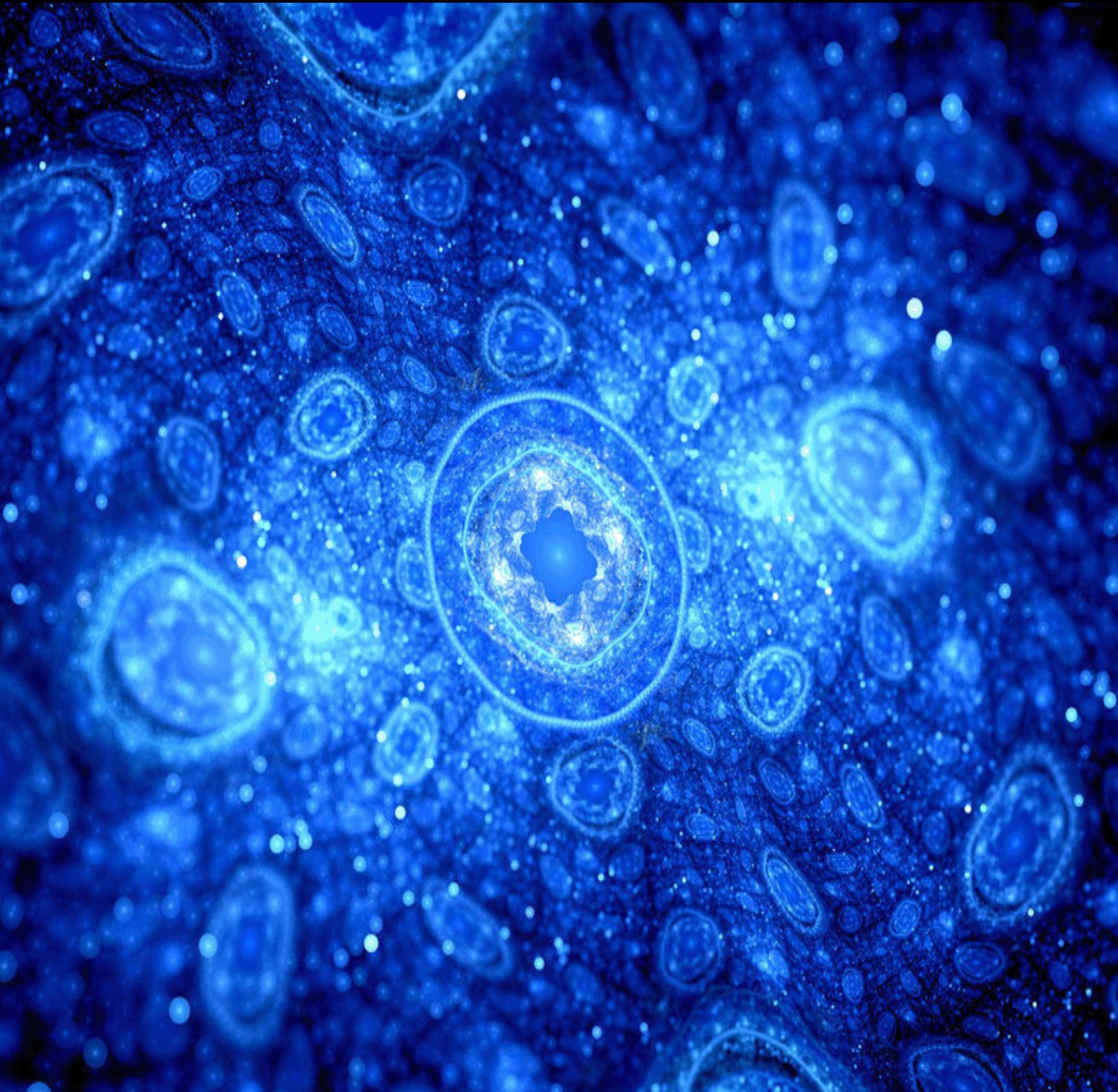


Journal for Pre-Health Affiliated Students

2016-2017 Volume XVII



JPHAS

*Journal For Pre-Health
Affiliated Students*

**Fall 2016/Spring 2017
Volume XVII**

JPHAS

Mission Statement

The Journal for Pre-Health Affiliated Students (JPHAS) was created in May 2001 to more fully recognize the broad spectrum of pre-health students at the University of Illinois at Chicago. JPHAS strives to offer students interested in the science field a valuable, informative resource and a forum to express, present, and exchange ideas. JPHAS aspires to strengthen the network of support for pre-health students.

PRESIDENT	VICE PRESIDENT	EDITOR-IN-CHIEF	FACULTY ADVISOR
Layal Dairi	Salmaan Zafer	Samer Hassan Salmaan Zafer	Saul J. Weiner, MD

EDITORIAL STAFF

SPECIAL THANK YOU TO

Executive Layout Editor-	University of Illinois at Chicago Honors College
Abigail Olsen	Ralph Keen
Section Editors-	<i>Dean of the Honors College</i>
Milan Patel	Saul J. Weiner, MD
Joe George	<i>Vice Provost of Planning and Programs</i>
Oluwadamilola Ajasa	<i>Professor of Medicine, Pediatrics and</i>
Sanjana Srinivasan	<i>Medical Education</i>
Section Layout Designer-	Sara Mehta
Abigail Olsen	<i>Honors Academic Advisor and Program Specialist</i>
Webmaster-	Andrea Vaughan
Sanjana Srinivasan	<i>Graduate Publications Advisor</i>

JPHAS CONTRIBUTORS

Features:	Research:	News:	Opinions:
Pal Shah	Abigail Olsen	Jomarie S. Arban	Aiswarya Baiju Fnu
Kevin Cao	Kenneth Booker	Atreya Mishra	Sarah Basheer
Kelly Fan	Jessica Poon	Maximiliano Vidales	Jacob Hill
Morgan Win	Med Jimenez		
Chioma Ndukwe	Alexander Kravets		
Claudia de Bruyn	Anastasiya Loos		
	Mitchell Sun		
	Arashpreet Kaur		
	Queena Luu		
	Shreya Thakkar		

DISCLAIMER

The articles and overall content presented in this publication do not necessarily represent the views of the University of Illinois at Chicago, the Honors College, the *Journal for Pre-Health Affiliated Students*, its editorial staff, or any of its affiliates and sponsors.

Table of Contents

Features

Bridging the Gap.....6

The Affordable Care Act Today:
What are *They* Saying?.....8

Conflicts with the Distribution of
Health Care for Refugees.....12

One Ticket to the
Marshall Islands.....14

Global Healthcare Shortage.....16

Worldwide Lack of
Resources for Trauma-Related
Mental Disorders.....18

Research

Why Don't Antidepressants
Work in Some Patients?.....20

Half Match Bone Marrow Wipes
Out Sick Cell in Select Patients.....22

Glutamate's Newfound Role in
Neuromuscular Development.....24

Schwann Cells: The Key to Unlocking
Epigenetic Nerve Regeneration.....26

The Ticking of the
Epigenetic Clock.....28

Shepherding Alpha-Synuclein
could be the Answer to
Treating Parkinson's Disease.....30

Rewiring the
Mitochondria's Energy.....32

The Effects of Zika Virus.....34

Do We Really Need Statins?.....36

Understanding the Prevalent
Fear of Dental Care.....38

News

Tech, Tots, and Teens:
The Impact of Media and
Technology on Today's Youth.....40

Yoshinori Ohsumi:
An Explorer of Autophagy.....42

World's First Baby Born
with New "3 Parent" Technique.....44

Opinions

Life After Death-
Without Permission....46

The Conundrum of Donations
from Living Organ Donors.....48

Advancements in Assisted
Reproductive Technologies.....50

BRIDGING THE GAP: *FEDERALLY QUALIFIED HEALTH CENTERS AND THE QUEST FOR GREATER HEALTH EQUITY*

BY PAL SHAH

A 60-year-old man stumbles into a North Carolina emergency room waiting area around midnight after being discharged only a few minutes before. The man was brought to the hospital via ambulance earlier in the afternoon after having distorted vision due to side effects of a medication, but after receiving treatment he could barely afford, the man has no way of getting to his home eight miles away. He has no money for a bus, no family near the hospital, and lives only with his disabled mother, so when his plea for help from the nurse in charge of the admissions-and-discharge station was denied, his growing frustration with his situation turned into despair. Now it seems that the man's only option is to stagger eight miles back home or spend the night in a hospital lobby waiting for help to find its way to him.¹

This situation, while tragic, is not uncommon for low-income Americans needing medical attention. Often these Americans are uninsured and lack access to primary care, so the only time they see a health professional is during an emergency situation. Many poor Americans in rural and urban areas alike cannot even afford the cost of transportation to or from the hospital. It is in these all too common tragedies that the vast inequity in health is most apparent. Health inequity is a product of income inequality. Income inequality in the United States is now at its highest point since 1928, with estimates of income earned by the one percent at 23% of the national total, and wealth held by the one percent to be 42% of the national total as of 2012.² While the economic and political repercussions of such vast disparities in wealth are well documented, the implications for access and quality of health care often go overlooked.

While the Affordable Care Act broke ground to provide millions of Americans with health insurance for the first time, 28.5 million nonelderly Americans still remain uninsured. The primary demographic of uninsured Americans is unsurprisingly people of color in low-income

families. Among uninsured Americans, at least 20% have forgone treatment or medication due to an inability to carry the financial burden, with over 50% having problems paying medical bills within the last year. Poor people of color are not only more likely to be uninsured, they are also far less likely to use, or even have access to, a primary care provider. According to the American Academy of Family Physicians, primary care is defined as "comprehensive first contact and continuing care for persons with undiagnosed signs, symptom, or health concerns."³ Primary care can not only identify low cost solutions to illness early on, but also leads to far fewer emergency room visits and procedures that lower costs overall. However, since a large portion of low-income Americans lack access to primary care, they are forced to use the emergency room for any and all medical services. According to a 2011 study conducted by the National Institute of Health, health care costs in emergency departments were between 320 to 728% higher than that of primary care clinics. This could have allowed for a savings of 69 to 86% if only the right facility were used.⁴ It is apparent that not only is the United States health care system less effective for low-income Americans, it is also far more expensive.

It is clear that health inequity is perpetuated by lack of access to primary care, so how can affordable quality care be provided to underserved communities? The answer may lie in federally qualified health centers (FQHCs) - comprehensive health facilities that provide primary care, dental, mental health and prescription services to underserved communities through Medicare and Medicaid subsidies.⁵ These care centers operate on a sliding pay scale, meaning that the cost of medical services varies depending on the income of the patient. FQHCs are primarily located in low-income, urban and rural areas where access to affordable primary and preventative care is scarce.

In fact, 71.9% of patients of FQHCs are at or below the federal poverty level.⁶ Not only are FQHCs more efficient for the distribution of health services than the emergency room, they are likely to pay for themselves the long run. In fact, a study from the Centers for Disease Control concluded that FQHCs are cost effective when considering the enormous cost saved compared to emergency room visits, reduction in hospitalizations, and greater access to preventive care.

FQHCs were initially allocated a \$2 billion investment from the American Reinvestment and Recovery Act of 2009. \$1.5 billion of this was to cover the cost of new equipment and facilities. A year later, another \$11 billion were appropriated towards the program due to its proven effectiveness. However, due to a restructured budget in 2012, funding for FQHCs through Medicare and Medicaid decreased, causing a limitation in expansion for these centers.⁶ While currently there may be 1,202 funded centers present in the United States, large rural states like Wyoming, North Dakota, and Nevada each have five or fewer FQHCs.⁵ As seen in the example of the 60-year-old man from North Carolina, the limited number of centers in such large states creates a transportation barrier to access to care. More funding must be allocated for the investment of centers in low-income rural states in order to bring down surging emergency room costs and to bridge health inequity in these heavily rural areas.

The disparity in care quality between those at the top and those at the bottom of the income bracket manifests itself in life span as well. Economists from the Brookings Institute found that there was a six-year difference in life expectancy between the top 10% and bottom 10% of male earners born in 1920. However, the difference in life expectancy for men from the top and bottom income brackets born in the year 1950 is a staggering 14 years.⁷ This is a problem that is dramatically escalating and will only worsen unless legislation is passed to fill the gap. Yet, as a result of the 2016 presidential election, the United States could be taking a giant leap backwards in health equity. If the President goes through with his early campaign promises of repealing and replacing the Affordable Care Act, then not only will 32 million Americans lose their health insurance, FQHCs across

the country are likely to lose all federal funding and be forced to shut down. Americans who are handed worse socioeconomic circumstances must still be treated as Americans and have access to the affordable, quality care that they deserve.

References

1. Cronk I. The Transportation Barrier. *The Atlantic Health*. August 15, 2015. <http://www.theatlantic.com/health/archive/2015/08/the-transportation-barrier/399728/>. Accessed November 4, 2016.
2. Lam, B. How Much Wealth and Income Does America's 1% Really Have? *The Atlantic*. March 12, 2016. <http://www.theatlantic.com/business/archive/2016/03/brookings-1-percent/473478/>. Accessed November 21, 2016.
3. Primary Care Web site. <http://www.aafp.org/about/policies/all/primary-care.html>. Accessed November 6, 2016.
4. McWilliams, A., Tapp, H., Barker, J., & Dulin, M. Cost analysis of the use of emergency departments for primary care services in Charlotte, North Carolina. US National Library of Medicine National Institute of Health [serial online]. July/August 2011. <https://www.ncbi.nlm.nih.gov/pubmed/22128684>. Accessed November 2, 2016.
5. What are Federally qualified health centers (FQHCs)? US Department of Health and Human Services Web site. <http://www.hrsa.gov/healthit/toolbox/RuralHealthITtoolbox/Introduction/qualified.html>. Published 2007. Accessed November 06, 2016.
6. Medicaid Service Delivery: Federally Qualified Health Centers. Center for Disease Control Web site. <https://www.cdc.gov/phlp/docs/presentation-fqhc.pdf>. Accessed November 6, 2016.
7. Bosworth, B., Burtless, G., & Zhang, K. Later Retirement, Inequality in Old Age, and the Growing Gap in Longevity Between Rich and Poor. Economic Studies at Brookings January 2016.
8. Key Facts about the Uninsured Population. Kaiser Family Foundation Web site. <http://kff.org/uninsured/fact-sheet/key-facts-about-the-uninsured-population/>. Published September 29, 2016. Accessed November 1, 2016.

THE AFFORDABLE CARE ACT TODAY: WHAT ARE *THEY* SAYING?

BY KEVIN CAO

It has been seven years since the Patient Protection and Affordable Care Act (ACA), otherwise known as Obamacare, was passed, and to many Americans, it seems as if the honeymoon phase is long over. With the election of Donald Trump and a newly empowered Republican congress, President Obama's landmark law has been thrown back into an uphill-downhill political trudge. In the background of a red hot political climate and moves to repeal the ACA, the new long-term unveiled data on the ACA tells a more objective story in delineating its faults, successes, and everything in between. While wild banter over the repealing of Obamacare conflicts with a brighter image on the left, the legislation's real success or failure lies with how it has impacted different healthcare constituents. The ACA's reform is a new chapter into healthcare in America and is heard through the many voices telling different stories on the landmark legislation. While policy scholars see that the law has its theoretical merits and shortfalls, the tangible impacts are in fact felt in individual experiences of everyday people, policy makers, and the insurers themselves. Some of these voices may not be as loud as others, but they are nonetheless important drops in a sea of healthcare reform.

Let's hear what *they* are saying.

What the Obama Administration said:

"We are at the threshold of a truly historic opportunity. The promise of positive transformative change in the U.S. health care system is at hand."¹

The United States Department of Health and Human Services website declared the aforementioned statement with a confident bolded size 16 font. The website detailed the strengths of the ACA, confiding in the American people that Obamacare was working. When viewed at face value by comparing the ACA to healthcare pre-2010, there are stark contrasts. Health insurance previously rejected millions based on claims of pre-existing

conditions and charged inefficient, unfair premium rates. President Obama's term came to an end with 16.4 million uninsured individuals gaining the coverage they needed. In addition to having attained the lowest ever percentage of the uninsured Americans, the ACA tells a convincing story of one of the hallmarks of President Obama's legislative legacy.¹

Even so, for the Secretary of the Department of Health and Human Services, Sylvia Burwell, the numbers don't exactly translate into complete success. In a 2016 interview with Politico, Sec. Burwell asserts that, "progress has been made, but we know and are focused on making more."² Burwell shines a light to the future, driving a positive momentum. "Can we do more? Can we do better? Yes. But is the basic trajectory, and has there been a market change? Yes." But with problems dogging the administration such as rising premiums, compatibility issues with insurance providers, and continual political push back, the "threshold of a truly historic change"² is truly a far cry from full-out victory.

The Center for Medicare and Medicaid (CMS) recently suggested improvements to address Burwell's cited issues. In response to the Department of Health and Human Services "reporting average of 25 percent in the 38 states using the federal HealthCare.gov website,"³ the CMS has suggested "using some of the fees from the federally funded marketplace for outreach to get more young people to sign up,"⁴ along with "strengthening rules for signing up to ensure that people are not waiting until they are sick to get coverage"⁴ to create a more bureaucratically stable operating model. For the Obama Administration, the fixes seemed to be directed towards making an unpredictable human customer market fit into the confines of a rigid system.

What someone without access to affordable healthcare is saying:

"Even if they were going to take me because of the preexisting condition, it would be hugely expensive. The affordable healthcare act means that I have a chance, that I don't have to stop treatment once the insurance runs out."⁵

For Martha Monsson, 2008 couldn't have been a worse time to be diagnosed with multiple myeloma, a bone marrow cancer. In the midst of the tumultuous recession, the then 54-year-old recounts, "when I was first diagnosed, my husband was the county attorney in Morgan County. And we had insurance through them. But his job was eliminated."⁵ When looking for insurance to cover the cost of her chemotherapy, she recalls, "since then, he has been doing contract work, which has kept income coming in, but, for insurance, all we have had is through COBRA. That expires at the end of February. If he doesn't have another job by the end of February, we would have to apply for private insurance. We would get turned down because of my preexisting condition."⁵ With the average cost of chemotherapy found in an American Health and Benefits study to be around \$125,000 (2015), an out-of-pocket approach would be financially crippling. For Martha, insurance was the line between life and death. When PBS NewsHour first introduced her story, Martha represented one of the 125 million patients that would have been rejected from a claim due to a pre-existing conditions or due to sexual/racial discrimination.⁶ With the introduction of the ACA, the banning of the pre-existing condition discrimination and the Medicaid expansion allowed people like Martha Monsson new hope for a longer life.

Martha Monsson has since passed away on Feb. 20, 2014, but her interview continues to bring endless cautionary wisdom. "People are one diagnosis away. And they don't realize it, to a large degree, but it's very true."⁵ Her heavy words to all again capture the importance of healthcare reform and the personal stories it encompasses.

What the Insurance Companies are saying:

"Overall, the financial performance in individual ACA compliant products has been disappointing, as membership has been short of our original expectations since its inception."⁴

President Obama's pitch of the ACA's Insurance Exchanges seemed simple enough. A federally regulated and funded state-wide marketplace would be created for consumers to purchase insurance, driving competition and increasing the options for personalized coverage - except for Pinal County, Arizona. This rural suburb of Phoenix stands as a ghost town for insurers in the Exchange market. With insurance provider Aetna's decision to leave most state markets, Pinal County stood option-less for subsidized coverage for 2017. Not a single plan was available to the residents. The once heralded option-filled market now hangs 9,700 people in Pinal County in the balance waiting for a desperate intervention.⁷ With a shortage of healthcare workers and a higher than usual poverty rate, Katherine Hempstead of the Robert Wood Johnson Foundation remarks that, "It's a dramatic case of a more general thing: There are weaker markets that are going to be less attractive for carriers."⁷ Since then, the insurance provider Blue Cross and Blue Shield have stepped in to provide for this and next year's only option for the people of Pinal County for only a limited time. But for the residents of Pinal county, the word "option" might be too far of a stretch.

In early April of 2016, UnitedHealthcare, the largest healthcare provider in America, announced it would be pulling out of the Obamacare markets in Illinois, Arkansas, Georgia, and Michigan with anticipated losses of \$650 million this year.⁷ UnitedHealthcare's impetus for dropping out is rooted in sharp losses due to a larger demographic of sicker, uninsured customers signing up in higher numbers than healthier ones. With the White House originally hoping that younger, healthier adults would make up 38% of enrollees to financially balance out less healthy claim holders, the current numbers find that they are only about 28% of the marketplace population, far less than expected.⁸ For insurance providers, this was simply an unsustainable rate to work at. As companies

withdrew from the marketplace, ideas of regional marketplace monopolization for companies able to operate at a loss were not farfetched.

Cynthia Cox, associate director of health reform and private insurance at the Kaiser Family Institute, remarks that, “the concern is that in future years, when there are more areas where insurers essentially have monopoly power, that that could lead to higher premiums.”⁹ With an estimated 6 in 10 counties that could lose 2 or more providers in 2017,⁹ President Obama’s plan for an affordable market competition may come to a halt.

What you are saying:

It has been a long way since former Governor Sarah Palin’s usage of “Obamacare death panels”¹⁰ and other hyperbolic vitriol, but arguments still exist nonetheless. While each person holds a different opinion of the ACA, current public polling has seen a dip to 39.2 favorability rating of the ACA (2016)¹¹ according to RealClearPolitics.com. Surprisingly though, 58% of respondents favor replacing the ACA with a federally funded healthcare system in a Gallup poll,¹¹ while about half of respondents would also be okay with keeping the ACA as is in the same poll. With such discontinuity in the data, the polling is more indicative of the unsettled national discourse than the actual policy itself.

What is to be said for the future...

“I like to think of this bill as like a starter home. It is not the mansion of our dreams. But it has a solid foundation, giving every American access to quality, affordable coverage.”¹²

The defence of Obamacare by former Senator Tom Harkin of Iowa elucidated a clear message in his 2009 Huffington Post piece: the ACA is a large step for healthcare reform to combat inequality, but finds itself in need of certain revisions. But with the election of Donald Trump, Harkin’s words seem like a distant memory as we now have an executive and legislative branch that are set on repealing ObamaCare from day one. When asked about how the ACA would be repealed, Trump acknowledged that taking twenty-one million people off of health insurance along with immediately abandoning marketplace hot spots was infeasible,

a more practical, uninflated contrast to his hot campaign trail rhetoric.¹³ But Politico’s Burgess Everett and Rachael Bade explain that the struggle to find a clear path to repealing the law may prove laborious. With the Obamacare Medicaid expansion, regulations on pre-existing conditions, and other cost efficient measures, the Republicans will find “pricey provisions that will complicate Republican efforts to merely gut the law.”¹³ As a result, Republicans are in a pernicious situation: they must come up with a viable alternative that will both satisfy the right wing of the party without completely alienating the people who had benefited from the ACA. Everett delineates the daunting task to, “satisfy conservative critics who want President Barack Obama’s signature initiative gone now, but reassure Americans that Republicans won’t upend the entire healthcare system without a viable alternative that preserves the law’s popular provisions.”¹³ With seven years since the ACA’s inception, we can only wait to see its rebuke or survival.

With the nation’s historically low uninsured rate hampered by a problematic insurance market, our nation’s pursuit of healthcare reform remains difficult and distant. With the Trump administration settling into the White House, we may again see the arduous trudge of politics in healthcare reform. With so many questions left unanswered by both the previous and current administrations, the slow march of political upheaval may indeed be the only clear prediction of what is to come.

References

1. Health Insurance Coverage and the Affordable Care Act. US Department of Health and Human Services (UDHHS). https://aspe.hhs.gov/sites/default/files/pdf/139211/ib_uninsured_change.pdf Published May 5, 2015. Accessed January 3, 2017
2. Health Plan Choice and Premiums in The 2017 Health Insurance Marketplace. ASPE. 2017. <https://aspe.hhs.gov/sites/default/files/pdf/212721/2017MarketplaceLandscapeBrief.pdf>. Accessed March 10, 2017.
3. US Department of Health and Human Services (UDHHS). Health Insurance Coverage and the Affordable Care Act ASPE. 2016. <https://aspe.hhs.gov/sites/default/files/pdf/212721/2017MarketplaceLandscapeBrief.pdf>. Accessed January 1, 2017.
4. Bryan, B. The government just announced some big changes to try to fix Obamacare. *Business Insider*. August 29, 2016. <http://www.businessinsider.com/obamacare-changes-cms-insurance-markets-2016-8>. Accessed December 20, 2016.
5. Carey, M. A. Sick Americans find solace in health reform’s pre-existing conditions guarantee. *PBS Newshour*. November 13, 2013. http://www.pbs.org/newshour/bb/health-july-dec13-healthstories_11-13/
6. Simas, D. Health Coverage Before the ACA, And Why All Americans Are Better Off Now. *Whitehouse.gov*. 2014. <https://www.whitehouse.gov/blog/2014/01/23/health-coverage-aca-and-why-all-americans-are-better-now>
7. Pradhan, R., Pradhan, P. D., Demko, P., Haberkorn, J., Madeleine K. Albright, Stephen Hadley and Nancy Lindborg, Cruz, T., . . . Thompson, A. The county Obamacare forgot. *Politico*. August 22, 2016. <http://www.politico.com/story/2016/08/the-county-obamacare-forgot-227251>
8. Kliff, S. Is Obamacare failing? *Vox.com*. August 24, 2016. <http://www.vox.com/2016/8/24/12538934/is-obamacare-failing> Accessed December 20, 2016.
9. Cox C. Preliminary Data on Insurer Exits and Entrants in 2017 Affordable Care Act Marketplaces. *Kaiser Family Foundation*. August 28, 2016. [- on-insurer-exits-and-entrants-in-2017-affordable-care-act-marketplaces/ Accessed December 19, 2016.
 10. Leonard, K. Is the ‘Death Panel’ Debate Dead? *US News and World Report*. July 9, 2015. <http://www.usnews.com/news/articles/2015/07/09/medicare-rule-revisits-death-panel-issue> Accessed December 18, 2016.
 11. Public Approval of Health Care Law. RealClearPolitics website. \[http://www.realclearpolitics.com/epolls/other/obama_and_democrats_health_care_plan-1130.html#\]\(http://www.realclearpolitics.com/epolls/other/obama_and_democrats_health_care_plan-1130.html#\) Published July 9, 2015. Accessed December 20, 2016.
 12. Harkin, S. T. The Senate’s “Starter Home” Health Reform. *Huffington Post*. March 10, 2010. \[http://www.huffingtonpost.com/sen-tom-harkin/the-senates-starter-home_b_407155.html\]\(http://www.huffingtonpost.com/sen-tom-harkin/the-senates-starter-home_b_407155.html\) Accessed January 3, 2017.
 13. Bade R, Everett B. GOP May Delay Obamacare Replacement for Years. *Politico*. December 1, 2016. <http://www.politico.com/story/2016/12/obamacare-republicans-repeal-replace-232025> Accessed December 19, 2016.](http://kff.org/health-reform/issue-brief/preliminary-data-

</div>
<div data-bbox=)

CONFLICTS WITH THE DISTRIBUTION OF HEALTH CARE FOR REFUGEES

BY KELLY FAN

The year 2015 ended with 65.4 million people displaced. Over half of the world's refugees come from only three countries: Somalia with 1.1 million displaced people, Afghanistan with 2.7 million, and Syria with 4.9 million.¹ These numbers draw attention not only to the enormity of the issue, but also to the huge disparity in displacement among different countries. Whether the result of government crisis and instability or situational emergencies, displacement is an issue that presents risks that can often lead to death. Those who are able to reach their destinations face altogether new challenges apart from the actual act of displacement. More often than not, migrants suffer from issues such as food deficits, sexual exploitation, shelter inadequacies, cultural ostracism, and lack of access to health services. Each of these issues poses a multitude of problems within themselves. Health systems around the world are faced with daily decisions on how to handle sudden population shifts caused by refugees entering and leaving different regions.

The task of providing health care to so many displaced people is made very difficult because of various factors. For one, many host countries lack the technology that allows them to efficiently and accurately update data. This issue leads to a major delay in supplying regions with the adequate information and resources to attend to their immediate needs.² Furthermore, refugees may be distrusting of the health systems in their host countries; they will only seek out medical attention if the situation proves dire.² Perhaps one of the larger pressing issues is that many immigrants live in their host countries illegally and are in hiding, hindering their ability to receive health care.² Many undocumented refugees and immigrants do not wish to seek out public assistance for fear of negatively impacting their potential to become citizens.³

Host countries are often ill-prepared to deal with caring for their own citizens, let alone refugees. For example, in Yemen, where many people suffer from drought, food shortages, and

high levels of unemployment, the health system struggles to meet the demands of even their own citizens and can hardly afford to accommodate the Somali immigrants' needs.² Additionally, the lack of treatment opportunities comes from professionals fleeing the country. In Iraq, violent groups target health care providers which leads to a massive shortage of physicians within the country. Once they immigrate, these health care providers are often forbidden to perform in their host countries, resulting in a loss for both their country of origin and the country to which they immigrated.² Sometimes after immigrating to the host country, a refugee's mental health can deteriorate.⁴ Because many immigrants spend time in refugee camps within their host countries, they are likely to live in harsh conditions and be exposed to violence. This can lead to the development of mental illnesses not experienced before displacement.⁴ Refugees can also be reminded of past trauma, leading to intensified post-traumatic stress disorder, anxiety, or depression.⁴ All of these issues complicate a system that is unable to satisfy refugee health needs and can be detrimental to both refugees and the people of their host countries.

Refugees arriving in their host countries can cause potentially large changes to those regions. For instance, if the number of arriving refugees makes up a significant percentage of a community's or country's population, the demand for resources such as electricity, water, land, food, shelter, and healthcare can greatly increase.¹ When countries that are taking in refugees are already struggling to adequately distribute these scarce resources to their own people, it can be extremely difficult to accommodate the influx of refugees. This leaves many people without access to health care and basic living necessities. Furthermore, excess human waste can contaminate water, increasing the risk of spreading disease not only among refugees but also among people of the host country.⁵ Clearly, when mass immigration occurs, the health needs of both

refugees and the people in their host country are very challenging to meet.

The massive displacement happening all around the globe poses serious problems for millions of people. Health care is only one of the many issues that displacement brings and is interrelated with many other facets of migration. The conflicts surrounding health care can perhaps be mitigated by future consideration of ways to eradicate discrimination. Cross-border cooperation should also be implemented so the rights of refugees are clearly outlined and guaranteed, and health systems should reach out to those in hiding.⁴ These considerations are just part of what may make it possible to achieve adequate health care for refugees and immigrants.

References

1. Edwards, A. Global Forced Displacement Hits Record High. *The UN Refugee Agency*. 2016. <http://www.unhcr.org/enus/news/latest/2016/6/5763b65a4/global-forced-displacement-hits-record-high.html>.
2. Mowafi, H. Conflict, Displacement and Health in the Middle East. *Global Public Health*. 2011; 6: 472-487.
3. Edberg, M., Cleary, S., Vyas, A. A Trajectory Model for Understanding and Assessing Health Disparities in Immigrant/Refugee Communities. *Immigrant Minority Health*. 2010; 13: 576-584.
4. Kirmayer, L. J., Narasiah, L., Munoz, M., et al. Common Mental Health Problems in Immigrants and Refugees: General Approach in Primary Care. *Canadian Guidelines for Immigrant Health*. 2011; 183: 959-967.
5. UNHCR Standing Committee. Social and Economic Impact of Large Refugee Populations on Host Developing Countries. *The UN Refugee Agency*. 1997. <http://www.unhcr.org/en-us/excom/standcom/3ae68d0e10/social-economic-impact-large-refugee-populations-host-developing-countries.html>.

ONE TICKET TO THE MARSHALL ISLANDS

BY MORGAN WIN

Now is the time to find tickets to the Marshall Islands because in a few years, the islands may be underwater! How is it possible that sea levels are rising high enough to overtake an entire country? The answer is climate change. It has been over 50 years since the first warning about global warming was brought to the attention of former Vice-President Al Gore, yet the world has only taken limited action to address it... until now.¹

In December of 2015, the United Nations Climate Change Conference took place in Paris, France and resulted in “195 countries adopt[ing] the first-ever universal, legally binding global climate deal.”² The deal aims to limit the increase in global average temperature to below 2° C by holding countries accountable for their greenhouse gas emissions and to bring countries together every five years to report and discuss the impact of climate change. Efforts to limit the effects of climate change include spreading awareness, providing aid to developing countries, and recognizing that climate neutrality needs to begin. Climate neutrality refers to the countries attempting to keep CO2 emissions low and compensate for any remaining emissions with climate protection measures. A location can be

considered “climate neutral” if harmful greenhouse gases are completely avoided.

Although this agreement is certainly a step in the right direction, it is only set to begin in 2020. That is about three years from now, which is far too long to wait. The most important outcome this agreement has had so far is in emphasizing the gravity of the situation if countries do not start taking climate change seriously. Data from climate scientists in 2016 revealed that the countries that emit the most carbon dioxide are the least concerned with climate change.³ This truly shows how dire the situation is when countries doing the most harm to the environment are the most uninformed. Referring to the graph below, the United States is one of the highest CO2 emitting countries with also one of the lowest climate change concern levels.

The world needs to be more informed about climate change and its consequences. Climate change not only affects the environment, but human health, too. Though developing countries are the most vulnerable to climate change, climate change affects all populations. Malnutrition, malaria, diarrhea, and heat stress are increasingly becoming major causes of death with the earth’s increasing temperature.⁴

People may not realize how critical this is to overall human health because they find solace in fewer winters or increased food production, but these events are not as beneficial as they seem. Infections breed in warm climates. For instance, tick-borne (viral) encephalitis has increased in Sweden as a response to warmer winters while cholera has been amplified in Bangladesh from the increased rainfall and water warming.⁵

These effects get worse as more time passes. It is predicted that climate change will result in 250,000 additional deaths per year and cost the United States \$2-4 billion per year by 2030.⁴ It is going to be a very sad future for our world if policies are not implemented to reduce emissions in the transport, food, and energy sectors. Currently, not many people can recognize that the climate poses a public health risk because our society has placed its concern on other issues. Climate change is steadily becoming more prevalent and creating detriments that will grow into the future whether we choose to acknowledge it now or not.

What can we do to make a difference? We can invest in clean energy systems, the same idea that was suggested 50 years ago! There are also little things that each and every person can do. Start taking the bus, train, walking, or cycling as often as possible. Furthermore, we can invest in fuel-efficient cars and also innovate new agricultural techniques that do not deplete a large portion of nature’s nutrients. For example, nutrient-rich environments suffer as new commodity markets grow.⁶ This marketplace depletes the natural resources (gold, oil, agricultural products, livestock, etc.), thus, draining the environment which propagates climate issues. Sufficient and affordable energy needs to be the goal, and it can be accomplished if activism and awareness about the issue are instilled in the population.

References

1. A. Paris Agreement. Climate Action - European Commission. http://ec.europa.eu/clima/policies/international/negotiations/paris_en. Published February 16, 2017. Accessed March 8, 2017.
2. Gillis, J. Climate Accord is a Healing Step, if not a Cure. *New York Times*. December 12, 2015.
3. Climate change, food systems and population health risks ... Accessed March 8, 2017.
4. Climate change and health. World Health Organization. <http://www.who.int/mediacentre/factsheets/fs266/en/>. Accessed March 8, 2017.
5. Climate change and human health: present and future risks - *The Lancet*. Accessed March 8, 2017.
6. Wike R. What the world thinks about climate change in 7 charts. Pew Research Center. <http://www.pewresearch.org/fact-tank/2016/04/18/what-the-world-thinks-about-climate-change-in-7-charts/>. Published April 18, 2016. Accessed March 8, 2017.

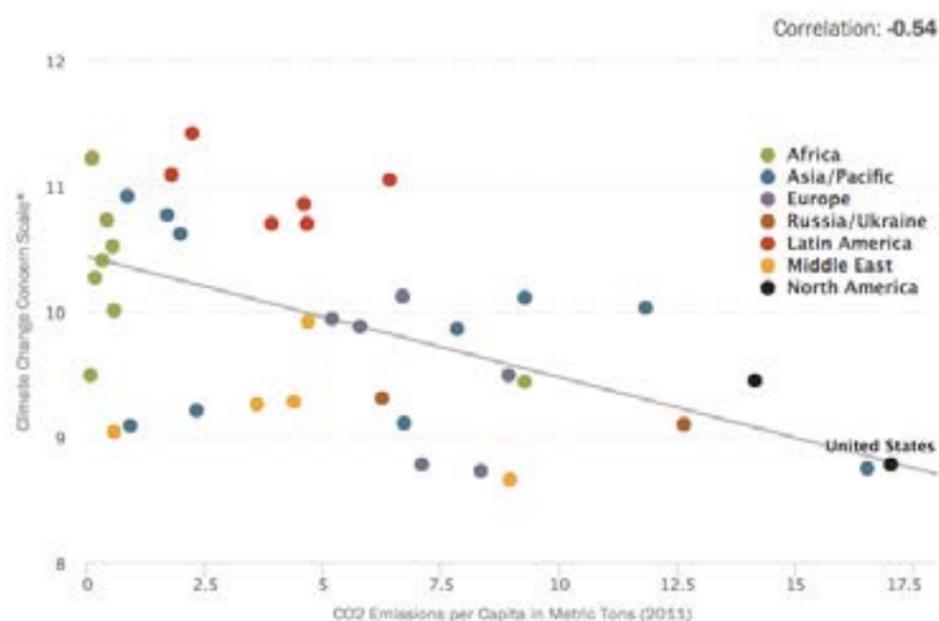


Figure 1: Correlation of Concern vs. Emissions per Capita³

GLOBAL HEALTHCARE SHORTAGE

BY CHIOMA NDUKWE

Over the past few years, laws including the Patient Protection and Affordable Care Act of 2010 have been passed in order to make healthcare more available to the general population. However, as more people gain access to healthcare, a problem that has been building over the past few decades has intensified. According to the World Health Organization, there is a 7.2 million healthcare worker shortage globally. It is projected that there will be a shortage of 12.9 million by 2035.¹ An aging physician workforce combined with a decline in the number of young physicians to replace them and a growing demand for medical services have contributed to this shortage. In the United States, this deficit affects rural and low-income areas more severely. However, other nations not only suffer from the same problems that the United States does, but must also overcome a lack of medical schools, as well as the emigration of physicians from their homelands. All countries have to come up with ways to address this problem.

In the United States, projections have shown that the physician shortage will become more severe in the coming decade. All specialties, from primary to specialized care, will face this problem. However, the surgical specialties will face the greatest shortage. Over one third of the physician workforce today is over 55 years old, so many of the physicians today are approaching retirement.² At the same time, the baby boomer generation is aging and will require a greater amount of medical attention, leading to a medical shortage in the coming years. The shortage will occur no matter what happens; however, there have been several proposals made in order to alleviate the problem. For example, a patient-centered medical home model would cut costs while making healthcare available to more patients. However, in order to address the physician shortage itself, it is believed that the cap on residency positions will need to be removed.³

Medically underserved areas (MUAs) will be the most affected by this shortage. The most common MUAs are rural and inner city areas. In rural areas, the medical shortage is due to the increasing specialization of physicians as well as a lack of

technology in these areas that deters physicians from practicing there. In contrast, the inner city medical shortage is due to inadequate access to health care.⁴ Although there is a high concentration of doctors in the city itself, there may be few to no clinics in certain parts of poorer neighborhoods. The Health Resources and Services Administration (HRSA), an agency of the United States Department of Health and Human Services, is dedicated to combating this inequity. By offering grants and scholarships to pay off student loans for primary care practitioners in exchange for working in one of the MUAs, the HRSA has attempted to entice physicians to work in these areas.

In order to stave off the looming healthcare worker shortage, the United States has imported practitioners from across the globe. In 2010, about 16% of all civilian healthcare workers in the United States were foreign-born.⁵ Hospitals and other agencies recruit these workers from their home countries, then offer them either temporary work visas or permanent visas to work for the specific hospital. The majority of these workers come from the Philippines, although a large number also come from countries like Canada, India, or Nigeria.⁶ However, due to this recruitment, the exporting nations suffer from the strain on their medical systems due to a shortage of medical personnel. They also bear the burden of the economic loss from the emigration of their educated citizens.

In order to compensate for the loss of their healthcare personnel, these nations implement programs and offer incentives to persuade their workers to remain. Governments increase healthcare spending in order to give the workers the tools they need to treat their patients. In some nations, healthcare workers are offered compensation, such as increased wages or allowances, to entice them to work in their homeland. Most importantly, medical schools themselves are recruiting new workers to overcome the shortage.⁷ Although these countries have come up with ways to alleviate some of the strain of a healthcare shortage, they, as well as developed nations, still must do more to address the looming problem.

References

1. Global health workforce shortage to reach 12.9 million in coming decades. *World Health Organization*. 2013. Retrieved from http://www.who.int/mediacentre/news/releases/2013/health-workforce-shortage/en/?_escaped_fragment_
2. New Research Confirms Looming Physician Shortage. *AAMC*. 2016. Retrieved from https://www.aamc.org/newsroom/newsreleases/458074/2016_workforce_projections_040_52016.html
3. Porter, S. Significant primary care, overall physician shortage predicted by 2025. *Annals of Family Medicine*. 2015. Retrieved from <http://www.aafp.org/news/practice-professional-issues/20150303aamcwkforce.html>
4. Harrah, S. Medically Underserved Areas: Regions Where U.S. Needs Doctors - The UMHS Endeavour. *The University of Medicine and Health Sciences*. 2013. Retrieved from <https://www.umhs-sk.org/blog/medically-underserved-areas-regions-where-u-s-needs-doctors/Caribbean-Medical-Schools>.
5. McCabe, B. K. Foreign-Born Health Care Workers in the United States. *Migration Policy Institute*. 2013. Retrieved from <http://www.migrationpolicy.org/article/foreign-born-health-care-workers-united-states/>
6. Brush, B. L., Sochalski, J., & Berger, A. M. Imported Care: Recruiting Foreign Nurses to U.S. Health Care Facilities. *Health Affairs*. 2004. 23(3), 78-87. doi:10.1377/hlthaff.23.3.78
7. Kumar, P. Providing the Providers — Remediating Africa's Shortage of Health Care Workers. *New England Journal of Medicine*. 2007. 356(25), 2564-2567. doi:10.1056/nejmp078091

WORLDWIDE LACK OF RESOURCES FOR TRAUMA-RELATED MENTAL DISORDERS

BY CLAUDIA DE BRUYN

The severity of mental illness and trauma is globally underestimated. This social problem stems from the current lack of adequate mental health care, the stigma surrounding mental illness, and differing cultural approaches to treatment. All these barriers work together to discourage people around the world from seeking help. Currently, health care systems worldwide do not properly address mental health issues. Instead, a public health approach must be implemented that works to educate and transform the current health care system to better support mental health and psychosocial recovery from trauma while further reducing widespread suffering.

The Ebola virus disease (EVD) outbreak is one such example of trauma.¹ EVD has led to significant mental and psychosocial effects for orphans and other affected family members. Such intense distress arises from fear of the virus as well as mandated quarantines. Physical isolation puts individuals at a higher risk for psychosocial problems and increases financial stress due to loss of income.²

Additionally, mental health challenges persist in countries like Syria that have experienced great trauma stemming from displacement and violent government protests. Brookings reports, “the Syrian refugee children are at great risk for mental health issues, having experienced very high levels of trauma: 79% had experienced a death in the family; 60% had seen someone get shot or physically abused; and 30% themselves had been shot at or physically abused.”³

Mental health resources remain difficult to access and fees that attempt to make medicine accessible create heavy financial burdens on many refugees who are below the refugee countries’ national poverty lines. Privatization of the health care system in Middle Eastern countries reinforces these barriers to care, allowing and encouraging higher user fees.² Many worry that if the mental health needs of vulnerable refugee children remain unaddressed, “their successful development into adulthood will be impaired, as the grim prospect of a ‘lost’ generation.”³ The world must invest now

in mental health resources in refugee countries for children before it is too late.

Further trauma in the context of armed conflict arises from sexual and gender-based violence. Sexual violence has historically and repeatedly been linked to armed conflicts. Such consequences of sexual violence include negative health outcomes along with rejection from society. Mental disorders reported include anxiety (including PTSD), major depressive disorder, substance use disorders, and suicidal ideations.⁴

Jordan, Lebanon, and Turkey’s current health care systems are not effective in helping overcome mental illnesses. Rather, a “multifaceted, community-based approach, informed by members of the community will create much stronger support systems for children.”³ This approach proves significantly more effective as well as cost-effective compared to individual-centered approaches in current therapy models.³ Such programs use four tiers of intervention: community level outreach and family visits, school based interventions (i.e. skill building programs), individual mental health counseling at schools, and individual mental health counseling (conflict and health). Additionally, partnerships with local humanitarian organizations can establish much needed trust for an effective health care model.

Such training programs must be implemented to help providers recognize the signs of trauma and help children develop the skills to cope with trauma. With increased awareness surrounding mental illness, families and individuals can work together with professionals to address trauma and mental illnesses to ensure culturally appropriate treatment.⁴ Currently, countries around the world do not provide complex, specialized mental health care; however, with implementations of public health programs, progress and change will soon follow.

References

1. IASC Reference Group on Mental Health and Psychosocial Support in Emergency Settings (2015). *Mental Health and Psychosocial Support in Ebola Virus Disease Outbreaks: A Guide for Public Health Programme Planners*. Geneva.
2. Karasapan O. Syria’s mental health crisis. Brookings. <https://www.brookings.edu/blog/future-development/2016/04/25/syrias-mental-health-crisis/>. Published 2016.
3. Tol WA, Stavrou V, Greene C, Mergenthaler C, van Ommeren M, Moreno CG. Sexual and gender based violence in areas of armed conflict a systematic review of mental health and psychosocial support interventions. *Conflict and Health*. August 2013. doi:10.1163/2210-7975_hrd-9928-3002.

WHY DON'T ANTIDEPRESSANTS WORK IN SOME PATIENTS?

BY ABIGAIL OLSEN

According to Mayo Clinic, depression is “a mood disorder that causes a persistent feeling of sadness and loss of interest.”¹ It affects how a person feels, thinks, and behaves on a day-to-day basis, and some individuals may feel like their lives aren't worth living. When treating depression, there are two main strategies: prescribing an antidepressant and/or counseling. Though antidepressants work for many people, about 30 to 50% of the depressed population do not feel relief.² No one knows why these individuals do not respond to antidepressants, but a 2016 study done in Europe may have an explanation.

In treating depression, doctors can prescribe many different medications. Selective Serotonin Reuptake Inhibitors (SSRI's) are amongst the most common, with Prozac being the most well-known.² SSRI's increase the level of serotonin, therefore increasing the number of messages being sent between nerve cells in the brain. Researchers from the European College of Neuropsychopharmacology (ECNP) argue that prescribing this drug does not allow people to recover from depression.² Instead, they have found that it alters the mindset of the patient. Researcher Silvia Poggini states that, “in a certain way it seems that the SSRIs open the brain to being moved from a fixed state of unhappiness, to a condition where other circumstances can determine whether or not you recover.”² In other words, it is the environment that depressed people engage with during the treatment that makes or breaks the possibility of getting better or worse- not the antidepressant itself.

Researchers from the ECNP tested this theory by obtaining a sample of mice and putting them under stressful conditions for two weeks. They started the mice on fluoxetine, a common SSRI antidepressant, and then split the group in half. Twelve mice continued to be stressed while the other 12 were accommodated with a relaxed environment. The team then tested the levels of cytokines - protein-related molecules released due to stress and which aid cell-to-cell communication in the immune system

of the mice.² The results were clear: the environment the mice were living in heavily impacted the response to the antidepressant. The levels of pro-inflammatory genes in the mice living in the more comfortable environment increased significantly with fewer signs of depression, while the stressed mice experienced a decrease in the pro-inflammatory gene level with more signs of depression. Being prescribed an antidepressant has been proven to not always be enough on its own- the environment also needs to be positive in order to obtain positive results.

An SSRI antidepressant has one main function- to “open” the brain to be influenced by the world around it. “SSRI's put you in the boat, but a rough sea can determine whether you will enjoy the trip,” Poggini stresses. It is the environment that dictates whether or not a depressed patient will feel a positive change in his or her life, not the antidepressant. This study brings up a controversial subject- the possibility of overprescribing antidepressants due to over- medicalization. Dr. Des Spence, Glasgow GP, states that “we use antidepressants too easily, for too long, and that they are effective for few people (if at all).”³ The definition of clinical depression, two weeks of low mood even after bereavement, is too loose according to Dr. Spence. Does this also contribute to the inefficacy of antidepressants in some patients? Do they not need them at all?

Though this study did not select a wide variety of SSRI's and used an animal model, it indicates a connection between medical treatment and the environment in which it works. This idea may be analogous with other medical disciplines and more research could be done to find out. Where do we go from here? Researchers from Cedars-Sinai Medical Center in Los Angeles, California have come up with a way to improve the quality of life for depressed patients called Future Directed Therapy. The results of the test showed that patients involved in FDT experienced “reduced hopelessness and increased positive future expectations.”⁴ Planning

to have a good attitude in the future when dealing with depression showed a positive result among the patients and supported the experimental results of the previous case. How will you view the world today?

References

1. Depression (major depression). *Mayo Clinic*. <http://www.mayoclinic.org/diseases-conditions/depression/basics/definition/con-20032977>. Published July 7, 2016. Accessed November 7, 2016.
2. Why don't antidepressants work in some patients? *ScienceDaily*. <http://www.sciencedaily.com/releases/2016/09/160920083019.htm>. Published September 20, 2016. Accessed November 6, 2016.
3. Are antidepressants overused? *ScienceDaily*. <http://www.sciencedaily.com/releases/2013/01/130122191404.htm>. Published January 22, 2013. Accessed November 7, 2016.
4. Improving Quality of Life for Patients with Major Depressive Disorder by Increasing Hope and Positive Expectations with Future Directed Therapy (FDT). *Innovations in clinical neuroscience*. <https://www.ncbi.nlm.nih.gov/pubmed/23630646>. Published March 10, 2013. Accessed November 7, 2016.

HALF MATCH BONE MARROW WIPES OUT SICKLE CELL IN SELECT PATIENTS: HAPLOIDENTICAL BONE MARROW TRANSPLANTS GIVE NEW HOPE FOR CURATIVE SICKLE CELL THERAPY

BY KENNETH BOOKER

For many people, the term “sickle cell” is little more than a bell-ringing phrase that suggests a stock image of a sick individual. For some, however, it is a stark reality. John Craig and his two-year-old daughter Madison are two of those people. Nicole Mclaurin, John’s spouse and Madison’s mother, recently passed away due to a pulmonary embolism, a secondary complication of her blood disorder.

Sickle cell disease (SCD) is a debilitating hemoglobin disorder characterized by a defect in erythrocyte formation. Its clinical complications include, but are not limited to, thrombosis, frequent episodes of extreme pain, and multiple organ damage due to impaired blood cell mobility.¹ The median life expectancy for those with SCD is less than 50 years.² While this represents an improvement in treatment over the past 30 years, quality of life for sickle cell patients is still a huge concern. “[Nicole] had to go get treatment usually three or four times out of the month,” said John. “She often had pain crises and either got little sleep, or was so exhausted she would finally [fall asleep]. It was a back and forth type of thing. When it got bad enough she had to stay in the hospital up to two weeks at a time for blood transfusions and pain management,” he added. “It took a lot out of her.” (J. Craig, personal communication, December 3, 2016)

Bone marrow transplantation (BMT) is a life-saving treatment that has the potential to correct SCD by restoring proper blood cell formation. The accessibility of the treatment, however, leaves much to be desired. Traditionally, BMT has been thought to be a lock and key procedure. In other words, a near perfect donor match is required. This is problematic given that less than 30 percent of people will have a perfectly matching donor. Outside of one’s immediate family, the chances of finding a full-matched donor fall to 10 percent. The numbers are even lower for minorities, who are underrepresented in national

registries, and who, paradoxically, comprise the majority of the SCD population.³

To circumvent these issues, many medical research institutions are exploring the utility of a half match, or “haploidentical,” BMT. At Johns Hopkins University, preliminary clinical trials showed that among 17 haploidentical transplants, 11 were successful, eight of which used donors who had no relation to the recipient. All patients received a pre-transplant reduced-intensity conditioning regimen of low-dose chemotherapy drugs and low-dose total body radiation. Post-transplant, high doses of the chemotherapeutic drug cyclophosphamide were administered. Cyclophosphamide destroys overactive immune cells from the donor’s marrow while preserving hematopoietic stem cells.^{4,5} After a two-year median follow-up, these eight patients were effectively cured of SCD and weaned off of immunosuppressants. Their new blood cells were now entirely derived from their donors’ marrow.⁴

While BMT as a cure for both malignant and nonmalignant blood disorders is not a new discovery, it has long been debated as to whether or not haploidentical BMT is effective. Compared to alternative methods, such as umbilical cord blood transplants, full-matched bone marrow shows greater instances of graft versus host diseases (GVHD).⁶ Half-matched marrow is expected to show higher GVHD, but so far research has been promising, yielding transplant results that are nearly comparable to those using unrelated full-matches to treat blood cancers. A study published in the journal *Biology of Blood Marrow Transplantation* compared full match transplant outcomes to those of the haploidentical BMTs in patients with blood cancers. The study, which was carried out in Thomas Jefferson University’s Department of Medical Oncology, examined three year follow-up data from patients who underwent either of the two procedures.

The findings were convincing, showing that 70% of patients in both groups continued to live cancer-free.⁶

When asked whether he and Nicole had ever considered the idea of a BMT, John’s response was an immediate “yes.” After being informed of the haploid BMT procedure, John grimaced at the seeming intensity of the protocol, but agreed it would be a relatively small imposition for a potentially life-saving treatment.

For many sufferers of both malignant and nonmalignant blood disorders, haploidentical BMTs are a promising horizon in medical research. The utility of the haploidentical BMT is to effectively increase treatment accessibility. While it’s far from likely to wipe out sickle cell disease, the advent of the haploidentical BMT will surely help the cause. Taking matters a step further, researchers from Johns Hopkins University School of Medicine have been working on a CRISPR-based gene editing approach to tackle SCD.⁸ CRISPR is a gene-based adaptive immunity mechanism discovered in bacteria that allows them to edit their own genome, removing the intrusive genetic material of infectious viruses.⁹ By carefully manipulating this biochemical mechanism, researchers can potentially correct the culprit SCD gene in patients’ own red blood cell samples in-vitro. This would eliminate the need for allogeneic marrow altogether. Indeed, more research is required going forward in sickle-cell patients to optimize the half-match approach before this procedure becomes common practice. Researchers are looking to expand clinical trials and find ways to minimize acute and chronic GVHD, which will prove challenging. For the foreseeable future, however, the prospects are bright.

References

1. Shenoy S, Eapen M, Panepinto JA, et al. A BMT CTN phase II trial of unrelated donor marrow transplantation for children with severe sickle cell disease. *Blood*. 128(21): 2561-2567. doi: 10.1182/blood-2016-05-715870
2. Platt OS, Brambilla DJ, Rosse WF, et al. Mortality In Sickle Cell Disease -- Life Expectancy and Risk Factors for Early Death. *N Engl J Med*. 330:1639-1644. doi: 10.1056/NEJM199406093302303
3. Hede, K. Half-Match Bone Marrow Transplants May Raise Odds for More Recipients. *JNCI*. 2010; 103(10), 781-783.
4. Half-Match Bone Marrow Transplants Wipe Out Sickle Cell Disease in Selected Patients. Johns Hopkins Medicine Web site. http://www.hopkinsmedicine.org/news/media/releases/half_match_bone_marrow_transplants_wipe_out_sickle_cell_disease_in_selected_patients. Published 2012, September 30. Accessed October 26, 2016.
5. Half-Match Bone Marrow Transplant Cures 22-Year-Old with Aplastic Anemia and PNH. Cleveland Clinic Web site. <https://consultqd.clevelandclinic.org/2016/05/half-match-bone-marrow-transplant-cures-22-year-old-aplastic-anemia-pnh/>. Published May 11, 2016. Accessed October 23, 2016.
6. Locatelli F, Kabbara N. Outcome of patients with hemoglobinopathies given either cord blood or bone marrow transplantation from an HLA-identical sibling. *Blood*. 122(6): 1072-1078. doi: 10.1182/blood-2013-03-489112
7. Thomas Jefferson University. Blood cancers: Half-matched donor bone marrow transplant may be as good as full match. *ScienceDaily*. October 7, 2015. www.sciencedaily.com/releases/2015/10/151007084531.htm. Accessed October 31, 2016
8. Blackstone A. Hopkins researchers offer new hope to sickle cell patients. *Baltimore Times*. March 27, 2015. <http://baltimoretimes-online.com/news/2015/mar/27/hopkins-researchers-offer-new-hope-sickle-cell-pat/>. Accessed November 01, 2016.
9. CRISPR/Cas9 and Targeted Genome Editing: A New Era in Molecular Biology. New England BioLabs Web site. <https://www.neb.com/tools-and-resources/feature-articles/crispr-cas9-and-targeted-genome-editing-a-new-era-in-molecular-biology>. Published January 2014. Accessed March 8, 2017.

GLUTAMATE'S NEWFOUND ROLE IN NEUROMUSCULAR DEVELOPMENT

BY JESSICA POON

For decades, scientists believed only one neurotransmitter, acetylcholine (ACh), was responsible for neuromuscular development. New studies have come to show that the neurotransmitter glutamate may have a role as well. It is well known that glutamate, the most common neurotransmitter in the brain, functions in invertebrate neuromuscular functions, and acetylcholine serves the same role in vertebrates. However, glutamate has been found to play a significant role in the neuromuscular development of vertebrates contrary to the decades-long belief that the sole neurotransmitter responsible is acetylcholine.¹

At the University of Buffalo and John Hopkins University, researchers have discovered that in mice, glutamate is employed in a vital position in muscle fiber maturation happening in the neuromuscular junction.¹ The neuromuscular junction is a cellular synapse where the motor neurons and skeletal muscle fibers exchange signals with each other. This junction allows for the translation of chemical messages that activate functioning.² For example, at the neuromuscular junction, motor neurons transmit signals to the muscle fibers, which causes muscles to contract.

With the discovery that glutamate is involved at this junction, the team tasked themselves with understanding the connections at the spinal cord and muscles during maturation. Newborns have muscle fibers that contact as many as 10 nerves. In adults, these are contacted by just a single motor neuron. Scientists claim that the nerve most effective in activating the muscle is the one that wins. The 10 nerves activating the muscle fibers at birth is narrowed down to the most effective one. Dr. Personius from the University of Buffalo (UB) found that nerves in humans release molecules that are converted into glutamate, which activates glutamate receptors like N-methyl-D-aspartate (NMDA) receptors.¹ These NMDA receptors are important to the central nervous system for controlling brain development, learning, and synaptic plasticity.

The researchers at UB hypothesized that glutamate receptor activation modulates the development of the neuromuscular system. They showed that the response of the muscle to glutamate is very strong at birth, but quickly disappears as mice mature, which indicates that the neuromuscular functioning has developed.

In one study published in the *Journal of Neurochemistry*, researchers at East Carolina University's School of Medicine analyzed neuromuscular junctions for glutamate regulation of the non-quantal releases of acetylcholine.³ Glutamate is found to regulate non-quantal ACh secretion from rat motor nerve endings. In support for the notion that glutamate has a role as a signaling molecule at the neuromuscular junction, glutamate transporter mRNA has been found in the cytoplasm of rat spinal motor neurons coupled with a glutamate-like immunoreactivity.³ Glutamate has been found in nerve terminals of rat motor neurons in association with synaptic vesicles. Through various studies at the Brody School of Medicine, a strong suggestion of glutamate being a mammalian neuromuscular junction signalling molecule resulted.

Another group of researchers at the Kazan Institute of Biochemistry and Biophysics has taken the initiative to analyze glutamate effects in the rat neuromuscular system for effects on spontaneous acetylcholine secretion processes.⁴ They base their research on the initial idea that glutamate is involved in rat motor nerve endings, is associated with synaptic vessels, and can be released simultaneously with acetylcholine.⁴ Prior to this study, there was no data on glutamate's effects on the spontaneous quantum and non-quantum secretion of acetylcholine in mature mammalian motor endplates. They found that glutamate has no effect on the processes of spontaneous quantum secretion of acetylcholine in mature neuromuscular junctions in mammals. Through their collected data, researchers from the Kazan Institute have gained ground to suggest that "glutamate secreted from nerve terminals along

with acetylcholine can activate NMDA receptors on the postsynaptic membrane of the muscle fiber."⁴ Therefore, glutamate can take part in the control of neuromuscular skeletal movement in mammals.

In addition, another study done at Ohio State University on glutamate receptors at neuromuscular junctions in mice finds that NMDA receptor subunits localize to the postsynaptic membrane and glutamate localizes specifically to this synapse in skeletal muscle.⁵ Interestingly, by knocking out NMDA receptor subunits, Ohio State Medical Researchers discovered that resulting phenotypes are similar to those typically associated with neuromuscular disorders. This indicates that since glutamate functions in activating NMDA receptors, in the absence of glutamate, NMDA would not be activated. This leads to the conclusion that glutamate plays a large role in neuromuscular development.

Overall, this finding paves the way to an understanding of why peripheral nerve trauma limits the return of the muscle function. This discovery promotes further study focusing on a new hypothesis: peripheral nerve traumas can be improved by manipulating NMDA receptors to reduce poor outcomes.

References

1. University of Buffalo. Glutamate plays previously unknown role in neuromuscular development. *Science Daily*. September 19, 2016. www.sciencedaily.com/releases/2016/09/160919094528.htm. Accessed March 9, 2017.
2. Vilmont VCA, Cadot B, Ouanounou G, Gomes ER. A system for studying mechanisms of neuromuscular junction development and maintenance. *Journal of Cell Science*. 2016;129(14). doi:10.1242/jcs.194613.
3. Malomouzh, A. I., Mukhtarov, M. R., Nikolsky, E. E., Vyskocil, F., Lieberman, E. M. and Urazaev, A. K. (2003), Glutamate regulation of non-quantal release of acetylcholine in the rat neuromuscular junction. *Journal of Neurochemistry*, 85: 206–213. doi:10.1046/j.1471-4159.2003.01660.x
4. Malomuzh, A.I., Mukhtarov, M.R., Urazaev, A.K. et al. *Neurosci Behav Physiol* (2002) 32: 577. doi:10.1023/A:1020497308865.
5. Mays TA, Sanford JL, Hanada T, Chishti AH, Rafael-Fortney JA. Glutamate receptors localize postsynaptically at neuromuscular junctions in mice. *Muscle & Nerve*. 2009;39(3):343-349. doi:10.1002/mus.21099.

SCHWANN CELLS: THE KEY TO UNLOCKING EPIGENETIC NERVE REGENERATION

BY MED JIMENEZ

When people think about the fundamental units of the brain, they often think of neurons. In reality, glial cells both outnumber neurons and play a pivotal role in the physical support of them. Structurally, glial cells lack axonal projections and dendrites, which are typical anatomical features of neurons. Glia also cannot generate action potentials, which is a form of cell signalling so they cannot conduct bioelectricity.¹ However, to compensate for these missing features, glia have one particular ability that neurons do not: nerve regeneration.

In the University of Wisconsin-Madison, Drs. Holly Hung, Rebecca Kohnken, and John Svaren studies the Schwann cell, a specific type of glia that is important for the myelination process in sensory and motor neurons in the peripheral nervous system. The myelin sheath is an insulation layer composed of fats that helps protect neurons. It also increases the bioelectrical signaling since neuronal electrical impulses propagate by a process called saltatory conduction.² This conduction allows for decreased resistance and faster conductance for faster cell communication, and was discovered by Nobel Laureate Andrew Huxley in 1949. In addition, Schwann cells have recently been discovered to play a crucial role in nerve regeneration.

After closely studying axonal regeneration in mice, scientists from the University of Wisconsin-Madison realized that when the organism had severed neuronal axons, specific genes were expressed that created proteins crucial for axonal repair due to the environmental stress.³ Structurally, axons are protrusions from the neuronal cell body that are important in many neuronal signaling pathways. Ablations in this part of the neuron are detrimental, as bioelectrical impulses, vesicles, or essential nutrients cannot pass, resulting in many types of defects, such as a blockage of the correct inputs and outputs in the sensory or motor relay. When Svaren found the activated genes and their protein products, he realized this was crucial in the neuroregeneration pathway. The environmental

stress caused changes in gene expression, better known as epigenetic modification. In this regulation, key enzymes such as histone acetyltransferase (HAT) or histone deacetylase (HDAC) can bind or loosen DNA through acetylation. Euchromatin, which is the conformation that chromosomes undergo when they are available for transcription, are modulated by this acetylation process. This process is essential in transcription (DNA to RNA) and later in translation (RNA to protein).⁴

In fact, the gene in question was polycomb repressive complex 2 or PRC2, and the activation allowed Schwann cells to go into a repair mode. In this mode, the Schwann cells degrade the old myelin and send out signals to hemoglobin in order to help clear the surrounding area. After the initial cleanup, a new nerve pathway is created, followed by the myelination of the newly formed neuron. However, the process of injury cleanup is very long.⁵ They hope that drug testing and mapping out the initiation process of PRC2 will lead to human clinical trials and serve as the go-to technique for nerve regeneration. It looks like glia are not lacking after all.

References

1. Carr F. Glia: Identity-driven. *Nature Reviews Neuroscience*. 2016.
2. Huxley AF, Stämpeli R. Evidence for saltatory conduction in peripheral myelinated nerve fibres. *The Journal of physiology*.1949; 108(3): 315-339.
3. Hung H, Kohnken R, Svaren J. The nucleosome remodeling and deacetylase chromatin remodeling (NuRD) complex is required for peripheral nerve myelination. *The Journal of Neuroscience*. 2012; 5: 1517-1527.
4. Verdin E, Ott M. 50 years of protein acetylation: from gene regulation to epigenetics, metabolism and beyond. *Nature Reviews Molecular cell biology*. 2015; 16(4) 258-264.
5. Ma KH, et. al. Regulation of peripheral nerve myelin maintenance by gene repression through polycomb repressive complex 2. *The Journal of Neuroscience*. 2015; 22: 8640-8652.

THE TICKING OF THE EPIGENETIC CLOCK

BY ALEXANDER KRAVETS

Thirty years ago, one German teenager formed a pact with his identical twin and childhood friend to pursue science with the intention of extending the human lifespan.¹ This German teenager grew up to become what can only be described as a “biomathematician,” conducting research studies in human epigenetics and biostatistics at the University of California, Los Angeles. Dr. Steve Horvath certainly remains true to his adolescent ambition; he is the sole author of the research paper that details his most significant contribution to aging and epigenetics research.²

Previous discoveries in aging research indicated that biomarkers in aging correspond to the epigenetic maintenance of the organism. This conclusion suggests that the biological age of an organism is determined by its epigenetic processes.² Dr. Horvath took this suggestion one step further: he sought to develop a software program that can accurately predict the biological age of an organism, dubbed the epigenetic clock.

By analyzing an unprecedented amount of DNA methylation data from healthy and cancerous tissues, Dr. Steve Horvath determined that the DNA methylation (DNAm) age measures the cumulative work done by the organism’s epigenetic maintenance system (EMS model). Not only does his software program accurately predict the DNAm age of an organism across a broad spectrum of cell and tissue types, he discovered direct correlations between aging-related conditions and the DNAm “ticking” rate.² This program confirmed Dr. Horvath’s postulation of the EMS model in the aging of human tissue. The development and implementation of this program had been unprecedented within the field of epigenetics.

Although Horvath’s software has led to major breakthroughs, its implementation has not been perfect. In an erratum paper— published two years after its release— Dr. Horvath retracted a statement in which he concluded that, “cancer is associated with an increased DNA methylation age

(.e. positive age acceleration) in most cancer types.”³ The erratum paper addresses an error he discovered in the software coding relating to the analysis of cancer tissue data. This error incurred a systematic overestimation of the DNAm age in the analyzed cancer tissues. Although this error had occurred, it did not affect the analysis of non-cancer tissue data, which still remains accurate. Having succeeded in creating the epigenetic clock, Dr. Horvath sought to use it in order to better understand the process of human aging.

One significant application of the software program addresses the effects of ethnicity/race and sex on DNAm age in a cross-sectional study conducted by Dr. Horvath et al. Note, no prior epigenetics study had been conducted to specifically compare the molecular aging rates among gender and ethnic/racial groups. The objective of this study was to “...explore relationships between epigenetic age and race/ethnicity, sex, risk factors of coronary heart disease (CHD), and the CHD outcome itself.”⁴

What had been concluded from this study is that the epigenetic aging rates differ between racial/ethnic and gender groups. Associations were statistically determined between risk factors and certain ethnic/racial groups, but not to the extent that a definitive correlation could be established.⁴ Doubts were also expressed in the analyses of DNA methylation data across the demographic groups; to supplement these doubts, an overall suggestion was made to conduct longitudinal studies within specified demographic groups. Ambivalently, the paper concludes in this fashion.

The actual importance of this study is implicit in the wide-scale application of the epigenetic clock in the analysis of racial and gender disparities in biological aging. Interestingly enough, this is only one vein of inquiry in which the unique potential for the application of this software has been explored. There are many more studies that Dr. Horvath has conducted— along with other researchers— that involve the use of the epigenetic clock. Yet, its

potential remains to be completely explored.

As the epigenetic clock continues to tick, Dr. Steve Horvath comes closer to prying it open.

References

1. Gibbs, W. W. Biomarkers and ageing: The clock-watcher. *Nature*. April 8th, 2014. Retrieved November 02, 2016, from <http://www.nature.com/news/biomarkers-and-ageing-the-clock-watcher-1.15014>
2. Horvath, S. DNA methylation age of human tissues and cell types. *Genome Biology*. October 11th, 2013. 14(10). Doi: 10.1186/gb-2013-14-10-r115
3. Horvath, S. Erratum to: DNA methylation age of human tissues and cell types. *Genome Biology*. March 19th, 2015. 16(1). Doi: 10.1186/s13059-015-0649-6
4. Horvath, S., Gurven, M., Levine, M. E., Trumble, B. C., Kaplan, H., Allayee, H., . . . Assimes, T. L. An epigenetic clock analysis of race/ethnicity, sex, and coronary heart disease. *Genome Biology*. 2016. 17(1). Doi: 10.1186/s13059-016-1030-0

SHEPHERDING ALPHA-SYNUCLEIN COULD BE THE ANSWER TO TREATING PARKINSON'S DISEASE

BY ANASTASIYA LOOS

You are sitting at the dinner table on Thanksgiving. Your family and friends surround you with laughter and joy. You admire the freshly cut turkey on your plate and eagerly stab into it with your fork. Now, you begin lifting it to your mouth, the warm gravy dripping back onto your plate as the turkey is raised higher and higher. Only, the turkey doesn't get to your mouth; you try to raise it but a force stops you- the trembling of your hands. Your guests quietly watch you struggle as your hands continue to tremble.

The above scene describes the embarrassment a Parkinson's patient experiences on a frequent basis; trembling of the body is a common symptom of Parkinson's disease. Parkinson's is a neurodegenerative disorder of the brain characterized by rigid muscles, stalled motor movement, and involuntary muscular spasms.¹ While medications exist to help patients cope with the symptoms, no cures exist. However, as of today, a cure may no longer seem impossible. Recent research by Giuliana Fusco, a graduate student at the University of Cambridge, has found evidence to suggest that treatment of Parkinson's will involve understanding the function of alpha-Syn, the protein created by the alpha synuclein gene.² This breakthrough could potentially lead to a cure for Parkinson's by addressing the mutations that affect alpha-synuclein and cause its improper functioning.

Although its mutation can result in Parkinson's disease, the alpha-synuclein gene is crucial for a healthy brain. Scientists understand that the alpha-synuclein gene encodes alpha-Syn proteins that regulate the flow of synaptic vesicles, which are fundamental to effective brain signaling.² The synaptic vesicles are used by neurons to carry information down a neuronal pathway with the help of synapses. Without this gene, too few or too many neurotransmitters could be released in a synapse, resulting in the acceleration or stalling of brain and

motor functions, as in the case of the aforementioned victim. Because the protein is integral in inhibiting or exciting synapses, it acts as a gatekeeper, or shepherd, for action potentials. For example, alpha-synuclein may release or inhibit the neurotransmitter dopamine, which, in addition to other things, activates feelings of happiness. In addition to regulating neuronal synapses, alpha-synuclein plays a role in other functions, such as facilitating neuronal plasticity, which allows neurons to grow.³

Nevertheless, mutations in the alpha-synuclein gene can result in Parkinson's disease. Because alpha-synuclein is responsible for the regulation of synapses, an extreme mutation will result in irreversible consequences- neuropathological lesions.⁴ Essentially, when mutated, alpha-synuclein is responsible for the destruction of tissue in the nervous system. In a similar manner, specific mutations of the gene can result in variations of Parkinson's disease. Researchers in the United Kingdom found that a missense mutation in the alpha-synuclein gene was found to cause a rare, familial form of Parkinson's disease, which may cause the degeneration of nerves that release dopamine as a neurotransmitter.¹ The laboratory's discovery shows that the mutations in alpha-synuclein are more complex than merely cause-and-effect because specific mutations will result in specific forms of Parkinson's disease.

While it is known that mutations in alpha-synuclein may cause Parkinson's, the wider scope of alpha-synuclein's functions remain unclear. Some scientists argue that as a result of Alpha-syn proteins impairing neuronal function, signaling is also affected.¹ While some scientists believe signaling inhibition causes Parkinson's, others believe that an aggregation of alpha-synuclein accounts for neurodegeneration.¹ The general consensus now is that while an alpha-synuclein mutation may be present in Parkinson's patients, the wider scope

of its effects are still unknown. Because the brain is sensitive and highly intricate, scientists cannot draw conclusions definitively regarding the effects of mutated alpha synuclein on the brain. Before any conclusions can be drawn, specific functions of the gene need to be further studied to understand hopeful treatment approaches for Parkinson's.²

Regardless of the uncertainty in the specific role that alpha-synuclein plays in inducing Parkinson's, the advanced discovery of alpha-synuclein's influence in the pathology of Parkinson's disease alludes to hopeful advancements in the near future. Most modern scientists believe that targeting alpha synuclein is a step in the right direction.⁵ As a result of this, much of today's research is directed toward developing strategies to increase or diminish the aggregation of alpha-Syn proteins.⁵

As a final note, it is important to recognize that a cure for Parkinson's has yet to be discovered; Fusco's research only suggests a potential cure by pointing scientists in the right direction— understanding the scope of alpha-synuclein proteins. In studying how the gene works when healthy, scientists can focus efforts on preventing mutations of the disease.

References

1. Goerdert M. Alpha-Synuclein and Neurodegenerative Diseases. *Nature Reviews Neuroscience*. 2001; 2: 492-501. doi: 10.1038/35081564.
2. Parkinson's Disease plays vital 'marshalling' role in healthy brains. University of Cambridge Website. <http://www.cam.ac.uk/research/news/parkinsons-disease-protein-plays-vital-marshalling-role-in-healthy-brains>. Published September 19, 2016. Accessed October 26, 2016.
3. Wooc-Kaczmar A, Ghandi S, Wood NW. Understanding the molecular causes of Parkinson's disease. *Trends in Molecular Medicine*. 2006; 12(11): 521-528. <http://dx.doi.org/10.1016/j.molmed.2006.09.007>.
4. Calo L, Wegrzynowicz M, Santivaney-Perez J, Spillantini MG. Synaptic Failure and alpha-Synuclein. *Movement Disorders*. 2016; 31(2): 169-176. doi: 10.1002/mds.26479.
5. Dehay B, Decressac M, Bourdenx M, et al. Targeting alpha-Synuclein: Therapeutic Options. *Movement Disorders*. 2016; 31(6): 882-885. doi: 10.1002/mds.26568.

REWIRING THE MITOCHONDRIA'S ENERGY

BY MITCHELL SUN

Macrophages are ubiquitous cells obtained from the differentiation of monocytes—white blood cells secreted from the bone marrow.¹ Depending upon the surrounding environment, macrophages can be subdivided into an array of functions ranging from interactions with B-cells to pro-inflammatory regulation. However, while current curricula split the macrophage subtypes into five distinct phenotypes, studies have shown that the barriers aren't as concrete as once thought; in some cases, scientists observe hybrids between the subtypes.² Macrophages are involved in metabolic cycles, including the citric acid cycle, immune responses, and possibly the crosstalk between these two processes. The citric acid cycle is a metabolic process concerned with the generation of energy through oxidation of acetyl-CoA localized to the mitochondrial matrix. Because of their adaptive property, macrophages have become a hot target for therapeutic approaches researchers have been interested in investigating.

During immune responses, macrophages play a role in the initiation, upkeep, and termination of the inflammatory response. They accomplish this by the secretion of certain cytokines and chemokines, proteins that mediate intercellular communication through the initiation of cellular cascade signaling. These proteins play a role in the initiation and maintenance of inflammation while their deactivation ends inflammation, allowing cells to repair damage.³

Recently, scientists from a collaboration between the Inflammation Research Group at Trinity College and the Medical Research Council Mitochondrial Biology Unit of Cambridge University have discovered that activated macrophages can recruit mitochondrial activation in order to amplify the immune response.⁴ From this discovery, researchers looked to explain this phenomenon by interrogating the metabolic pathways. They found that activation of macrophages by lipopolysaccharides (LPS) reprogrammed these cells from the oxidative phosphorylation pathway to the glycolysis pathway. This would mean that the ATP production would switch sources and

succinate levels would rise from glycolysis. Succinate is a key intermediate of the citric acid cycle, and whose major role lies in the generation of energy through metabolism. However, new studies reveal a possible role for succinate in inflammation through the stabilization of the hypoxia-inducible factor 1 (HIF-1), a complex conserved in the presence of low oxygen levels but degraded in normal oxygen levels.⁵ When HIF-1 is stabilized, it can activate interleukin-8, a crucial inflammatory chemokine. In addition, the increased production of succinate would augment oxidation by succinate dehydrogenase (SDH) via the mitochondria, leading to the rise of mitochondrial reactive oxygen species (ROS) as well as mitochondrial membrane potential. Mitochondrial ROS promotes inflammation through the activation of interleukin 1- β (IL-1 β). Further studies show that it is necessary to have both succinate oxidation and mitochondrial membrane potential to create such ROS.

Looking towards factors that antagonize this process of inflammation, the teams found that the inhibition of the succinate oxidation by dimethyl malonate (DMM) led to an anti-inflammatory state. Because the succinate was oxidized, it accumulated in the cytosol. Other pathways that also prevent the inflammatory process include blocking ROS production by either mitochondrion uncoupling or treatment with the alternative oxidase. Knowing how to target and regulate this pathway could strike a balance between inflammatory response and wound healing – potentially optimizing recovery while limiting the proliferation of infections.⁶

Activated macrophages reroute metabolic pathways to encourage the inflammatory response through ROS production. This study highlights how each molecular player is crucial in the overall health of the body-- similar to how a choreographed dance relies on the performance of each individual. When this dance is disrupted, order is broken and disease proliferates. However, with better understanding of interactions between the players in each group, we can modify the dance to restore order.

References

1. Ginhoux F, Jung S. Monocytes and macrophages: Developmental pathways and tissue homeostasis. *Nature Reviews Immunology*. 2014; 14, 392-404.
2. Martinez FO, Gordon S. The M1 and M2 paradigm of macrophage activation: Time for reassessment. *F1000Prime Reports*. 2014; 6.
3. Fujiwara N, Kobayashi K. Macrophages in Inflammation. *CDTIA Current Drug Target -Inflammation & Allergy*. 2005; 4, 281-286.
4. Tannahill G, Curtis A, Adamik J, et al. Succinate is a danger signal that induces IL-1 β via HIF-1 β . *Nature*. 2013;496(7444):238-242.
5. West AP, Brodsky IE, Rahner C. TLR signalling augments macrophage bactericidal activity through mitochondrial ROS. *Nature*. 2011; 472:476–480.
6. Mills E, Kelly B, Logan A, et al. Succinate Dehydrogenase Supports Metabolic Repurposing of Mitochondria to Drive Inflammatory Macrophages. *Cell*. 2016: 167.

THE EFFECTS OF ZIKA VIRUS

BY ARASHPREET KAUR

Zika virus disease results from the Zika virus, which spreads mainly through the bites of *Aedes* mosquito. What might sound like a mere infection can take a complex turn as this infection has no known vaccine or medicine—it is supposed to go away on its own in a few days. Apart from causing common infection-like symptoms like fever, rash, or joint pain, this infection is also related to chronic diseases like microcephaly in the fetuses of pregnant women.¹ When pregnant women acquire Zika infection either through insect bites or sexual transmission, they can pass this infection to their fetus in the womb or during the birth of the child. This leads to the development of microcephaly in the babies. Microcephaly is the condition in which the infants have a smaller head size than is normal, which leads to smaller brains and intellectual disabilities in some cases, according to the Center for Disease Control and Prevention. Recent studies have found that brain disorders are not limited in infants with Zika infection, and that even adults infected with Zika are prone to such disabilities as well.²

Zika infection targets the neural progenitor cells in adult brains, which mature to form neurons in healthy individuals. Over the course of a few years, these progenitor cells become resistant to the Zika infection after they fully transform into neurons—this is the reason why adults were earlier thought to be less susceptible to developing brain disorders due to Zika virus. Zika infection does not affect the entire brain in adults like it does in babies—instead, the major effects are on two portions of the brain, which are the sub-ventricular zone of the anterior forebrain and the sub-granular zone of the hippocampus.² This indicates that Zika virus can also reduce the number of progenitor cells in adults by targeting them, which can lead to smaller brain volume.² These two target areas of the brain are associated with memory and learning, which means that these two functions are most severely affected by the Zika virus in adults. The trial studies done by David O’Conner and his colleagues at University of Wisconsin in Madison reveal why and how Zika virus is capable of causing

such brain damage, especially in the fetuses of pregnant females, which follows them throughout their lives. The researchers introduced this virus into two groups of monkeys—a pregnant group and a non-pregnant group. The researchers found that the virus was eliminated naturally within 10 days of infection from the monkeys that were not pregnant. On the other hand, the virus stayed in the body of pregnant monkeys for over two months. The researchers found that the virus infected the fetus, which would shed the infection back into the mother’s bloodstream, and the suppressed immune system of the pregnant mother was unable to eliminate this infection. The infection resulted in brain shrinkage in the developing fetus, which provided scope for further research.³ The Zika virus is capable of entering the brain and can lead to either swelling or shrinking of the two major zones mentioned above, which then disrupts the proper functioning of the brain according to the Medical Daily.

The medical community has been startled by other studies indicating that Zika infection can lead to Alzheimer’s disease as well. Because the infection targets the immature cells in the brain, these cells die and the brain is deprived of formation of new neurons, which are involved in neuroplasticity as well as learning and memory function.⁴ The results of this deficit are declining cognitive ability and neurological diseases like Alzheimer’s disease. An after-effect of Zika infection is the rare occurrence of Guillain-Barré Syndrome (GBS)—an autoimmune disease where the immune response generated by the body damages its own nerve cells, resulting in muscle weakness and complete paralysis in some cases. Even though there are medications and treatments available for GBS, the effects of the disorder can last for a long time. The severe effects of Zika virus are not limited to pregnant women only—instead, the horizons of this infection have spread to engulfing the brains of adults too. So far, the results of this infection have only been observed in mice brains, which were genetically engineered to represent human brains—but several cases in different areas of the world have brought

to light that these effects are not only limited to genetically engineered mice. These global cases represent the suffering affected once the Zika virus is able to make its entry into the human brain. Further studies are being conducted to ameliorate our understanding of this correlation.

References

1. Broutet N, Krauer F, Riesen M, et al. Zika virus as a cause of Neurologic disorders. *New England Journal of Medicine*. 2016. doi:10.1056/nejmp1602708
2. Rockefeller .Virology: Zika virus infects brain cells. *Nature*. 2016. 531(7593), 143–143. doi:10.1038/531143b
3. Rockefeller. Zika infection may affect adult brain cells, Suggesting risk may not be limited to pregnant women. August 18, 2016. Retrieved November 5, 2016, from <http://newswire.rockefeller.edu/2016/08/18/zika-infection-may-affect-adult-brain-cells-suggesting-risk-may-not-be-limited-to-pregnant-women/.html>
4. Griffin, A. Zika virus could have Alzheimer’s-like effect in adults. *The Independent - Science*. August 19th, 2016. Retrieved from <http://www.independent.co.uk/news/science/zika-alzheimers-effect-adults-symptoms-causes-what-happens-latest-study-a7198876.html>

DO WE REALLY NEED STATINS?

NEW RESEARCH PROVIDES INSIGHT ON THE RELATIONSHIP BETWEEN CHOLESTEROL AND CARDIOVASCULAR RISK REDUCTION

BY QUEENA LUU

Lipitor and Crestor have become familiar names in many households across America. This may not come as a surprise because they are common brands for a group of drugs called statins. These statins work by lowering cholesterol levels. This is critical for people who currently have or are at risk for cardiovascular disease.¹ To put this into context, according to the CDC, cardiovascular disease is the leading cause of death in the United States, killing over 610,000 Americans per year.² Furthermore, 71 million American adults (33.5%) have high levels of low-density lipoprotein cholesterol (LDL-C), commonly referred to as “bad” cholesterol.³

The logic behind the mass prescription of statins for heart health rests on biomedical research. LDL-C is well-established as a significant risk factor for cardiovascular disease such as atherosclerosis, stroke, and heart failure. Thus, statin-based therapeutic treatments serve critical roles in effectively reducing this risk. On the other hand, there is a lot of debate around the effectiveness of alternative, non-statin-based therapies.

A new meta-regression analysis study, published in the September 17, 2016 edition of the *Journal of the American Medical Association* (JAMA), contributes to this knowledge base. Michael Silverman, M.D. and colleagues at the Brigham and Women’s Hospital and Harvard Medical School investigated the association between lowering low-density lipoprotein cholesterol and cardiovascular risk reduction among statin and non-statin therapeutic treatments.⁴ The researchers conducted a meta-analysis and review of 49 therapy trials published in scientific journals. The study included 312,175 patients with 39,645 vascular events from nine different interventions that focused on lowering LDL-C through different mechanisms. For analysis, these interventions were divided into four groups: (1) statin-based therapies; (2) non-

statin-based therapies that primarily upregulated the expression of LDL-C receptors through methods such as diet, ileal bypass surgery, or ezetimibe (i.e., a drug that decreases cholesterol absorption in the small intestine); (3) non-statin-based therapies that reduced LDL-C by methods other than upregulating its receptors, such as prescribing fibrates and niacin (i.e., Vitamin B3); and (4) interventions that used PCSK9 inhibitors, which resulted in LDL-C decrease.⁴

The researchers compared the reduction of LDL-C due to each intervention with the risk for major vascular events such as acute heart attack and stroke. They found that for statin interventions, reduction in levels of LDL-C was associated with a lower risk for vascular events.⁴ This supports existing research that statins are effective in addressing cardiovascular disease.

Additionally, the data showed a similar association between the reduction in levels of LDL-C and relative risks for major vascular events for non-statin-based therapies that acted by predominantly upregulating the expression of LDL-C receptors.⁴ More specifically, each 1-mmol/L reduction in LDL-C level was associated with a 23% relative reduction in the risk for major vascular events. The resulting reduction in LDL and the risk reduction for CVD events in the non-statin-based therapies were comparable to the results for the statin-based therapies.⁴

This data provides insights into the effectiveness of alternative therapies that use different mechanisms to address LDL-C levels. Because these treatments are still being researched, current American Heart Association guidelines stand to recommend statins as the first line of treatment as provided by physicians.²

As more research is gathered, perhaps non-statin-based interventions may be effective alternatives to statin regimens in lowering LDL-C

and improving cardiovascular health. Given the increasing research and emphasis on personalized medicine, alternative therapies may be beneficial to consider for patients with different co-morbidities. From there, one can truly ask, “Do we always need statins?”

References

1. Cholesterol-lowering Medication. *Centers for Disease Control and Prevention*. http://www.cdc.gov/cholesterol/treating_cholesterol.htm. Published March 16, 2015. Accessed March 8, 2017.
2. Heart Disease Fact Sheet. *Centers for Disease Control and Prevention*. http://www.cdc.gov/dhdspl/data_statistics/fact_sheets/fs_heart_disease.htm. Published June 16, 2016. Accessed March 8, 2017.
3. Vital Signs: Prevalence, Treatment, and Control of High Levels of Low-Density Lipoprotein Cholesterol --- United States, 1999--2002 and 2005--2008. *Centers for Disease Control and Prevention*. <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6004a5.htm>. Published February 4, 2011. Accessed March 8, 2017.
4. Silverman MG, Ference BA, Im K, et al. Association Between Lowering LDL-C and Cardiovascular Risk Reduction Among Different Therapeutic Interventions. *JAMA*. 2016;316(12):1289-1297. doi:10.1001/jama.2016.13985.

UNDERSTANDING THE PREVALENT FEAR OF DENTAL CARE

BY SHREYA THAKKAR

Fears associated with dental care are complicated and widespread. It is estimated that 45% of American adults have moderate levels of dental fear, whereas 10% to 20% describe high levels of fear.¹ In many nations, it is noted that approximately 43% of children have dental fear.² Dental fear can influence the tendencies of patients to obtain dental treatment and thereby manifest significant consequences for oral, psychological, and overall health.¹ Refraining from routine dental treatment can increase the risk of diseases such as heart disease and diabetes, and can decrease self-esteem.¹ It is well-understood that research pertaining to dental fear and its many intricacies is necessary in order to formulate solutions and interventions for patients. Recent research conducted to quantify and analyze dental fear includes one study performed at the West Virginia School of Dentistry that ascertains the relationship between gagging and dental fear.

Gagging is a biological mechanism associated with the pharyngeal reflex that helps individuals avoid choking. While gagging may be prompted reflexively, dentists are typically confronted with gagging in the form of a behavioral response. Such a behavioral response may be produced through stimulation of the anterior portions of the oral cavity; this implies that conditioning and psychological variables play a significant role in the etiology of recurrent gagging.³ Gagging episodes can disrupt dental procedures, and if acute or recurrent, can potentially result in a deferral of care. Frequent gagging may also lead to a need for special care or additional time for procedures to be completed. It is still indefinite why some gag and others do not. Many individuals will gag upon stimulation of the posterior pharynx and glossopharyngeal nerve, which is less frequently observed. Other patients will gag due to sights, sounds, and odors without any stimulation of areas correlated with producing a gag reflex. Variation in the regularity and incidence of gagging during dental treatment between patients is possibly due to differences in psychological variables from

person to person.³

The study had the objective of assessing gagging and its possible association with fears pertaining to dental care. Participants were enlisted from the oral diagnosis clinic waiting area at the West Virginia University School of Dentistry; many of the recruited participants were there due to dental emergencies, while others had come for new patient screenings. The patients filled out a gagging behavior questionnaire, the Dental Fear Survey, the Fear of Pain Questionnaire, and the Revised Dental Beliefs Survey prior to their oral examinations, in the aforementioned order. The study was performed to assess the frequency and acuteness of gagging pertaining to dental treatment, with the principal query being whether there is a relationship between gagging and dental fear. It was hypothesized that patients who reported problems with gagging during dental care would describe relatively greater fear pertaining to dental treatment, greater fear of pain, and more adverse opinions about dentists and dental care when compared to individuals that gagged less often or not at all.³

The authors of this study found that patients who gagged less frequently described less dental fear and adverse opinions about dentists and dental care relative to participants who experienced a moderate to high frequency of gagging. Among participants who did report gagging issues at dental appointments, those who experienced gagging due to less intrusive stimuli reported higher levels of dental fear.³

According to the literature, many individuals with dental fear and anxiety try to obtain care when pain becomes intolerable, as opposed to pursuing preventive care. Five to 10 percent of individuals in the United States forgo visiting the dentist due to anxiety and fear. The US Surgeon General's Report corroborates this and underscores that good oral health is a requisite for good systemic health.³ The study at the West Virginia University School of Dentistry are crucial stepping stones to

better understanding the phenomena of dental fear. Further research pertaining to dental fear will prove beneficial for its alleviation and for better oral health both nationally and globally.

References

1. Randall CL, Shaffer JR, McNeil DW, Crout RJ, Weyant RJ, Marazita ML. Toward a genetic understanding of dental fear: Evidence of heritability. *Community Dentistry and Oral Epidemiology*. 2016; 1-8.
2. Armfield JM, Stewart JF, Spencer JA. The vicious cycle of dental fear: exploring the interplay between oral health, service utilization and dental fear. *BMC Oral Health*. 2007; 7(1): 1-15.
3. Randall CL, Shulman GP, Crout RJ, McNeil DW. Gagging and its associations with dental care-related fear, fear of pain and beliefs about treatment. *Journal of the American Dental Association*. 2014; 145(5): 452-458.

TECH, TOTS, AND TEENS: THE IMPACT OF MEDIA AND TECHNOLOGY ON TODAY'S YOUTH

BY JOMARIE S. ARBAN

On a regular sunny day around 25 years ago, young people could be seen outdoors, perhaps drawing with chalk on a sidewalk, riding their bicycles, or going for a walk. Nowadays, however, they can be found indoors staring at screens of their televisions, smart phones, or video games. Generally speaking, technology and media play major roles in young people's daily lives. In many ways, the use of technology can have positive effects when used wisely and productively. On the other hand, using technology can negatively impact children and adolescents, especially in their mental, physical, and emotional development.

Many debate whether technology and media can be helpful or harmful for young people's well-being and development. Technology supporters argue that it can more efficiently facilitate learning by providing easier access to a wide range of scholarly information found on the Internet and freeing students from traveling to libraries. Fellow supporters argue that today's technology offers better methods of communication amongst people, aiding in the healthy social development of today's youth. However, there are major downsides to having such access to what kinds of content are available and how often technology can be used for social interaction, such that there can be negative effects on the social, physical, cognitive, and emotional development of children and adolescents.

As mentioned by Cris Rowan in "The Impact of Technology on the Developing Child," studies have shown that "elementary aged children use on average 7.5 hours per day of entertainment technology."¹ It has also been seen that busy parents are regularly "leaving their children in the corner of a room with an iPad doing the parenting" and not spending enough time with their child doing other activities such as playing outside or reading books.² This not only means that using technology and media is the first choice of a young person to entertain one's

self but also that so many parents are limiting their children to turning to digital technology as a means of entertainment instead of encouraging them to do something more productive or beneficial. In addition, many homes have very easy access to the Internet, social media sites, and other technologies in general, such as video games and television, so young people could remain at home and easily turn to using those items if they get bored as opposed to other activities. Time spent using technology takes a significant amount of time away from carrying out other activities, especially exercising. Many studies have shown that there is a direct relationship between an increase of accessibility of technology with an increase in the rates of obesity and in the amount of time that people remain sedentary. Due to quick and easy access to online content, as well as an overreliance on technology for social interaction, many children in the U.S. are becoming less active and more obese, with about 17% of children in America categorized as obese.³ Those young people dedicating many hours to screen time and media usage "have been shown to have increased obesity, reduced physical activity, and decreased health."⁴ Being sedentary for long periods as opposed to getting the healthy amount of physical activity time crucial for the body and the development of the brain is causing a disruption in the youth's development of tactile stimulation that aids in healthy functioning of the motor and sensory areas of the brain.¹ Sensory input is important, as people need constant movement and to have physical contact with other humans and nature.¹ Playing with other children outdoors would greatly aid in fulfilling these needs.

Generally speaking, less face-to-face interaction with other people can deter social development.⁵ Relying on communication via screens and typed messages results in a difficult transition from screen conversations to ones where people are physically together. Face to face conversations

and maintaining eye contact are actions they end up struggling with. They have a harder time learning how to deal with social situations and interactive with other people, often causing anxiety and distress. A lack of this typically causes people to say things they typically wouldn't say in person, leading to online harassment, bullying, or threats. Since the internet and media are generally public, anything and anyone can be searched and viewed, and adolescents are at a great risk to be exposed to inappropriate and harmful content. Cyberbullying, sexting, pornographic material, harassment, etc. can all be linked to depression, suicide, anxiety, and isolation.⁶ Their effects can be profound and long-lasting on the emotional development of a child or an adolescent, affecting their sense of trust, self-esteem, and feeling of safety.

Next, studies have shown that a heavy dependence on technology to solve problems causes weakened critical thinking skills and limited creativity and imagination.⁷ Relying on technology-based toys as opposed to non-technological means of play restricts the imagination of young people to pre-existing games with pre-set rules and pre-determined strategies. Also, the immediate feedback from technology has impacted the ability of children to maintain focus, attention, and control, resulting in poor academic performance.⁸

As a whole, digital technology and media have admittedly made life more convenient and efficient, but for them to really benefit people's lives, they have to be correctly utilized. Overusing digital technology and media can be counterproductive to the growth and development of young people. Bavelier and his colleagues validated this idea and reason that this is "because children are at the forefront of the technological revolution and because the developing brain is more malleable in response to experience than is the adult brain."⁹ Oftentimes, children and adolescents are not getting out and exercising enough because they feel they can have all the entertainment they need indoors with their technology. Their attention spans are becoming even shorter than a goldfish's.¹⁰ These issues affecting the social, mental, physical, and emotional development of today's youth can be combatted if parents educate their children about the dangers of technological dependency and

place limits to ensure young people don't go on dangerous websites or overuse technology.

References

1. Rowan, C. (2013, May 29). The Impact of Technology on the Developing Child. Retrieved October 11, 2016, from http://www.huffingtonpost.com/cris-rowan/technology-children-negative-impact_b_3343245.html
2. Dredge S. Why YouTube is the new children's TV... and why it matters. *The Guardian*. <https://www.theguardian.com/technology/2015/nov/19/youtube-is-the-new-childrens-tv-heres-why-that-matters>. Published November 19, 2015. Accessed March 9, 2017.
3. Childhood Obesity Fact. *Centers for Disease Control and Prevention*. <https://www.cdc.gov/obesity/data/childhood.html>. Published November, 2015. Accessed March 26, 2017
4. Rosen L. et al. Media and Technology use Predicts ill-being among children, preteens, and teenagers independent of the negative health impacts of exercise and eating habits. *National Institutes of Health*. 2014(35): 364-375. doi:10.1016/j.chb.2014.01.036.
5. Dunckley, V. Screentime and Arrested Social Development. *Psychology Today*. <https://www.psychologytoday.com/blog/mental-wealth/201606/screentime-and-arrested-social-development>. Published June 30, 2016. Accessed March 9, 2017.
6. Farber B. Children, Technology, Problems, and Preferences. *Journal of Clinical Psychology: in Session*. 2012 68(11): 1225-1229. DOI: 10.1002/jclp.21922
7. Wolpert S. Is technology producing a decline in critical thinking and analysis? *UCLA Newsroom*. <http://newsroom.ucla.edu/releases/is-technology-producing-a-decline-79127>. Published January 27, 2009. Accessed March 9, 2017.
8. Schacter J. The Impact of Education Technology on Student Achievement What the Most Current Research Has to Say. *Milken Exchange*. 1999;20:1-12. <http://www2.gsu.edu/~wwwche/Milken%20report.pdf>. Accessed March 9, 2017.
9. Bavelier D. Children, wired – for better or worse. *National Institutes of Health*. 2010; 67(5): 692-701. doi:10.1016/j.neuron.2010.08.035
10. McSpaden K. You Now Have a Shorter Attention Span than a Goldfish. *Time*. 2015. <http://time.com/3858309/attention-spans-goldfish/>

YOSHINORI OHSUMI: AN EXPLORER OF AUTOPHAGY

BY ATREYA MISHRA

Autophagy [Aw-Tuh-Fey-Juh]

NOUN:

1. controlled digestion of damaged organelles within a cell.
2. the maintenance of bodily nutrition by the metabolic breakdown of some bodily tissues.¹

The process of autophagy has historically been a topic shrouded in mystery for biologists. Autophagy research began in the 1950's when Belgian scientist Christian de Duve revealed a previously unknown structure within the cell known as a lysosome. De Duve, along with others, discovered that this membrane bound organelle contained many degradative enzymes. They discovered that, under the right conditions, these enzymes would tear apart proteins as well as other organelles.²

After de Duve's work, research in autophagy became stagnant until the 1990's when Dr. Yoshinori Ohsumi, a Japanese cell biologist, began autophagy research. "I don't feel comfortable competing with many people, and instead I find it more enjoyable doing something nobody else is doing," said Ohsumi. "In a way, that's what science is all about, and the joy of finding something inspires me."³ Ohsumi began his research of autophagy within yeast cells. At the time, researchers believed that autophagy was only useful in specific circumstances such as cell starvation. Yet, due to Ohsumi's research, scientists have since understood that autophagy is important in many other circumstances.

Ohsumi's father, a professor of engineering at the Kyushu University, introduced him to academics early on in his life. This introduction fostered an interest in the natural sciences in young Ohsumi, prompting him to attend the University of Tokyo to learn chemistry. While he was in college, however, Ohsumi developed an interest in molecular biology and graduated with a Bachelors in Science followed by a Doctor of Science. For his post graduate years, Ohsumi went to the Rockefeller University in New York for a postdoctoral fellowship. After, Ohsumi was

offered a research associate position at the University of Tokyo where he started his research on autophagy. Before long, he was appointed as a lecturer, and later, Associate Professor.

Ohsumi's research began with an initial investigation of the lytic function of the vacuole organelle within cells. At the time, nothing was known about the degradative properties of the vacuole. Ohsumi started investigating the function of the vacuole through the use of light microscopes and later used electron microscopes to observe autophagosome formation and vacuole fusion within yeast cells. He then proceeded to investigate the genes involved in autophagy and analyze these specific genes (known as ATG genes). Through studying these genes, Ohsumi was able to further understand the processes behind autophagy.⁴

As a result of Ohsumi's research, autophagy is now understood to be essential to a cell's health, and complications in autophagy can have far-reaching consequences. Several diseases are now being better understood as being due to issues with the process of autophagy. These include neuronal damage in Alzheimer's, Parkinson's, and other neurodegenerative diseases. Due to Ohsumi's uncovering of the mechanisms of autophagy, scientists now believe that this crucial process also plays a role in preventing diabetes and cancer.⁵

Ohsumi was awarded the 2016 Nobel Prize in Medicine and Physiology for his research advancements. Autophagy is critical for cells to stay healthy and survive. His research within yeast can be applied to human beings as well. The autophagy genes and metabolic pathways he studied within yeast are also present in more complex organisms like humans. His work led to a new field of study and inspired other researchers to follow his lead in studying autophagy.⁶

References

1. Autophagy [Def.1, 2]. (2017). In Random House Dictionary. Retrieved 3 March 2017, from <http://www.dictionary.com/browse/autophagy>
2. Gorman, C. (2016). *Medicine Nobel Recognizes "Self-Eating" Cell Research*. *Scientific American*. Retrieved 5 November 2016, from <https://www.scientificamerican.com/article/medicine-nobel-recognizes-self-eating-cell-research/>
3. Devlin, H. & Sample, I. (2016). *Yoshinori Ohsumi wins Nobel prize in medicine for work on autophagy*. *The Guardian*. Retrieved 5 November 2016, from <https://www.theguardian.com/science/2016/oct/03/yoshinori-ohsumi-wins-nobel-prize-in-medicine>
4. Sedwick, C. (2012). *Yoshinori Ohsumi: Autophagy from beginning to end*. *The Journal of Cell Biology*. Retrieved 25 November 2016, from <http://jcb.rupress.org/content/197/2/164#ref-list-1>
5. Samuelson, K. (2016). *5 Things to Know About Nobel Prize Winner Yoshinori Ohsumi*. *TIME Health*. Retrieved 25 November 2016, from <http://time.com/4516341/yoshinori-ohsumi-nobel-prize-winner/>
6. Kolata, G. & Chan S. (2016). *Yoshinori Ohsumi of Japan Wins Nobel Prize for Study of 'Self-Eating' Cells*. *Nytimes.com*. Retrieved 5 November 2016, from http://www.nytimes.com/2016/10/04/science/yoshinori-ohsumi-nobel-prize-medicine.html?_r=0

WORLD'S FIRST BABY BORN WITH NEW “3 PARENT” TECHNIQUE

AN ANALYSIS ON THE INTERACTION BETWEEN GENETICS AND THE FORMATION OF FAMILIES

BY MAXIMILIANO VIDALES

One hundred and thirty million babies are born every year. Approximately 3-4% of these births include a major birth defect or genetic disorder.¹ The genes we inherit from our parents put us at risk of developing innumerable diseases and disorders such as cystic fibrosis, sickle cell anemia, heart disease, cancer, diabetes, and arthritis.¹ Researchers across the globe have attempted to eliminate these genetic predispositions, but few have been able to create a solution that is both replicable and without additional complications. This story is not necessarily about a groundbreaking revelation in the field of genetic engineering, but rather a refinement on the discovery with the intention to further apply it.

The parents of this baby boy suffered the hardships of four miscarriages spanning many years and eventually were able to give birth to a baby girl. Unfortunately, the child was diagnosed with Leigh Syndrome, a genetically-inherited disorder that makes it nearly impossible for a child to mature properly. The average child born with Leigh Syndrome is conflicted with vomiting, diarrhea, hypotonia, dystonia, dysphagia, ataxia and countless other complications.² Their child passed away at the age of six and the couple attempted to have another baby who passed away after eight months.

The process of removing the mutation of the genes responsible for Leigh Syndrome (SURF1 and MT-ATP6) was obtained by a process called “spindle nuclear transfer.”³ A donor egg has its nucleus removed and the nucleus of the mother is inserted. This egg (now consisting of DNA information of two mothers) is then fertilized by the father’s sperm. The overall genetic makeup of this child will include mitochondrial DNA from a donor, nuclear DNA from the mother, and DNA from the sperm cell.³

The concept of a child born with more than one parent isn’t necessarily original. This situation regarding the couple is a success story. These

methods are viewed differently by each nation, some of which view the process as acceptable and others as immoral. The history of mitochondrial donation began with the embryologist Jacques Cohen. In 1997, he discovered the technique called “cytoplasmic transfer,” where the cytoplasm of a healthy egg is injected into the parent egg.⁴ This egg is then fertilized with the father’s sperm and inserted into the mother’s womb for further development with the hope it would grow normally. This method of transferring the cytoplasm, rather than the mitochondria, was abandoned due to the unexplainable mutations in the child’s DNA. In 2014, the Food and Drug Administration met to speak on the morality of conducting this method, with uncertainties in mind, and decided that the risks far outweighed the benefits.⁴ This decision may have made the ethical line clearer for researchers in this field but many would say this only hinders medical sciences ability to aid the public.

This technique in genetic engineering (with the purpose of correcting genomes and allowing parents with genetic disorders to have healthy children) is considered a miracle to some and a scientific advancement to those in medical field. Reducing the amount of error in such a procedure is the first momentous step in being able to adapt this technology to improve additional aspects of our lives.

References

1. Matthews A. (2010, June 8). Inherited Disorders and Birth Defects. Net Wellness. 2010;1<http://www.netwellness.org/healthtopics/idbd/2.cfm>
2. Ruhoy IS, Saneto RP. The genetics of Leigh syndrome and its implications for clinical practice and risk management. *The Application of Clinical Genetics*. 2014;7:221-234. doi:10.2147/TACG.S46176.
3. Hamzelou J. (2016, September 28). Exclusive: World’s first baby born with new 3 Parent Technique. 2016; 1<https://www.newscientist.com/article/2107219-exclusive-worlds-first-baby-born-with-new-3-parent-technique/>
4. Kula S. (2016). Three-Parent Babies Have Been Here Since the Late '90s. *Slate Magazine*. 2016; 1 http://www.slate.com/articles/technology/future_tense/2016/02/three_parent_babies_have_been_here_since_the_late_90s.html

LIFE AFTER DEATH- WITHOUT PERMISSION

BY AISWARYA BAIJU FNU

When 17-year-old Chen Aida Ayash was hit by a car and subsequently killed, her parents requested that physicians freeze and harvest her eggs. After appealing to the courts of Israel, her parents were eventually granted permission to extract Chen's eggs and cryogenize them for future use.¹ It was here, though, that the courts disagreed and denied the family permission. Their reasoning was that there was no proof that Chen had desired to have children. The ethical dilemma comes in two parts: first, whether or not it was right for the parents to be able to extract the eggs of their daughter; and second, whether or not they should be allowed to fertilize the eggs and thus produce Chen's children.

Being a very complex case, a strong argument can be made for both sides of the issue. Extracting her ova would be considered advantageous for the parents only if they were also granted permission to fertilize the ova with sperm. At this point, the fertilized ova could lead to the eventual birth of their grandchild, or someone who could fill the void left by their daughter. Even though she may have passed away, Chen may be able to leave behind a beautiful child that could ease a bit of her parents' agony and sadness. However, Chen's ova are being considered property and the wish of the deceased owner is not accounted for in this circumstance. There's a difference between donating organs and harvesting the ova or sperm of an individual because the donated organs aid in the survival of a person- they don't create a being or a family. The creation of life outside of normal processes is a momentous act in itself, and even more complex with the addition of donated gametes or a surrogate mother. For donation of ova or sperm, verbal or explicit prior consent must be given.

Doctor Bahadur, author of *Death and Conception*, believes that the issue of posthumous reproduction is ethically unjustifiable.¹ He says the topic of posthumous assisted reproduction (PAR) may sound morbid, but the issues it raises are the most challenging and sensitive, as the use of gametes and embryos in PAR is almost inevitably emotionally charged.² In a sense, the harvesting of eggs is

unethical. The ova retrieval make the physician face an array of difficult ethical issues, but the use of ova to reproduce a child using a surrogate also adds social and legal complexity to the status of the child.³ A child born under these circumstances may be confused or feel uncomfortable knowing he or she was conceived months after his or her mother passed away, and may want to know who his or her true biological parents are.⁴

The decision of whether or not to have a child is a private matter and a fundamental right. This needs to be respected even after death. Birth after the death of the parent is an enigma that is a blend of tragedy and joy. The critical issue with Chen's case is that we do not even know if she would have wanted to have children after her death. Rosamond Rhodes, director of bioethics education at Mount Sinai School of Medicine in New York, said that regardless of the reproductive possibilities, Chen will not be alive to take care of her own child. Extracting ova from a dead child to produce another child is not the same as using organs from the dead to save the living. It has a very different meaning. Judith Daar, Professor of law at Whittier Law School in California, said that since the patient cannot give consent, the doctor would need to be assured that a suitable substitute decision-maker is in place to provide consent. "Families must try to set aside their understandable desire to keep a part of their child and focus on what their child would have actually wanted."¹

By this line of reasoning, the court made the right decision in denying Chen's parents the ability to fertilize her eggs. We must above all consider Chen's autonomy and the potential harm that may be done if the eggs are indeed fertilized. Finally, if the courts were to allow for the fertilization of the eggs, it sets up a dangerous precedent for allowing the storage of eggs and creation of children in situations outside of the context given in this case: for example, the possibility of storing eggs of a mother with good or desirable genes, or the buying and selling of eggs as if they were any other product. The ethics behind genetic manipulation continue to be widely debated, but in this specific scenario, there is no contest.

References

1. Bahadur, G. Death and conception: Opinion. *Human Reproduction*. 2002. 17(10), 2769-2775. doi:10.1093/humrep/17.10.2769
2. Bahadur, G. Posthumous assisted reproduction (PAR): cancer patients, potential cases, counselling and consent. *Human Reproduction*. 1996. 11, 2573-2575.
3. Conley, M. Harvesting Dead Girl's Eggs Raises Ethical Issues. *Public Health and Policy*. August 11, 2011. <http://www.medpagetoday.com/publichealthpolicy/ethics/28009>
4. Bahadur, G. The Human Rights Act (1998) and its impact on human reproductive issues. *Human Reproduction*. 2001. 16, 785-789.

THE CONUNDRUM OF DONATIONS FROM LIVING ORGAN DONORS

BY SARAH BASHEER

In prolonging life via the connection between human beings, organ donation represents medicine's beauty. When we are born, we are given one set of eyes, a heart, lungs, liver, and other organs that are assumed to last us a lifetime, but accidents happen and unforeseen traumas come into our lives. When calamity strikes, we are forced to turn to our human brothers and sisters. Even though we may be strangers to one another, our human connection gives us the ability to leave a lasting impact on another's life. Organ donations ensure that tragic deaths are not in vain, as they serve as second chances for others by allowing daughters to save mothers or brothers to save sisters, and everyday people to become heroes. While we may have heard about organ donation or vaguely recall it being mentioned at the DMV, many of us overlook organ donation until we are placed in situations that require us to be informed about its benefits and drawbacks.

Though organ donation is a relatively new medical practice, it has quickly become a commonplace procedure in our current times. The first successful organ transplant in history was in 1954 when Ronald Herrick gave his kidney to his identical brother.¹ Since then, organ transplants and affiliated research have flourished. Success stories of organ transplant patients are well-publicized, but less frequently do we hear about the true heroes, the often anonymous donors who perform these altruistic acts of kindness and then vanish. It seems unfair that these people are plagued with debt, depression, illness, or other repercussions for saving the life of another human being. Unfortunately, these are the risks of being a living donor.² Although, many organ donations do come from deceased donors, these donations are not enough to satisfy the high demand of organs required by today's population. Instead, we must turn to living donors, who possess the miraculous ability to regrow skin and liver, and to replenish blood or bone marrow, making it possible to donate vital tissues to those in need.² But the cost of transplant, and recovery times often makes people

of high or moderately high socioeconomic class the only people willing or able to donate organs. When only a few elite members of society are persuaded to donate organs, we are faced with the ongoing issue of serving many patients who require organs and only few people to support them. By addressing these issues, we can make it possible for a wide variety of individuals from all socioeconomic levels to donate organs.

The organ donation industry puts a great emphasis on the patients who require organs, but arguably not enough on those who donate them. Often donors feel as if they are only as valuable as the organs they provide, and after these organs are extracted, they are ignored or abandoned by the very agencies and organizations that have been involved throughout the donation process.³ For example, while insurance agencies do cover some costs of complications that donors may face because of transplant surgery, they do not cover all the costs. Such costs are compiled from recovery and medical bills as well as travel and specialty care. There is also the issue of time off, job security and psychological repercussions. These burdens too often plague donors who merely sought to help someone in need; little did they know that they would be bombarded with these difficult circumstances.

Additionally, donors make the decision to give up their organs and other parts of their bodies. Thus, it seems unwarranted to make travel expenses and recovery bills also part of their responsibility. Some alterations can be made to improve this process. First, informing the public of the risks is one of the most critical actions taken in the donation process, and must be carried out early. This grants individuals the opportunity to assess whether they are in financial situations stable enough to shoulder the burden before they donate. It has become standard procedure to inform donors of the medical risks but it is beneficial to both donors and the hospital to implement financial screenings into the process. Financial screenings will determine how government

support will be distributed to organ donors who meet certain criteria. If donors are unable to cover costs of recovery or care, the individual receiving the donation should first be asked if they are willing to pay for these costs. If neither party can, then these payments should either be paid by a portion of tax dollars allocated for such situations or be funded by private donations and fundraising.³ These efforts can ease the financial burden that living organ donors are met with when they are uninsured or of lower incomes.

If the government can somehow find a way to pay for special cases in which neither donor nor recipient can pay for these costs, the American medical industry can easily incorporate more eligible living donors into the registry, while also assisting donors with costs and care. Many employers give paid leave for jury duty and a few give paid time off for new mothers, but it is mostly unheard of for employees to receive paid time off or even extended time off without pay for organ donation.⁴ At the very minimum, employers should offer extended time off for employees who provide verifiable documentation that they are in fact participating in an organ donation, and it should be a right of employees to have job security that ensures they will have their position waiting for them when they return. This may create an undue burden on employers, and therefore to incentivize them to pursue this plan, employers can be granted tax credits for ensuring job security among their employees who engage in charitable acts such as organ donation. It is possible that these hurdles implemented by American employment, make many people hesitant to donate organs. By drafting legislation that guarantees more rights for employees who donate organs, we may be able to increase organ donations and transplants nationwide.⁴

Living organ donation is a contested issue and the idea of potentially causing harm to a healthy patient to save another's life raises ethical concerns. Thus, it is of the utmost importance that we take every step possible to ensure a complete and successful transfer of organs from the donor to the organ recipient. That is the real success. We must guarantee that both the patient and the donor can successfully return to their lives without psychological trauma, debt, or unemployment. By evolving the

organ transplant industry to address the needs of donors and provide financial support and security, we can increase the number of organ donations and potentially save many more lives. Removing the burdens of cost to donate and complications in job security can make organ donation more appealing and accessible to a wider variety of people, allowing us to meet the great level of demand for organs and ensure that every American is given their second chance.

References

1. Organ Transplant History. *LiveOnNY*. <http://www.liveonny.org/all-about-transplantation/organ-transplant-history/>. Accessed November 12, 2016.
2. Truog, M.D. R. The Ethics of Organ Donation by Living Donors. *The New England Journal of Medicine*. August 2005:444-446. doi:10.1056/NEJMp058155.
3. Fry-Revere S. Where's The Safety Net? Living Organ Donors Are People, Too. http://www.huffingtonpost.com/sigrid-fryrevere/-living-organ-donors-are-people_b_10229038.html. Published June 26, 2016. Accessed October 20, 2016.
4. National Kidney Foundation Urges Support For Living Donor Protection Act. *National Kidney Foundation*. <https://www.kidney.org/news/national-kidney-foundation-urges-support-living-donor-protection-act>. Published February 25, 2016. Accessed November 16, 2016.

ADVANCEMENTS IN ASSISTED REPRODUCTIVE TECHNOLOGIES: *AN ETHICAL DILEMMA*

BY JACOB HILL

Consider the following hypothetical scenario: the time is twenty years from now, and a couple decides they are ready to have a child. The potential parents visit the local hospital and supply the necessary ova and sperm. Using this genetic material, physicians create over one hundred embryos, and the couple is presented with a report of how the laboratory has interpreted each embryo's DNA. It is then up to the couple to decide which embryo should be implanted in the mother's uterus. Should they choose the embryo which will become athletic or the one who may be gifted in music? Should the embryo who is at risk of having a genetic disorder such as Duchenne Muscular Dystrophy be avoided?

Hank Greely, a Stanford law professor who specializes in the social and legal implications of biomedical technologies, believes that this scenario will become a reality in the near future.¹ Greely predicts that procreation will begin to occur more frequently in laboratories – not bedrooms – as parents are given the ability to determine both the physical and cognitive characteristics of their children. The technology for “designer babies,” or humans whose genetic makeup is prearranged, does not yet exist, but reproductive technologies are rapidly advancing. Indeed, advances such as pre-implantation genetic screenings (PGS) and diagnoses (PGD) are already in use. Pre-implantation genetic screenings, in which a single cell is removed for analysis from an embryo created through in vitro fertilization, are currently used to select embryos based on sex, usually with the intent of avoiding a sex-linked disorder.² However, harvesting egg cells, a necessary step for in vitro fertilizations, is an expensive process, so Greely suspects that an alternative method – creating sperm and eggs from induced pluripotent stem cells, or IPS – may be more successful. In addition to being easier to produce, IPS can be used in lieu of embryos. Those who consider deriving stem cells from human embryos to be a

moral offense would thus find IPS to be a significant ethical advantage over the donation, freezing, and destruction of embryos that PGS involve.³

Ronald Bailey, an award-winning writer for Reason magazine, is an ardent supporter of the advancement of early screenings and other reproductive technologies. He believes that restricting the use of PGD blinds a child's family to dangerous medical risks and prevents them from taking necessary steps to limit those risks.⁴ For instance, if a screening shows that a child has a predisposition for lung cancer, parents who smoke may be more likely to quit this dangerous habit, as smoking could further exacerbate the situation for their child. Or if a child is determined to have a high chance of developing diabetes, an appropriate diet and exercise regimen can be enforced in order to help prevent the disease.

Though Bailey may contend for the benefits of pre-birth diagnoses, he fails to address fears about what reproductive technologies may become and how they may be used in the future – it is this issue, after all, that the most prominent ethical dilemmas surround. Indeed, the idea of determining a child's genetic makeup has been deemed morally reprehensible by many bioethicists. Even pre-birth screenings have been criticized, as they violate a child's right to an “open future.”⁴ Those who oppose PGS and PGD argue that parents who discover their fetus is at-risk for disorders like trisomy 21 or cystic fibrosis may elect for abortions, even though PGD can produce false positives.⁵ And when pregnancies are not terminated, children with pre-birth diagnoses might be burdened with the knowledge of their genetic predispositions for latent illnesses.

Additionally, being able to select which embryos should be implanted and which should be discarded is a disconcertingly powerful ability. As Dr. Leslie M. Whestine points out in the Journal for Child Neurology, this is especially worrying in a

nation like the United States, which has a shameful history of “sterilizing marginalized individuals.”⁵ It is possible to make pre-birth screenings only legal for identifying disorders, thus preventing the use of reproductive technologies for liberal, or “positive,” eugenics – that is, the practice of parents freely choosing which desirable traits children should inherit.⁶ But enforcing such a law would be impossible, as deciding what exactly constitutes a disorder or a disease is largely subjective. Deafness is a somewhat extreme – but interesting – example of this. The deaf community has argued that deafness is not “a disability but a matter of culture,” and some deaf parents have requested PGS in order to implant a congenitally deaf embryo.⁵ The reason for concern here is clear. If a parent physically deafened a baby, the child would undoubtedly be removed from the adult's care and the parent would be prosecuted.¹ The deliberate physical deafening of a child is obviously illegal, so perhaps the use of PGD for what is ultimately the same purpose should be illegal as well. While the process of attaining a deaf child through these two means is vastly different, PGS effectively allow for the same results. While the legality and morality of this issue is heavily debatable and also somewhat confusing, it is an ethical quandary that cannot be ignored.

Furthermore, the expense of advanced reproductive technologies would compound financial and health disparities. Even if pre-birth screenings and other developing procedures become less costly, they will not be available to everyone; they will only be a viable possibility for financially secure individuals. This could create a societal imbalance where parents who can afford advanced reproductive technologies have perfectly healthy children, while those who cannot afford such technologies must leave their children vulnerable to illnesses and with less desirable genes. This could replace nature's “survival of the fittest” with an artificial “survival of the richest.” Because of the sheer magnitude of this problem, Greely believes that modernized countries will subsidize the child-making process.¹ And yet, this only makes the issue an international one: affluent nations could eliminate genetic-linked disorders from their populations while undeveloped nations are left vulnerable. In an article for *Reproductive*

BioMedicine Online, Mário Sousa and Alberto Barros maintain that “social inequalities are already the present rule in our societies,” and thus they believe that the danger of developing reproductive technologies should be ignored.⁷ However, disregarding the potential worsening of a problem by acknowledging that it already exists is both a careless ethical philosophy and poor reasoning.

The advancement of assisted reproductive technologies may be an exciting part of the rapidly evolving field of medicine, but the numerous uneasily answered ethical quandaries it creates suggest it will continue to be widely contested. It is hard to predict if and when these questions will be resolved, but we should seek to ensure that the moral standards which society eventually agrees upon are reached by public consensus and not determined by a handful of law professors, doctors, and bioethicists— after all, as Greely suggests, this is an issue that affects everyone “in such basic ways.”¹ Until that ethical solidarity is reached, changes in human reproduction should be approached with great caution.

References

1. Lorge G. Changes in human reproduction raise legal, ethical issues. Stanford Medicine Web site. <https://med.stanford.edu/news/all-news/2016/04/changes-in-human-reproduction-raise-legal-ethical-issues.html>. Published April 7, 2016. Accessed October 10, 2016.
2. Brezina PR, Zhao Y. The ethical, legal, and social issues impacted by modern assisted reproductive technologies. *Obstetrics and Gynecology International*. November 25, 2011. <https://www.hindawi.com/journals/ogi/2012/686253/>. Accessed October 10, 2016.
3. Kamp T, Murphy W. What are IPS cells? University of Wisconsin-Madison Stem Cell & Regenerative Medicine Center Web site. https://stemcells.wisc.edu/sites/default/files/What_Are_IPS_Cells_o.pdf. Published 2013. Accessed October 10, 2016.
4. Bailey R. The moral case for designer babies. *Reason*. 2014; 46(2): 20-21. Available from: Academic Search Complete, Ipswich, MA. Accessed October 10, 2016.
5. Whetstine LM. Ethical challenges in assisted reproduction: the place of preimplantation genetic diagnosis in a just society. *Journal of Child Neurology*. 2015; 30(5): 547-550. doi:10.1177/0883073813511151
6. Goering S. Eugenics. The *Stanford Encyclopedia of Philosophy*. 2014. <https://plato.stanford.edu/archives/fall2014/entries/eugenics/>. Accessed 8 March, 2017.
7. Sousa M, Barros A. A moral case study for discussion: designer babies and tissue typing. *Reproductive BioMedicine Online*. 2004; 9(6): 596-597. doi:10.1016/S1472-6483(10)61764-6

