out in the morning and you can't come back until the afternoon. If you're recovering from surgery, having terrible diarrhea, or having back pain, you have to leave the shelter and wander around all day. We were supposed to provide, and we have over the years evolved a respite program that fills in that gap between acute hospital care and shelter. My reason for framing this is that Boston was very unusual in that it is blessed because the homeless health care works with the hospitals. This is one of our huge blessings.

The biggest thing that is missing is when you go to take care of a population like homeless people you realize that the burden of illness that they bear is very high and usually that's a substance abuse problem presently or from the past. Often there's a serious mental illness there and for many of them in addition to that one or more chronic medical conditions that they're trying to take care of. There are a lot of aspects of our health care system that I think homeless people shed a real light on. There are the medical problems cared for under Medicaid, mental health under their capacities, substance abuse programs under their branches. They all have different funding and record systems. An individual who needs all those services has to go through three separate systems.

I think Boston has been slowly learning to integrate the care for those folks. In my practice I care for the people on the streets who are even too fragile or independent to come into the shelters. For those folks, integrating that care requires that we go out as a team to see them because you can't expect them to go to three different facilities for each of those things. That's what I see as the biggest challenge. And we have seen a great deal of progress with that over time.

You mentioned that a psychiatrist goes along with your group.

The integration of behavioral health in this program is interesting. We started out without it because the shelters insisted that we would not do mental health services. It turns out that the shelters in 1984 and 1985 were horrified by the number of mentally ill people that were living in them. They thought, I think very justifiably, that the 1960s deinstitutionalization caused large populations of people released from these hospitals to go to the shelters. While deinstitutionalization was a completely wonderful idea, the shelters were protesting that the planned supports never materialized for these patients when they were emptied from the hospitals.

The shelters were protesting that, as a class action suit basically, saying that this was not fair to people with mental illness. They didn't want us at BCHCP to do services that would deter the government from realizing that these people needed mental health services. It wasn't until 1994 that we started doing mental health services and it was when we had grown up enough that we could work in the clinics. When we opened our own place, the Barbara McInnis House in 1993, was when we realized we had some people that were really sick, had mental illnesses that would flare up with their other illnesses and that we really needed to have mental health services at the shelters and they were fine by that time with us doing that.

Our mental health component has been growing since then. Beginning around 1999 or 2000, we've had a psychiatrist working on the street team with us and four years ago Mass General Hospital gave us the money for a full time psychiatrist to be on our street team. It's great.

How well is Boston equipped to aid its homeless population in the case of a natural disaster or state of emergency?

I have a lot of respect for how the city of Boston has paid attention to not only homeless but also emergency services for homeless people and people in shelters. In all the time I've been doing this we've only had two mayors and both have had a firm commitment to taking care of homeless people and they really have stood by this commitment.

One of the commitments is that there is a shelter bed for any person in Boston who needs one. Almost all of the shelters don't require you to be sober to come in so that's really good. When we look at the people living outside in Boston in the cold weather, those are people who could have a bed but for whatever reasons choose not to go into the shelter. Some people can't stand to be in a big crowd or find the rules of a shelter infantile. And others just have disorders that make them scared to be in a shelter. I see that group that stays outside as a particularly vulnerable subgroup of the homeless population.

Boston has had a disaster plan going for years. I remember when I first started in 1985 there had been a hurricane warning and they started practicing what to do. The Emergency Shelter Commission of Boston, which is supreme, has always organized people around town so we have a disaster plan. During this most recent hurricane we had a large number of women who slept on our lobby floor on cots to make sure they were safe and away from the storm. Boston just has one particular problem because people are bused out to the city of Boston shelters out on Long Island, and during a hurricane that can be difficult. There are shelters here that plan how to take care of people. It's really remarkable.

What are your goals looking forward into the future of the program?

Our mission is pretty straightforward: to provide the best quality care to any man, woman, or child who is experiencing or has experienced homelessness in the city of Boston. I think the first 25 years was learning how to get out of the hospital mentality and be out in the shelters and out in the streets taking care of people where they are as a way to provide primary preventive care to them instead of them having to come to us.

The nurse, who taught me everything I know, Barbara McInnis, when I showed up at Pine Street Inn in 1985, says that if you wait for people to come to you then you've already lost the game. We did a pretty good job of getting out and making sure we were everywhere where homeless people were. In fact

I worry that the homeless people think that we're all over the place. We're in 70 different shelters, soup kitchens, and adult homes. We have a street team. We learned how to coordinate electronic medical records in the mid 1990s. We've developed a respite program where we now have 104 beds for people coming out of emergency rooms. This model has stood the test of time. Now, as we learn more about homelessness, the solution is clearly housing.

How do you take people who have been homeless for years and get them into housing? And over the last five or six years, Boston has been trying to bring housing services to people without forcing them to qualify for sobriety first.

The Pathways to Housing study found that for the chronically mentally ill, if you get these homeless people into housing before they are technically eligible, it often prevents illnesses and emergency room visits. We've been working alongside these efforts and the federal government realized that the goal was to allocate the money to housing first and manage this problem. We've also been involved with agencies around town that are working on housing. As a program, we don't do housing but these are people we've been working with for a long time so we know a lot about the services they may need. We've been able to partner with Pine Street Inn, Homestart, and the Boston Housing Authority. As they get people housed we start do services for them. About a third of our long-term folks have been placed in homes around town and our team its now learning how to do home visits.

Last year we did about 1200 home visits to people that were all previously on the streets. And we are reminding ourselves as a program that homelessness is not a permanent state. It's a marker for people that live in such abject poverty and have so few resources that only one little perturbation can end them up in the streets or homeless shelters. When they're in housing they're still very fragile and need lots of support. As a program, I think our next twenty-five years is learning how to realize that when these people get into housing there's still another challenge and to keep that continuum of care.

Lastly, how do you stay in touch with all your patients?

It's kind of fun. As people get into housing we visit them frequently. We keep in touch by phone, knock on a lot of doors. You have to be very careful because it's easy to think that now if they're in housing they're going to be ok. Their health is still at risk. They might isolate themselves, and even do all the things they might have done on the street except now they do it in their own efficiency apartment. We've learned that for many of those folks we've found we have to regularly check in with them, make sure they're okay, and do our primary care visits like you'd do with elderly home visits. They're very complicated people because many are people still suffering from mental-health issues, drug abuse issues, and other health issues that require integrating the process. It's the new frontier for us.

ORIGINAL ARTICLE

Prenatal Cannabis Exposure and its Effects on Learning and Memory: A Critical Review

Robert E. Ventura

*The various effects of substances on children in the womb have been extensively documented for quite some time now. From the outcomes associated with fetal alcohol syndrome to the consequences noted in the Surgeon General's warning on cigarettes, there are countless reasons to ensure that there are no aberrations in the delicate environment of the developing human body. Marijuana (*cannabis sativa*) is a commonly used substance by pregnant mothers, especially by mothers aged 18-25. Although in popular culture marijuana is considered a "softer" drug for its allegedly non-addictive properties, there are an estimated 61 different cannabinoids in marijuana, including delta-9-tetrahydrocannabinol (Δ^9-THC), which can interfere with the human's endocannabinoids. The CB_1 and CB_2 receptors, stimulated by the artificial cannabinoids of marijuana, are shown to be readily involved in neural development, from axon guidance to gliogenesis, and the presence of cannabinoids potentially affect the function of these receptors. Prenatal marijuana exposure can also lead to learning and memory deficiencies, based on psychological tests of children whose mothers self-reported marijuana use while pregnant. This is most likely caused by a decrease in long-term potentiation in the brain (LTP). There is still a need for more research in this field, however, potentially looking at how the cannabinoids affect the nervous system on a receptor level in different animal models.*

INTRODUCTION

Background

Marijuana, or cannabis sativa, is one of the most popular recreational drug. Its frequent use emerged in the late 1960s and 1970s in the United States, and use has sparked plenty of controversy in recent years (particularly in California) over its decriminalization and potential legalization. Marijuna is now as popular as it was in the 1970s with over 25% of all women from ages 18-25 using the drug in the year 2002.[1] Unfortunately, due to the popularity of marijuana, it is all too common for pregnant women, especially young adult and teenage individuals, to partake in marijuana use.[2] Estimates made in 1990 reveal that each year, anywhere between 125,000 and 835,000 babies are born with the risk of being prenatally exposed to marijuana.[1] Like most illegal substances, marijuana can negatively affect prenatal development if used by the mother. Multiple studies have been carried out studying the precise effects of maternal intake of marijuana on the neural development of the fetus, ranging from laboratory studies done on mice and rats to human longitudinal studies based on self-reported statistics from mothers and observations of the children as they develop. Considering the critical nature of neural development, the effects of the drug on the brain can often lead to learning and memory difficulties later in life. The different studies vary in their methods, hypotheses, and experimental procedures, but this review will attempt to synthesize the various data and conclusions found in the articles to further elucidate the precise effects of marijuana on the developing brain, specifically regarding learning and memory.

The Science of Marijuana and the Brain

Marijuana is classified as a psychoactive drug, and it is made up of 421 different chemicals, or constituents.[3] Of those constituents, 61 are types of cannabinoids, with delta-9-tetrahydrocannabinol (Δ^9-THC) being the major cannabinoid responsible for the effects of marijuana.[3] Some of the other major cannabinoids include cannabidiol (CBD) and cannabinol (CBN), neither of which inherently possess any pharmacological properties but both of which have been shown to be important to the activity of Δ^9-THC.[4] These cannabinoids are the molecules that interact with the brain to cause the high that marijuana users feel after exposure to the drug.

The molecules in marijuana are usually activated when the plant is heated, allowing the molecules to vaporize and be inhaled or consumed; through this mechanism, the cannabinoids can enter the system and cross the blood brain barrier.[3] Δ^9-THC can then bind to the G protein-coupled cannabinoid receptors (CB_1 and CB_2) by mimicking endocannabinoids, in doing so suppressing the release of neurotransmitters in the neurons and inhibiting the outcomes associated with cannabinoid receptor activation, which causes many of the effects marijuana has on the brain.[5]

The CB_1 receptor is expressed mainly in the brain and thought to play a role in reducing pain and inflammation by preventing excess neurological activity from occurring.[5] Additionally, CB_1 receptor activation is closely linked to the reduction of glutamate and GABA neurotransmission, as CB_1 receptors are often located at glutaminergic and GABAergic neurons (Figure 1D).[6] Both receptors are primarily located at presynaptic axon terminals, explaining their ability to decrease neurotransmission, which needs to be inhibited presynaptically.[7] The CB_2 receptor is expressed in the immune system and has been shown to play a role in enhancing immunity and nociception, like the CB_1 receptor.[5,8]

The strange behavior of Δ^9-THC in both inhibiting and stimulating cannabinoid receptors contributes to the dual excitant and depressant effects of marijuana.[5] When Δ^9-THC is inhibiting cannabinoid receptors from releasing inhibitory transmitters (such as GABA) onto acetylcholine, glutamate,

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or dopamine-releasing neurons, it can stimulate various sensations, and when it is acting on CB_1 receptors to inhibit the release of glutamate onto GABAergic neurons, excess GABA can cause the inhibitory effects.[5] It is this inhibition of dopamine and glutamate release that affects brain development critical to learning and memory.

Focus of the Review

Given this knowledge, we can gather that Δ^9-THC and the other cannabinoids are very complex agonists and antagonists. By applying this knowledge to the developing brain and nervous system, it is clear that exposing a fetus (particularly its developing nervous system) to any foreign substances (such as Δ^9-THC) can potentially cause neurological problems later in life for the offspring, especially pertaining learning and memory, two of the most important mental tasks of the human brain. The connection between learning and memory and cannabinoids such as Δ^9-THC is evident considering the decrease in the activity of tyrosine hydroxylase (TH) in the brains of children perinatally exposed to cannabinoids.[9] The activity of this enzyme represents the rate-limiting step in dopamine (DA) synthesis, and this connection will be looked at in greater detail in the following discussion.[10,11] I will be trying to reveal how prenatal and perinatal marijuana exposure affects the learning and memory abilities of the offspring, which will determined based on the findings of several papers on how marijuana cannabinoids, especially Δ^9-THC, interferes with the developing nervous system and contributes to the increased activity of tyrosine hydroxylase.

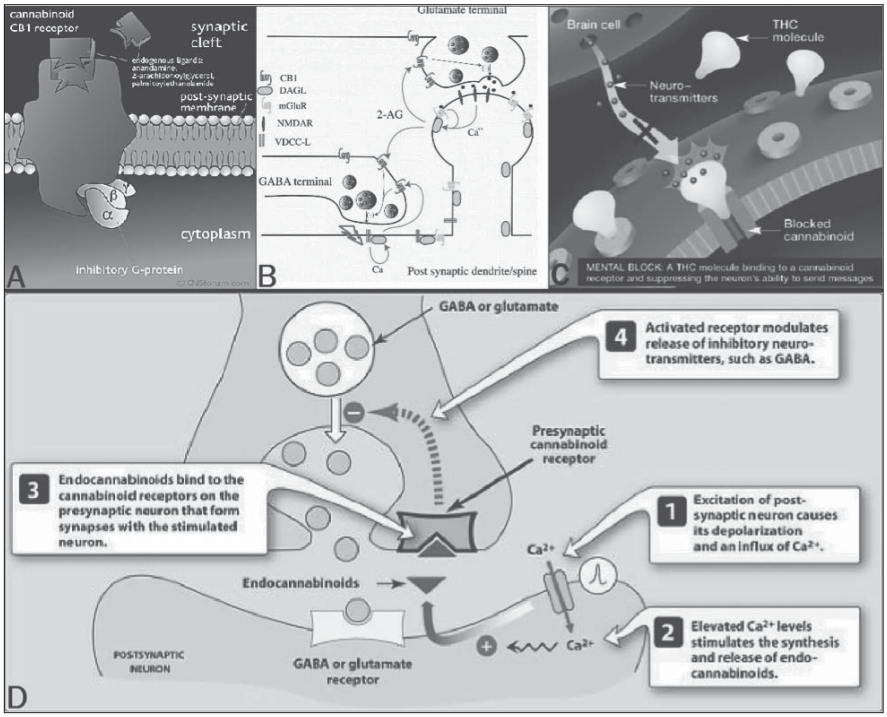

Figure 1. *(A) Adapted from The Lundberg Institute. A visual model of a cannabinoid-1 recep-tor, which includes the three-subunit G protein, the orientation of the receptor in terms of the synaptic cleft, and how ligands such as 2-AG1 and Δ⁹-THC attach to the receptor, and a more complete view of the entire neuron is shown in (B) Adapted from Patel, 2010. The primary role of endocannabinoids such as 2-AG1 is retrograde synaptic suppression. They diffuse to presynap-tic axon terminals where they activate CB_1 receptors and cause a decrease in neurotransmitter release. The CB_1 receptors are located on both GABAergic and glutamatergic axon terminals synapsing onto principle neurons. Δ⁹-THC blocks 2-AG1 from bonding to cannabinoid receptors and prevents all of these things from happening. (C) Adapted from the American Association for Cancer Research. Δ⁹-THC blocks cannabinoid receptors and prevents neurotransmitters that are coming from across the synaptic cleft from activating the receptors, which is also seen in a more complete way in (D) Adapted from 10.11 in Harvey and Champe, 2008, which shows and ex-plains the order of effects as a result of endocannabinoid release and cannabinoid receptor activa-tion. 12-AG stands for a 2-Arachidonoylglycerol, an endocannabinoid that is often blocked from binding to cannabinoid receptors as a result of the agonism of Δ⁹-THC.*

DISCUSSION

Endocannabinoids, Cannabinoid Receptors, and their Role in the Developing Nervous System

The CB_1 receptor is one of the most common G protein-coupled receptors in the human brain, and can be found in the early stages of brain development.[12] This equates to day 11 in the developing central nervous system of the mouse, day 14 in the rat, and around 5 or 6 weeks in the human.[12,13] Strangely enough, most of the places that cannabinoid receptors are found in the developing brain do not mirror areas where they can be found in the matured adult brain, and this fact reveals that the endocannabinoid system is involved in early development of the nervous system and not just with the normal functions it has in the fully developed brain.[13] Multiple papers have been written addressing this aspect of the endocannabinoid system and how it is involved in neurogenesis, neuronal migration, axon guidance, synaptogenesis, dendritogenesis, and gliogenesis.[1,12,14] This is due to the fact that the CB_1 receptors are expressed in the neural progenitors and localized in order to assist in developing axonal projections for axon guidance.[1] It has been shown that CB_1 expression levels reach a maximum when synaptic connections are established between cortical pyramidal cells and GABAergic interneurons.[15] The exact mechanism of how improper endocannabinoid system function can affect development is not exactly known, as papers written as recently as 2011 still only discuss the results of the dysfunction. It is known, however, (thanks

to genetic ablation experiments done on the CB_1 receptor) that the endocannabinoid system is very important to neurogenesis, neuronal migration, and axonal pathfinding.[16] Because the cannabinoids in marijuana act as agonists and antagonists for the cannabinoid receptors in the nervous system, it can be concluded that the introduction of foreign cannabinoid mimickers is likely to disrupt some steps of development in the brain, particularly the completion of neural connections.[16] That experiment demonstrated that during development, unlike in the adult brain, CB_1 receptors are expressed in the subventricular zones, which play a role in cell proliferation, and white matter regions, in particular transverse commissural tracts, which are essential for cell migration and axonal elongation.[13] Considering the inhibition of some of the neural connections that could be important for forming memories and learning later in life, the idea of prenatal marijuana exposure causing memory and learning problems in grown offspring seems reasonable. Considering similarities demonstrated by animal and human studies in social interactions, behavior, learning and memory and the similar brain development patterns observed between vertebrates (which comprised all of the animals used in the studies) and humans, the deduction can be made that the mechanisms between the two models are markedly similar.[2,12,16,17,18,19,20] The differences between the animal and the human studies are irrelevant when just considering long term effects and the involvement of cannabinoid receptors as development of the two is so similar.

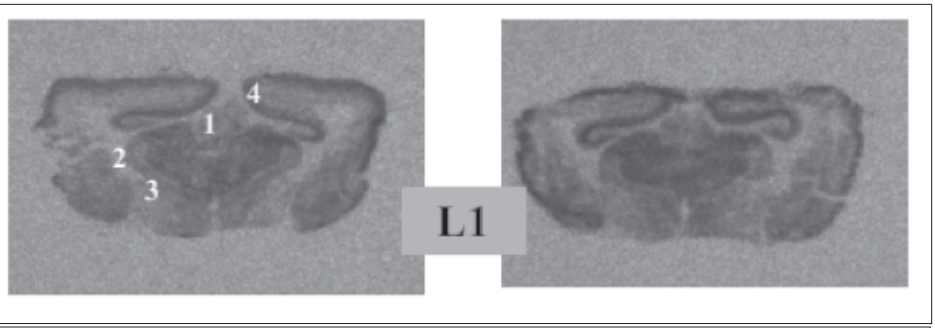

Figure 2. *Adapted from Gómez, 2003, Figure 2 on top and Fernández-Ruiz, 2004, Figure 1 on the bottom. Autoradiograms showing the levels of L1-mRNA in several brain structures of male fetuses that had been daily exposed to Δ^9-THC or vehicle (left panel) since day 5 of gestation. The increase in area shows an increase in L1 expression, and therefore CB1 presence. (1) Cere-bral cortex, (2) corpus callosum, (3) cortical subventricular zone, (4) striatal subventricular zone, (5) caudate-putamen, and (6) septum nuclei on top and (1) habenula, (2) fimbria, (3), stria termi-nalis and (4), cerebral cortex on the bottom.*

Physical Effects of Altered Cannabinoid Receptor Activity

Once the damage has been done and development is complete, the results can often be observed through study of the animal models and observation of the brain. It is in these cases that animal studies are favored over human studies, for the obvious reason that the brains of human fetuses are typically not tagged, stained, and sacrificed for research in the manner of rodent brains. Because of this, it is difficult to study the effects of exposure to the chemicals in marijuana on the development of the brain specifically regarding humans. In the experiment carried out by Gómez, observation was done via in situ hybridization after administering an oral dose to rats of 5 mg/kg of Δ^9-THC extract daily from the 5th day of gestation. Gómez concluded that Δ^9-THC exposure increased the gene expression of neural adhesion molecule L1, whose expression has been shown to correlate with the anatomical distribution of the CB_1 receptor.[21] However, the increased expression of L1, hypothesized to be an effect of Δ^9-THC CB_1 receptor activation, still throws off normal development by impairing normal neurotransmitter development. A study done by Fernández-Ruiz directly correlates with Gómez's study, as he used the same exact procedure and procured the same results (Figure 2).[13] Both Gómez and Fernández-Ruiz saw more L1 expression in male brains than in female brains, interestingly enough, which will be addressed later in the review.[13,21] In a study done by Gianutsos, it is concluded that the role of nucleic acids in the learning process is vital to consider when looking at the altered RNA synthesis that is a result of marijuana exposure.[18] Another study done with a slight increase in the dosage (with rats being given 10 to 15 mg/kg marijuana extract during gestation) revealed a significant decrease in DNA, RNA, and protein in the developing brain of the offspring, which again is relevant considering the relevance of protein and nucleic acid in learning.[22] This effect on the learning process will continue to be discussed as other articles concerning the consequencesof prenatal marijuana exposure on learning and memory are analyzed.

Direct Neurological Effects Related to Learning and Memory

Issues in learning and memory, or at least some sort of mental deficiency, have been cited in most of the papers written about the developmental neurobiological effects of prenatal marijuana exposure. In human models, longitudinal studies looking at children born to mothers having smoked marijuana have shown a definite trend of learning deficits and memory issues, although obviously no facts of causation can be drawn from these studies.[12,17,23,24] Although the studies done on the development of children born to mothers who had reported using marijuana during pregnancy are useful for observing how the exposure affects the children's brains as they develop, the potential of a self-reporting bias from the mothers reporting their marijuana intake is too significant for any direct conclusions. Additionally, the exposure of marijuana cannot be controlled (for obvious ethical reasons), and even though the surveys given to mothers concerning their marijuana use can be detailed enough to gain almost all the information needed to classify the magnitude of the exposure, there are still incredibly wide variances that exist between the different

types of cannabis prepared and grown in terms of their cannabinoid concentration. Therefore, the amounts and types of cannabinoids that the mother and the fetus are exposed to can never be known for sure or replicated by any laboratory preparation of cannabinoids or marijuana extract. Lastly, the assumption can easily be made that if these mothers are using marijuana while pregnant, they very well may be doing many other substances that are equally or increasingly detrimental to fetal development, and although this can be noted in surveys, it cannot be used to draw conclusions. However, these results have been mirrored in animal studies, add to their validity due to the increased control and deceased variability.[20]

In a study done by Gianutsos, a fairly different preparation of marijuana was used. Instead of pure Δ^9-THC extract, cannabis sativa extract was used at 250 mg/kg doses daily on days 8 to 11 of pregnancy in rats. However, one issue with cannabis sativa extract is that the amount of Δ^9-THC and other cannabinoids can vary, although this did not seem to affect the results in any way, based on replication of the resulting learning problems in other studies.[20,25] In this study, the rats born to the parents exposed to cannabis were allowed to mature for 65 days. There was a statistically significant increase in the times that the rats took to complete the maze, with the experimental (fetal marijuana exposed) rats taking close to 800 seconds longer on average than the placebo rats. Interestingly enough, it was noted that females generally performed worse in the maze in comparison to males, which contradicts the findings of Gómez and Fernández-Ruiz, both of whom determined that males are more sensitive to the effects of Δ^9-THC than females. This deviating result could be due to the fact that the males in these studies did indeed show more L1 growth after marijuana exposure, and although Gómez and Fernández-Ruiz both proposed this would cause impairment in neurotransmitter development, the increase in CB_1 receptors as shown by increase in L1 could have caused impairment of neurotransmitter development to not be as great as they were in females. It is also a possibility that Gianutsos' results should be considered an outlier, as no other papers reviewed mentioned a learning difference between sexes or involved such a maze learning task in the studies. Additionally, Gianutsos did not provide any data comparing the times to complete the maze of control mice for both sexes to times for experimental mice for both sexes. Although these studies all show that a connection between prenatal marijuana exposure and learning and memory issues exist, none of them actually explain the precise processes of the brain and why these effects occur, which is what will be investigated next in order to fulfill the original intent of this review.

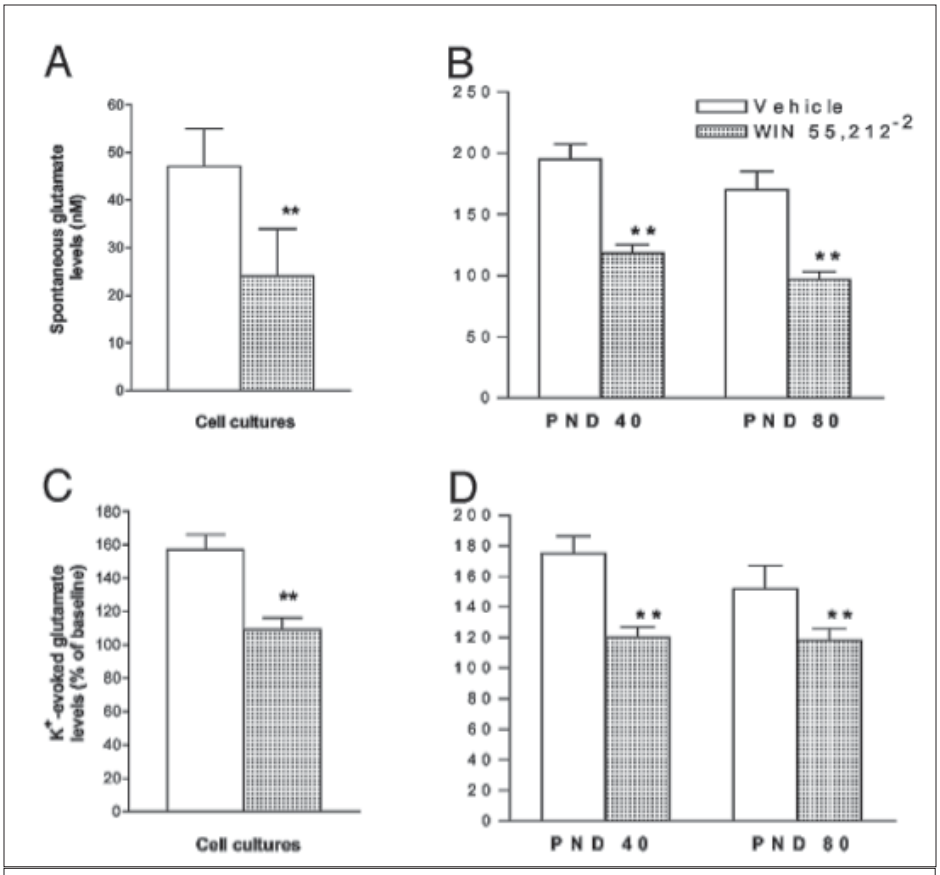

Figure 3. *Adapted from Mereu, 2003, Figure 4. Ef-fect of prenatal exposure to WIN on extracellular hippo-campal glutamate levels in cell cultures (A and C) and in vivo at 40 and 80 days of age (B and D). The white repre-sents the control and the gray represents the experimental.*

Molecular Models of Learning and Memory Problems

Now that it has been shown in multiple studies that there is indeed a correlation between prenatal marijuana exposure and problems with learning and memory, it is necessary to explain the mechanisms of what is occurring in the brain and why exactly the cannabinoids from marijuana are resulting in these issues. To get a better look at the ties between CB_1 receptor agonism and learning, a study that slightly deviates from the classic marijuana study can be considered. Such as study was carried out by Mereu, who analyzed the effects of a chemical that works in similar ways to marijuana endocannabinoids. This chemical was WIN 55,212-2 (or just WIN) and is a CB_1 receptor agonist, just like Δ^9-THC. As such, these two chemicals can be considered to have very similar effects, although it is noted that WIN has been found to be 3–10 times more potent than Δ^9-THC, depending on the administration route, causing the amounts used of WIN to correspond to a low dose of cannabis. This study determined that the memory

impairment caused by interaction with CB_1 receptor is linked to decreased glutamate release in the hippocampus and altered hippocampal long-term potentiation (LTP).[19] LTP is a long-lasting strengthening in signal transmission between two neurons that results from stimulating the neurons simultaneously. LTP is one of the major neural mechanisms that allows for learning and memory. Mereu's findings show that there is a significant decrease in the amount of glutamate in hippocampal cells treated with WIN.[19] Considering the fact that glutamate is one of the main excitatory neurotransmitters in the brain and vital for exciting neurons and causing LTP to occur, the effect of increased GABA release as a result CB_1 receptor agonism mentioned in the Introduction seems reasonable. Since GABA inhibits glutamate, with a decreased amount of glutamate, less LTP is bound to occur (Figure 3).[19] Mereu does note that additional studies are needed to confirm that the effects of WIN are reproduced by Δ^9-THC. Luckily, an experiment carried out by Suárez tested a very similar concept using Δ^9-THC instead of WIN and received similar results.[14] In this study, the amounts of glutamate transporter were measured after daily prenatal exposure of 5 mg/kg orally of Δ^9-THC from day five of gestation.[14] Presence of glutamate transporter is directly related to the amounts of glutamate, as increased glutamate requires increased amounts of transporter. Suárez's data also showed that males exhibited more glutamate transporter reduction than females, which further decreases the credibility of Gianutsos' study, which asserted that females were more affected, contradicting the findings of Gómez and Fernández-Ruiz, as mentioned earlier.[14]

Another potential mechanism lies in the connections between dopamine and learning and memory and the connection between the enzyme tyrosine hydroxylase (TH) and dopamine neurotransmission. The first study considered addressing this topic involved rats receiving injections of 15 mg/kg of Δ^9-THC per day from the fifth day of gestation to the second day postnatal, which is significantly more than Suárez, Gómez and Fernández-Ruiz were using in their studies.[26] The rats were sacrificed after 62 days postnatal and their brain slices analyzed via in situ hybridization histochemistry. The results revealed decreased dopamine receptor 2 expression, and considering the ties between dopamine and learning, this is a significant in determining the precise effects of marijuana on learning development (Figure 4).[26] Dopamine is known to be the main neurotransmitter involved with learning, especially learning that is reward-based. On top of this, dopamine expression can be increased through the enzyme TH, which limits the rate at which dopamine is synthesized.[10,11] Δ^9-THC has been shown to increase the gene expression for TH, causing more TH to be produced, and therefore resulting in less dopamine synthesized.[11,27] Finally, there is a progressive increase in the amount of CB_1 receptors in the hippocampus throughout development, and as mentioned, more CB_1 receptors means more dopamine inhibition, implying that dopamine deficiencies could occur in the hippocampus as well, causing memory issues.[28]

CONCLUSION

There is still much more research that can be done on this topic, especially considering the fact that the connection between glutamate, dopamine, marijuana exposure, and memory and learning has yet to be experimentally tested. The review of the articles should have elucidated the fact that prenatal and perinatal marijuana exposure affects the learning and memory of the offspring through incomplete neuron development, decreased LTP, excess tyrosine hydroxylase enzyme activity, and decreased dopamine and glutamate activity. There are existing explanations for each marked deficiency in learning and memory from prenatal marijuana exposure in the literature, based on tyrosine hydroxylase presence and dopamine deficiencies for learning and on glutamate deficiencies and LTP decrease for memory. Although this is a good start, future directions for this topic should address this issue at a receptor-sized level and investigate how blocking of the cannabinoid receptors during development affects neuronal development. Studies could involve an animal whose embryo is easily observed throughout development, such as a chick or a frog. Such experiments could finally reveal what exactly Δ^9-THC and other cannabinoids are doing to CB_1 receptors during development and how these effects alter the formation of the nervous system.

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A full list of references for this article can be found at TuftScopeJournal.org

OPPOSING VIEWPOINTS

Is Gender Selection of a Fetus Ethical?

***Brian Wolf** argues that gender selection should be permitted, but **Kathleen Li** discusses its negative consequences.*

The opinions expressed in these articles do not necessarily reflect those of the author.

YES

The issue regarding the selection of a child's gender continues to produce a wide variety of positions. The main argument in favor for gender selection rests upon the notion that individuals have a choice in the selection of the sex of their offspring. While this practice may be quite controversial, it is essential to understand how and why this technique is being utilized, and to create an approach that appeases both those who oppose and support gender selection.

The way in which individuals can know the gender of their child is through the post conceptual method of in vitro fertilization (IVF) and preimplantation genetic diagnosis (PGD). PGD has been noted as an important tool in determining whether the child presents single gene defects and sex-linked disorders. Additionally, this is a method that enables a strong possibility of a pregnancy with a fetus of the chosen sex and a close-to-zero possibility of a pregnancy with a fetus of the non-chosen sex.[1] Only within the past decade, a technique for sex selection which does not include pregnancy termination has been presented.

An argument that supports the need for gender selection is the high risk of maternal mortality in certain countries in the world. As stated in a study by World Health Organization (WHO), the report notes "the disturbing statistics of maternal mortality for developing countries, where women are more than 400 times as likely to die from complications during pregnancy than women in Southern Europe."[2] Maternal mortality and morbidity can be linked to series of consecutive pregnancies, in addition to having children at a very young age.[1] An example of a situation in which women must bear successive pregnancies occurs when a family's religion demands that they produce sons.[1] If a family has the option to choose their first child as male using PGD, the women would not be burdened with multiple pregnancies

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Image Source (http://www.flickr.com/photos/lunarcaustic/2128618333/)

NO

While embryonic gender selection via preimplantation genetic diagnosis (PGD) is beneficial for medical purposes, such as screening out embryos with sex-linked disorders, single gene defects, and chromosomal disorders,[1] the issues that arise from non-medical gender selection pose concerns about ethical obligations, are damaging to the economy and medical advancement, serve to reinforce gender stereotypes, and may lead to the establishment of selection of genetic predispositions as a right.

Embryonic sex selection is a process of in vitro fertilization (IVF) whereby a woman's embryo is fertilized with a man's sperm in a lab. After three days incubation, a doctor can extract a single cell from the embryo to determine its gender. The would-be mother then has the choice of whether or not to implant the embryo.[2] Evidence suggests that children born from PGD methods are not any more likely to have physical health problems.[3,4,5]

The ability to choose the gender of a healthy child is so appealing that eager parents are willing to incur the steep financial burdens that accompany it. These procedures are costly, often up to $18,000 for a single procedure. Sometimes, a procedure might not even produce any usable, chromosomally normal embryos.

The gender selection industry makes over $100 million a year performing 4,000-6,000 procedures.[6] There is reasonable fear about human resource allocation; for example, fertility doctors may decide to stop treating infertility and pursue gender selection instead. Advertising for gender selection procedures have begun to scope out interested individuals among the masses, posting and advertising on social networking sites such as Facebook, Twitter, and Youtube, attempting to drive up the demand. Framing gender selection as an industry, and advertising it as a commodity, we have parents such as Megan Simpson addressing the success of the procedure in a grossly inhumane manner. "My husband and I stared at our daughter for that first year. She was worth every cent. Better than a

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until a male is born. While it is necessary to promote gender balance and sex equality throughout the world, the choice of gender selection has a strong potential to save many women's lives.

However, studies on gender selection need to be understood before opinions are formed on this matter. As described in the following study:

"*1001 British men and women were asked about their gender preferences. About two thirds of the respondents stated that, if given a choice, they would like to have a family with an equal number of girls and boys. Most of the remaining third claimed not to care about the sex of their children. Asked whether they wish their first-born child to be male or female, 16 per cent liked their first child to be a boy, 10 percent liked their first child to be a girl, and a vast majority of 73 percent said they did not mind what sex their first-born child was. Finally, when asked to imagine they could have just one child, 19 percent preferred their only child to be a boy, 17 percent preferred it to be a girl, and 57 percent stated they did not care about the sex of their only child (Dahl et al., 2003).*"[3]

While there may be a slight preference for child to be male (19 v. 17 percent), does this indicate that all these parents who prefer a male for their only child will utilize PGD and in-vitro fertilization to select the gender of their child? Probably not. It should also be noted that, according to data from American and British "Gender Clinics," individuals who are willing to subject themselves to these invasive and costly treatments are couples who have two or three children of the same sex and would want another child of the opposite sex.[3] A possible solution to the utilization of gender selection "can be addressed by permitting sex selection only for second or subsequent children, rather than by absolute prohibition."[1] This allows sex selection for purposes of family balancing in countries where no distinct male-dominance prejudice occurs and for parents who are ethically neutral on gender selection.

The clinics that offer this service of gender selection are given the liberty to offer, to curb, or to reject a prospective patient when deemed necessary. As described in various studies, there is no conclusive evidence for a severe sex ratio distortion to occur in various countries (e.g., England and United States), but the possibility of gender bias in other societies needs to also be considered. The clinics providing this service must understand that when there is a clear and present danger due to sex bias they must use reasonable judgment to refute this service. Therefore, the post-conceptual method of IVF and PGD should be permitted, but only under certain circumstances.

References for these articles can be found at TuftScopeJournal.org

new car, or a kitchen reno."[7]

Simpson is a middle class, married woman who grew up in a family of four girls. She wanted a daughter because she desired to engage in stereotypically female bonding activities, such as "sewing, baking, doing hair and makeup," which she had enjoyed as a child. Other women share similar sentiments. Jennifer Merrill Thompson, self-published author of "Chasing the Gender Dream," states her reasoning simply: "I'm not into sports. I'm not into violent games. I'm not into a lot of things boys represent and boys do." A report published by the Ethics Committee of the American Society for Reproductive Medicine indicates the potential of psychological harm placed on sex-selected offspring, with parents expecting their child to behave in a certain manner in accordance to gender stereotypes.[8] This in turn could also lead to reinforced gender stereotypes in society as a whole.

Also, the casual normalization of sex selection might lead to the creation and prevalence of other selective procedures in the future. The fears of the 1997 science fiction film "GATTACA" may be realized; people may start evaluating others based on genetic traits. In the world of GATTACA, natural conception is a choice only those in lower social classes would make. There is rampant genetic discrimination, those born without perfect genetic traits such as heart defects, nearsightedness, possibility of developing mental disorders, as well as other unnecessary enhancements such as height and hair color are considered "invalid" in their society and only have access to low-paying, manual labor jobs. Encouraging selectivity in the general population about children we want born may strengthen the social gap and the wealth gap.

Right now, doctors in the United States can make the decision of whether or not the patient will receive the sex selection procedure. The issue of ethical obligations arises. Should a doctor discourage sex selection, based on all the potential negative impacts, or should they respect their patient's autonomy? There are economic incentives for doctors to condone embryonic sexual selection, a whole market of women who are interested in undergoing the expensive and unnecessary procedures. The United States is one of the only countries in the world that still legally allows PGD for non-medical reasons. Kerry Bowman, bioethicist at University of Toronto's Joint Centre for Bioethics in Ontario brings up the point that "the gender of a child is not directly related to the health and well-being of a child."[9] We cannot have a society that will allow the choosing of children based on the fact that they are a boy or girl.

"There is reasonable fear about human resource allocation."

INSIGHT

Innovations in the Fight Against Cervical Cancer

Alison Pinkerton

Thanks to the advent and availability of the Pap smear, American women are much less vulnerable to cervical cancer. Just forty or fifty years ago, cervical cancer was the most fatal cancer for women in the United States. Now, regular Pap smear tests can detect precancerous cells in the cervix before they become malignant, giving women a greater chance for survival. Unfortunately, this screening option is not readily available across the world, and cervical cancer poses a public health crisis in many developing nations. The World Health Organization (WHO) reports that 80 percent of cervical cancer cases and deaths occur in low-income, undeveloped countries.[5] After breast cancer, cervical cancer is the most common type of malignancy in women across the globe. About 500,000 women in developing countries will be diagnosed with cervical cancer each year, and half of these women will succumb to the disease.[5]

As shown by the past few decades in the United States, the Pap smear test could dramatically reduce the mortality associated with cervical cancer around the world. Of course, developing nations do not have the funds to institute such screening processes, so these hundreds of thousands of women become victims to an unfortunate health inequity. Donald G. McNeil, Jr. of *The New York Times* explains that trained cytologists must stain and evaluate Pap smear tests in equipped laboratories that countries such as Botswana and Thailand just cannot afford. In these countries, doctors are promoting a much simpler screening test to mitigate the dangers of cervical cancer.[4]

"80 percent of cervical cancer cases and deaths occur in low-income, undeveloped countries"

The new testing method is so simple, in fact, that it "requires only vaginal spoons, vinegar, and a bit of training," writes *National Public Radio*'s Jason Beaubian.[2] In his article "Botswana Doctors Stop Cervical Cancer with a Swab," Beaubian recounts an interview with Johns Hopkins obstetrician-gynecologist Dr. Ricky Lu. Lu works with Jhpiego, a Hopkins-based international public health group, to bring reproductive health care measures into underserved communities in the world. As part of this initiative, Lu is pioneering the vinegar-swab test with hopes that he can reduce cervical cancer-related fatalities. To administer the test, a trained nurse swabs a woman's cervix with either vinegar or diluted acetic acid. The nurse can then look at the cervix and clearly see areas of white tissue: these areas are precancerous lesions. The nurse can then immediately remove the lesions and send the patient on her way after only a few short minutes of screening.[2] Dr. Doreen Ramogola-Masire, a practicing obstetrician-gynecologist, performs this same test to women at her clinic in Botswana. Dr. Ramogola-Masire uses nitrous oxide to "slough off" the top layer of precancerous cells. Because the test is quick and simple, it is a much more feasible option than the Pap smear in impoverished countries.[2]

Botswana, too, has another unique women's health problem. The country has one of the highest human immunodeficiency virus (HIV) infection rates in the world- some estimates indicate that about one in four Batswana adults are infected with the disease.[2] Unfortunately, the presence of this horrible disease may signal the presence of another: human papillomavirus. The World Health Organization reports that 99 percent of all cervical cancers are related to the contraction of human papilloma virus (HPV).[4] Because of the connection between cervical cancer and HPV, and the connection between HPV and HIV, many HIV-positive women may develop cervical cancer if their disease progresses. In Botswana, this means that the threat of cervical cancer is very high. Dr. Ramogola-Masire notes an interesting paradox about this issue in Beaubein's article: when the HIV/AIDS epidemic first came to light, cervical cancer was not a problem for this population because affected women did not survive long enough for the cancer to develop. Years later, HIV/AIDS treatments have advanced and doctors can now extend the life of an HIV-positive patient. However, these HIV-positive women are likely to fall ill with HPV and, subsequently, cervical cancer.[2] Dr. Ramogola-Masire morosely describes advanced cervical cancer as "a horrible disease to die from." Until countries plagued with these diseases can institute the inexpensive screenings such as those in Dr. Ramogola-Masire's Botswana clinics, cervical cancer will continue to pervade and take the lives of numerous women, HIV-positive or not.[2]

On the other side of the globe, and much closer to the United States, Dr. Miriam Cremer is hoping to bring a more advanced but equally effective cervical cancer screening tool to Salvadoran women. Donald G. McNeil's *The New York Times* article "Cervical Cancer: El Salvador Gets a Screening Test That Women Can Administer at Home" identifies the test as careHPV, produced by Dutch technology company Qiagen.[4] This screening method is simple enough to administer in third-world countries, yet *The Lancet Oncology* reveals that it is twice as likely to identify the possibility of cancer in the cervix. Instead of illuminating precancerous lesions, though, careHPV tests a woman's cervical tissue for papilloma virus

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DNA. The swab test is easy enough that some woman can even perform the test themselves at home, bringing another level of ease and comfort to the screening process.[4] Dr. Cremer works with Basic Health International, an organization whose website proudly declares "a mission to eradicate cervical cancer and improve women's health in Latin America and the Caribbean."[1] Dr. Cremer and her staff hope to be able to screen about 30,000 women in El Salvador and, in time, make their mission a reality with the help of the careHPV test.[4]

Another group of innovative physicians is studying a gene silencing cervical cancer treatment that would be accessible to cancer patients in underdeveloped countries. This treatment is just that- a treatment, not a screening test- but it shows promise in both early and late stage cervical cancers. Dr. Paul Lambert of the University of Wisconsin McArdle Laboratory of Cancer Research conducted the study on laboratory-bred mice and published his promising findings in Cancer Research. Dr. Lambert and his team based their research on the knowledge that two oncoproteins, E6 and E7, play an integral role in the development of cervical cancer and cervical inter-epithelial neoplasias (CINs).[3] These proteins, they discovered through researching cultured cell lines, cause not just ovarian cancer, but also anal, head, and neck cancers. Dr. Lambert began to question if "turning off" the oncoproteins would decrease the severity of the cancer, or even erase it: this technique is called gene-silencing therapy. E7, it turns out, is the more potent of the two proteins, and is much more involved in the cancer-causing process.[3] When Dr. Lambert and his team experimented on lab-bred mice, they learned that when they blocked the E7 protein and left the E6 protein on, "the cervical cancers and CINs melted away."[3] This finding is particularly important because it means that E7 blocking can stop cervical cancer at all stages. The gene-silencing therapy was effective not just on full-blown cervical cancer but also on cancers linked to HPV and precancerous lesions. These lesions, or CINs, can pose certain difficulty: high-grade CINs often turn into cervical cancer, and doctors note that surgically treating the CINs can cause infertility and great amounts of bleeding.[3] In developing countries, this surgery is even riskier or, worse, completely unavailable. Screening tests, too, are scarce in these locations, so gene-silencing therapy will be able to give underprivileged women a fighting chance even if doctors did not catch their cancers early on.

Mothers, sisters, aunts, daughters, and nieces across the globe have great reason to celebrate these findings. All too often, medicine advances and modernizes in Western societies but remains stagnant in more vulnerable areas. Women in the United States still contract cancers, of the cervix and otherwise, but can be grateful that ever-improving technology continues to offer new ways to detect, prevent, and treat these ailments. Regrettably, women of other nations cannot feel the same way. Lacking medical infrastructure, funds, and education, these countries cannot provide women with the proper resources to diminish the risks of cervical cancer. Doctors Ricky Lu, Doreen Ramogola-Masire, Miriam Cremer, and Paul Lambert are now picking up where these countries left off. The exciting new treatments that they are pioneering are as simple as vinegar and as complicated as genetic silencing, but they all share a common virtue: they are egalitarian treatments and will leave no woman behind. These doctors believe that global medicine can be as effective as Western, American medicine, but need not be as costly or inaccessible. In fact, medicine for the developing world simply cannot be as costly or inaccessible as American medicine. Laboratories in Botswana are not equipped to read Pap smear results, so instead they can use vinegar swabs to achieve the same results.[2] In El Salvador, doctors and nurses are not abundant enough to regularly screen women for papilloma virus cells, so public health groups distribute careHPV tests that women can administer themselves.[4] And when all else fails and the cancer advances, doctors will soon be able to silence the cancer-causing genes and provide women who cannot get screenings or operations with the same fighting chance that a cervical cancer patient in America has.[3] With hope, these measures will bridge the gap between developing and developed medicine; no woman should be more vulnerable to a horrible disease because she was born in a struggling country, and these heroic doctors will make sure of that.

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MD Anderson Takes a Giant Leap for Mankind

Ariel Lefland

Forty-one years ago, President Nixon signed what became know as the war on cancer: the National Cancer Act of 1971.[1] Fifty years ago, President John F. Kennedy famously challenged the United States to go to the moon. "We choose to go to the moon in this decade and do other things, not because they are easy, but because they are hard, because that goal will serve to organize and measure the best of our energies and skills, because that challenge is one that we are willing to accept, one we are unwilling to postpone, and one which we intend to win, and the others, too."[2] Inspired by JFK's 1962 speech at Rice University, the University of Texas MD Anderson Cancer Center has proposed its own "Moon Shots Program" to significantly decrease the mortality rate of cancer in this decade. The ambitious and innovative project is putting MD Anderson at the forefront of cancer research so that cancer can be better prevented, treated and detected.

In the past forty-one years, cancer research has come a long way. Researchers and doctors have discovered that cancer is a complex disease with many forms and multiple causes. The American Cancer Society estimates that there will be 11.3 million cancer survivors in the United States by 2015, but cancer is still one of the most devastating diseases. This decade alone, 100 million people worldwide are expected to die from cancer. The mortality rate of cancer exceeds that of cardiovascular disease, tuberculosis, HIV and malaria combined. In a published statement, the MD Anderson Cancer Center calls its new program "an unprecedented effort to dramatically accelerate the pace of converting scientific discoveries into clinical advances that reduce cancer deaths." The program looks to directly impact patients; MD Anderson's president, Ronald A. DePinho, M.D. believes we have many of the techniques and instruments needed to fight cancer systematically "with the precision of an engineer." [3]

Moon Shots is focusing on developing effective drugs and personalized therapies through molecular techniques. A new Center for Co-Clinical Trials will study animal and cell models from MD Anderson's large tissue repositories to profile the mutations and proteins responsible for the onset of certain cancer types.[4] Researchers at Johns Hopkins University School of Medicine in Baltimore have noted that molecular markers such as DNA mutations, alterations in gene expression or alterations in protein function have been associated with all types of cancer.[5] These markers can be used to detect and monitor cancer. A news release published earlier this year by MD Anderson also points to the importance of genomics in cancer suppression. Researchers found that Grb2 controls an important cell-signaling pathway involved in FGFR signaling. The research helps to explain why mutations in the gene sequence may promote cancer formation and growth.[6] Genomics is a powerful tool for doctors when choosing appropriate treatments for patients and is becoming a more affordable technology. Knowing key gene sequences can help determine whether or not a patient will benefit from a specific therapy. [7] The Moon Shots Program has a single platform to unify all of its research teams, emphasizing clinical genomics and bioinformatics. The initiative will also look to implement policies to prevent cancer and promote early screening and detection.

The Moon Shots Program will initially target eight cancers through six moon shot teams. Acute myeloid leukemia (AML) and its precursor myelodysplastic syndrome (MDS), chronic lymphocytic leukemia (CLL), melanoma, lung cancer, prostate cancer and triple-negative breast and ovarian cancers were chosen based on current knowledge of prevention, treatment, survivorship, the probability of reducing the number of deaths and the strength of assembled teams.[8]

Myelodysplastic syndromes are a group of malignant diseases affecting blood cells. Fifty percent of patients suffering from MDS develop AML, the most common form of leukemia in adults. Approximately 16,000 Americans each year are affected by AML and MDS; however, no curative therapy exists for patients with MDS. The Moon Shots Program aims to identify the molecular mechanisms that drive MDS to become AML in order to develop inhibitors of this process. Resistance to current medications is a major barrier in finding an effective cure for MDS. Understanding why AML/MDS becomes resistant to intervention is a major goal for this moon shot team so that outcome in patients can rapidly be improved.[9]

CLL is the most common form of leukemia seen in the United States and Europe. The prognosis for patients with CLL can range, making it a challenge to treat.[10] Its genetic makeup can be studied easily in detail because it flows in the bloodstream.[11] Out of the eight cancers under study in the program, CLL is closest to being cured. Researchers hope to create a "gene map" to determine risk factors, new drug combinations for personal therapies and new screening methods.

Lung cancer is the leading cause of cancer-related deaths in the United States. 220,000 people per year are diagnosed with lung cancer in the US, and it kills approximately 160,000 Americans each year. Its most common cause, tobacco smoking, however, is also its most preventable cause of death. Detecting lung cancer too late is also a leading cause of poor prognosis in lung cancer patients.[6] Better detection methods and educational programs can make a huge impact on the number of lung cancer cases and deaths due to lung cancer

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each year. Moon Shots aims to use new smoking prevention programs to reduce tobacco use by 15% among youth and adolescents. The program also wants to use molecular profiling to increase the number of patients cured with early-state and locally advanced lung cancer by 10-20%.[12]

Melanoma is the most severe form of skin cancer. The survival rate for most patients with advanced melanoma is two years; Moon Shots aims to make it over 3-5 years. There is an exciting new therapy in which a patient's immune system cells are trained to attack the cancer cells. T cells are collected, exposed to antigens found on tumor cells and then injected back into the patient.[13] Whether or not this therapy can be used successfully for long-term remission remains to be seen.

Prostate cancer is the most common cancer and the second leading cause of death in men in the US. Currently, one in six men gets prostate cancer; incidence is expected to increase with the age of the male population. Researchers aim to develop screening techniques and tools to identify molecular targets to prevent unnecessary treatment and extend the lifetimes of patients not benefiting or responding to current therapies.[14]

"...the tools needed to fight cancer already exist."

The final group of cancers targeted by the program are triple negative breast and ovarian cancers. Breast and ovarian cancers are the most lethal and aggressive forms of cancer in women. It is estimated that 229,000 women will be diagnosed with breast cancer and approximately 40,000 will die from breast cancer in 2012. Out of 22,280 diagnosed cases of ovarian cancer in the US per year, 15,000 women will die. Both are associated with BRCA1 and BRCA2 breast cancer genes. Mutations in these genes increase the likelihood that the cancer will develop. The moon shots team's goal is to identify women and families at risk for these cancers and develop programs to decrease their risk for breast and ovarian cancers. The team is also studying animal models for potential new drug targets.[15]

The Moon Shots Program recognizes the great advances cancer research has made in the past forty-one years; however, it also recognizes that we still have much to learn in order to be able to wage a successful fight against cancer. The program is ambitious, but it also serves to raise confidence in the scientific community. As MD Anderson's president noted, the tools needed to fight cancer already exist. The $3 billion dollar project set to launch in February 2013 is structured to use these tools in a systematic and unified way. It aims at a dramatic reduction in mortality by not only finding genetic targets but also by creating programs for better screening methods, earlier detection, and improved allocation of resources. The fight against cancer will certainly not be an easy battle to win, but it is a challenge MD Anderson intends to win.

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ORIGINAL ARTICLE

Spineless: Placing Profits before Patients

Rachel Dillinger

Although the spine is resiliently crafted to withstand great stress while retaining flexibility, sometimes it fails. Around 700,000 vertebral compression fractures (VCFs) occur each year in America, mostly in people whose spines have already been weakened by osteoporosis. A VCF is a painful condition which can be remedied through either of two procedures: Vertebroplasty or Kyphoplasty. Both utilize bone cement products and offer instantaneous relief to patients at a very high success rate, ~90%.[1] Between 2002 and 2004, physicians testing products for the medical device company Synthes treated 31 VCFs with Norian XR, a bone cement.[2] The problem? It was only approved by the FDA for use in the arm, and three people died as a consequence of its misuse.

Generally speaking, off- label usage has proven beneficial when pursued with the right intentions. For instance, Avastatin, a drug proven to treat colon cancer, was investigated for effectiveness in treating Age-related Macular Degeneration (AMD), a disease which leads to blindness and affects 1.6 million Americans. Avastatin was found to be equally effective in treating the disease as Lucentis, the established AMD drug. This was a significant finding for researchers, especially considering Lucentis costs thirty-nine times as much as Avastatin. Not only does this respect the patient's pocketbook, but Medicare could also save three billion dollars per year.[3] There is nothing wrong with testing a product in a new manner, especially with the benefit of others in mind.

If a physician cannot separate their clinical decision making processes from this industry, then not only are the companies spineless, but the physician is as well.

However, the FDA has strict regulations that corporations must follow if they want to engage in off-label testing. Unless all of the following six conditions are satisfied, the investigational use of marketed drugs, biologics, and medical devices needs FDA consent via approval of an Investigational Device Exemption (IDE):[4]

1) It is not intended to support a significant change in use or labeling.

2) It is not intended to support a significant change in the advertising for the product.

3) It does not involve a route of administration or dosage level, use in a subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.

4) It is conducted in compliance with the requirements for IRB review and informed consent.

5) It is conducted in compliance with the requirements concerning the promotion and sale of drugs—21 CFR 312.7 (products cannot be touted as safe or effective)

6) It does not intend to invoke 21 CFR 50.24 (informed consent is not necessary when other treatments are unsatisfactory or unavailable, or when subjects are incapable of making decisions due to their medical conditions).

Originally, Synthes was granted FDA approval for the use of Norian XR in the arm.[5] The company then set out to see if it was suitable for use in the spine, despite preliminary studies which found the cement had the potential to react with blood and form clots.[2] Of the conditions stipulated by the FDA, several were not met: (1) In changing the treatment area to the spine, a significant change in labeling would need to occur, considering that the original label warns strictly against usage there. (3) Use in the spine poses significantly more risk than use in the arm, considering it proximity to major arteries in addition to the aforementioned label warning. (4) The subjects in this unauthorized study were never told that the product used on their vertebrae was not made for spinal fractures. No informed consent was given concerning the off-label usage. (5) Misbranded shipments of Norian XR were sent to Texas, Maryland, California, Indiana, New York, Pennsylvania, Alabama, and Florida. These shipments lacked some of the product information, including the labeling prohibiting use for VCFs.[2]

As a result of the product testing, three subjects died. No blame was placed until four top executives from the company were tried in 2010. In a letter read in court, former Synthes spine division president Thomas Higgins stated, "I didn't think at the time that we were doing anything illegal," even though preliminary studies showed that not only could blood clots form if the cement was used in the spine, but that they could travel to the lungs and cause death within 30 seconds.[5] In late 2011, Higgins was sentenced to nine months in jail along with former Synthes North America President Michael Huggins. Former Director of Clinical and Regulatory Affairs, John Walsh, was given a five month sentence, while former VP of Synthes, Richard Bohner, had his sentencing postponed. All four were fined $100,000.[7] The presiding federal judge thought that the hunger for profit caused executives to disregard "the sanctity of human life".[5] This case outcome proved that those at the helm of corporations could be held responsible and truly penalized for wrongdoing.

Was justice fully realized? Greed can be a powerful source of motivation. Opening up the market for VCF treatment

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would have undoubtedly provided excellent financial returns for Synthes. The vital question is this: does the blame rest solely on the manufacturer, or does it extend to the physicians using the product as well? In 2011, results from a study financed by the National Institutes of Health were released, entitled: "Financial payments by orthopedic device makers to orthopedic surgeons." In 2007, 939 orthopedic surgeons were paid more than $198,000,000 (over $210,000 per physician). A year later, 526 orthopedic surgeons were paid more than $228,000,000 (over $430,000 per physician).[8] Endorsing products provides excellent financial returns for physicians. While payment to push medical products is not currently considered unethical, is it good practice?

Physicians are traditionally expected to investigate treatment options and give unbiased opinions regarding which medication or device to use, if any. Economic influence from corporations negates that expectation. Parties involved (save the physician) stand to possibly incur more expenses, and patients stand to potentially take unneeded medication or undergo unnecessary procedures.[9]

Although the physicians trained for the Norian XR trials were given altered documents which hid certain properties of the product, they still should be held partially accountable. They have a responsibility to be thoroughly knowledgeable about the products they use and to test them without bias towards a specific outcome. Those employed in another Synthes study (ProDisc™) in 2006 were not in a position to be objective. The Attorney General of New Jersey, Anne Milgram, wrote that, "The investigation revealed that a majority of the physicians who participated in these clinical trials had significant investments in the products — investments that would have been worthless had the product failed to obtain regulatory approval from the FDA".[10] Financial conflicts of interest cloud physicians' minds, whether they accept money to favor a product or find it safe for market use.

For that reason, safety and efficacy must be tested impartially. Monetary incentives and close proximity to the corporation create subjectivity, and can even lead to dishonesty. Several doctors who worked for Synthes, including Dr. Barton Sachs, trained other doctors to use Norian XR. "On January 10 and 11, 2004, defendants Synthes and Norian held the first surgeon forum, which was approved by defendants Huggins, Higgins and others, at which approximately 30 surgeons were trained to use XR to treat VCFs, and at which the companies delegated to Dr. Sachs the task of explaining the warning on XR's label, 'not intended for treatment of' [VCFs]. The evidence shows that Dr. Sachs re-worded the warning".[6] In doing so, he played an active role in the alleged deceit of practitioners, patients, and the FDA. Additionally, Sachs was involved in the previously mentioned ProDisc™ study. He published several papers validating usage of that product,[11] and likely had certain "significant investments" referred to by the Attorney General.

Had the physician researchers in the Norian XR trials been more objective and thorough, they would have requested preliminary study information. They would have inquired as to why an Investigational Device Exemption was not needed. They would have noted that the substance was too liquid and prone to leaking. After each fatality, they should have questioned if it was the product which was deadly and not the happenstance of surgery. Ultimately, they should have refused to endorse a flawed product by continuing trials and jeopardizing human life.

In practice, physicians are welcome to employ off-label usage. The FDA only states that, "If physicians use a product for an indication not in the approved labeling, they have the responsibility to be well informed about the product, to base its use on firm scientific rationale and on sound medical evidence, and to maintain records of the product's use and effects".[4] Synthes failed as a corporation when they commenced unlawful clinical trials with a product they knew was unfit for use in the spine. The physicians failed when they let monetary incentives impair their ability to recognize a faulty product.

The responsible corporate officer doctrine was enacted in this case and dealt sufficient justice to one guilty party. It sets a precedent for future cases and serves as a warning to corporations who are employing the same unethical practices. Still, it is not enough. The government's next step should be to create legislation that would make physicians like Dr. Sachs who knowingly participate in unlawful trials and perpetuate harm more accountable for their actions. Further laws to regulate physician payouts (both cash and stock) by pharmaceutical and device companies, to increase the transparency of these transactions, and to require the investigation of both new and established products by truly independent sources could help deter financial conflicts of interest. More research is needed to document how widespread these questionable ethics are.

Clearly, at present, some biomedical device companies are willing to sacrifice positive patient outcomes in the pursuit of profits. If a physician cannot separate their clinical decision making processes from this industry, then not only are the companies spineless, but the physician is as well.

References for this article can be found at TuftScopeJournal.org

ORIGINAL ARTICLE

ARSENIC EXPOSURE IN THE BENGAL BASIN: DISCOVERY, CAUSE, EFFECTS, AND SOLUTIONS

Alon Slutsky

Arsenic is a naturally occurring element in the earth's crust. It is also a recognized Group A carcinogen by the U.S Environmental Protection Agency. The consumption of contaminated drinking water is the primary route of exposure to arsenic in humans. Chronic exposure leads to a wide-range of detrimental health effects, including cardiovascular diseases, such as peripheral vascular disease, ischemic heart disease, and cerebrovascular disease. Numerous other vital organs are affected as well, including the skin, brain, and liver. The World Health Organization recommends a maximum arsenic concentration of 10 ppb in drinking water. In Bangladesh, arsenic concentrations have been reported as high as 2,300 ppb. More than half of the tube-wells in Bangladesh are not in compliance with the WHO guidelines and approximately 70 million Bangladeshis are chronically exposed to unsafe levels of arsenic-contaminated drinking water. The situation in Bangladesh is considered to be the largest mass poisoning in history. This paper provides an in-depth analysis of the arsenic crisis in the Bengal Basin beginning with the factors that led to the discovery of the crisis and the origins that brought it about. Descriptions of the health effects and a discussion of potential solutions follow.]

INTRODUCTION

The West Bengal Government never acknowledged, appreciated or helped my work on the prevention of arsenic poisoning. – Dr. K C Saha[6]

The 1980's had its share of catastrophic environmental disasters. In 1984, thousands were killed and hundreds of thousands more permanently disabled due to a leak of methyl isocyanate from a Union Carbide plant in Bhopal, India.[1] In 1986, the Chernobyl nuclear power plant in Ukraine exploded, releasing harmful radiation into the environment and causing a significant increase in the incidence of cancers and birth defects.[2]

While these now notorious events took place, another massive environmental disaster was taking place in South Asia. This disaster was not man-made and the detrimental health effects were not immediate, two likely reasons why the situation was largely ignored by the Indian government and the international community for almost two decades. Few people seemed to notice that the largest mass poisoning in history was taking place in Bangladesh and India, where millions of people were being continuously exposed to arsenic contaminated drinking water.[3,4]

The arsenic crisis in the Bengal basin, which includes Bangladesh and West Bengal India, began when the people of the basin began to transition from a dependency on surface water to ground water in the 1970's.[5] The shift to ground water was borne out of necessity. Poor sanitary conditions compounded by heavy rainfall and flooding made surface water virtually non-potable, due to the presence of fecal matter, as well as pathogenic bacteria and viruses. The immense water supply located underground was widely believed to be free from the contaminants found on the surface and therefore safe for human consumption. With this assumption the United Nations Children's Fund (UNICEF) began a massive tube well drilling operation across the Bengal basin.[5] The immediate health benefits were remarkable. Infant mortality levels due to diarrheal diseases dropped steeply, similar declines were also seen in maternal mortality rates.[5] Many took the decline in waterborne diseases as a confirmation that ground water was safe. However, not everyone was convinced.

In 1982, two patients with mysterious skin pigmentations were referred to Dr. Saha, a dermatologist from the School of Tropical Medicine in Calcutta.[6] After his examination of the two patients, he disagreed with an original diagnosis of Addison's disease and instead suggested arsenic poisoning. It was his first encounter with arsenic poisoning, but he recognized the symptoms from his days as a medical student. Upon receiving news that other villagers were exhibiting similar symptoms, he travelled to Gangapur and tested the tube well. He returned with water samples, as well as nail and hair samples. He found it difficult to convince his colleagues at the university to run the costly arsenic tests, especially without sufficient evidence. After some urging they agreed and the results confirmed his suspicion. Arsenic was present in the water at levels reaching 500 parts per billion or 500 μg/L.[6] Dr. Saha notified the villagers not to drink from the contaminated water and to find other sources of water. With no safe water available, the villagers sent mass petitions to the government demanding arsenic-free water.

Dr. Saha was shocked when he was told by a government minister to stop inciting villagers against the government. He ignored the request and continued to investigate the scope of the problem and publicize it. What began with one affected village is now known to affect the entire Bengal basin with an area of 569,749 sq. km.[6] Arsenic concentrations have been reported as high as 2,300 ppb.[7] The World Health Organization recommends a maximum arsenic concentration of 10 ppb in water.[8]

SCOPE OF THE PROBLEM

The people of the Bengal basin are not the only ones suffering from arsenic exposure. Naturally-occurring high

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arsenic concentrations have been reported in China, Vietnam, Taiwan, Thailand, Nepal, Pakistan, Myanmar, Cambodia, Mexico, Chile, and Argentina.[7] It is believed that other contaminated areas will be discovered in the future.[7]

It is estimated that a quarter of the tube wells in Bangladesh contain arsenic concentrations above the 50 ppb standard.[9] 57% of tube wells were found to exceed the WHO's 10 ppb standard. The extent of contamination is diffuse, but the brunt of exposure is concentrated in the south-east of the country.[9] With 97% of the rural population deriving its drinking water from tube wells, somewhere between 35 and 77 million people are being exposed to arsenic.[9,10] In West Bengal, it is estimated that 1.5 million people are exposed to arsenic-contaminated drinking water and that 200,000 people are already suffering from arsenicosis.[10] The numbers are growing but approximately 100 million people worldwide are being exposed to dangerous levels of arsenic.[5]

The risk of arsenic exposure is not only limited to groundwater. Arsenic has also accumulated in rice paddies of Bangladesh. Rice is a staple providing 73% of the caloric intake for Bangladeshis.[5] Rice was found to contain 46 μg/g in affected areas, compared to 10 μg/g in areas with low arsenic concentrations.[11] The rice is contaminated both by the large quantities of water it demands, as well as the contaminated soil from which it grows.

"This disaster was not man-made and the detrimental health effects were not immediate..."

GEOCHEMISTRY OF THE ARSENIC CRISIS

A number of hypotheses have been put forth to explain the geochemical mechanism by which arsenic dissolves, becomes soluble, and contaminates ground water in the Bengal Basin. The most accepted explanations that are applicable to the Bengal basin include the oxidation of sulfides containing arsenic, and the reductive dissolution of arsenic-bearing oxides and hydroxides.[12] Until recently it was believed that these two mechanisms could only exist independently. However, recent evidence suggests that they are most likely occurring simultaneously.[12] This could explain why arsenate is stable in oxidizing environments, and arsenite is stable in reducing environments.[13] In ground water dissolved arsenic is found almost completely as arsenate [As(V)] or arsenite [As(III)].[13] Arsenite is the most toxic form of arsenic.[13] Although both mechanisms are believed to play a role, the role of reductive dissolution is the primary driver of arsenic contamination in the Bengal basin.[14]

Defining the mechanisms by which arsenic dissolves in ground water is difficult because of the multitude of factors that likely play a role, including microbial activity, pH, and the presence of other elements. These factors lead to a striking variability of arsenic concentrations over intervals that range from centimeters to meters apart.[15]

Some conditions that lead to elevated risk are aquifers that are rich in organic matter, nitrogen (because of its oxidizing power), phosphorous, and elevated concentration of microbes (that assist in creating anoxing conditions).[15] A correlation has also been found between arsenic concentration and diagenetically available Fe.[16] It is interesting to note that the concentration of arsenic in sediment is not indicative of the concentration of dissolved arsenic in ground water.[17] Rather, one needs to take note of the above risk factors.

In the Bengal basin, arsenic rich sediment is primarily found in the Quaternary alluvial, deltaic, and Holocene sediments transported by the Ganges-Brahmaputra-Meghna river system.[6] Deeper and older sediments such as Pleistocene have low arsenic concentrations.[6] It is commonly believed that arsenic concentrations have increased over time. However, research has not proven this.

HEALTH EFFECTS OF ARSENIC POISONING

The consumption of contaminated drinking water is the primary route of exposure to arsenic in humans. Therefore, it is also the most heavily studied route of exposure.[18] Because of the widespread arsenic exposure in the Bengal basin, among other locations, the health effects of chronic arsenic poising have been well-documented. On the other hand, there is a relative shortage of epidemiological studies dealing with acute arsenic exposure.

Chronic exposure to arsenic has been linked to a wide range of health outcomes. Chronic arsenic exposure has been linked to cardiovascular diseases, such as peripheral vascular disease, ischemic heart disease, and cerebrovascular disease.[9] Neuropathy has been documented in many arsenic contaminated areas (West Bengal, Alaska, Mexico) and has been shown to correlate with arsenic exposure.[19] Exposure has also been linked to the development of type 2 diabetes in five different studies conducted in Taiwan and Bangladesh.[19]

A linear relationship has also been established between the incidence of hepatomegaly and arsenic exposure.[19] The most recognizable effect of arsenic exposure is the occurrence of hyperpigmentation that causes black spots to form on the skin.[20] Hyperpigmentation is usually a precursor to the development of Bowen's disease, which is the most common form of skin cancer induced by arsenic.[20]

Inorganic arsenic is a recognized Group A carcinogen by the U.S. Environmental Protection Agency (EPA).[21] Besides skin cancer, arsenic has been linked to lung, bladder, liver and kidney cancer. Some researchers believe that the potential cancer burden in Bangladesh due to arsenic exposure will double from 103.5 to 229.6 per 100,000. [22]

After being ingested, arsenic enters the blood stream and comes in contact with many vital organs.[23] A reliable method of determining levels of arsenic in the blood stream is to measure how much arsenic is accumulated within keratin-based tissue, such as nail and hair. This method is useful because it provides a long-term history of arsenic exposure in an individual.[23] Inorganic arsenic is also metabolized into methylarsonic acid (MMA) and dimethylarsinic acid (DMA), which is then excreted in the urine. Analyzing urine samples for MMA and DMA levels can give a recent history of arsenic exposure,

as well as determine how much inorganic arsenic has been metabolized into less toxic MMA and DMA.

Due to the developmental differences between adults and children, arsenic affects these populations differently. A study conducted in North West Argentina in 1998, compared arsenic levels in adult women to children chronically exposed to concentrations around 200 μg/L.[23] The children were found to have nearly double the levels of inorganic arsenic in their urine, but lower levels of DMA.[23] This supports the contention that children are not as efficient in metabolizing arsenic, and therefore produce less DMA. This data lead researchers to believe that children may be more prone to arsenic's detrimental health effects than adult populations.[24] Differences in health effects have been noticed when stratifying by gender, age, and nutritional status.[23]

In the past decade new research has linked chronic arsenic exposure to decreased cognitive development in Bangladeshi children. The results of this study have been corroborated in similar studies conducted in Taiwan and rural China.[25]

Researchers from the Columbia University's Department of Psychiatry conducted the first systematic study measuring the effect of arsenic exposure on children's intellectual function.[25] The sample consisted of 201 children 9.5-10.5 years of age from the town of Araihazar, Bangladesh. Along with information regarding economic class, demographics, and education level, the primary water source used and urinary arsenic concentrations were recorded. The Wechsler Intelligence Scale for Children was used to obtain a standardized intelligence quotient, after adaptation of this instrument for Bengali culture. Water arsenic concentrations varied from 0.094 μg/L to 790 μg/L. As hypothesized, the researchers found a dose-response relationship between increased arsenic exposure and decreased intellectual function after adjustment was made for sociodemographic covariates.[25]

The study conducted by Wasserman et al. from Columbia University was corroborated by the findings of S.Y. Tsai and researchers from the Dept. of Neurology in Tzu-Ai General Hospital, Taiwan. Tsai et al. conducted a cross-sectional study examining arsenic's effect on cognitive development in adolescents. 49 junior-high students were grouped into high exposure and low exposure (520629.0+/-605824.2 and 13782.2+/-12886.0 ppm, respectively). The participants were then matched with controls for age, sex, education, body height, body weight, body mass index, and socioeconomic status. Each group was given four neurobehavioral tests. Dose-response was seen in all four tests. The high-exposure group performed worse on three out of the four tests. The researchers believe that the "unstable result" was due to the small sample size.[26]

The results of these studies are troubling. It is unclear how long the negative developmental effects last or if they are permanent. What is clear is that the cognitive development of an entire generation of children is being significantly affected.

(IMPROVED) DUG WELLS

A decade after the arsenic problem penetrated the consciousness of the Government of Bangladesh, a national water policy was adopted that encouraged a transition away from contaminated tube wells and back to dug wells that rely on surface water.[27] A study found that only 0.6% of dug wells surveyed exceeded the 50 ppb limit.[28] Dug wells are the oldest source of drinking water in Bangladesh, so the possibility of partially returning to a dug well system is undoubtedly possible.[29] However, in the days when dug wells predominated, almost 1 in 4 children under the age of 5 died of water borne diseases.[5] This tragic statistic is not easily forgotten or should it be. The Government of Bangladesh insisted that if dug wells were built with a strict adherence to WHO sanitary guidelines than the dramatic decrease in waterborne diseases would not be reversed.[27] Three important conditions required for building a safe dug well are: (a) at least 30 feet away from a latrine (b) away from penned animals (c) a safe distance away from possible is contaminating areas (industrial sites or croplands).27 Regular chlorination of dug wells has been shown to keep coliform levels low, and should be done at least every two weeks.[27] The cost of the Government of Bangladesh's pilot dug well program equaled approximately 5-7 USD per person served.

A dug well program initiated in West Bengal has reported similar findings. The dug wells successfully provided an alternate water supply with arsenic levels below 50 ppb.[30] However, attempts to regularly disinfect the dug wells succeeded in only 65% of the dug wells, while the other wells contained high levels of coliforms.[30] The researchers claim that despite the levels of coliforms in a percentage of the wells, no outbreaks of disease were reported.[30]

In theory, the dug well solution can work very well in decreasing the dependence on contaminated tube wells. But, the improper use and construction of dug wells carries significant risk and the risk of being exposed to deadly water borne diseases should not be the alternative provided to the population.

Improper construction and/or disinfection can expose the population to risk greater than the risk posed by arsenic contaminated water.[31] In addition, the technologies required to keep dug well water safe requires infrastructure and regular maintenance, a difficult and expensive task to provide in over 80,000 villages.[5] However, the pilot programs in Bangladesh and West Bengal demonstrate that on a community level with the appropriate oversight and infrastructure, dug wells can potentially provide safe water.

No matter what alternative water source is used, it is widely agreed that frequent monitoring of bacteria and heavy metal contamination, including arsenic, needs to be an integral part of any intervention. Consistent monitoring will allow appropriate adjustments and repairs to be completed before negative health outcomes have a chance to occur in the community. The arsenic problem had the opportunity to become such a wide scale crisis, in large part due to an absence of monitoring.[27]

RAIN WATER HARVESTING

Rain water harvesting has been used in South Asia for the past 1000 years.[32] The Bengal basin is subject to heavy rains during the monsoon months, so naturally attempts to tap rainfall as an alternate water supply have been considered

and implemented to some degree. Rainwater is free from the soluble arsenic found in the sediment of the Bengal basin and is also free from anthropogenic contaminants found in surface water.[33] Calcutta, the capital of West Bengal, receives an average of 1765.1 mm (69.5 in) of rain a year.[34] Some parts of Bangladesh receive 2400 mm (94.5 in) of rainfall annually.[35] Rain water is successfully harvested in other countries, such as in the rural parts of Argentina.[36] Bangladesh receives 80% of its rainfall during the monsoon and therefore harvested rain water can only be useful if it lasts throughout the dry months, which can be as many as 9 months.[37] The issue than becomes one of storage. How does one store enough water for the dry months, while also keeping it free from contaminants?

The size of the tank, determined by the intensity of rainfall and the size of the catchment area is the most expensive part of the system.[35] The catchment area is most likely the roof of a house connected by gutters to a storage tank. The most efficient roofs for rainwater harvesting are cement roofs.[35] This aspect of the system makes it untenable for the poor whose roofs are thatched and unable to catch rain water.[35] Other methods have been designed for these communities, such as using plastic sheets or polyethylene.

Although the rain is pure when it falls, it deteriorates in quality during the process of harvesting. The first run off from the roof is always discarded due to the presence of bird droppings, dust, and other impurities. While in the tank, treatment with bleach is required at least twice a year to minimize algae growth.[35] Upon the testing of 40 rainwater harvesting systems in Bangladesh, the mean pH was found to be 9.33, with the highest measurement being 10.9.35 The reason for the high pH is believed to be from the calcium oxide found in the material used in the storage tanks. To make matters worse, rainwater also may leach lead out of certain roof materials.[35]

Despite these issues, appropriately maintained and installed rainwater harvesting systems are relatively low risk and can be used in high rainfall areas as an alternate safe water supply. To date, the rain water harvesting systems have been used most frequently and successfully in schools.[35]

DEEP TUBE WELLS

One of the more promising alternate water supply options being funded by international aid organizations is deep versus shallow tube wells. A benefit of deep tube wells is that it does not require a change in behavior; 90% of the population currently use shallow tube wells.[38]

From a geological standpoint, deep tube wells are very enticing. The majority of arsenic making its way into the ground water is leaked from rocks found in the geologically young Holocene sediment.[39] The sediment is divided into three aquifers, upper aquifer, main aquifer, and deep aquifer.[39] Because of the geographical differences throughout the basin it is difficult to define these aquifers using strict measurements.[40] The majority of water presently withdrawn in the Bengal basin is removed from the hydraulically connected Upper and Main aquifers and is commonly contaminated with arsenic. According to the British Geological Survey, 99% of deep tube wells (reaching past 150 m) contain arsenic levels below 50 ppb, and only 5% were above 10 ppb.[41] In addition, a study reports that the prevalence of diarrheal decreased twice as much in households utilizing deep wells compared to households utilizing shallow wells (approximately 45m deep).[42]

However, researchers have been slow to fully embrace deep tube wells. The geographical layout of the basin is not uniform, and areas exist that do not have a water-impermeable layer separating shallow and deep aquifers. These areas will likely produce arsenic free water at first, but as the sediments mix the deep aquifer water will become contaminated.[35] This has already occurred in the villages of Jessore and Sylhet where deep tube wells are contaminated.[35] On the other hand, the coastal areas of Bangladesh have an impermeable layer between aquifers and water is replenished in the aquifer through horizontal water movement. These locations will most likely provide arsenic free water permanently, but will still require operational oversight.[35]

An extensive analysis of the geological milieu was published in 2006 by the Government of Bangladesh. The analysis determines where deep aquifers begin across the country and which aquifers are suitable for deep tube wells.[40] The analysis is ongoing and hopefully will provide a sufficient understanding of deep aquifers and how to tap its possibly safe waters. The painful lessons learned from the indiscriminate drilling of millions of shallow tube wells have been learned. As a result, deep tube wells have been dug only in select areas until further research is completed.

Already we have created, may be inadvertently, many problems for the shallow groundwater resources of the country. We should not do the same for the deep aquifer as this kind of ultimate frontier for water supply of the country; we need to protect the deep aquifer for the coming generations. In order to protect the deep aquifer we need to understand the geology, hydrogeology, hydraulics, geochemistry of the deep aquifer.[40]

ARSENIC REMOVAL TECHNOLOGIES

A number of methods have been designed to remove arsenic from water on the household and village level. These technologies strive to be affordable, easy to maintain, and user-friendly. An important goal of these devices is to filter a sufficient amount of water in a reasonable amount of time. If they fail to do so they risk being rejected by the population. This paper will examine two specific arsenic removal projects, one in West Bengal and the second in Bangladesh. The project in West Bengal will serve as an example of a failed intervention, while the project in Bangladesh will demonstrate what a successful intervention may look like.

By the 1990's, the arsenic crisis in West Bengal was becoming more well-known and national and international organizations were scrambling to develop possible interventions that could mitigate peoples' exposure to unsafe levels of arsenic. By 2007, more than 2,100 Arsenic Removal Plants (ARPs) were installed at an average price of USD $1,500 per unit and totaling USD $3.15 million.[41] Researchers from Calcutta's School of Environmental Studies decided to monitor the effectiveness of the ARPs by following the installation of 19 plants in the district of Baruipur for 2 years.

The 19 ARPs were designed by 11 manufacturers some Indian and some international. They found that 13 of the ARPs (69%) failed to reach the target arsenic concentration set by the manufacturers.[42] It should be noted three of the manufacturers cited arsenic-free water as their goal. The researchers deemed this goal impractical, if not impossible.[42] Six of the plants (46%) failed to reduce arsenic below 50 ppb. Two plants successfully filtered water with arsenic concentrations below 50 ppb consistently. None could lower arsenic concentrations enough to meet WHO guidelines of 10 ppb.[42] When the researchers came back in 2005 to assess the ARPs, only 3 out of the original 19 ARPs were still in operation.42

The researchers outlined three reasons why the ARPs failed: (a) poor maintenance (b) clogging (c) lack of user-friendliness. They extended their scope to 202 other ARPs and deemed 90% of them not useful.[43] It was the opinion of one of the researchers that the ARP manufacturers were testing their products on the villagers before the devices were ready for human use.[41]

A completely different story arises in Bangladesh regarding the design and distribution of the SONO filter. The first important difference to note is that the Government of Bangladesh created BETV-SAM, which stands for Bangladesh Environment Technology Verification-Support to Arsenic Mitigation, in the year 2006.[43] No arsenic removal technology may be installed in Bangladesh without prior approval by BETV-SAM. (This author was surprised to note that a lead partner for BETV-SAM is the Canadian International Development Agency, which was also a lead partner in installing the ARPs in West Bengal a few years earlier. Perhaps they wished to correct past mistakes.) As of now, the SONO filter is one of four technologies to have the green light to operate in Bangladesh.[43]

The device is fairly simple. It is composed of two buckets. The first bucket is filled with iron chips and coarse sand, and the second bucket is filled with wood charcoal and fine sand.[44] The technology relies on inorganic arsenic's affinity for metallic iron, while the charcoal removes organic impurities in the water.[44] All the materials are found locally. Its ability to remove arsenic from water is remarkable.

In multiple experiments, the SONO filter was able to remove 800 ppb of arsenic (III) to below detection limit (< 2 ppb).[44] The filter also reduced the concentration of soluble iron from 6000 ppb to 200 ppb (permissible level is 300 ppb).[44] The filtration system cost USD $35, is projected to last for a minimum of 14 years, and can filter up to 100 L a day.[45] Another filter has been designed for communities that can filter 100 L an hour.[45] As of 2010, 225,000 filters have been installed in Bangladesh with a few hundred installed in India and Nepal as well.[45]

The SONO filter is easy to use, does not require virtually any maintenance, is locally made, environmentally friendly, affordable, and most importantly effectively removes arsenic from water. It is by far the most promising technology currently available.

CONCLUSIONS

Since Dr. Saha identified the first few cases of arsenic poisoning in Gangapur in 1983, much has been learned about the scope of the crisis. However, much still remains to be learned. More time and funding needs to be allocated to explaining the mechanisms by which arsenic becomes mobile in ground water, as well as possible treatment options for people currently suffering from arsenic related illnesses, by the international community and the governments of India and Bangladesh. There are undeniably other priorities facing these countries, but there is no excuse for leaving millions of people without access to arsenic-free water for 20-30 years. The long list of health effects mentioned in this paper highlight the urgent need for an emergency intervention in the most affected areas.

Based on my research, low-risk and affordable solutions such as rainwater harvesting and the SONO filters should be immediately installed in Indian and Bengali villages. Immediately after the areas safe for deep tube well drilling are identified a large scale re-drilling operation should be implemented. All interventions should be carefully monitored for arsenic and hazardous coliforms with reports made publically available to community members. Knowledge regarding the arsenic problem alone does nothing to protect individuals from exposure. Useful and applicable solutions need to go hand-in-hand with the most recent information.

Although this research paper focused primarily on the Bengal basin, much of the lessons learned in India and Bangladesh are applicable to the other countries faced with arsenic exposure. By joining efforts and sharing information affected governments can more provide data driven and field tested solutions.

The shear magnitude of the crisis in the Bengal basin makes a solution appear impossible. However, the people of the basin have proven to be remarkably resilient and they deserve the best solutions and research available today. The crisis has come a long way from the early days of denial and shock. Solutions and support must be supported by community involvement and government resolve.

References for this article can be found at

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ORIGINAL ARTICLE

A Health Care Crisis: My Experience in Nepal

Alana Fruauff

Health care reform has become one of the most pressing issues for nations throughout the world today because it is such an important aspect in maintaining a fair standard of living. Perhaps the most urgent concern is the health care of developing countries because these nations have such poor populations and limited access to resources. The people of these nations suffer from immensely inadequate health care if they receive any health care at all. These countries also often have a strong history of traditional medicine and thus, the development of modern facilities is impeded by these cultural customs. My desire to better understand the reality of health care in developing countries led me to design a study focused on the health care issues in Nepal. The isolated nature of Nepal and its strong cultural heritage made it a perfect location to study the development of modern medical facilities in coexistence with traditional systems. After spending the summer in Nepal navigating health care facilities, interviewing health care personnel, and becoming familiar with the people of Nepal, I gained invaluable knowledge and experience that has allowed me to effectively reflect on health care policies in Nepal.

Because Nepal has a long history of inadequate allopathic facilities, traditional medical facilities have always been a major source of relief for Nepalese people. Ayurveda, Tibetan Medicine, and Chakra are three of the most prominent traditional systems present in Nepal. These alternative medicinal systems are still ubiquitous in Nepal today, even with the advancement of allopathic facilities. This speaks to the cultural and social importance of these medical systems to Nepalese people. These systems have been passed down for generations, and they incorporate many spiritual aspects important to religious life. Traditional systems are particularly important in villages, where allopathic medicine is very limited. In the absence of modern medicine, many villagers use their local resources for healing, and thus herbal systems such as Ayurveda persist. Although alternative medical systems are present in urban centers, they aren't as dominant or as authentic as those in more rural places. Traditional systems in the city are normally used as an alternative option. Several doctors and administrators informed me that alternative medicine in the city tends to be used by people with specific diseases, especially chronic ones, such as gastritis, arthritis, jaundice, and mental illnesses. Additionally, urban residents use alternative medicine when they feel that modern medicine has failed them. Whether traditional systems are used as an alternative option or as the primary care system, it is apparent that traditional medicine is integral to society. Most Nepalese people believe in these traditional systems and a substantial amount of people even prefer traditional medicine because they are skeptical of modern medicine and its side effects.

Although traditional medicine is a major component of Nepalese health system, the development of allopathic medical facilities has allowed increased emphasis on allopathic services. The allopathic health care sector in Nepal is divided between public facilities run by the government and private amenities that are independently funded. A large portion of my experience in Nepalese health care took place at Paropakar Women's hospital, which is a government hospital in the capital, Kathmandu. Government hospitals tend to be much more affordable than private ones and as a result, a majority of patients in these facilities come from the lower and lower-middle classes. Because there is a shortage of medical facilities, the hospitals are extremely overcrowded with patients. There is also a great shortage of faculty resulting in a very hectic, congested environment not conducive to productivity and optimal patient care. In 2004, the World Health Organization (WHO) reported that there were only two physicians and two professional nurses for every 10,000 Nepalese people.[1] The shortage of physicians in the country is worsened by the fact that many physicians want to leave the country to find work elsewhere. An article from the Himalayan Times sited a "lack of security, poor remuneration, and limited opportunities for professional development" as reasons for doctors leaving the country.[2] As a result of the shortage, government hospitals are known for having long queues and slow service. This has caused a distinctive form of health care to emerge in Nepal. Physicians are forced to strategize—choosing only certain tests and medicines—in order to efficiently diagnose and treat patients while also keeping costs low. Physicians must also be extremely efficient so that they may tend to the large number of patients awaiting care. In many cases, however, this means that treatment is compromised because physicians are less thorough and attentive. In the gynecology outpatient department of the Paropakar Hospital, for example, physicians spent roughly four minutes on each patient—barely enough time for a few questions and a quick physical exam.

The high ratio of patients to physicians is only one of many urgent problems facing this poor country. To make matters worse, the hospital has greatly inferior facilities that debilitate the staff's ability to perform. In general, the technology is about fifteen to twenty years behind the Western world, and the technology that does exist is immensely inadequate. For example, there is only one ventilator at Paropakar Hospital, and at one point two newborns needed the ventilator, which resulted in one baby eventually dying. Additionally, the city lacks technologists and as a result many machines have

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no operators or repairmen. The mammography machine at Paropakar hospital was out of service for months simply because they had no technologist to work it. Another prime example of the lack of adequate facilities can be seen by the government's attempts to initiate transplant services. In 2004, the government tried to start kidney transplant services at a city hospital, but failed because of "a lack of expertise and adequate equipment."[3] Even now that hospitals have started transplants, they are so under-resourced that only one transplant occurs a week and appointments are booked for eight months in advance.[3] This is the case for a lot of care: patients are forced to wait weeks or months for procedures due to a lack of staff and equipment. In addition to inadequate facilities, basic accommodations are deficient and sanitation efforts are dismal.

Although care in the capital is inadequate in many ways, there is still a reasonable amount of accessible facilities. This cannot be said about many areas in Nepal where health care facilities and personnel are even more scarce. The WHO reported that in 2002, there were only 4.26 hospital beds per 10,000 people in Nepal.[1] There are considerably more beds in urban areas, whereas rural areas suffer tremendously from deficient beds. The hilly terrain and scattered populations of rural Nepal make it very hard to access remote villages, let alone provide care to them. The facilities that do exist in more remote places are difficult to staff because few physicians or nurses want to work there. The structure of the health care system itself illustrates the lack of widespread facilities. There are seventy-five districts in Nepal and each only has one district hospital. Below this, there are primary health care centers, which only have one physician each. Lastly, there are health posts that completely lack physicians. Additionally, district hospitals only have general physicians, so in order to see specialized doctors, patients have to go to zonal, regional, or central hospitals that are much more scarce. Most of the time, cases are sent to central hospitals in Kathmandu; however, this journey isn't practical for many patients because the transportation system is abysmal and the cost of travel is too high. Several physicians told me terrible stories about families that carry their sick relatives miles to reach a hospital.

Not only is health care sparse, but also it is unattainable for a considerable portion of the people in the country because it is such poor country. In 2005, thirty percent of the population was below the poverty line.[1] Several administrators told me that one of the greatest struggles for Nepal is making health care easily accessible and affordable for the masses. Although the care in government hospitals is significantly discounted and there are several programs to aid low-income patients, these measures are not sufficient. Every hospital only uses five percent of its government funds and five percent of their own profits for the care of the poor.[1] Although primary care is fairly accessible for most patients, higher care, such as surgeries is largely inaccessible because the costs are too high even after receiving aid. Many patients also struggle to pay for medicine, which is not normally discounted through the hospital. To make matters worse, most people are not aware of the importance of looking after their health. Hygienic measures aren't practiced among many people leading to propagation of diseases. In 2005, only thirty-nine percent of the population had adequate sanitary disposal facilities available.[1] Systemic preventative care is also largely non-existent. Patients usually come in late stages of their illness, making it hard for doctors to treat them and increasing the costs of their treatment.

The issues I faced while working in the allopathic facilities were alarming. Everywhere I turned there seemed to be inadequacies resulting in inferior delivery of health care services. Most of the health care problems stemmed from poor government administration and insufficient funding. In 2003, only 5.1 percent of the national budget was devoted to healthcare measures.[1] The country depends largely on aid from other countries but this aid is not enough. Furthermore, poor administration prevents efficient use of this funding. For the past ten years, Nepal has seriously struggled with political instability and incompetency. The nation has been desperately trying to institute democracy and a constitution but these measures have been largely unsuccessful. The constant power struggle that ensues prevents productive administration and policies cannot be effectively implemented. This severely debilitates health care reform. In order for health care reform to be effective, the Nepalese government must be reformed. If the Nepalese people can successfully institute democracy and instate a more effective government in the next few years, it would be instrumental for the nation's health care. Thus, it is very important for international aid to help initiate effective health care policies and it may even be important for foreign authorities to help ease the country's transition into democracy.

Although political reform is crucial, health care reform must coincide with government reorganization in order for progressive measures to be made in the health care sector. The wide range of daunting issues plaguing Nepalese health care must be addressed in order to preserve the country and its health. International intervention is essential in this quest because without positive influences, Nepal will remain as it is. First, foreign aid must continue with even greater amplitude because without funds, no changes can be made. Additionally, it is essential that the medical community donate equipment to Nepal so that the country can build up its supplies. Shipping money and equipment to Nepal, however, will not be sufficient because the same mistakes will persist. International intervention must increase drastically to fix the multitude of problems. Foreigners need to take action in Nepal and promote a more positive role for the government in health care. International aid should train technicians and initiate programs that can continue to train them. Also, aid must help create new health facilities so that existing ones aren't so scarce and overcrowded. In order to staff the facilities, Nepal must begin to promote careers in the health sciences. Measures must also be made to reach out to the Nepalese people to inform them about the importance of maintaining healthy lives. Although these are just minor steps, they will help lay the foundation for a greater future for Nepal.

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ORIGINAL ARTICLE

The Gambian Health Care System:
An Investigation Into the State of Prescription Drugs

Jonathan Lis

This piece aims to detail a seven-week medical volunteering trip to The Gambia during the summer of 2012 and to identify and offer solutions for the problems facing the state of health care. Most notably, the lack of quantity and diversity of prescription medication is addressed. The state of prescription medication is viewed through the lenses of the central government and the practices of the nurses. This piece does not intend to demand change for The Gambia, it simply outlines the apparent problems and suggests methods of improvement.

I distinctly remember my first thoughts upon entering Banjulunding. They were nearly all some form of bewilderment. This sandy, humid, yet strikingly beautiful place was to be my home and worksite for seven weeks. As we approached the health center compound, children emerged from behind walls and trees to see us "toubabs" (white men) entering their home. It was barely dawn, but already the humidity had caused me to perspire through my shirt. I didn't have the luxury of changing, because my bag had been sent to Conakry and was happily exploring Guinea, 1100 km to the Southeast. That first day was nearly overwhelming, but I soon gathered myself and assimilated into the community to the best of my abilities.

I had come to The Gambia (the smallest country in continental Africa), with Operation Crossroads Africa, a nonprofit organization that has been sending American college-aged youths to Africa to work on a variety of service projects for over fifty years. My assignment was to work in the Banjulunding Health Center, assisting the nurses and providing inpatient and outpatient services to the patients. Most of the patients turned out to be pregnant women, women who had recently delivered children, and children under the age of five years. The nurses who worked at the health center were quite knowledgeable, and were well trained in common ailments of sub-Saharan Africa, such as malaria (mostly the P. Falciparum form) and septic wounds.

On my first day of work, it was painfully clear that this health center lacked basic tools, technology, and sanitation. The labor ward was the first ward in which I worked, a small one-window room with a dysfunctional ceiling fan that rendered it scorching. I witnessed a birth of a baby girl to a young woman. The only tools at the midwife's disposal were latex gloves, a small wooden instrument with which it was possible to hear the fetal heartbeat, and some scissors and forceps that were bloodstained from the last birth that took place a few hours earlier. The mother lay on her back on a flat, black bed that better resembled a trainer's table than a true hospital bed. The baby, once born (without any painkillers or epidural for the mother), was wrapped in cloth that the mother brought with her, and the placenta was taken care of with a similar self-brought cloth. Blood covered the floor and bed, and flies began to swarm in even larger quantities than before. Soon after, an old male orderly came by to mop it all up.

As incredible and beautiful it was to witness the entrance of a child to the world, it became difficult over time for me to understand the poor health care system. Accessibility, it seemed, was not an issue. Anyone and everyone who wanted access to health care could achieve it, because of the low cost (about fifteen cents per visit) and many locations of health centers or clinics. Children under the age of five were seen for free, and were given a special chart to document patient information and all previous ailments and vaccinations. Thus it is logical that children under the age of five made up the bulk of the patients we saw.

Apart from the easy access to medical care, the system was indeed extremely inefficient and unacceptable by Western standards. First, patient records and medical histories were essentially nonexistent. There was a register in which the patient's name, ailment, and treatment were documented, but this register was never consulted when examining a patient. It was as if every patient was a brand new patient, even if he or she had been there only a few days earlier. This makes diagnosis very difficult, and is part of the reason why the nurses there treat symptoms rather than attacking the cause of the disease.

Additionally, there is quite simply a dire lack of proper tools and technology. The utilization of old, unsanitary tools renders patient care less safe, with a higher possibility of transferring pathogens and bodily fluids from patient to patient. The Banjulunding Health Center only had one working thermometer and one (barely) working blood-pressure cuff. These instruments were not cleaned or wiped between uses, as cleaning supplies themselves were scarce. Often the blood-pressure cuff or thermometer would be transferred from a patient in the outpatient ward to one in the labor ward to one in the inpatient ward. The lack of technology, especially in a diagnostic sense, was also apparent. Frequently patients would arrive complaining of headache, fever, and vomiting. We would test these patients for the P. Falciparum form of malaria using a simple assay, and more often than not this test would come back negative. Then, with no further tests at our disposal, the nurse would prescribe a painkiller and a generic antibiotic. Nearly every patient received these two prescriptions.

The state of prescription drugs was especially interesting to me, since much of my work at the health center was directly dependent upon the inventorying and dispensing of

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medication. Prescription drugs were available to patients at no additional cost if the health center had the medication in stock. The government would ship prescription medication to the health center monthly, but often these shipments were late or insufficient to meet patient needs. Other than vaccinations for children under five years, nearly every prescription drug ran out at some point. The supply simply could not keep up with the demand for the drugs, especially the antibiotic Septrin and the painkiller acetaminophen (the two medications prescribed to nearly every patient). This meant that people would have to go to the pharmacy and buy the drugs themselves, which they rarely did due to a lack of funds.

Unfortunately, when there was a rare surplus of medicine at the health center, the head nurse would typically ration it. In order to make the drugs last longer, the nurse would limit the amounts dispensed to patients. One may argue that rationing drugs is illogical, because they should be given to whoever is sick at the time. However, since the health center was not truly a 24-hour facility, the sicker patients typically showed up in the morning. Thus, those who showed up in the afternoon were often denied prescriptions and were forced to go to the pharmacy if they wanted drugs.

But who can be to blame for the scarcity of medicine? Surely it cannot be the fault of the sick, who have barely any control over their medication needs. I believe that the fault lies with the central government and the practices of the nurses. No one entity is entirely to blame, but I believe it to be a mixture of both.

The majority of the fault I believe lies in the hands of the central government. There simply needs to be a more efficient method of medication purchasing and distribution to the national health centers. The government would argue that they are doing their best to provide for the people, but there is much more that can be done. For one, creating electronic patient records and improving treatment documentation would greatly aid the nurses in diagnosis and in prescribing the proper medication. Having access to a patient's medical history is crucial to targeting illness and disease. However, in order to achieve this, a stable power grid is essential. Having electricity only fifty percent of the day makes this electronic patient history useless. If the government can achieve a stable power grid and set up an electronic patient record, the prescription process would become more efficient, perhaps using less or different medication to better treat illness.

There is even more than can be done. Ensuring that people actually pay their taxes can increase tax revenue, and this increase in tax revenue can be used to purchase more prescription medication, hire a few workers to oversee its efficient distribution, and perhaps even purchase goods such as bandages and sanitary supplies. If the government were half as dedicated to its people as its billboards state, it would be more serious about collecting tax revenue and distributing it to meet the needs of its people's health.

In addition to bolstering tax revenue for health care spending, there needs to be an attitude change within the Gambian government. There is still much hesitation about Western medicine (especially with AIDS), as the president His Excellency Dr. Prof. Sheikh A.J.J. Jammeh feels AIDS medication to be poison and believes with the utmost conviction that he can cure AIDS with more traditional herbal methods.[2] The World Health Organization maintains that there is no current cure for AIDS, and no valid third party has verified the president's claims. Regardless, the arrogance toward Western medicine is fueling the negligence for medication and supplies for the Gambian people. The government needs to embrace modern medicine, not shun it. This attitude change begins at the top, and either the president needs to adopt this change or the people need to adopt a new president. (The Gambian people seem to think positively of President Jammeh, however, and he has been in power since 1994.) Unfortunately, the Gambian economy is simply not advanced enough to handle a privatization of medical care and insurance. Therefore, the most powerful institution in the country, the government, needs to take control of improving the state of health care.

The government's inadequacies concerning medication are not the only flaw in the Gambian health care system. The practices of the nurses are also partly to blame for the frequent lack or rationing of medication. I do not blame the nurses themselves, as they are simply doing what they have been trained to do. I do, however, blame their practices and

Table 1: List of prescription medication (tablets or capsules) available at the health center[1]

Medication:	**Use:**
Priton	Common cold
Diclo	Painkiller
Salbutamol	Asthma
Acetaminophen	Painkiller
Septrin	Antibiotic
Amoxicillin	Antibiotic
Oral Rehydration Salt	Dehydration
Flagyl	Abdominal pain, Diarrhea
Bico	Vitamin B deficiency

methods, given to them by their teachers and superiors.

Many modern doctors are very hesitant to prescribe antibiotics, and do so only when necessary. The recent rise in discoveries of antibiotic resistant bacteria has forced the medical world to be wary of prescribing antibiotics in cases where they are unnecessary. This caution has not found its way to The Gambia. The antibiotic Septrin was given to roughly three quarters of all patients who received a prescription, and the nurses also prescribed amoxicillin rather liberally. Patients complaining of a simple fever (no malaria) were frequently given an antibiotic to fight a possible infection, and patients with septic wounds often received antibiotic pills when simple topical creams would have sufficed. This eagerness to prescribe antibiotics is not only dangerous to public health, but it causes the inventory of available prescriptions to decrease to the point of rationing or exhaustion.

What can be done to change this? This answer I believe to be much simpler and much more easily achieved. There needs to be intervention, either from Gambian doctors or from foreign professionals, to address the issue of over-prescription. Educating the nurses to prescribe medication more conservatively, yet still effectively is key. The multitude of foreign doctors who work in the main hospital in Banjul, the capital city, have an obligation to educate the nurses and others prescribing medicine about proper and efficient antibiotic prescriptions. It shouldn't take very long for the nurses in the main hospital to pass their new practices onto the nurses in the health clinics, as nurses travel between the hospital and clinics often.

Unfortunately, change is often slow. Advances in Gambian medicine have taken a back seat to infrastructure improvements such as road paving and the construction of new government buildings. I believe that stable electricity may be necessary before my suggestions for health care improvement can occur. I believe that the economy must grow and new industries must arise to create jobs and increase GDP. I also believe that the prescription process and Gambian health care as a whole can become more efficient and better serve the nation within a few years. I hope that upon my return, whenever that may be, I am able to witness a vastly improved health care system operated by the same jovial and selfless health care professionals with whom I became great friends.

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RESEARCH HIGHLIGHTS:

Depression May Be Related to Survival of Patients with Renal Cell Carcinoma

Ariel Lefland

A recent study published by PLOS ONE identified symptoms of depression and dysregulation of cortisol as key factors in predicting survival in renal cell carcinoma (RCC) patients. The study provides the first evidence of this association, controlling for disease- and treatment-related factors such as age, sex, ethnicity and disease risk index.

In a prospective study, researchers followed 217 patients with RCC, a life expectancy greater than four months, a Zubrod performance status of less than or equal to 2 and no other serious illnesses. Patients gave blood and saliva samples and completed several psychosocial questionnaires (i.e., the Centers for Epidemiologic Studies - Depression, or CES-D). Whole-genome transcriptional profiling was performed on samples from 15 patients with the highest levels of depressive symptoms. Transcript analyses indicated an up-regulation of genes involved in inflammation, immune response and negative regulation of programmed cell death and a down-regulation of genes involved in cell trafficking, adhesion, oxygen transport and hemostatis. in patients with high CES-D scores, 116 transcripts were found to be up-regulated by an average of 50% or more, and 57 transcripts were down-regulated by 50% or more. Furthermore, individuals with high CES-D scores had significantly greater tumor-associated macrophages compared to patients with low CES-D scores. Researchers also found that cortisol regulation may play a role in the correlation between symptoms of depression and cancer progression.

While this study cannot show that depressive symptoms lead to the progression of RCC, it demonstrates an important connection between psychological wellbeing and disease prognosis. More research must be conducted to determine whether depressive symptoms decrease survival rates or if RCC, in fact, causes these depressive symptoms.

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ORIGINAL ARTICLE

The Adirondack Region Medical Home Pilot:
Advances in Adirondack Health Care and Continuing Challenges for Rural Seasonal Workers

Daniel Farrell

The Adirondack Park in Upstate New York is a six million acre mountainous area that past generations of Americans had the foresight to limit from overdevelopment. However, the very conditions that maintain this wilderness have created a rural population that rely on service and public sector jobs, many of which are seasonal. The Adirondack Region Medical Home Pilot is an 'experiment' that began in January of 2010 to address the low numbers of physicians in the area, and the rising costs of healthcare. Through a series of interviews with those involved in the Pilot, both physicians and administrators, I learned about the changes of the Medical Home model and what it has done for the region's health care system. Through interviews with seasonal workers and people involved in insurance policy, I learned of the challenges that remain in the area for seasonal workers to secure health insurance coverage.

The fact that many seasonal workers go without insurance or struggle to find coverage brings to light deficiencies in the traditional system of health care and health insurance, a system that is experiencing many changes. One change is the Adirondack Region Medical Home Pilot, which is working to reduce health care costs and establish a more productive system of health care delivery. While the Medical Home Pilot does not directly increase health care access for seasonal workers, it can benefit them indirectly because it is an important step in making health care in the Adirondack region more efficient and affordable.

A Medical Home is not a place, rather it is a model of health care geared specifically toward the patient that provides extra support when necessary and improves efficiency. Financially, a big change has been that insurance companies are paying health care providers an extra $7 each month for each insured patient at their practices. Deciding which patients are considered members of the Medical Home was a difficult back and forth process between the insurance companies and the health care providers, but it has improved during the two and a half years the Pilot has been running.[1,2] The extra money has funded the start up and/or improvement of care management and electronic medical records (EMR). While each practice uses the money in varying ways, the practices share an end goal of providing better quality care, as opposed to the traditional goal of seeing as many patients as quickly as possible.[3,4] This is a big change for the health care system, as insurance companies are replacing the traditional "fee for service" model with a new "pay for performance" model, at least for the duration of the five year Pilot.[4] More specifically, Dr. Alison Guile has found "a real change" to be the regular meetings of physicians in the community. Physicians and administrators from different practices now discuss how they want the Medical Home funds to be used and what they want to achieve as a group.[5]

The Medical Home Pilot began as a collaborative effort between three major health centers in the region, as well as their surrounding primary care practices, as they were all experiencing a sharp decline in primary care practitioners. Dr. John Rugge, one of the leading organizers of the Pilot, related that they wanted a model that would make physicians "feel rewarded and satisfied, not just financially" and he believes the Medical Home can draw and keep physicians in the area. Champlain Valley Physician's Hospital (CVPH) President Stephens Mundy has attested that since the start of the Pilot he has seen better success at recruiting physicians, more physicians staying in the area, and more use of nurse practitioners and physician assistants. One physician currently has a medical student who knew about the Pilot shadowing at her practice.[6] However, with the high ratio of patients to doctors in the region, the efforts of the Pilot have only allowed Dr. Heidi Moore to see more patients and "drown a little less slowly."

The results of the Pilot are ongoing, and while the jury may still be out on cost savings, there are indications of increased efficiency that could make health care more financially accessible. Frequent users of the system, who drive up costs, receive more care management now, such as extra follow-up and referrals to services such as diabetic educators and nutritionists.[2,3,4] Special focus has been placed on recently discharged patients in an effort to reduce "preventable" readmissions (readmissions to the hospital within 30 days of discharge for the same condition). At CVPH, the preventable readmission rate has decreased from 15% in May 2011 to 7% in April 2012, suggesting significant cost savings if each readmission runs approximately $10,000 (a low-end estimate).[4] Emergency Room (ER) visits are also beginning to decrease in some areas, and there has been a huge push to educate patients about appropriate use of the ER, as well as to call patients who have used it inappropriately.[2,3,6] The Medical Home administrators are currently trying to pool together the data collected during the Pilot to demonstrate the cost savings to the insurance companies.[4,2,7] Although the Pilot is a five year agreement, physicians and administrators are confident that insurance companies will continue to work with and fund the health care providers

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because it is in their "best interest to share savings, share information and encourage better models of care." [1]

Despite the advances in the medical care of the Adirondacks that can be attributed to the implementation of the Medical Home Pilot, seasonal workers still have limited health insurance options. Erika Walker, a Community Health Advocate, receives calls from many seasonal workers and uninsured individuals, whom she helps to find low cost health insurance. Her position is not a result of the Pilot but was started with grant money from the Affordable Care Act (ACA), and she currently covers six counties in the region. Walker related that while seasonal workers can be on Medicaid or state programs in the off season, they often no longer qualify for these plans once they report income from a seasonal job. Other premium-based health insurances exist, such as Healthy NY and the NY State Bridge Program for pre-existing conditions, but these can be expensive with monthly premiums of at least $181 along with a deductible of $1200, which still represents a significant sum of money for someone working seasonally.[8] Michelle Be, a young seasonal worker, said that it is "hard for us in the Adirondacks because our income varies so much from week to week, month to month, year to year" and explained that health insurance is simply something she cannot afford to think about when she has a hard time just paying rent. When available plans are unrealistic for somebody, Walker looks for health centers that offer discounted payment plans based on income, or even suggests that individuals try to pay up front in cash at doctors offices and request the lower Medicaid rates. Regarding the option of buying directly from insurance companies, the individual market typically has higher cost and lower benefit plans, and at over $1000 a month, this is never an option for a seasonal worker.[8,9]

Additionally, employers of seasonal workers are faced with many reasons not to provide insurance. With the nature of seasonal work being short term and having high turnover rates, it is not typically in the best interests of employers or insurance companies to offer plans. There is also lot of "unrealized expense" involved in taking people on and off a health insurance plan, and there is a potential for high use in a short period of time.[9] David McKillip, Human Resources Director for ORDA, a large seasonal employer in the Adirondacks, said that as much as 75% of their employees during the peak season do not qualify for the health insurance, and that it would simply be too expensive to offer a seasonal health plan. Another potential concern for some employers is that some seasonal workers may have under the table jobs. If these individuals were to actually report all of their income, the burden of paying for health insurance might not remain on the seasonal employer who does fully report earnings. Due to these financial considerations, employers will limit the amount of time seasonal workers are hired so they are not able to qualify for health insurance.

The common financial decision of seasonal workers to forego health insurance brings up the question of accountability in the health care system. Michelle Be believes "insurance could be a great system if it was done with more concern for the individual's financial cost/benefit" and feels that insurance companies unfairly profit off of a contrived system. The current insurance options for seasonal workers are so limited that continuously switching between low cost plans and Medicaid based on the time of year and variations in income levels could be considered comparable to having another job.[9,10] Mary Ilacqua, a long-time seasonal worker, only recently invested in Healthy NY after years without insurance. Clearly some sort of accountability is necessary as the uninsured are still treated in the ER. While some see no way to cover the uninsured without a government mandate, others see a mandate as an attack on the individuals who already cannot afford insurance. Physicians in the area generally consider it a tragedy people go without insurance in the U.S. because of cost, and believe people deserve at least some level of basic care.[5,2,6,11] A fair amount of health care providers see a solution through the ACA, and while many believe a national approach is not the way to go, we certainly have a "national failure" of high cost and poor result health care.[2] According to Dr. Rugge, "we have the least developed primary care system of any nation" and this emphasizes the unbalanced nature of a health care system that financially promotes physician specialization instead of more cost-effective and accessible primary care. It is difficult to say who should be accountable for our country's uninsured; as the case of seasonal workers shows, the traditional system of a year-round employer providing insurance coverage is not always adequate.

Under the traditional system of health insurance, seasonal workers do not work enough to qualify for insurance through an employer, and they work too much to qualify for state programs.

Any attempt at health care reform that could provide coverage to seasonal workers needs a highly efficient and cost effective health care system, which is what the Medical Home Pilot is beginning to establish in the Adirondacks. The Pilot has seen improved cost efficiency in areas such as ER visits and preventable readmissions, and while its changes have been gradual most health care professionals in the area consider it a step in the right direction. Although paying for insurance is still the biggest obstacle to seasonal workers, the efforts of the Pilot can hopefully halt the decline of doctors in the area, as this is an obstacle to care for everyone. Unfortunately, under the traditional system of health insurance, seasonal workers do not work enough to qualify for insurance through an employer, and they work too much to qualify for state programs. The fate of the United States health care system is currently a controversial issue, and the complexities of finding coverage for people who work seasonally will hopefully not be forgotten.

References for this article can be found at

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SCIENCE REPORT

ENCODE: Unraveling the Human Genome, One Function at a Time

Joseph St. Pierre

PREFACE

Since the discovery of the double helix, the influence of DNA over the structure and function of organisms has long been the topic of extensive biological study, underscoring the basic tenants of biology, and arguably serving as the core for the science as a whole. In 2003, almost 50 years after the discovery of DNA, The National Human Genome Research Institute (NHGRI) completed the Human Genome Project, a landmark undertaking which oversaw the sequencing of the approximate three billion base-pairs comprising the human genome, as well as assessing the presence of an estimated 30,000 protein-coding sequences.[1] However, despite the substantial trove of knowledge the project attained, many questions remained unanswered. In particular, researchers were amazed to find that only one to two percent of the entire human genome's base pair sequence actually coded for transcribed proteins,[2] leaving the function of the remaining margin to be little more than the subject of speculation. Enter the Encyclopedia of DNA Elements (ENCODE) project, brainchild of the NHGRI and successor to the human genome project.[2] Less than two months ago, the project unveiled the fruits of almost a decade's worth of genomic analysis across a plethora of cell types through the publication of thirty research papers[2] detailing a massive reserve of data which assigned at least one biological function to 80.4% of the human genome.[3] Extending beyond protein-coding sequences to encapsulate protein binding sites as well as an extensive array of RNA functionality, ENCODE paints a new portrait of the human genome, one that is far more regulated and multidimensional than previously fathomed.

AIMS

The ENCODE project affords a mass of statistical and qualitative data detailing elements of the entire human genome. However, the data is quite complex, necessitating the inclusion of a brief overview of the role of DNA in gene expression prior to any examination of ENCODE. In addition to defining the locations of all known gene loci, as annotated by the ENCODE's subproject, GENCODE,[7] the project highlights several other functions of the human genome. Finally, several implications of the ENCODE project, including the revolutionary manner in which its data is presented, will be discussed. Therefore, the aims of this paper are as such: to provide a brief summary of DNA and gene expression, to summarize ENCODE's statistical findings pertaining to protein coding loci, RNA expression, DNA binding sites, and areas of histone modification, and to conclude with a brief discussion of the project's various implications.

DNA: A BRIEF SUMMARY

All information pertaining to the structure and function of a living cell is preserved and maintained within one or more molecules of DNA. It is this information that is passed from a cell, or any multicellular organism for that matter, to its progeny. Structurally, DNA is composed of two helical strands running antiparallel to each other and bound to each other through complementary hydrogen bonding that occurs between a series of four nitrogenous bases lining the molecule's interior. Through a process known as gene expression, information stored in the form of nitrogenous base-pair sequences within the DNA molecule is used to create a variety of polypeptides, which form proteins capable of performing a variety of tasks. This process begins with transcription, during which a sequence of DNA is copied onto a molecule of single-stranded RNA, and ends with translation, the process of translating the base sequence of a transcribed RNA molecule into a polypeptide.[9]

A variety of elements exists to regulate and fine tune this process. For example, not all transcribed RNA is translated into protein. Prior to translation, RNA is spliced into various new sequences, with only portions known as exons possessing the potential to be translated. Furthermore, not all exons are translated into polypeptides, as many are folded and modified into what are known as non-coding RNAs, which perform a variety of tasks associated with gene expression.[9]

In addition, DNA molecules of humans and other eukaryotic organisms, coil around proteinaceous bodies known as histones. The resulting aggregate is known as chromatin. Histones are often modified, controlling how coiling occurs in a given portion of DNA, as well as how accessible its sequence is to a variety of proteins associated with genetic transcription.[9]

ENCODE: A SUMMATION

Essentially, ENCODE is the compilation of a variety of experiments testing for specific genomic sequences or facets performed across a varying array of 147 cell types.[3] The project focused primarily on several cell lines: GM12878, a cell line produced from immature lymphcytes; K562, an immortal cell line derived from cancerous leukemia cells;[4] and the embryonic stem cell line H1-hESC.2 Expanding upon its predecessor's study of protein-coding regions, ENCODE outlines a list of exactly 20,687 said regions, discerning a mean of 6.3 alternatively spliced transcripts per locus,[3] as well as listing 11,224 pseudogenes,[3] nonfunctioning gene analogs. Still, protein coding regions, that is, exons of protein-coding genes, were shown to comprise only 2.94% of the genome's base pairs,[3] leaving the bulk of the project's discovery to genomic regions serving different purposes.

One such function is the transcription of RNA, a nucleotide which serves variety of genetic roles, most notably its

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intermediary status in the translation of DNA sequences to protein. A staggering 62% of the genome was found to be expressed in the form of RNA molecules measuring more than 200 base-pairs in length, with only 5.5% of the aforementioned percentage accounting for protein-coding exons.[3] In addition, using a method known as CAGE-sequencing to capture, methylate, and sequence RNA molecules, 62,403 transcription start sites were pinpointed across the genome, with a significant number of such sites located within exons and untranslated regions. Other project-specific data shows a statistically significant portion of these start sites to exhibit "cell-type-restricted expression"— gene expression ascribed only to specific cell types,[3] further supporting the idea that portions of a human's genome, or that of any multi-cellular organism for that matter, are expressed only in specific cell types.[3] Furthermore, sequences coding for long and short non-coding RNAs were found to account for a significant portion of the genome,[3] suggesting a higher amount of genomic regulation, particularly with respect to cell type, than previously considered.[7] These molecules, known for their roles in RNA translation as tRNAs and alternative splicing as sNRPs,[9] have also been recently speculated to possess a multitude of significant roles in organismal development.[6]

Beyond transcriptionally expressed elements, the project found a substantial portion of the genome to be involved with the facilitation of physically binding to proteins and other molecules. Using the procedure known as ChIP-seq to identify proteins through specific antibody binding, ENCODE accounts for the binding sites of 119 DNA-binding proteins across 72 cell types. 8.1% of the genome is involved with such functions.[3] Particular emphasis appeared to be placed on transcription factor binding sites, which accounted for 87 of 119 DNA-binding sites studied, as well as their correlation with the presence of a strong DNA-binding motif,[3] a sequence of DNA associated with the increased affinity for DNA binding proteins to the sequence in which it is contained.[11] In addition, to map areas of DNA accessibility, sensitivity to the nuclease DNase1 was also documented across the entirety of the genome and cross-referenced with each area's affinity for DNA binding proteins. Interestingly, DNase activity was significantly higher in regions with lower affinity than in regions with higher affinity, suggesting that such low-affinity regions to be associated with other, as-of-yet unspecified factors. [3]

In addition to transcription factors, areas involved with histone activity were also the topic of substantial study. The locations for as many as 12 histone modifications were studied across 46 cell types. Overall, histone modification varied across a the cell types studied in correlation with various transcription patterns, with areas of intense modification substantiating 56.1% of the genome,[3] further verifying claims in previous studies on the consistent transcriptional impact of histone modification across varying cell types.[10]

Furthermore, areas where DNA was bound directly to outside molecules were the subject intense statistical analysis. In particular, locations of DNA methylation of cytosine in CpG dinucleotides, a phenomenon correlated with both DNA repression and increased transcriptional activity,[3] were analyzed across 82 cell lines, with 96% areas of methylation varying across different cell types.[3] This high percentage indicates strong statistical correlation between differential methylation and transcriptional expression across various cell types.

Finally, the connections between various sequences at differing areas across the genome were assessed. Using an approach known as 3C carbon copy(5C)y to analyze chromosomal positioning and activity, the interactions with transcription start sequences (TSS's) located on separate chromosomes across four cell types were cataloged through the analysis of many statistically-significant correlations for various activities. TSS's studied were found to interact on average with 3.9 other distant elements. The project considers such activity to be indicative of the presence an undiscovered and interconnected dimension to the genome involving long-range physical interaction between sequences.[3]

CONCLUSION: BEYOND ENCODE

In summation, according to ENCODE's data, 80.4% of the genome has now been assigned at least one biological function. The wealth of information afforded by such a feat is staggering, and is already developing into a core reference for researchers across a wide spectrum of study. The data itself is publicly available on several online databases, including the those of ENCODE and the National Center for Biotechnology Information.[8]

To understand the magnitude of what such availability implies, consider the analogy posed by NHGRI program director Elise Feingold, Ph.D., who likened the data to a genetic version of Google Maps:

"Simply by selecting the magnification in Google Maps, you can see countries, states, cities, streets, even individual intersections, and by selecting different features, you can get directions, see street names and photos, and get information about traffic and even weather. The ENCODE maps allow researchers to inspect the chromosomes, genes, functional elements and individual nucleotides in the human genome in much the same way."[8]

With respect to the project, much remains undiscovered. Note that percentages mentioned in this paper do not sum to 100%, showing a significant portion of the genome to be involved with more than one of the aforementioned functions. Alas, while the data provided by ENCODE is by far the most complex comprehensive study of the human genome to date, the work the project began is far from complete, as a vast array of cell types have yet to be tested. Therefore, it is not unreasonable to posit that a variety of genomic elements, as well as a myriad of functions not yet ascribed to previously-studied sequences, remains undiscovered. However, the ENCODE's approach, as well as its revolutionary presentation of data as a free online resource, has paved the way for similar endeavors. Indeed, the fruits of ENCODE may well be seeds of a coming age of genomics, one in which a comprehensive view of humanity from the molecular level upward may finally be realized.

References for this article can be found at

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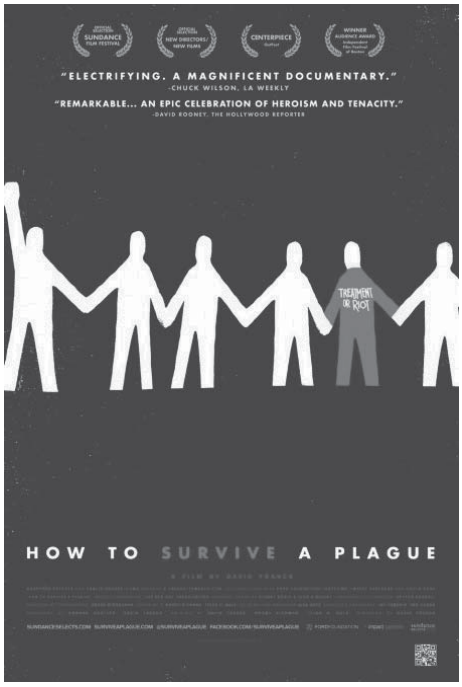
How to Survive a Plague

Directed by David France; Reviewed by Alejandra Garcia

In an inspiring and heartbreaking 129 minutes, director David France chronicles the story of two groups of activists whose work turned AIDS from a death sentence into a livable condition. *How to Survive a Plague* chronicles the work of ACT UP and TAG (Treatment Action Group), two colorful and improbable groups of individuals fighting a battle to end the AIDS crisis. Compiling coverage from nearly twenty years of filming, the documentary takes us year-by-year, beginning in 1987, when there was little to no focus on the epidemic.



Located in the heart of New York City's eclectic Greenwich Village, ACT UP and TAG congregated at weekly meetings as support groups for the gay and lesbian community to strategize their course of action. At the beginning of the documentary, the groups direct their focus at the lack of support from the government and health care industry. Many thought that a cure was being purposely hidden from the hundreds of thousands of Americans affected by AIDS. Evidence that better treatment options existed in other countries inspires very powerful scenes of these activists protesting outside of FDA headquarters and other governmental buildings. "Health care is a right, health care is a right," they chanted, as they were aggressively removed and assaulted by police officers and anti-gay groups.

Throughout the film, scenes from the groups' protests and demonstrations place the viewer in the midst of the era. From "kiss-ins" to staging protests outside of government buildings, hospitals, and churches, we see that the work of these activists will not end until their mission has been fulfilled. We see powerful messages like "silence=death" and "fight AIDS, fight back" plastered all over the activists' signs and bodies. We see bodies being trampled by police officers, people being physically removed from the demonstrations responsible for putting the AIDS crisis on the radar for the entire country.

Throughout the film, the death toll of the number of lives taken by AIDS scrolls across the screen. Rapidly increasing as the years recounted progress, the desperation for a treatment that works becomes even more imperative. With the prices for the only available medications at the time sky-high, stopping the vicious killer was close to impossible. A decent society does not just put people out to pasture and die because they've done a human thing. The heroic actions of this improbable group of people moved everyone in the theatre to tears.

The film is not only the story of a disease; but also the story of a movement. Plague conveys the story of a movement of people who refused to sit idly and accept their disease as their executioner. One of the movement's key activists, Peter Staley, stated that living with AIDS during the 1980s was like living in a battlefield. "I'm going to die from this," Staley commented, "it's like living in a war, all around me friends are dropping dead." In an emotional interview, another woman stated that she has no friends who she has known longer than five years, blaming this misfortune on the rapid spread of AIDS. Although these fighters accepted the probable fate that they would not survive to see an end, the community of LGBT activists never lost hope.

Through the telling of personal stories, the viewer develops a connection with the victims of the epidemic. Documenting the same individuals over the course of 20 years, Plague evokes strong emotions of grief as we watch the lives of many fighters deteriorate as the years pass. In an incredibly memorable scene, we see one of the activists in his final days of life. Remaining positive and hopeful even though the disease had already consumed his body, he speaks of his dreams for all of his friends to have the opportunity to live as complete of a life as he did. In the end of the film, the viewer is presented with many familiar faces—faces of those who never dreamt that they would live to see a treatment that worked. With greying hair and wrinkles to boast, many of these young men and women who were wholeheartedly responsible for the AIDS revolution are still here to tell their story.

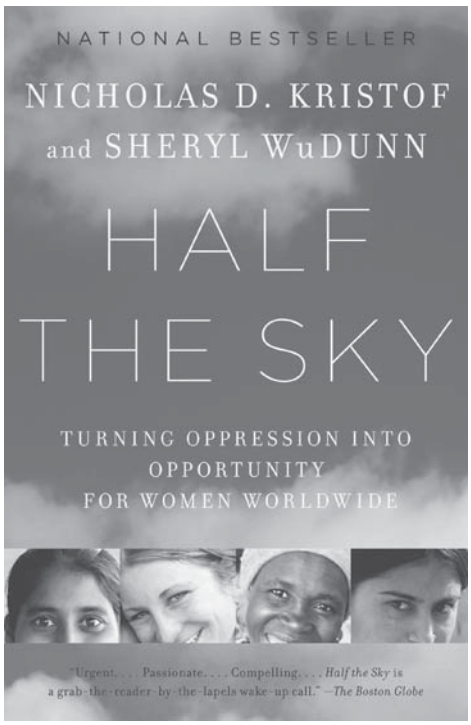
The strong presence of AIDS awareness today makes it easy to forget about the fight that led to where the movement currently stands. Although the crisis is by no means over, there are various treatment options available to enable HIV positive individuals to live long, fulfilling lives. The progression of these treatments is without a doubt a result of the hard work performed by these heroic individuals for the past 25 years. An extremely important film about an extremely important era, *How to Survive a Plague* is both inspiring and heartbreaking.

Alejandra Garcia is the New Media Editor of TuftScope

Half the Sky:
Turning Oppression into Opportunity for Women Worldwide

Book by Nicholas D. Kristof & Sheryl WuDunn; Reviewed by Eriene-Heidi Sidhom

In *Half the Sky*, Nicholas Kristof and Sheryl WuDunn, preface by describing a "gendercide" of women. Due to the high life expectancy of women, there should be a higher number of women in the world than men. However, in countries where women face inequality, such as China, India and Pakistan, men outnumber the women. Calculations estimate that the number of women that die due to this gendercide in a single decade is more than all the victims of genocide in the twentieth century. These unsettling and shocking statistics are the premise of an investigation of the various forms of gendercide in primarily Asia and Africa.



While Half the Sky could run the risk of sounding sermonizing, their personal interactions with the many victims of gender inequality, lends a sincerity and verity to the stories of these incredible women. Similarly, while issues of rape and honor killings could lead to a dark account of unimaginable cruelty, Kristof and WuDunn strike the balance between the reality of gender inequality and the inspiring women who have gained a sense of independence and freedom.

Each chapter begins with an overview of an obstacle that women face around the globe. The current efforts in combating this issue, the reasons for their successes and failures, and stories of individuals who have become victim to such discrimination and cruelty are introduced. The second half of each chapter then details a particular organization or individual who has been able to establish a model for eliminating or mitigating the effects presented in the first half. This format gives the reader the context allowing it to be accessible to even those with no background in the field and introduces the reader to the many ways they can be involved. Kristof and WuDunn, do not claim that there is a single silver bullet for any of the given forms of gendercide. They make an effort to highlight successful outreach and educational efforts, while simultaneously acknowledging their potential limitations.

The book begins by discussing prostitution with a focus on eastern Asia. It speaks about the deception used to bring young girls into brothels, the violence they endure from the pimps and the difficulties even when they are given the chance to start a new life due to drug dependence and feelings of worthlessness.

Beyond brothels, the book discusses the authority men gain over women through rape and extreme sexual violence, particularly in places like the Congo. Kristof and WuDunn tell the inspiring stories of women like Mukhtar Mei, a gang rape victim, who through the support of her family, demanded the prosecution of her attackers and used the money to start a school. The necessity of education in empowering women and the economic advantages of doubling the work force and intellectual and political communities of a nation, through the incorporation of women, are themes that are carried throughout the book.

The latter half of the book focuses on women reproductive health issues, in particular the devastating effects of complications in childbirth leading to fistulas. While, these are commonly thought of as "women's issues," Kristof and WuDunn emphasize this is an issue of human rights; as Stephen Lewis said to the UN Secretary General Ban Ki-moon, "We're talking about more than fifty percent of the world's population… If you can't stand up for the women of the world, then you shouldn't be Secretary General."

The book also speaks of the efforts of children and adults here in the United States whose seemingly small contributions, grew into national efforts. Twelve year old Zach Hunter started a campaign against modern slavery called Loose Change to Loosen Chains, and raised $8,500 in his first year. Jane Roberts, a retired French teacher, responded to the 2004 announcement to deny the $34 million voted by Congress for the United Nations Population Fund, by writing to her local paper, asking for 34,000,000 women to donate $1 each to the UN Population Fund. The UNFPA, while at first doubtful of this small effort, was soon overwhelmed by mail; to date, they have raised $4 million.

Half the Sky is not merely a narrative of dozens of inspiring women worldwide, but a call to action by showing the need for equality and the importance of every contribution.

Eriene-Heidi Sidhom is the Editor-in-Chief of TuftScope.

EDITORIAL

Sugar Tax Sugarcoats Problem of Obesity

Ayal Pierce and Avery Epstein

Obesity is a growing problem around the world, especially in the United States. The amount of obese people in our nation has more than doubled since 1980 and this number is steadily increasing at a rate of approximately 4-5%.[4] A major contributor to obesity, heart disease, and diabetes is soda. Although there have been a plethora of proposals on ways to reduce sugary drink consumption, an article in *The New England Journal of Medicine (NEJM)* sparked a nationwide debate when recommending a one-cent-per-ounce tax on sugary beverages, roughly a 20% overall increase on the price of most soda.[1] The government involving itself in the regulation of food through taxation, however, is not the answer. The causes of the problem are people choosing to eat unhealthy foods and the easy access of unhealthy foods in lower socioeconomic environments. Taxes do not address this cause.

A sugar tax would not effectively combat obesity because it attempts to use a legislative solution for a social and economic problem. It ignores the social determinants of health-— the environment and conditions in which people are born, grow, live, work, and age, which are shaped by the distribution of money, power and resources at the global, national and local levels, according to the World Health Organization. It does not directly address the various reasons why people choose to drink soda or other sugary beverages, but rather assumes that beverage choices are exclusively based on price. Two reactions to an increase in price of unhealthy beverages could occur. The desired effect would be the reduction of sugary beverage consumption in favor of the healthier, cheaper options. However, one must also consider the effect of choosing not to buy the healthy drinks, like bottled water or natural juice, in order to save for the better tasting unhealthy drinks, like energy drinks and soda.

Although the revenue generated from this tax could be helpful for funding further research related to obesity, the cost of the tax would outweigh the benefits. People of lower SES would be unfairly burdened by the tax, and will continue to buy sugary drinks unless cheaper, healthier alternatives are also made available. Kelly Brownell, director of Food Policy and Obesity at Yale, coined the term "toxic food environment" to describe the "ubiquitous availability of food at outlets ranging from gas stations and drug stores to bank lobbies and elementary schools; and the incessant advertising of high-fat, low-nutrition foods," which has led to the rising obesity rates.[2] A tax is not going to change the "toxic food environment" and the availability of unhealthy foods, and without alternatives to unhealthy foods, the tax is not going to alter consumer behavior either. A more effective solution would be to subsidize healthier foods, restrict advertising of unhealthy foods, and improve dietary practices in public schools.

One possible, yet controversial, intervention to reduce the exorbitant quantity of soda consumed would be similar to New York City Mayor Michael Bloomberg's proposal of eliminating the sale of large sugar-sweetened drinks in any cup larger than 16 oz. Should a consumer want a 32-oz drink, he need only buy two 16 oz drinks. No price raise. No taxes. No elimination of freedom to consume as much as one wants. Just clever psychology to discourage the ever so easy option of choosing the extra large drink for a couple cents more.

A public health media campaign to raise awareness about the health implications of drinks that have a high concentration of sugar has the potential to change social norms and behavior related to food choices, similar to the anti-tobacco campaigns to reduce smoking. Cigarette smoking used to be considered cool when the health risks were unknown. After the Fairness Doctrine in 1966, in which the FCC mandated that the media be used to serve the public interest and portray both sides of an issue, education about the detrimental health effects of smoking greatly increased. Through this education, the public learned about the carcinogenic effects of cigarettes and the causal link between smoking and lung cancer; the consumption of cigarettes also greatly decreased as smoking became considered a stigmatized behavior.[3]

The relationship between smoking and cancer, however, is more apparent than that of sugary drinks and heart disease. Despite the fact that heart disease is the leading cause of death in America, the threat of cancer is a much scarier and immediate one. The goal must then be to make Americans realize the true dangers of consuming soda in large quantities and to strive to create new social and behavioral norms.

Obesity is a growing problem in the United States. It is the responsibility of the government to educate the public of the detrimental health effects of the gluttonous consumption of sugary drinks. It is not the responsibility of the government to make an easy buck in the name of public health. Education is the key to changing the social norms that dictate individual behavior and consumer choice, not increased taxes. Unless healthier options are available and there is a shift in the overall "toxic food environment," the tax will only hurt the people it is intended to help.

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