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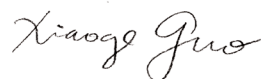
From the Editors

The University of Rochester is host to a variety of innovative research facilities, ranging from Optics laboratories to Women's Studies research centers. Within each academic discipline, undergraduate students collaborate with faculty members to create new research methods, develop original hypotheses, and make valuable contributions in their respective fields. From the first day of Freshman Orientation, undergraduate students are encouraged to participate in research and to explore ways of learning outside the classroom. Research can be an incredibly rewarding experience, and plays a vital role in the academic and creative enrichment of a large portion of the student population. Through research, students learn to become independent thinkers and develop critical thinking skills.

The Journal of Undergraduate Research (*jur*) strives to provide a medium through which undergraduates can present their original research to the rest of the student body, as well as to faculty members and other universities throughout the United States. We encourage submissions from a wide range of academic fields, from history or anthropology to biology or psychology. *jur* distinguishes itself from many other academic journals by presenting information from all academic disciplines; we believe that research in any field is significant. Through publishing original undergraduate research, *jur* hopes to promote curiosity and encourage other students to participate in research.

This current issue showcases promising and unique research from undergraduate students at the University of Rochester. The ideas and discoveries presented are diverse, but all reflect the intellectual curiosity and academic potential of the University of Rochester's undergraduates.

Sincerely,



Xiaoge Guo



Rachel Sitts

Editors-in-Chief

Journal of Undergraduate Research

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Associate Professor, Department of Biochemistry

jur: What are you currently doing in your field of research?

Culver: In general, I'm looking at the factors that are inside the protein coding sequence that influence the amount of protein that is made. In particular, I am interested in how the genetic code itself, the synonymous codons that are chosen, affect the amount of protein. I got there in a circuitous way, doing an experiment with Eric Phizicky and Stan Fields in a functional genomics experiment, where we made a library of every yeast gene fused to a purification tag. We did that because we had a set of 6,000 strains, and each one expressed a particular polypeptide. We could use that to assay for a biochemical activity and then know what gene caused it because you could purify every one of those genes by an affinity method, put it in a pool of 100 proteins, assay for a biochemical activity, and get right back to the strain that was responsible for it. So, that was called biochemical genomics. That was where I started making genomic libraries. And then, I made [a genomic library] with Eric and Mark DuMont and Mike Snyder at Yale. The weirdest thing is that you have a thousand-fold difference in expression in this library where you have the same promoter, same terminator, the exact same context, and the only difference is the protein coding sequence. That meant that the protein coding sequence has a lot to do with how much is actually made. We weren't the first people to know that codons affect things. So that's what I study now; how the actual genetic code that codes the proteins affect how much is made.

jur: Education-wise, how did you become interested in your current field?

Culver: I went to an all-female Catholic high school, and at the time that I attended, not that many people went on to college. A few people were going to the University of Illinois, and other people were going on to two-year colleges. My mother had gone off to St. Louis, and she was one of the few women in her generation who had gone to college. She then went to Johns Hopkins to get her bachelor's degree. My dad was a doctor, so my parents were encouraging. I went to a small college in Appleton, Wisconsin, called Lawrence University. From there, I had classes with all of the biochemistry majors. It was amazing. It was great because it was a

real confidence builder. I left there, went to Cornell, and worked with Jeff Roberts. Then I worked on bacteriophage *lambda* and the Q protein. I wanted to move on to eukaryotes, but onto something that I can grow quickly. I moved on to work with yeast at the University of California at San Francisco. Because of the combination of the two people I worked for, I was really lucky. Both [mentors] were fantastic and very different. Jeff was extremely smart, very analytical, and really deep. I learned a lot from him. Ira, who died a few years ago of cancer, was very creative and imaginative; so, it was like a study of contrasts. But I just thought I got really lucky that it worked out in both labs I was in. The people there were smart; they were fun. The whole field was also smaller. It was much easier to imagine yourself solving great problems.

jur: Why do you think research is important?

Culver: Basic researchers are the prospectors, finding the areas that people who do translational research later on might in fact find interest in. We contribute [to the fact] that there's information there to be manipulated. It changes the spectrum of drugs available. I think that both types [of research] are very important, but they are fundamentally different. I think there are people whose research is directed at problems that they know impact health, and there are people who are interested in addressing questions that have potential but need to be figured out first. Basic researchers also develop the tools. An example is the genome sequence – when a genome was first sequenced, in a sense, you could say it was a string of As, Gs, Cs, and Ts. You need to figure out how you're going to make use of that information; there's no guidebook.

Every single functional genomics technique that was developed in yeast, as well as others that have been particularly useful have also been applied in some way or another to mammalian organisms. The importance of comparing genomes from closely related organisms to find the important signals was first done studying yeast. And then, of course, what are they doing with humans and chimps and everything else? They're using the same techniques to extract information. If you think about my field, which is genomics, last year I think it was, fifty diseases were linked to particular differ-

ences and their tendencies to occur in the human genome sequence. Those are not genetic diseases in the sense that, like cystic fibrosis where a gene causes it; these are really complicated diseases where the tendency to develop the disease is associated with a particular mutation within the genome. I think that's fascinating that in ten or twelve years, we've gone from genome sequencing to being able to do that.

jur: You've mentioned a few changes already, but how else has your field changed over the years?

Culver: A lot. I started out in bacteria and bacteriophage, absolute biochemical, and what I did for my thesis was to purify a protein that had never been purified before to demonstrate its activity in vitro, which would affect gene regulation. I moved out of bacteria and into yeast. I was doing gene regulation in yeast, and then, I moved from there into functional genomics. Now I'm doing work that's between functional genomics and translation. The techniques I've used have changed. I used to do much more biochemistry, and now I do a much stronger component of molecular biology and genetics.

jur: Are there any roadblocks that you have faced?

Culver: There are huge roadblocks. There are times when what you're doing doesn't work and you have to rethink yourself. Sometimes you have to go a different way than you might have thought, and find something to do in there that works.

jur: You mentioned earlier that you were part of five chemistry students - was that hard for you?

Culver: That was actually easy. The Biology department had a lot more students. I had actually taken college chemistry and never taken any high school chemistry, and when I went into it, the professor said that the last five students who did this failed it. He said that if you get into any trouble and don't understand the lecture, come in and ask me. And I did that. And I understood it all, but that kind of attention was really good. And in graduate school, there was one other woman in my class. So, I wasn't completely alone. I didn't really encounter any sexism in graduate school or as a post doc. I did on the job market—that was the first time—in that somebody said, "Our wives are good biologists, but we husbands have the jobs." I've never quite forgotten that.

jur: Do you have any advice for students who are pursuing something similar to what you are doing?

Culver: I think students and all young people should do what they love to do, but the other part to that is that you don't always know what that is. So, in the end, you pick something and try it, and you can't be afraid to pick. And if you pick something that's not right for you, don't be afraid to change. My dad told me that you're going to spend a lot of your life working, so you have to like it.

Britain, Bengal, Burton, and Beer: George Hodgson and the Development of India Pale Ale

Nicholas J. Hamlin, 2009

Adviser: Stewart Weaver, Ph.D.

Department of History

Sir Henry Cotton *understood* heat. As soldiers in the Indian Civil Service in the late nineteenth century, Cotton and his fellow expatriates had to contend with the sweltering climate of the subcontinent, a shocking contrast to their temperate native England. In his memoirs, he describes riding “under a blazing sun and in the teeth of a fiery wind.”¹ Fortunately for those stricken by torrid temperatures and a longing for familiar comforts, like Cotton, the British East India Company shipped a solution to both problems: beer. According to legend, George Hodgson of East London’s Bow Brewery developed the only beer that could survive the trip across the sea by purposefully increasing the hop levels in his brew to bolster its shelf life. Once the shipments arrived, “India Pale Ale” became famous throughout the region for its dry and refreshing taste, and soon every beer drinker in India knew Hodgson’s name.

This story, which appears regularly on modern beer packaging, is mere historical fiction. Hodgson did not send the first beer shipments to India, nor was he a visionary who designed his product specifically to last the voyage. By the late 1700s, a soldier could find an imported pint of London beer, but this heavy, viscous, and semi-sweet libation suited cool British weather better than oppressive tropical humidity. Luckily, Hodgson offered his alternative. His beer, which contained extra hops, matured quickly from the ship’s movement and the changing ambient temperatures. With its distinct flavor and appearance, IPA became the drink of choice for thirsty expatriates. After dominating the overseas markets for forty years, Hodgson’s India Ale eventually lost its following when rival brewers from the town of Burton-on-Trent created their own versions of the drink and cut a new deal with the East India Company. Within a decade, the Burton exports eclipsed Bow’s, and India Pale Ale developed into a fixture of the English brewing tradition at home and abroad. By tracing the rise of India Pale Ale from Britain to Bengal and back, we can see how, through a lucky break, George Hodgson managed to influence commerce, industry, and society across the globe.

Industry, Technology, and Trade in Hodgson's England

The early nineteenth century was well suited to a burgeoning brewing industry in the British Isles, mainly because of the ongoing rise of industrialization. With a growing economy caused by the Industrial Revolution, British citizens could diversify their occupations beyond subsistence trades like farming. For those that did remain in agriculture, developments like the seed drill and mechanized reaper made the process more efficient.² Capitalizing on the tools at their disposal, farmers, including those growing the barley that brewers needed for their beer, could generate a surplus of available raw materials. A rising population combined with the effects of Parliamentary Enclosure led to a shortage of available land for small farmers, which pushed many of them into industry.³

Furthermore, the British Industrial Revolution laid the groundwork for developing breweries through the growth of new technologies that facilitated beer production. The greatest mechanized contribution to the establishment of sizable English breweries arrived in James Watt’s steam engine. This new power source simplified the labor-intensive components of the brewing process. Without this, the brewers could not have generated enough profit to support the sustained growth of the trade. Alongside the steam engine, brewers integrated thermometers into their available set of tools. While Avicenna and Galileo had developed temperature-measuring devices centuries earlier, cumbersome size and imprecise readings made thermometers impractical for beer production until the technology had matured around 1760.⁴ Another innovation in brewing technology, the saccharometer, provided a means for measuring the amount of dissolved sugars in a sample of beer and gave brewers a precise chemical makeup of their product. British brewer David Booth extolled the device’s virtues in his 1852 brewing treatise by declaring, “The utility of such an instrument is at once evident; by it you...can maintain a regular strength of liquor, which otherwise was a mere matter of chance, for the same quantity of malt does not always produce the same amount of saccharine.”⁵ Thus, the saccharometer eliminated irregularities and ensured uniform quality in the brewing process. Brewers like Hodgson used this standardization to deliver the exact flavor that their

faithful customers expected in every sip. As Roberts put it, “it may be remarked, without hyperbole, that since the introduction of the thermometer and hydrometer, [i.e. saccharometer], the art of brewing has ceased to be a mere mechanical operation... It has, in fact, attained in many respects the rank of a science.”⁶ With new technology in hand, British brewers stood poised to flourish in the nineteenth century.

Increasing globalization and international trade fostered a climate favorable to rising big brewing. The British East India Company, founded in 1600, provided a new seaward link between Europe and Asia, which allowed for both an increased westward flow of spices, silks, and other exotic goods and a movement of English wool and linen to the east.⁷ By the mid 1800s, the Company had evolved from a simple trading organization into the main regional governing body. A rising tide of Englishmen filled major outposts at Bombay, Madras, and Calcutta. The opportunity to make one’s fortune appealed to many on the cusp of entering a new social status, in spite of dangerous long voyages and foreign tropical diseases.⁸ The booming English population in the area and the increased shipping speed improved trade for British goods. As a result, the socio-economic conditions in India by 1800 were perfectly suited to shift from the beverage *status quo* to support a new iconic drink.

The Prevalence of Porter

By the time George Hodgson was born, the brewing industry was already a fixture of British social culture and domestic commerce. Thirsty workers loved their beers, which stood as a point of English pride for those who made and consumed them. Most late eighteenth century brewers focused their efforts on dark, rich, and hearty “porter”, which brewer Frederick Accum referred to as “the most perfect of all kinds of malt liquors.”⁹ Making a good porter required soft water, dark-roasted malt, and, sometimes, a small amount of elderberry juice.¹⁰ Consequently, the surrounding water supply’s low mineral content and the availability of other necessary ingredients made London perfectly suited to porter production. Until IPA’s creation, parched Englishmen at home and overseas favored porter as their drink of choice. Contrary to modern six-pack lore, British merchants and soldiers in India already had plenty of options to slake their thirst, including high-quality porter, before Hodgson’s first eastbound shipments of India Ale. Like modern print media today, the *Calcutta Gazette* featured numerous beverage advertisements aimed at piquing consumer interest; one popular ad described a combination of foreign liquors with exotic local fruits.¹¹ With the enormous trade across the Empire, shippers imported beverages from around the world, including Caribbean rum or gin from Britain. Wine, especially Madeira, also had a large following among expatriates, as the advertisement in Figure 1 demonstrates. Similarly, in his 1810 *East India Vade-Mecum*, Thomas Williamson pointed out that upon arrival in India, one should avoid exertion and, “take care never to avoid more than four to five glasses of the best Madeira.”¹² Eventually, the wine trade into India grew to the point where the government had to appoint officers to oversee its sale.¹³

The prevalence of alternative alcoholic options at first

appears to suggest that beer was unavailable in eighteenth-century India. Brewing historian Peter Mathais declares that, “Only the strongest malt liquor brewed would stand any chance of survival in the long journey through the tropics.”¹⁴ However, this is untrue. In fact, the East India Company shipped more and more domestic products, including beer, to satisfy the cravings of the growing oversea settlers’ community.¹⁵ As early as 1784, well before Hodgson’s shipments, the *Calcutta Gazette* advertised “London Porter, and Pale Ale, light and excellent.”¹⁶ Williamson mentioned that on the voyage from Britain, “The ordinary beverage is table beer, or perhaps porter...sometimes, indeed, the whole crew are supplied with from one to two quarts daily.”¹⁷ Aboard ships before modern sanitation and food storage techniques, barrels of water would grow dangerous bacteria and quickly become non-potable. Thus, sailors drank beer as a hydration source with a built-in antiseptic. Though certainly not “clean” by today’s standards, the alcohol at least kept disease at bay until sailors could find fresh liquids at the next port. While the available selection may have been limited, plenty of beer clearly reached India where British settlers heartily enjoyed it, as shown in Figure 2.

If those living in British India already had access to beer, then what drove George Hodgson to enter the existing market? Fortune was on his side in many ways. First, his brewery in Bow happened to lie nearby the East India Company docks on the Lea River. In search of a new beer supplier, the Company considered Hodgson as a convenient choice.¹⁸ Modern legend explains how he added extra hops to some batches of beer to survive a trip to India. At first glance, this seems like a reasonable conclusion. However, brewers recognized the preservative qualities of hops as early as the Middle Ages, and

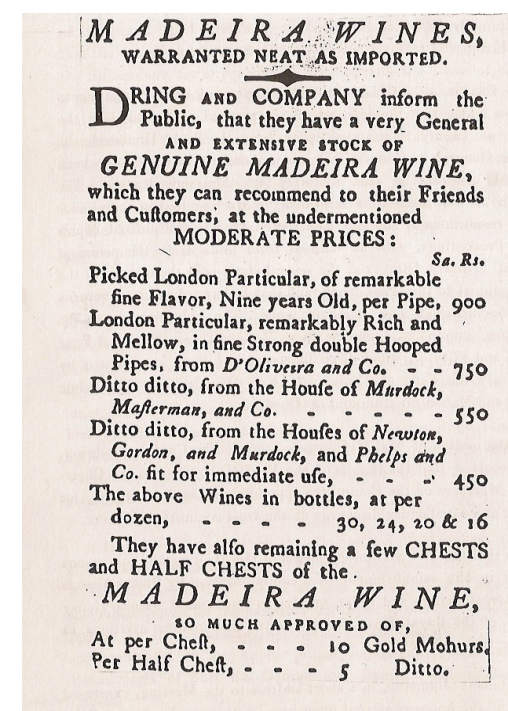


Figure 1. Advertisement for Madeira, demonstrating availability of alcoholic beverages in the Indian settlement, as published in the *Calcutta Gazette*, 13 February, 1817.

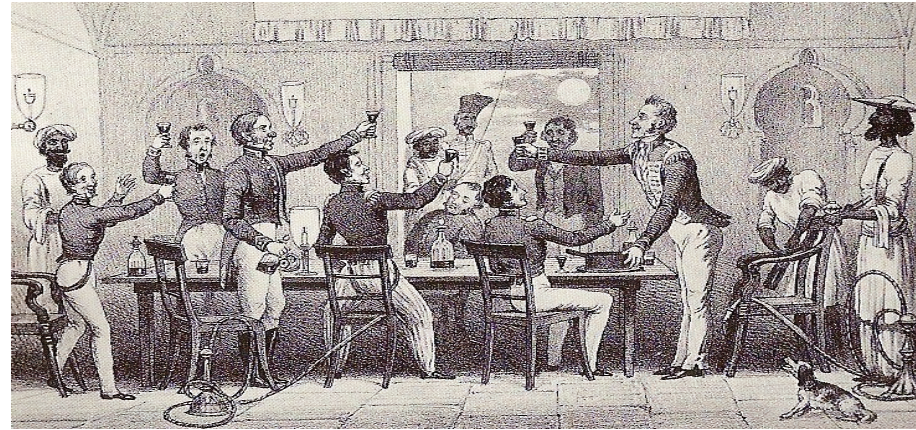


Figure 2. English soldiers enjoying a happy group libation. Rich settlers like these were the most common consumers of beer in India, including Hodgson's. Published in Brian Harrison, *Drink and the Victorians*. (London: Faber and Faber, 1971).⁴²

any drinker knows the odor of spoiled ale. Period recipes for India Ale feature specific lists of the types of hops to use and the elevated amounts to include in each batch. One account suggests that, "seldom less than twenty-two lbs [of hops] will suffice."¹⁹ In contrast, recipes for porter only required twelve to fourteen pounds for the same amount of finished product.²⁰ While evidence suggests Hodgson's India Ale differed from other beers of the time only through increased hop levels, irrefutable proof of beer's availability in the East Indies before Hodgson repudiates the idea that hops was required for preservation.

How could Hodgson have been so successful when British settlers already had access to alcoholic beverages? The answer lies not exclusively in hops, but in the use combined with the voyage. According to brewing historian Martyn Cornell, "The slow regular temperature changes and the rocking the beer received in its oak casks as the East Indiamen ploughed the waves had a magical maturing effect. By the time the beer arrived...it was as ripe a brew six times its age that had slumbered unmoving in an English cellar. The expatriate British loved it."²¹ While his beer sloshed in the holds of ships sailing through gradual weather shifts, its flavor evolved in a way that Porter's could not. Brewer David Booth commented on the need for agitation of IPA for flavor development by asserting that casks should be rolled at least once every day.²² Clearly, brewers did recognize the importance of temperature shifts and gentle motion to the quality of India Pale Ale. Nevertheless, nothing suggested that Hodgson himself had any idea of these factors when he made his initial shipments to India. Simply put, he was extremely lucky.

"And amid the constellations did the star of Hodgson rise"

Around 1800, Hodgson's business with the East India Company took off, making his name synonymous with beer in India. To foster the partnership, Hodgson regularly gave company shippers a long credit period of sometimes up to eighteen months. Also, fortunately for Hodgson, outbound shipping charges to India were substantially lower.²³ This commercial imbalance combined with his British East India Company relationships let Hodgson ship his beer for minimal cost, which, in turn, allowed him to flood the foreign market. Around this time, the ads in the *Calcutta Gazette* shifted from

featuring generic porters and ales to almost exclusively Hodgson beers. In the summer of 1822, the paper mentioned the arrival of the vessel *Sir David Scott*, which carried onboard, "Hodgson's warranted prime picked pale ale of the genuine October brewing, warranted fully equal, if not superior, to any ever before received in the Settlement."²⁴ The dominance of his India Ale even led one Indian newspaper to extol its virtues through verse, depicting it as the drink of choice even amongst the gods:

"Take away this clammy nectar," said the King of Gods and Men,
 "Never at Olympus' table let such Trash be served again."
 Terror shook the limbs of Bacchus, paly grew his pimpled nose,
 And already in his rearward felt he Jove's tremendous toes.
 When a bright idea struck him: - "Dash my thyrsus! I'll go bail,
 For you never were in India, that you know not Hodgson's ale."
 "Bring it," quoth the Cloud Compeller, and the wine god brought the beer.
 Port and claret are like water to the glorious stuff that is here.
 Then Saturnius drank and nodded, winking with his lightning eyes,
 And amid the constellations did the star of Hodgson rise.²⁵

By this time, George Hodgson had made a fortune and transferred control of the Bow Brewery to his sons Mark and Frederick. With their product firmly entrenched in the British-Indian culture, the Hodgsons set out to further increase their revenue. In the early 1820s, they phased out the Company middlemen and took control of all aspects of the export business themselves, with disastrous results. Tizard noted the problems with the new approach by stating that, "The pressing calls of 1821 for an increased supply, let Hodgson, of London, to enlarge his brewery, and induced some to enter into arrangements for monopolizing the market: this...ended in severe losses to all concerned."²⁶ Confident that no one could match their product, the Hodgsons raised prices and stopped offering long-term credit to shippers, insisting on immediate cash payments.²⁷ They booked India-bound vessels themselves, infuriating the Company. When others tried to capitalize on the Bow Brewery's greed by sending their own beer east, the Hodgsons simply increased their shipping volume and temporarily lowered prices, driving competitors from the market. With a massive operation already firmly established, they could overwhelm and undersell all newcomers. That is, until angry merchants convinced brewers from Burton-on-Trent to take a shot at the India Ale giant.

Why Burton Was Built on Trent

Like Hodgson's fortunate spot near the East India docks, the town of Burton-on-Trent benefited from lucky surroundings. Its location on the river Trent allowed easy access to shipping lanes that connected to the world via the port at Hull. More important to the brewing industry, however, was the unique local water supply that provided Burton's "*raison d'être*."²⁸ Runoff from nearby mountains contained high amounts of gypsum. This increased hardness made Burton water perfectly suited to producing higher quality and clearer pale ales.²⁹ Only when making paler beers did Burtonians realize the water's full potential. Local author William Molyneux vocalized this epiphany in his 1869 discussion of his town's "history, water, and breweries," where he described, "those remarkable supplies of water to which tradition at least assigns the ecclesiastical origins, and from which modern science determines the commercial importance and the flourishing condition of the town of Burton-on-Trent."³⁰ Although it was not initially recognized as such, Burton's water was wet gold. Even before discovering the importance of its water, the town had an established brewing tradition. In fact, the Abbot of Burton's Wetmore Abbey leased land from the town for his monks' brewing purposes as far back as 1295 CE.³¹ This original facility expanded into many others by the nineteenth century. However, these expanded breweries met much less success in their attempts to produce Burton's ales because they had different water sources. Thus, until the rise of India Ale, London brewers controlled England's beer markets.³² Yet, with its history of brewing, Burton stood to challenge the capital for domestic brewig dominance.

Of the many companies comprising the Burton brewing industry before the advent of India Pale Ale, two firms played a critical role in the town's history because of their size and longevity. The leader of the first, Michael Bass of Bass, Radcliff, and Gretton pioneered techniques in brand-management and marketing after IPA's arrival. In 1876, he established his company's distinctive red triangle logo, Britain's oldest registered trademark and still the symbol of Bass Ale today.³³ The owner of the second firm, Benjamin Wilson, built critical relationships with merchants headed north to ship his beer. These contacts, in turn, promoted the growth of Burton's pre-IPA commerce. Wilson's heir, Samuel Allsopp, also shipped porter across

England before commandeering Hodgson's recipe, but the India Pale Ale trade boosted his brewery to the forefront of the British industry.³³ Before this could occur, though, something needed to unseat Hodgson, the reigning king of IPA. This turning point that started the revolution lay not in India, but in Russia.

With its connection to Hull via the Trent, Burton brewers could easily ship their beer to the Baltic Sea, a porter-drinking region that accounted for most of the town's export market, shown in Figure 3. The Russians loved British beer to the point where William Molyneux proclaimed, "both Peter the Great and Empress Catherine are said to have been immoderately fond of the beverage, which was then high-coloured and sweet, and over remarkable strength – qualities which appeared specially suited to the Russian temperament."³⁴ However, due to the Napoleonic Wars severing trading connections with the Baltic and the Russian government's increase of import tariffs in 1822, the economic feasibility of selling "Piva Burtonski" in the Baltic region quickly evaporated.³⁵ This market loss, combined with the 1823 reduction on malt duty, led to a surplus of beer in Burton.³⁶ The Hodgsons' alienation of their East India Company shipping contacts opened the door for Burton Brewers to redirect their efforts from their former northern trade to more eastern destinations for their extra product.

The Shift of Power

According to Martyn Cornell, at the initial meeting between Campbell Marjoribanks, a representative of the East India Company, and Samuel Allsopp, the shipper convinced the brewer that entering the Indian market would allow him to improve upon his former Baltic business. Furthermore, the shipper complained that, "We are all now dependent on Hodgson, who has given offence to most of our merchants in India."³⁷ At the Company's behest, Allsopp's brewmaster, Job Goodhead, brewed the first incarnation of the Burton IPA in a teapot in 1822.³⁸ Upon scaling up the recipe, Allsopp sent his initial shipment eastward, where it sold rapidly in Calcutta despite a cost that was twenty percent higher than Hodgson's.³⁹ Shortly thereafter, the Hodgsons' luck soured. The existing production facilities and brewing experience in Burton allowed the city's breweries to begin shipments of their own India Pale Ale immediately. When

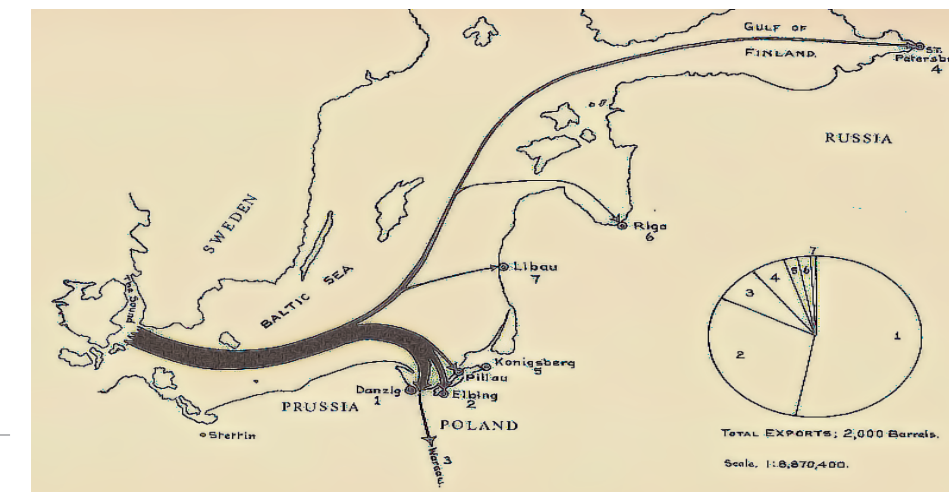


Figure 3. Map of Benjamin Wilson's shipments to the Baltic region, as published in Colin C. Owen, *Burton upon Trent: The Development of Industry*. (Chichester: Phillimore & Co., 1978.)

the Hodgsons resorted to their standby tactic of flooding the market and underselling their rivals, they could no longer keep up with the competition arriving from Burton-on-Trent. This became a major turning point in the beer shipping relationship between Britain and India; the Hodgson monopoly fell apart, the available products diversified, and overall market volume shot up. Though some fluctuation did occur, beer shipments to Calcutta steadily increased from 1830-1840 because of Burton's entry to the Indian market, as shown comparatively in Figure 4.

Beer producers and consumers alike noted the magnitude of the Burton-India trade as soon as it began. Tizard commented, "The beers now most saleable, and which command the highest quotations are those of Messrs. Alsop and Son, Bass and Co., and Ind and Smith, especially the former on account of the superior lightness and brilliancy of their shipments."⁴⁰ Burton brewers also discovered an additional measure to maintain their IPA's shelf life even after the beer reached its destination. By boiling their product longer than domestic porters, they could substantially increase the lifespan of their product.⁴¹ Later, the sea voyage simply smoothed out any rough flavors created by this extra boiling. While many praised the Burton brewers for their quality alternative product, the Hodgsons refused to surrender control of the Indian beer market. In fact, thirsty expatriates commented on their enjoyment of both products. After his description of the group of women eagerly consuming Hodgson's Pale Ale, George Jhonson continued to explain how he also, "Watched a lady after dinner put away six quarts of Allsopps without moving from her chair."⁴² Along the same lines, Sir Henry Cotton discussed the use of Burton beer as a means of combating the weather. He remarked in his memoirs how, "at the time of which I write [the 1870s] Bass's bottle beer reigned supreme. Hodgson's Pale Ale had had its day... I can remember the twelve-bottle men... who could get through twelve quart bottles of Bass at a sitting."⁴³

However, Hodgson had lost his stranglehold on the Indian market and his business suffered accordingly. Burton brewers were simply more equipped to produce ale that could flourish in India. Since the city had been brewing well before the arrival of

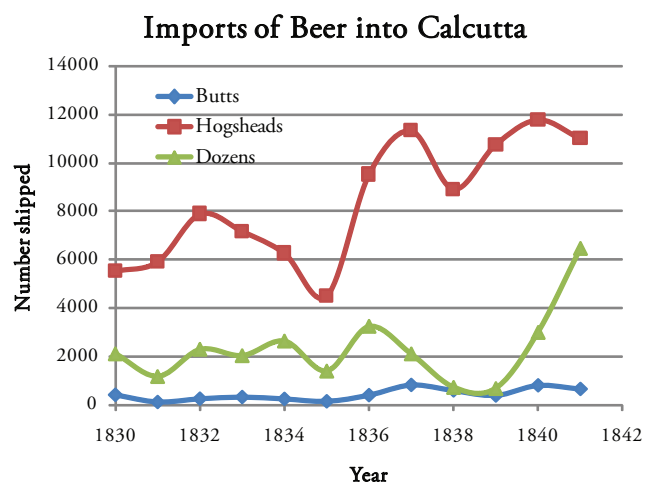


Figure 4. Calcutta Beer Imports in Various Packaging. Statistics from William L. Tizard, *The Theory and Practice of Brewing Illustrated* (London: printed by the author, 1846).

IPA, local brewers were all second-generation owners of their businesses; they had the experience in international trade and producing beer specifically for this purpose.⁴⁴ They were also among the first brewers to include scientific experts on their payroll. With chemists specifically hired to analyze the quality and components of their product using new thermometer and saccharometer technology, Burton brewers ensured that all their beer was of ideal quality for overseas sales. By the 1850s, Burton's name had become so synonymous with India Pale Ale that Hodgson was almost forgotten. Only thirty years after Burton's entry to the trade, the public already recognized its complete dominance, sometimes not even crediting George Hodgson with the creation of the initial recipe. Historian R.G. Wilson points out that, "After the mid-1820s...Burtons leading brewers drove a far more vigorous Indian export trade and produced far superior pale bitter ale to those hitherto brewed in the capital."⁴⁵ Another historian, Colin Owen, goes even further and declares that by 1840 Burton had "secured almost complete control" over the Indian market.⁴⁶ Hodgson had finally met his match.

IPA's Impact at Home and Abroad

Once Hodgson had developed India Pale Ale and the Burton brewers had subsequently co-opted the market for it, the international trade boomed, influencing the lives of people across the British Empire. Beyond the direct benefits of having a more refreshing thirst quencher widely available in the torrid Indian heat, the IPA trade carried other ramifications for the settlers. Once the beer arrived, consumers immediately sought ways to chill it. One account describes how locals soaked the bottles in water and saltpeter, which reacted to become cold enough to chill them.⁴⁷ An alternative, and probably safer, method appeared in the 1830s, when Frederic Tudor, a Boston entrepreneur, discovered a means of sending New England ice to warmer climates and made his first Indian shipment to Calcutta in 1833.⁴⁸ Hodgson's beer helped to create a market for Tudor's ice, which, in turn, eventually led to a massive ice trade between India and New England.⁴⁹ Also, Hodgson's IPA helped to spark brewing on the Indian peninsula. John Mackinnon, a British expatriate himself, established the first modern brewery in India in 1834.⁵⁰ Though Mackinnon could never compete with the volume of product arriving from Burton and London, he managed to make a living. When lighter German-style lager imports edged English beers from the Indian market at the end of the nineteenth century,⁵¹ Mackinnon's business survived and inspired a surprisingly substantial local brewing tradition. By 1901, brewers in India itself produced over 5.5 million gallons per year.⁵² Without Hodgson's original lucky creation, this industry could never have developed as it did.

Back in England, many factors contributed to the domestic rise of IPA. First, transporting beer posed serious difficulties; it was heavy, it sloshed back and forth, and it required a tight seal in watertight vessels. Raw materials needed to move from place to place as well. Fortunately for brewers, the marked growth of the rail system allowed them a quick, far-reaching, and stable means of transportation through which they could convey their beers to public houses across England. Also, since British railroads were continuously developing during this period, areas

like Burton could easily adapt the network to meet their changing needs. As its domestic pale ale trade burgeoned, in 1839 Burton-on-Trent saw the construction of the new Birmingham to Derby Line, which ran next to the major breweries, including Bass and Allsopp, and connected the area to the main English overland shipping routes for the first time.⁵³ This allowed Burton beer to easily reach all of Britain and, with the number of shipments booming, production volume also growing, as shown in Figure 5. The railroad, combined with the increased number of liquor sales licenses made available by the 1831 Beer House Act, sparked a surge in pale ale sales beginning around 1850 that in turn caused the local brewing industry to triple the size of its overall production and workforce every decade for the next thirty years.⁵⁴ This monumental growth firmly planted Burton at the center of the British brewing world.⁵⁵

The British rail system was not the only domestic industry that profoundly contributed to the nineteenth century beer trade; India Pale Ale especially played a key role in the growing glass industry because of its distinct color and clarity. London porter, when stored in cloudy hand-blown bottles, could look "vile, black, [and] turgid" to potential drinkers.⁵⁶ In contrast, the IPA's brightness combined with the bottles' transparency made it a visually appealing beverage that looked clean and refreshing, especially to thirsty expatriates in India. R. G. Wilson observes that the new beer, "was novel, bright, fresh, and pale. He said that beer looked good in the new glassware and it was the high-fashion beer of the railway age."⁵⁷ These clear yet robust bottles could sustain rougher treatment than hand-blown vessels, minimizing breakage and raising shipping volumes.⁵⁸ As a complementary good, glass caused nearby areas to follow Burton's rapid industrial expansion. St. Helens, a town on the River Mersey near Liverpool, swiftly grew into the center of a newly revitalized major British industry. With innovative automation techniques for production and readily available raw materials nearby, St. Helens' glassmakers could create new glass products quickly and efficiently, including bottles for the new bright and clear brew coming out of Burton.⁵⁸ Thus, complementary goods required by the growing pale ale brewing industry worked in favor of the similarly rising numbers of glass-makers in Industrial Britain.

In addition to its driving economic causes, the Hodgson-sparked rise of IPA in England also reflected social changes while also making its own influential marks on British society during the Industrial Revolution. During this period, per capita income rose with increasing industrialization and availability of factory jobs. With the extra money, English citizens could afford more luxury goods, including more expensive alcoholic beverages. Though IPA from Burton-on-Trent via railroad regularly sold, at first, for twice the cost of the same volume of London porter, the middle class could now support such an industry.⁵⁹ Consequently, Burton IPA evolved into a recognizable status mark for the newly well-to-do.⁶⁰ Without this fundamental social change, the domestic IPA trade could not have survived. Additionally, the more regulated daily lives of factory workers gave them a strict schedule. Factory workers worn down by their dangerous, repetitive, and monotonous jobs could all retire to their "local" at the same time after work for their evening pint. Not only did these social gatherings happen

Burton Beer Production, 1831-1900

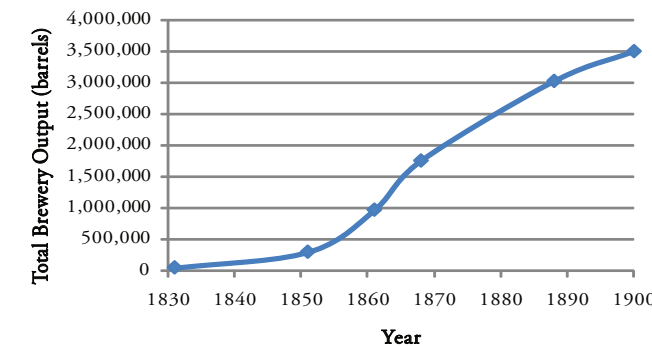


Figure 5: Overall Burton Beer Output, based on data from C.C. Owen, *The Development of Industry in Burton on Trent*. (Phillimore & Co: Chichester, 1978).

because of the regularity of industrial life, they also provided a form of escapism and pain reduction for those in taxing and hazardous new occupations.⁶¹ Moreover, the increase in industrial jobs required a large concentrated urban workforce. To meet the demand for factory employees, migrant workers moved from the countryside into the cities. With a large number of people suddenly thrust into an unfamiliar and often squalid living situation, drinking alcohol, IPA included, as a means of combating frustration and fear became a part of life.⁶²

The development of IPA had important ramifications for Britain as a whole, but what about for the denizens of Burton itself? As the local beer gained notoriety, other brewers rushed to establish their own facilities there, as much for name recognition as for enhanced quality and output. To exemplify this phenomenon, Charrington and Co., one of the top five London brewers of ale and table beer in 1820, combined with Steward Head of Stratford in 1872 to become Charrington, Head, and Co., now of Burton-upon-Trent.⁶³ Like others that followed suit, Charrington used the new location in Burton to ride the coattails of the prospering industry.⁶⁴ The growth of the brewing community, combined with the crush of outside brewers looking to capitalize on the town's success, caused a shortage of available space and labor. Architects had to shoehorn buildings into place; barley and hop farmers planted their fields in whatever strange shapes that could maximize agricultural production for brewers who constantly needed raw materials.⁶⁵ The breweries also required such a large workforce that they actually had to import migrant laborers from East Anglia to meet growing demand, causing Burton's influence on the region to stretch far beyond the city limits.⁶⁶ Other industries also benefited from the success of the local beer. Paradoxically, Burton's "extreme industrial specialization" actually generated diversity in other areas by creating a need for complementary goods and services.⁶⁷ Brewers could not do their jobs without maltsters to provide raw materials, coopers to build shipping containers, or mechanics to maintain steam power to the brewing facilities. Trades without a direct relation to brewing still prospered by using resources brought to the city by its breweries. This practice began even before the rise of India Pale Ale, as local textile manufacturers capitalized on Benjamin Wilson's contacts in the Baltic to create a market for their cloth.⁶⁸ After IPA took off in Britain and

around the world, this type of relationship continued to flourish, causing a boon for Burton's entrepreneurs in a wide range of occupations.

IPA Today

Clearly, without George Hodgson's inadvertent creation of a nineteenth-century international phenomenon, brewing in England would not have evolved into the major industry that it became. It still survives today, as modern large-scale breweries continue to carry on the traditions of Hodgson and the Burton brewers. Though most modern drinkers have forgotten the name of Hodgson, the brewing traditions that he helped to shape still prosper. Perhaps James Herbert put it best in his exuberant admonition that:

There is no beverage so wholesome and invigorating as beer, nor any so generally palatable. It may, indeed, be justly considered as our national drink, and therefore to give a good genuine article, brewed from the very best materials, is the right way for the tradesman to sustain his reputation and give satisfaction to his customers.⁶⁹

In the end, this is the goal that all brewers, in Hodgson's day and in ours, seek to attain.

Author's Note

My personal interest in this topic stems from a previous job in making packaging for a small microbrewery. After folding thousands of IPA six-pack holders by hand, I knew the anecdote about Hodgson's alleged innovation in beer preservation techniques well. It was only through research for this paper though that I attempted to determine the story's veracity, which, as the historical record shows, is often misrepresented in modern folklore.

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Student Interview

Jarrold Bogue, 2010



jur: How did you first get involved with undergraduate research?

Bogue: During my BIO 112 class freshman year, taught by Dr. Terry Platt, I become interested in research so I asked him for a recommendation of who I could do research with. He recommended Dr. Culver, who was new here at the time, and I worked in her lab for a little over a semester.

jur: What research have you done during your career here?

Bogue: Well, I worked in the Culver lab during my freshman year, and I also did some clinical research at Strong Hospital during the fall of my junior year. It's actually a funny story—I had no idea how to use the new Gmail student email system and I meant to email all the residents on my floor (I was an RA) telling them about a volleyball game, but I accidentally emailed all of my contacts, including someone at the hospital who I had emailed a while ago asking about research opportunities. She emailed me back saying that she couldn't make it to the volleyball game, but wondered if I was interested in doing some research on Autism with a developmental pediatrician fellow. It was a really great experience, and I was assigned to fill out patients' charts and go on rounds in the hospital.

jur: What kind of research are you involved in currently?

Bogue: I'm currently continuing the research I started last summer, when I had the opportunity to work in a lab at Yale. Junior year in a molecular biology class, we learned about riboswitches, which are essentially segments of RNA that change shape in response to a small compound and this change of shape turns a gene on or off. I thought they were very cool, so I found out who was doing research on them and decided to email Dr. Breaker from Yale, who told me that I could work with him if I could find funding. I ended up getting money through the REACH program here, and during the spring of my junior year I emailed different members of the lab to learn more about their projects and to see what I was most interested in. I had a really great experience and ended up classifying a new type of riboswitch. In the next

couple of weeks I'll hopefully get my research published in a paper written by a member of the Breaker lab. After my summer at Yale, I wanted to continue this research here, so I enrolled in an independent study (395) course. I work with Dr. Joseph Wedekind in the Biochemistry & Biophysics department in the medical center on X-Ray crystallography to learn more about the specific molecular structure of the riboswitch before and after it changes shape.

jur: What are the kinds of techniques or approaches you use with your research that makes it different from other people who are conducting the same research in your field?

Bogue: I'm pretty much just going by the book in terms of techniques and methods, but I guess my research is unique in the sense of what I'm working on. For now, this is all unpublished research. Nobody else really knows about it, so theoretically I'm the only one in the world crystallizing this specific RNA in the world, which is an exhilarating feeling.

jur: What kinds of projects do you hope to pursue in the future?

Bogue: Next year I'm heading to medical school. I really like research but ultimately I enjoy the person-to-person aspect that comes with being a doctor. I may do more research while I'm in medical school, but it's not what I plan to do with my career.

jur: What is one highlight of your different research experiences?

Bogue: Definitely hearing that my work is going to be published. I was so excited when I got the email!

jur: What advice would you give to undergraduates interested in research?

Bogue: I would say to always be looking for opportunities and email everyone you can. Find something that you're interested in and just go for it. You never know what can come with a simple email expressing interest in research.

Michael Rizzo, Ph.D.

Assistant Professor of Economics



jur: Could you tell us a little about your educational and professional background?

Rizzo: I went to Amherst College and I graduated in 1996. I was a physics major my whole life until my senior year when I decided I couldn't do advanced quantum dynamics. I ended up majoring in Economics and wrote a senior thesis, comparing the quality of public and Catholic schools in the United States. It was my first time doing empirical work and I liked it. Then I worked for a few years after that as an investment banker. I went to Cornell from 1999 to 2004 in the economics program and I graduated with my Ph.D. The primary field for my dissertation was in Labor Economics and the topic was in the Economics of Higher Education. I asked questions about why some states spent more and some spent less on higher education; were there other factors that crowded in or crowded out that spending? It's a little bit more complicated than that. I also did a field in Environmental Economics in which I ended up teaching a course here. Then, I dabbled in a few other things. I did experimental economics and some public economics.

jur: When did you first participate in scientific research?

Rizzo: I started thinking about doing research during my junior year of college, either in Physics or Economics. Then, I figured I had a better chance doing something in Economics. I spent the first 4-5 months doing background research, reading a lot and being really confused about the econometrics. And then, my second semester of my senior year, I did the data work. I spent a lot of time collecting the data. But fortunately, Professor Steve Rivkin, who was just an assistant professor trying to get tenure, spent a lot of time with me. He even ran some of the regressions and cleaned some of the data for me, at least in the beginning. It was from the "high school and beyond" survey that people still use [to] this day. That was great. It was a tedious process. I don't know how much I liked it. I didn't feel like I was as creative as some people. I did more research until my second year of grad school near 2000. Again, that's a little bit unusual. I had the good fortune of getting picked as a research assistant for one of the top economists at Cornell, Ronald Ehrenberg. He has it as one of his life goals to get people

involved in his research. Basically, the summer between my first and second year, he handed me a pile of papers. He said, "Read these and tell me what's in them." And I did it. That started a long and productive relationship. I probably co-authored five or six (maybe more) pieces with him. And from an early time, I think I was in second year, he helped fund me to go to the various Labor Economics conferences where I would present the work. And I hated it. I hated getting up in front of people. When you're a student, who's not very confident about what you're doing, it's a challenge. [During] my whole entire grad school career, he basically encouraged me to do that.

jur: What kind of research were you involved in as an undergrad and as a grad student?

Rizzo: All the types of research I do are empirically-oriented (you collect some data and test some theories) and all of it was virtually in education. So as an undergraduate, I was focusing on K-12 education because, again, when you're in college, that's the education you know. You see kids around you who went to really good schools. I went to a regular Catholic school in New York City that wasn't that great, but when I was there, I thought it was great. So, I just wanted to understand what made certain schools better than others. Maybe it's funding, maybe it's the quality of students. I was trying to dig beyond that and find some other factors that are less easy to observe that may account for the differences in quality. I started to find things like discipline and other sort of intangible factors that really made a school a good school. And then in grad school, I don't know if it was because it was my interest or because I knew I could do some good work in it, I focused purely on higher education. It was an under-researched area at the time. I was always interested in the public side of things, so how states make funding decisions and various questions like that. Most of my work was empirical and virtually all on education. That was through grad school. Since then, I've changed my interest a little bit.

jur: What are your current research interests, and how did you get interested and involved in that specific field?

Rizzo: I originally took a tenure track position right after grad school. You have to be very traditional... You publish a few papers and you become a research person and you get your tenure and you do whatever you'd like. I didn't quite like it. I did like my teaching more but beyond that, I didn't want to do higher education all the time.

Now my research is basically motivated the other way. I put myself in the position of saying: suppose I'm a bright kid/person at a dinner party, and someone has an interesting economic question but they don't want to have read book after book after book. I tried to write papers and articles that would help them understand those things, or at least to be equipped at a dinner party to say something interesting. Generally I focus my intention on taking some complicated issues and making them digestible for the general audience. I was truly motivated by my teaching, not the other way around. That's not the right way to go. Many other people have a very good and important research agenda. The frontier is on the theory. That's not where I'm going. I'm going right back to the basic theory and saying "Look, this is really useful to explain almost everything you see around you." So, I generally write about most topics now, not just on education.

There's this notion that as we get really rich in society, you get these technological improvements that bring the costs of very many things down dramatically, such as computers, refrigerators, cell phones. But there are still many sectors of the economy that are largely very labor-intensive or very service-oriented where we [find it] hard to imagine that you would get these productivity gains. A theory out there says that over time you should expect the relative costs of those service sectors to get higher or to take a bigger share of the budget. Over time you see health expenditures going up as a share of our budgets. They are expensive but not just because the procedures are more expensive. It's just that there are technological limitations to productivity. Similarly in the arts, you don't get to see technological improvements. Therefore, artworks are getting more expensive relative to everything else. You can't mass produce a Monet and if you did, it's wouldn't be a Monet. So there's a theory called the Baumol's cost disease theory. I want to ask first the question, "How true is it?" It makes a very nice theory but do you actually see it? I want ask that question in [relation to] higher education, because I don't believe it. Again, I shouldn't go into the research with a [preconception].

Nominally you see higher education costs going up, and one argument is that teachers like me can't improve their productivity as fast as people like me in other sectors of the economy. So in order for Rochester to attract me, they have to pay me a wage that would be reflective of my productivity elsewhere, which makes sense. If I were a software engineer, I can just write lots of software and sell hundreds or thousands and it wouldn't cost any more than writing the first piece. But look at teaching, you know even here I teach what I think are big classes. Could I teach 400, and then 500, and then 600? There's going to be a limit. But I wonder if there is a limit. I wonder if there's not a way to effectively improve your teaching. In fact, this might be a way to do that. I don't view technology as substitute for my ability to teach. I probably view it as complimentary. There's going to be a cost efficiency you gain because of technology so we're going to do some research asking those questions in higher education.

Generally, other things I'm working on are bookish projects

and other small research papers with some students. One project is I want to put together is a pamphlet or a book on history on all the resources we've ever used and look at their real prices. To the extent that we view something that we've called a resource, there's this prevailing notion that oh well we running out of it, it's fixed. There's only a certain amount of copper in the ground or tin or antimony or lead or whatever it is. And the prevailing whiz in this is that overtime, that's just going to get more expensive and we're going to run out of it. It turns out if you look at the data, virtually any resources we've ever used has gotten substantially cheaper, which seems to throw the theory of limited resources on its head. Now, I'm not going to write a polemic about it. I wanted just to put all data together in one place: raw data versus all the different wages that would reflect the cost of living changes and let people use it for their own goods.

jur: What kind of applications could your research have?

Rizzo: I'm doing work on university financial aid policy and it turns out that many institutions are inefficient about how they work financial aid, in some cases, over-awarding students, and in some cases, under-awarding students that would have been profitable to enroll. The point is we could probably more effectively manage our financial aid budgets to keep the same enrollment or increase it and actually use fewer resources to lower costs for everybody. I [say] that because I have data for almost 250 schools on their entire admitted applicants and their financial aid package. We could estimate what sorts of things affect your probability of enrolling and we can see how much at the margin more money or less money would have changed that. When you put all data together you could start asking questions that no researcher has been able to. If you look at an individual school (that's typically how these projects are), you can't ask questions about how students' decisions are affected by the type of school, for example. But I have 250 schools, and suddenly I can start looking at: are financial aid decisions different at public versus private schools? State versus...? Or what would happen if schools dramatically cut their tuition? I can never do that if I model out University of Rochester because they never had a time when they dramatically cut their tuition. But when you have lots of different schools in your data set, you can then control for all the factors that make a school [similar to] UR, and then look at places that have widely different tuition rates to proxy what might happen if Rochester, say, dropped the tuition by half. They would never try it now, because if it didn't work, they would be out of a lot of students and a lot of money. So, I would be able to answer some micro questions using these data sets, which should be hopefully marginally useful.

jur: How did you collect all the data?

Rizzo: In grad school, I had a job offer from a consulting firm that does this sort of work. I never took it but I stayed on as a consultant and as part of that [firm]. Those data sets were accumulated as part of the projects they got hired for. It's very proprietary data but it's useful because you could merge it in with publicly available institutional data to do some interesting analysis. In fact, I've started work with undergraduates on this project. It will be a very long term project. Hopefully, they have a

good experience doing it.

jur: In what ways do you interact with undergrads?

Rizzo: Generally, what I'm trying to do is to ramp up a small research program or basically any research I could do with my undergraduates. I'm here as a full-time, so any research I do is really just grading. It's not part of my renewal of my job. So, it's a good opportunity to get students involved in my work or otherwise I might not have the incentive to do it. The book on resource prices has some students working with me on financial aid. I have another student doing some preliminary work on the costs of various health care procedures to see where the costs are going up. Why don't you see efficiency in health care? With all the technology we have, you might expect prices to be going down for x-rays and MRI's, but it's going up. But, for the same kind of technology, computer prices are going down. So it seems weird. I have a student working on that. And then generally, I have 6-7 students doing independent studies with me. They are largely motivated by their interests but they first ask me "Hey! What's an interesting question?" And then I have them work on those kinds of things.

jur: How can undergrads get seriously involved in research in your field?

Rizzo: In Economics, it's just a matter of being excited about [something]. All of us are very happy to work with students as long as you have an interest. Some of us who are doing empirical work have work that's just much more amenable to have students help you, but that doesn't preclude you from doing theoretical work with somebody. So first, you have to be interested. And I think the second part is, I'd like to see students doing stuff on their own, not necessarily in research. I have a student that's very interested in the financial market. I actually believe him because he reads the paper all the time and various websites. He's very engaged, even though he doesn't know what he wants in research. If someone wanted to work with me on a question in environmental economics, it would be really helpful if they're very aware of current issues. That would be a nice start in any field, not just in economics, for students to really take an interest on their own. The other thing they could do is, it may sound a little strange and might be a little bit over ahead, virtually any department, especially ours, has three or four outside speakers come in every single week. Some of them are very high level and technical but it would be OK to pop your head to see how those seminars go and see what the academic research process looks like. You'll see how my colleagues interact with the speakers very collegiately but [also] challenge them. You could sort of see how serious the process is [and] get used to seeing the pattern of how our research projects happen. I think around campus, there are really a lot of those opportunities. It takes no more than an hour out of your time to do it. We'd like to see students do a little more of that.

jur: Do you have any advice for undergrads considering a research-oriented career, particularly in your field?

Rizzo: As an undergraduate, what you want to do is to form relationships with faculty and people at internships who can talk about your creativity, your diligence, and your acumen for doing research.

You want to be able to put yourself in a position so we can say something. Even if you had not yet done the research, you want to have us say "Look, this person is very creative or they're interested and they're intriguing. I suspect that if she were in grad school, she would be this successful." You can do that certainly by becoming a research assistant for a faculty member, but you can even do that through your coursework. It's OK to go beyond the required readings and see what else is there. The second thing I would want to argue is that by the time you're juniors or seniors, you want to try to get research experience, whether it [be] a summer internship or a program that we have on campus. There are several programs [that provide] funding for undergraduate research and you really want to try to do that. It's becoming competitive because other students at other schools have these opportunities, but it does prepare you and it gives you a flavor for whether that's what you want to do. You don't want to be 35 like me and say "I got lucky." I said research is not really for me, but fortunately I like to teach and I do research as sort of the byproduct of it. I think the other thing is, if you're an economics student, you really want to improve your math skills, even though I don't personally believe they're vital to being a very good economist. They are important to become a good researcher. They're a very good signal of your ability to tolerate something that's high level and succeed at it. You want to sort of develop the tools now while you have the time because it's going to be really hard once you've graduated and you've [gone on with] your life. You could do it but it's much harder because other things in your life become important.

jur

The Effects of RAD001 on Neuroendocrine Differentiation and Prostate Cancer Progression

Alexandria K. Maurer, 2010

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ABSTRACT
An estimated 192,000 men in America will be diagnosed with prostate cancer in 2009. Androgen ablation (deprivation) is currently the primary method of treatment for advanced prostate cancer. Though in most cases such therapy is initially effective, the cancer frequently recurs in an androgen-independent state. Previous studies have suggested that neuroendocrine differentiation contributes to androgen-independent prostate cancer development. Notably, others have documented a potential role for the PI3 Kinase/AKT/mTOR pathway in neuroendocrine differentiation. In this study, we sought to explore the effect of inhibiting this pathway with a novel inhibitor RAD001, a drug shown to have inhibitory effects on the pathway. We used a mouse model of prostate cancer to determine whether inhibiting a crucial signaling pathway by RAD001 (a derivative of rapamycin which blocks the function of the molecule mTOR) impedes neuroendocrine differentiation and androgen-independent prostate cancer development. Our study demonstrated no significant impact of RAD001 on neuroendocrine differentiation and prostate cancer progression because we were unable to detect a significant difference between the group treated with RAD001 and the control group treated with a placebo. Direction for future studies is discussed.

INTRODUCTION

Prostate cancer is the second leading cancer in men in the United States. Currently, the primary mode of treatment for advanced and metastatic prostate cancer is hormonal therapy (androgen ablation or inhibition of androgen action).⁷ For the majority of men, hormonal therapy induces an immediate remission of the cancer; however, within three years of treatment, an androgen-independent or castrate-resistant form of prostate cancer typically emerges.^{4,5} Recently, studies have suggested that neuroendocrine differentiation may contribute to the development of androgen independent prostate cancer.¹² For example, a recent study showed that the PI3 Kinase/AKT/mTOR pathway is critical for neuroendocrine differentiation in prostate cancer.¹³ This pathway has been shown to be activated by androgen deprivation in LNCaP cells.

Additionally, rapamycin derivative RAD001 has been shown to inhibit the pathway.^{3,6,14,15,17} Based upon this observation, we hypothesized that androgen deprivation induces neuroendocrine differentiation, which contributes to androgen-independent prostate cancer growth; additionally, inhibition of the molecule mTOR by rapamycin may inhibit neuroendocrine differentiation and, therefore, androgen-independent prostate cancer progression.

This hypothesis was tested *in vivo* using a mouse model of prostate cancer. Mice were injected subcutaneously with LNCaP cells, an androgen-dependent human prostate cancer cell line, to induce tumor development. The mice were castrated after tumor development. Animals in the experimental group were administered RAD001, a derivative of rapamycin, to determine whether androgen-independent tumor recurrence would be inhibited. Tissue was collected as the mice died. Twenty weeks after castration, all surviving mice were sacrificed, and tumor tissue was examined for presence of neuroendocrine markers. An absence of neuroendocrine markers in the experimental group receiving RAD001, and conversely an absence of neuroendocrine cells in the control group, supported the hypothesis that inhibition of the PI3 Kinase/AKT/mTOR pathway inhibits neuroendocrine differentiation, which prevents androgen-independent prostate cancer development.

MATERIALS AND METHODS

1. Cell culture

LNCaP cells (American Type Culture Collection, Manassas, Virginia) were cultured in RPMI (61870; Invitrogen Corp., Carlsbad, California) supplemented with 10% fetal bovine serum (S11060; Atlanta Biologicals, Lawrenceville, Georgia), 1% sodium pyruvate (11360-070; Invitrogen Corp., Carlsbad, California), and 1% penicillin-streptomycin (15140; Invitrogen Corp., Carlsbad, California). The cells were incubated at 37°C in humidified atmosphere with 5% CO₂ and were passaged when flasks reached approximately 95% confluency.

2. Injection of LNCaP cells into animals

Twenty 8-week-old athymic nude mice were obtained from Maryland (NCI-Frederick, Frederick, Maryland) and housed in

the vivarium under normal conditions. Mice had free access to a normal diet and water supply. The experiment was approved by the University Committee on Animal Resources.

Mice were injected subcutaneously with LNCaP cells prepared in the following manner: when flasks of cells were 100% confluent, adherent cells were detached with 1x trypsin (25200; Invitrogen Corp., Carlsbad, California), re-suspended in RPMI and counted using a cell counter Vi-Cell XR. The concentration of cells was found to be 5.22 x 10⁶ viable cells/ml. For each injection, 192 µl of cell suspension was mixed in 100 µl Matrigel (354234; BD Biosciences, San Jose, California) and loaded into a syringe. The Matrigel/cell mixtures were kept on ice until the injections were administered. The final concentration of LNCaP cells was 1.00 x 10⁶ cells per injection. Each mouse was given one injection in each flank region.

Concurrent with the injections, testosterone supplement was implanted subcutaneously in the interscapular region to facilitate hormone-dependent tumor growth. Testosterone (T-1500; Sigma-Aldrich Corp., St. Louis, Missouri) was prepared in Silastic® laboratory tubing (Dow Corning, Midland, Michigan) and implanted.

3. Castration

Nine weeks after injections of LNCaP cells, sixteen mice had developed visible tumors ranging in size from 5 mm to 22 mm. These mice were castrated, and their testosterone implants were removed.

4. Administration of experimental substance

Following castration, the mice were divided into two groups, each containing eight mice: each experimental group was administered the experimental substance while the control group received a placebo. Administration of the experimental substance, RAD001, and the placebo began immediately after castrations. Substances were administered biweekly by oral gavage. The experimental group received RAD001 while the control group received only vehicle. RAD was obtained from Novartis formulated as a micro emulsion concentrate at 20

mg RAD per 0.25g micro emulsion concentrate. Both RAD and the placebo were administered at a concentration of 10 µl/g with the total administration volume dependent on the mass of the mouse. Administration of substance continued until the animal died naturally but ceased by 20 weeks after castration. At 20 weeks after castration, all surviving mice were sacrificed.

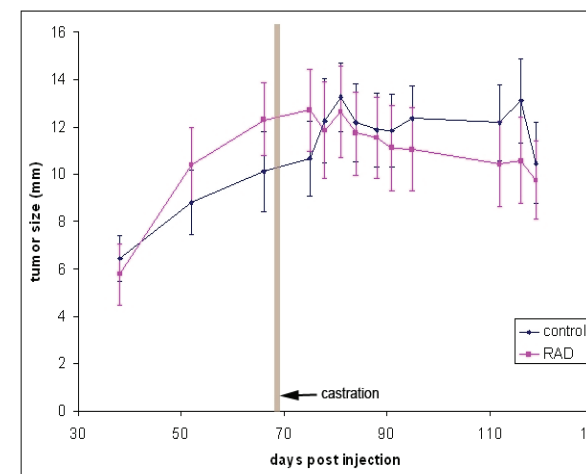
5. Analysis of tissue

Tumor tissue was collected after the mice were sacrificed. The tissue was fixed in formalin and embedded in paraffin blocks. An H & E stain and a DAB stain for the neuroendocrine marker Chromogranin A were performed on each section.

RESULTS AND DISCUSSION

Typically, when implanted into a preclinical model, hormone sensitive tumor tissue grows until it is deprived of androgens, at which point tumors begin to regress. Following regression, however, many tumors once again increase in size. It is hypothesized that at a particular point following castration, the androgen-independent tumor cells begin to predominate and cause the tumor to grow in size following androgen deprivation. If RAD001 properly inhibits castrate-resistant tumor growth in this model, then we would expect xenografts in treated animals to not experience androgen-independent growth.

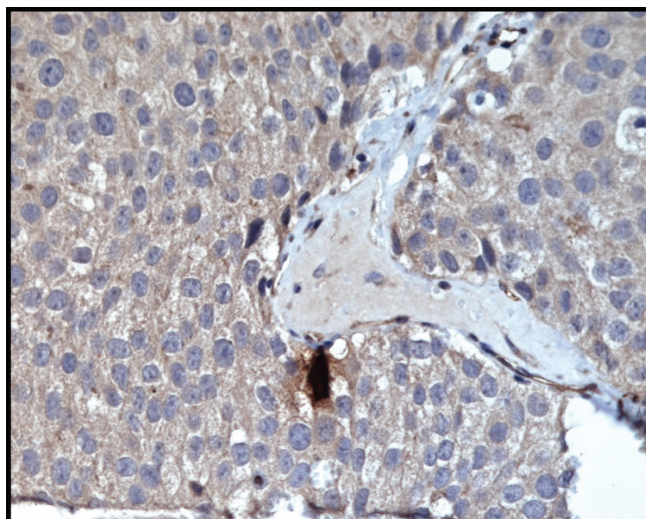
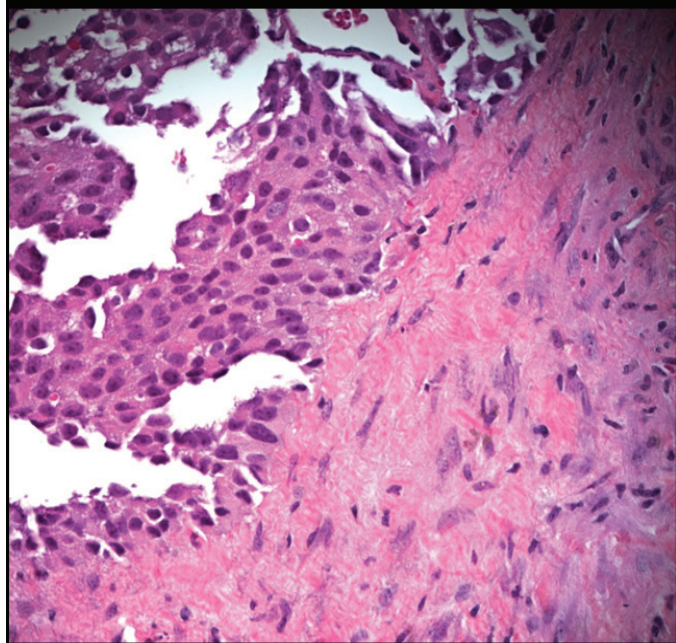
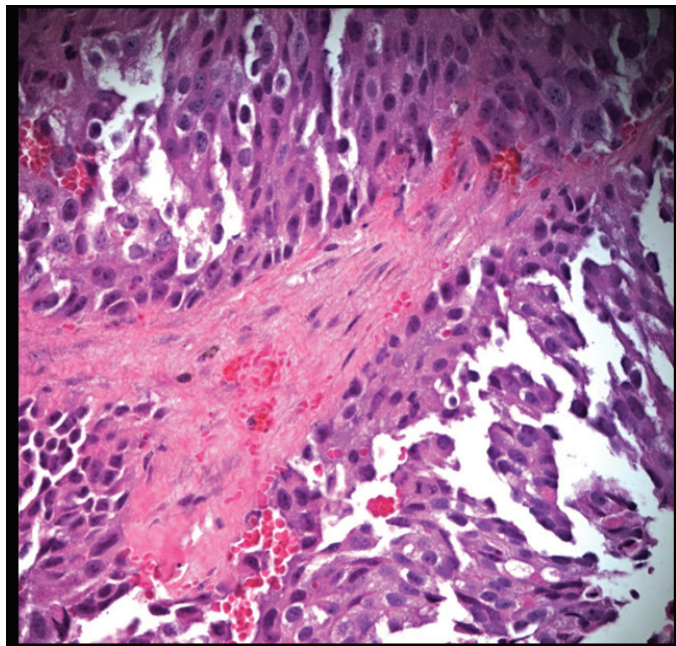
Our results showed no significant difference between the tumor growth curves of the experimental and control groups (See Graph 1). This outcome suggested that tumor growth following castration was not inhibited in the experimental group more than in the control group. A statistical analysis of tumor growth was performed using a two-sample T-test at select time points during the experiment. Results from this analysis are shown in Table 1. A P value < 0.05 implies that the two sample populations differ significantly. If this experiment were to verify our hypothesis, the experimental and control groups ought to differ significantly in tumor size during the later time points following castration. However, the smallest P value obtained using the T-test was 0.15, suggesting that tumor sizes of the two groups were



Graph 1. Tumor growth curve in both experimental (RAD) and control mice. Tumors were measured biweekly beginning when the tumors were palpable. Mice were castrated around day 70 after injection of LNCaP cells. No significant difference was seen between the Rad and the control group.

| | Day 0 | Day 16 | Day 47 | Day 79 | Day 131 |
|------------------------|-------|--------|--------|--------|---------|
| Mean-Ctrl (mm) | 11.4 | 14.6 | 13.9 | 13.4 | 13.2 |
| Mean-RAD (mm) | 12.6 | 13.1 | 10.6 | 11.1 | 11.6 |
| Std. Error-Ctrl | 1.52 | 1.43 | 1.62 | 1.72 | 1.61 |
| Std. Error-RAD | 1.36 | 1.72 | 1.60 | 1.76 | 1.84 |
| T test P value | 0.58 | 0.50 | 0.16 | 0.35 | 0.51 |

Table 1. Mean values and standard error of tumor measurements were used in a two-tailed two sample T-test. The table shows the results. P<0.05 indicates a significant difference. P>0.05 indicates no significant difference between the values. The T-test was performed at various time points starting the day of castration when treatment began (Day 0).

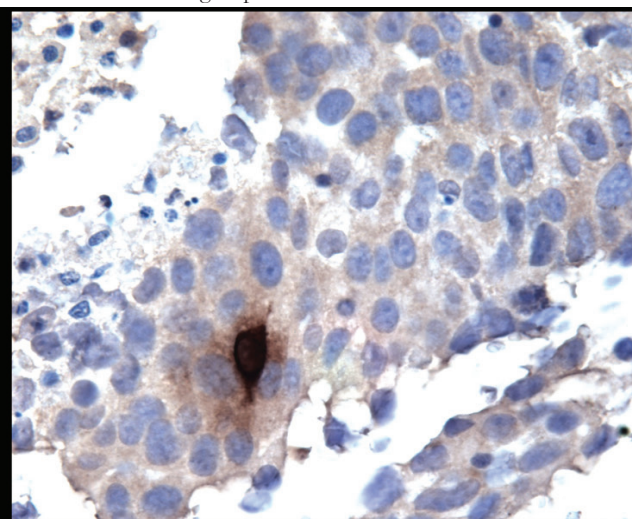


insignificantly different at all points during the experiment. Because the sample size for both populations was small ($n=16$), a T-test, which was meant to analyze larger populations, may not be the most accurate means of analysis. Therefore, a Wilcoxon Rank Sum Test was performed on the data because it is meant for small population sizes. In the Wilcoxon test, $P < 0.05$ was considered a significant difference. However, the smallest P value obtained using the T-test was 0.16, suggesting that tumor sizes of the two groups were insignificantly different at all points during the experiment.

Figure 1 shows representative sections of RAD001-treated and placebo-treated tumor tissue stained with hematoxylin and eosin (H&E). As shown, no difference was detected between the two groups. Figure 2 shows tissue sections stained for neuroendocrine marker Chromogranin A. Section A is from a mouse in the experimental group and B is from a mouse in the control group. No CgA positive cells were found in sections from the experimental group, and a total of only three CgA positive cells were found in sections from the control group. An absence of CgA positive neuroendocrine cells initially appears to support our hypothesis. (Recall that we are using RAD001 to interrupt the PI3K/AKT/mTOR pathway which is crucial to neuroendocrine differentiation. If the pathway is interrupted, neuroendocrine cells should not be found in the tumor tissue). However, we would expect that neuroendocrine cells would be

Figure 1 (left) H&E stained sections of tumor (40x). Injected human LNCaP cells can easily be distinguished from mouse kidney and epithelial cells. Human cells have distinct, rounded nuclei (dark purple), while mouse cells appear more striated (lighter purple). These sections confirm that the injected human cells did incorporate into the mouse tissue, and that the tumors were formed from these human cells.

Figure 2 (below) Sections of tumor stained for neuroendocrine cytoplasmic marker chromogranin A (CgA) using a DAB stain (counterstained in hematoxylin). [A: 20x, B: 40x] Both cells were found in sections from control mice; no positive cells seen in 5 of 8 control mice or any experimental mice. However, the absence of positive cells does not necessarily indicate that RAD stopped NE cell growth in the experimental sections since an insignificant number of positive cells was seen in the control group.



consistently present and at higher proportions in the control group; this result was not observed. Therefore, we do not have sufficient evidence to conclude that in this experiment, RAD001 successfully inhibited neuroendocrine differentiation.

The xenograft model of human LNCaP prostate cancer cells in a mouse is well-established.^{8,9} Additionally, LNCaP cells, which are normally androgen-dependent, are known to exhibit neuroendocrine phenotype when deprived of androgens for extended periods of time. Therefore, we must consider why this experiment yielded unexpected results.

LNCaP cells have been shown to exhibit neuroendocrine characteristics when cultured in an androgen-deprived state for prolonged periods *in vitro*. However, evidence for the same phenomenon in xenograft models using LNCaP cells is scant and conflicting.^{1,10,11,16} Several studies have reported that LNCaP xenograft tumors in castrated male mice contain significantly more neuroendocrine cells than tumors in non-castrated male mice. Other studies have been unable to corroborate this result; instead, neuroendocrine cells were not found in androgen-independent xenograft tumors using LNCaP cells. In future experiments, androgen-dependent cell lines other than LNCaP could be used for xenograft creation with the expectation that the neuroendocrine phenotype will be induced following androgen deprivation.

It was expected that the tumor sizes would decrease following castration and in the control group, would begin to grow again in an androgen-independent state following regression. This effect, which is a well-documented outcome of androgen-deprived prostate cancer progression, was paradoxically not observed in this study. That is to say, our control arm did not behave in the way we expected. It is possible that the castration was inadequate; though unlikely, there is a possibility that the orchietomy ineffectively removed the testes, or that the tubing in which the testosterone implant was encased was breached prior to removal. This would result in incomplete testosterone supplement removal. Therefore, suboptimal androgen deprivation would result in the continuance of androgen-dependent growth of the tumor cells, and the mice would not actually have been androgen deprived. Serum testosterone levels could have been analyzed to ensure androgen deprivation. It is also possible that the mice were exposed to exogenous androgens in their environment, perhaps through their diet. A more likely scenario would be a cell line contaminant. It is feasible that cells from an androgen-independent cell line contaminated the LNCaP population, and the resulting tumor did not consist of androgen-dependent cells as we intended. This could be tested by examining the cells for characteristic LNCaP markers, such as the androgen receptor (AR) which would be present on LNCaP cells, but not androgen-independent lines such as PC3 and DU145 cells.

A complicating factor in the analysis of our results was that most of the mice (13 out of 16) died before the projected endpoint of the study. In fact, two-thirds of the mice only survived for half of the anticipated experiment timeline. A possibility is that

the mice simply did not live long enough for the androgen-dependent tumor to regress and the androgen-independent tumor to develop. Had they survived to the endpoint (20 weeks after castration), perhaps we would have observed not only the characteristic growth curve discussed above, but also the expected proportion of neuroendocrine cells in the control group. It should be noted that the excessive tumor size is ultimately what caused these mice's demise. Had the tumors been smaller, the animals likely would have survived longer. So, death of the mice is secondary to the lack of tumor regression observed. Furthermore, the initial inoculum's size injected into the mice could have been in excess. 1×10^6 cells were injected into each flank. Perhaps using such a large number of cells caused the tumors to grow too large. We observed that the bulky tumors became necrotic, and many mice died from the burden of such tumors. If the inoculum's size were smaller, perhaps the cells in the tumor would not necrotize and could be more easily manipulated by the experimental drug.

Additionally, we were unable to detect a significant number of neuroendocrine cells in the control group, so it is not possible to determine whether the RAD001 was effective in the experimental group. We have shown that androgen-deprived LNCaP cells exhibit a neuroendocrine phenotype *in vitro*; however, there is conflicting data concerning whether LNCaP tumors actually exhibit neuroendocrine cell phenotype *in vivo*. Perhaps the *in vivo* conditions were not appropriate for the expression of neuroendocrine cells. To more definitively answer this question, we could examine more sections of tissue through the entire section. In further studies, we could use different methods for detecting neuroendocrine cells, such as immunohistochemistry for other neuroendocrine markers, like NSE, or perform RT-PCR on non-formalin fixed tissue.

In essence, the results garnered in this study were inconclusive; the control group, which did not receive RAD001 treatment, did not behave in the expected manner. Therefore, there are no meaningful comparisons which could be drawn between the control group and the experimental group to determine whether the experimental drug did indeed have an effect on neuroendocrine cell differentiation as was originally hypothesized. It is unclear at this point why the control group behaved unexpectedly; as discussed, problems could have arisen with the original LNCaP cells that were engrafted into the recipient mice, or a complication could have arisen because of the overgrowth tumor observed in some of the animals. In future studies, the cell line ought to be evaluated prior to injection to verify that they are the appropriate phenotype. Additionally, primary cells derived from a patient could be used to avoid changes that occasionally occur in immortalized cell lines.

In subsequent studies, we could examine, at the molecular level, whether the PI3K/AKT/mTOR pathway was active in the control and whether it was, indeed, inhibited in the mice treated with RAD001. This analysis could be done by evaluating activity of the molecule mTOR and other downstream mTOR substrates.² We could also determine the actual concentration

of RAD001 within the experimental tissue. Perhaps the drug did not actually reach the target tissue or did not remain in the tissue long enough to be effective against neuroendocrine cells. This could be a consequence of gavage as the route of delivery. Perhaps a more effective route of delivery would be injections of the drug at the site of the tumor or, alternatively, an implant near the tumor itself.

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Reaching for Words and Non-Words: Isolating Stages in the Response Dynamics of Younger and Older Adults

Leon Tsao, 2010

Advisers: Ashley S. Bangert, Ph.D., Richard Abrams, Ph.D., David A. Balota, Ph.D.
Department of Psychology, Washington University in St. Louis

When our brains receive information from the outside world, how do we process this information and break it down? One of the goals of cognitive neuroscience is to isolate stages of information processing. This can be rather difficult because most cognitive operations are multifaceted. We have developed a novel paradigm to explore the differences in information processing between older and younger adults.

In a classic paper, Sternberg developed a procedure to isolate stages of cognition.¹ To illustrate an experiment that isolates these stages, I can take a string of letters (such as the word GREEN, or the non-word FLIRP), and degrade it (in other words, mask it with dots—see example in “Stimulus Degradation” step in Figure 1). If a subject is flashed this degraded stimulus on a computer screen and has to decide as fast as possible whether the string of letters comprises a word or a non-word, there are two variables involved in processing this stimulus; the brain first has to eliminate the mask of dots and then decide whether the string of letters make up a word. In Sternberg’s procedure for isolating stages of cognition, when there is more than one variable involved in processing a stimulus, these variables are additive. According to Sternberg, these variables are additive because the time it takes to process the degraded string of letters equals the time it takes to eliminate the mask plus the time it takes to decide whether the string of

letters make up a word. The speed of this decision is influenced by word frequency (e.g. frequent words like DOG are processed faster than rare words, e.g., SILO). Since the variables are additive, they are not interactive. “Interactive” means these two variables are dependent on each other; the time it takes for the brain to deal with one variable in this word/non-word decision task influences the time it takes to deal with the other variable. According to Sternberg, the brain works with one variable first, and then works with the other in a completely separate stage of processing.¹

The proposal of the diffusion model by Ratcliff et al. motivated our research into differences in information processing between older and younger adults.² They postulated a theory of how age-related differences can occur in a word/non-word decision task, and we wished to investigate the validity of their claims. According to the diffusion model, word/non-word decisions are made as informational criteria for word or non-word from a stimulus that accumulates across time. For instance, I may see a stimulus (the masked GREEN as shown in the “Stimulus Degradation” step in Figure 1), and my brain has to figure out whether I am seeing a word. In order to make a decision, I garner information from the stimulus to decide if it fits the word or non-word criteria. When information meets the criteria boundary for either word or non-word, a response

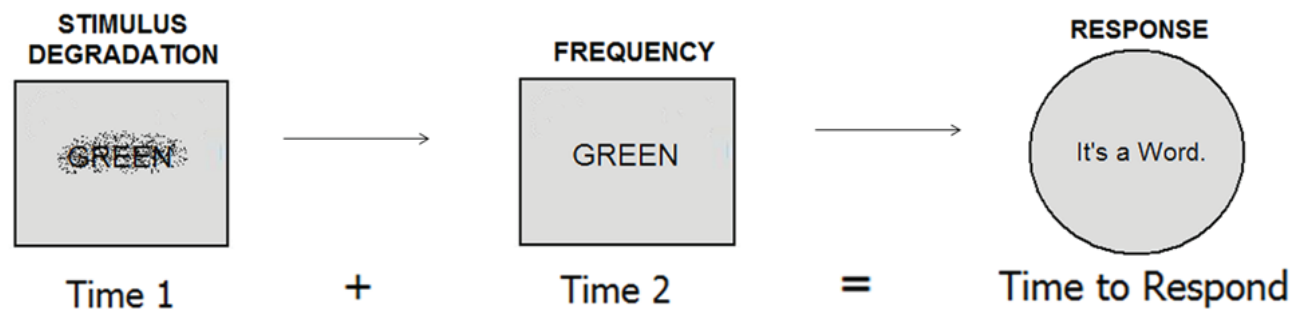


Figure 1. Two-stage processing model. In the “Stimulus Degradation” step, the brain has to eliminate the mask. In the “Frequency” step, the time it takes to decide whether the letter string is a word depends on the frequency of the word (GREEN would be a relatively frequent word). Clear stimuli (one without a dotted mask) would be processed faster than degraded stimuli, since only one step is involved (the “Frequency” step). If variables are interactive, the two-stage model does not apply, since it is non additive.

is executed. I may finally decide the degraded stimulus GREEN makes up a word, and I would then press the “1” key on a keyboard (the “1” key signifies word, and the “2” key signifies non-word). In the diffusion model, age-related differences in lexical decision have been explained by differences in setting of the response criteria, with older adults setting more conservative criteria than younger adults. This means that they wait for more criteria from the stimulus before making a decision (Figure 2).

We used a novel arm-reaching response paradigm in which a subject (an older or younger adult) sees a letter string (clear or degraded), and reaches across a computer screen with his or her arm to select “word” or “non-word” as a response (Figure 4). This is different from previous studies that used a simple key-press (key “1” on a keyboard for word, and “2” for non-word), and therefore could only track responses and response times (sFigure 3). The current study is the first to explore age-related changes in movement dynamics of lexical decision responses. The advantage is that not only can it track responses and response times, but it can track the onset of the arm movement and the trajectory of the movement made. For instance, in a trial, a subject may initially move his or her arm towards one response circle but end up selecting another response circle with it. If older adults set a more conservative response criterion, one may expect the effects of word frequency and stimulus degradation to occur primarily in the time before movement onset, whereas, for younger adults, there may be less of an influence in movement onset latency and more of an influence of these variables in movement dynamics.

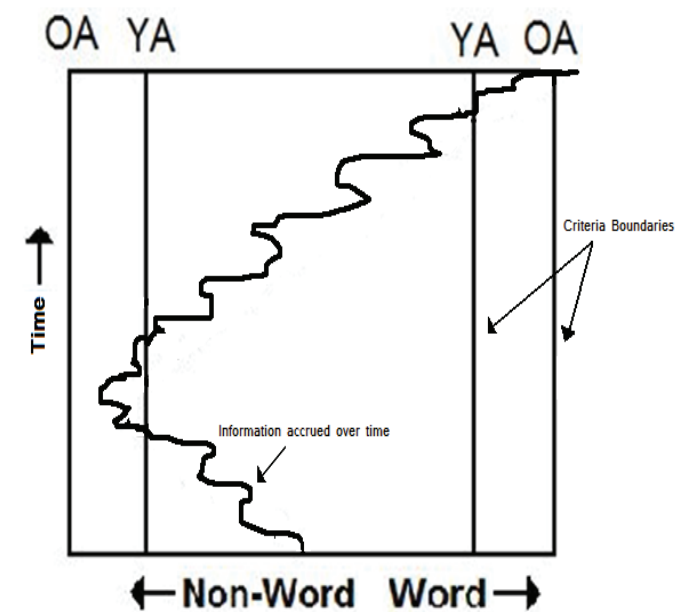


Figure 2. Diffusion model. The plotted line represents criteria/information accrual over time. The vertical lines represent where older and younger adults (OA and YA) set their criteria for initiating word and non-word responses. Older adults set more conservative (farther) boundaries. In this diagram, the perception of the stimulus is initially biased towards Non-Word. Once a boundary is crossed, the subject may press a key to indicate a response. Older and younger adults may have different responses due to their boundary-setting differences.

Methods

- 27 older adults (10 males/17 females), mean age = 77.8 (± 8) years
- 20 younger adults (8 males/12 females), mean age = 19.7 (± 1) years
- Participants were seated on a tall chair about 1 foot from a screen-facing-upwards computer monitor upon which stimuli were presented. A glove on their right hand had an Ascension Flock of Birds® magnetic sensor attached to the right index finger. A detector tracked the location of the sensor in 3 dimensions (up/down, left/right, and forward/backward) while participants made reaching movements (see Figure 4).
- 400 experimental trials, half of which were degraded with a random dot mask.
 - 100 High-Frequency (HF) words
 - 100 Low-Frequency (LF) words
 - 200 Pronounceable Non-Words (NW)
- Dependent variables:
 - Movement Onset Time - time from stimulus appearance to movement initiation
 - Accuracy
 - Positional variables:
 - X position - horizontal position of finger throughout movement in cm
 - Y position - vertical position of finger throughout movement in cm
 - Change in position over time

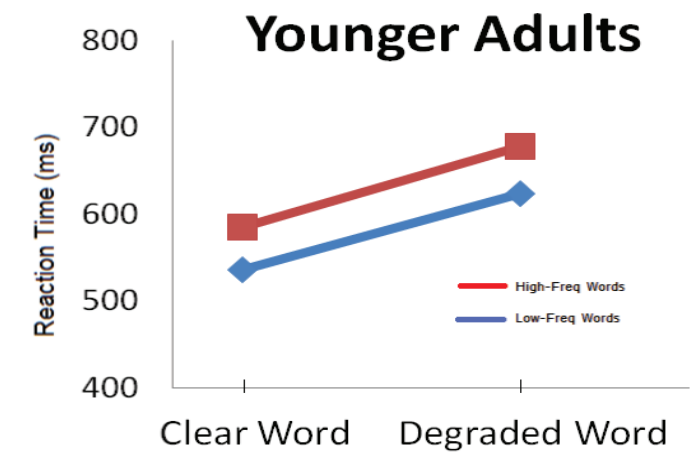


Figure 3. Plot of additive effects on a button press. The red line is for low-frequency words and the blue line is for high-frequency words. Yap and Balota gave young adults a word/non-word decision task in which strings of letters were either clear or degraded.³ The additive effect is apparent since the lines are nearly parallel with ~50ms difference between them for clear word and degraded word conditions. This means that stimulus degradation and word frequency do not interact and occur in separate stages of processing. Since this is a button press experiment, it can record response and response times of subjects but not their response dynamics.

Results

The results shown in Figure 5 suggest that younger adults set a more liberal criterion and initiate their responses before full analysis of the stimulus. An interactive effect is apparent in Figure 5 for younger adults because the lines in the graph for this group are not parallel. Older adults wait for a full analysis before initiating movement, which is apparent from the parallel lines in the graph similar to that in the younger adults of Figure 3. Keep in mind that the y-axis for Figure 3 is reaction time, and the y-axis for Figure 5 is movement onset-latency, which can only be measured with a movement paradigm. Given the ability to move towards a target rather than a simple button-press, younger adults employ a different strategy from older adults, as evident in the fact that their effects are now interactive instead of additive.

In Figure 6, there is a steeper shift in the X position relative to the Y position for older adults than younger adults. Younger adults are more likely to move their arm towards the wrong response first before landing their fingers on the correct response circle, therefore averaging a smaller X position relative to Y position. This implies that older adults are more likely to commit to a response prior to movement onset than younger adults, thus indicating that they set a higher criterion to initiate movement.

Age-related differences in criteria-setting are also apparent in Figure 7. Older adults show a greater bias towards the X position as compared to the Y position when compared to younger adults even early on in the movement. Again, this indicates they have made their word/non-word decision before initiation of the response and were pulled in the dimension (horizontal) that discriminates words from non-words.

Conclusions

We developed a novel reaching paradigm to explore the mental chronometry of younger and older adults' cognitive performance in a word/non-word decision task, and their subsequent response dynamics. In contrast to the standard button press studies, younger adults showed an interactive effect of word frequency and degradation in the onset latencies, whereas older adults produced clear additivity, consistent with the standard button press studies. In other words, given the ability to move towards a response circle, the older adults followed the 2-stage model of processing as illustrated in Figure 1. For younger adults, processing between variables occurs interactively rather than in two separate stages. The reason for this contrast is that the button-press can only record responses. The button-press forces the subject to process word degradation and frequency prior to initiating a response. Given the ability to move in our study, strategic differences are revealed between younger and older adults.

These findings reveal qualitative differences between younger and older adults' speeded binary judgments, and are consistent with recent developments of the Ratcliff et al. diffusion model of aging and lexical decision performance.² Younger adults initiated movements earlier than older adults because younger adults have more liberal criteria to initiate their response. For younger adults, the stimulus was not fully analyzed before they initiated their response. Changes in criteria were also supported

by the observation that older adults were more likely to commit early on in the horizontal dimension to a target than younger adults, despite having a more delayed onset latency.

Why do older adults engage in a more complete analysis when acting compared to younger adults? It is possible that older adults compensate their slower cognitive processing and physical movements by waiting to obtain more information about the environment before initiating movements. Younger adults can afford to act with more liberal informational criteria than older adults because they can quickly adjust the direction of their movement if they find that they made the wrong move. Older adults may have set more conservative informational criteria to minimize the cost of mistakes or injury. For example, if a young adult were to walk down a staircase, she may move her foot to the next step of the stair without needing to process the location of the next step as thoroughly as an older adult. This is because if she did make a mistake in processing, she can change the direction of her foot more easily than an older adult can. An older adult, due to his slower movements, knows that he cannot change the direction of his foot as quickly. Therefore, he strategically spends more time processing the location of the next step prior to moving his foot in order to prevent falls. More research on the differences between younger and older adults in response to dynamics, however, is necessary to corroborate these conjectures.

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3. Yap, MJ et al. 2008. On the additive effects of stimulus quality and word frequency in lexical decision: Evidence for opposing interactive influences revealed by RT distributional analyses. *Journal of Experimental Psychology: Learning, Memory, & Cognition*, 34, 495-513.

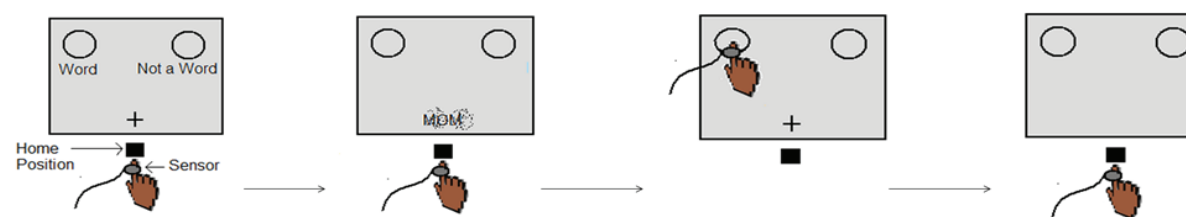


Figure 4. Demonstration of procedure. On each trial, participants placed their right index finger at the home position. Once a letter string was presented, they pointed to the appropriate word/non-word response circle. They then brought their finger back to the home position to start the next trial. Feedback about incorrect responses or problems with movement was given after each trial.

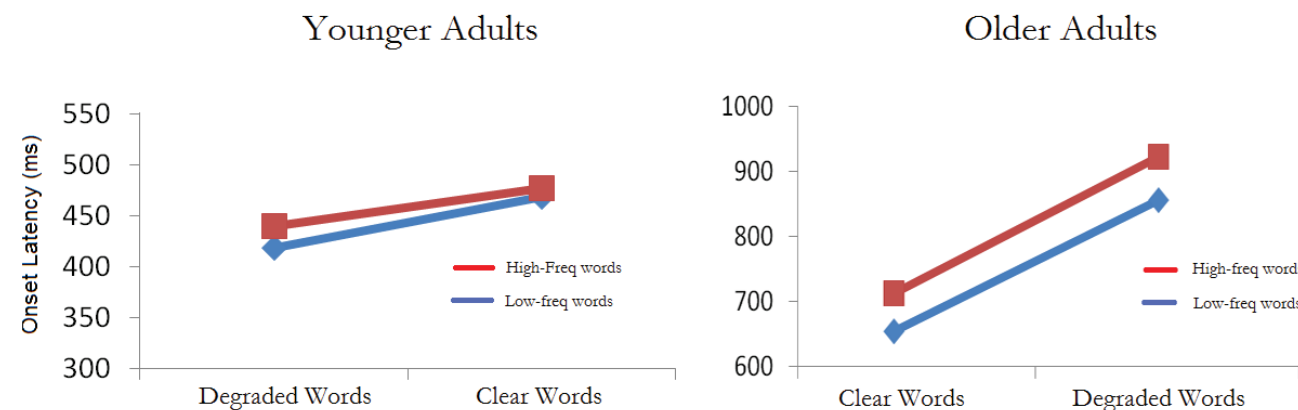


Figure 5. Plot of onset of arm movement latency by word frequency and degradation in younger and older adults. The red line is for low-frequency words and the blue line is for high-frequency words. Both groups show strong effects of frequency and degradation (all $p < .001$). Younger adults show an interaction between these factors ($p < .01$) while older adults do not ($p > .40$). There are no significant differences in accuracy between the two groups despite differing onset latencies ($p > .90$).

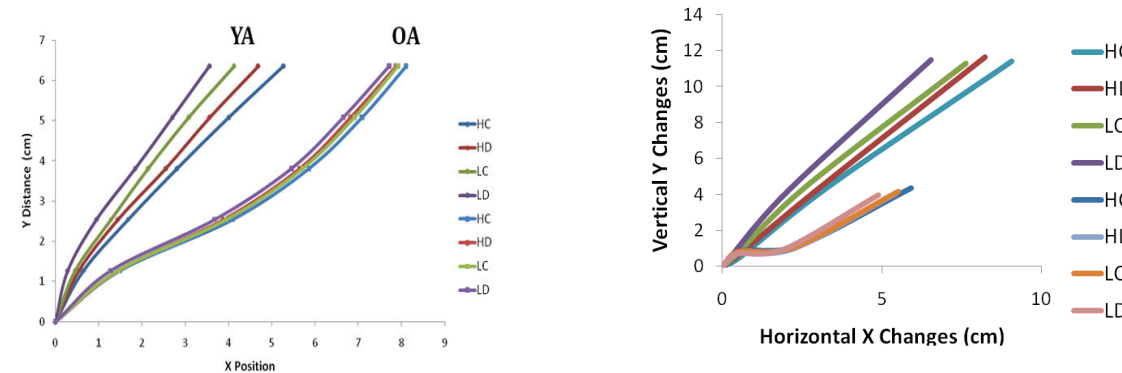


Figure 6. The average X position for specific distance changes of finger in the Y position (see Methods for explanation of X and Y position) for younger and older adults (YA and OA). The H in HC and HD means "high-frequency words" and the L in LC and LD means "low-frequency words." The C in HC and LC means "clear words" and the D in HD and LD means "degraded words." X positions for movements to the left were flipped so that all movements were evaluated in the same space. Positions farther to the right indicate that movements were closer to the appropriate response circle. Younger adults show large effects of frequency ($p < 0.001$) and degradation ($p < 0.01$). Older adults show an effect of frequency ($p < 0.05$) but not of degradation ($p > 0.10$). Neither group reveals a significant interaction between these variables (all $p > 0.70$).

Figure 7. Change in X position and Y position at 100, 200, and 300 ms after movement initiation (see Methods for explanation of X and Y position). The H in HC and HD means "high-frequency words" and the L in LC and LD means "low-frequency words." X position changes for movements to the left were flipped so that all movements were evaluated in the same space.

Fly Me to the Moon, Cheaply

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We investigate two related problems in the Planar Circular Restricted Three Body Problem (PCR3BP): 1. The path of minimum force connecting two points in phase space, and 2. The most probable path connecting two points in phase space for a particle experiencing random forces. We then show that these two paths are in fact the same if the random force is small. Using numerical methods, we find paths to the moon which minimize the square of the applied force.

1. The PCR3BP

In the PCR3BP it is assumed that two massive bodies, called primaries, orbit each other in circular motion according to the Kepler problem. We then derive the equations of motion for a third particle of negligible mass in the gravitational field of the two bodies. The Lagrangian for this system is given by

$$L = \frac{1}{2}(\dot{\xi}^2 + \dot{\eta}^2) - U(\xi, \eta, t)$$

where ξ and η are the coordinates in the inertial frame. It is convenient to transform the Lagrangian into a rotating reference frame in which the potential is time independent.

$$\begin{pmatrix} x_1 \\ x_2 \end{pmatrix} = \begin{pmatrix} \cos \omega t & -\sin \omega t \\ \sin \omega t & \cos \omega t \end{pmatrix} \begin{pmatrix} \xi \\ \eta \end{pmatrix}$$

To find how the velocities transform we take the time derivative, which yields

$$\begin{pmatrix} \dot{x}_1 - \omega x_2 \\ \dot{x}_2 + \omega x_1 \end{pmatrix} = \begin{pmatrix} \cos \omega t & -\sin \omega t \\ \sin \omega t & \cos \omega t \end{pmatrix} \begin{pmatrix} \dot{\xi} \\ \dot{\eta} \end{pmatrix}$$

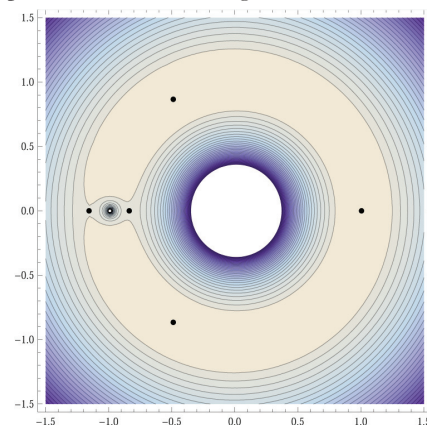
The Lagrangian in the rotating frame is then

$$L = \frac{1}{2} [(\dot{x}_1 - \omega x_2)^2 + (\dot{x}_2 + \omega x_1)^2] - U(x_1, x_2)$$

$$U(x_1, x_2) = -\frac{Gm_1}{\sqrt{x_2^2 + (x_1 - r_1)^2}} - \frac{Gm_2}{\sqrt{x_2^2 + (x_1 - r_2)^2}}$$

Where r_1 and r_2 are the radii from the origin to m_1 and m_2 , respectively.

The potential in the rotating frame is shown below.



1.1 A System of Units

From the circular two-body problem the following relations are known

$$r_1 = \mu r_{12}$$

$$r_2 = (1 - \mu) r_{12}$$

$$\mu = \frac{m_2}{m_1 + m_2}$$

$$\omega = \sqrt{\frac{G(m_1 + m_2)}{r_{12}^3}}$$

We define a system of units where the sum of the masses, the frequency of rotation and the distance between the primaries are all equal to unity. Using this system of units and the above relations, it can be shown that the Lagrangian and potential simplify to

$$L = \frac{1}{2} [(\dot{x}_1 - x_2)^2 + (\dot{x}_2 + x_1)^2] - U(x_1, x_2)$$

$$U(x_1, x_2) = -\frac{(1-\mu)}{\sqrt{x_2^2 + (\mu - x_1)^2}} - \frac{\mu}{\sqrt{x_2^2 + (x_1 + 1 - \mu)^2}}$$

1.2 Equations of Motion

From here the equations of motion are easily derived from Euler's Equation

$$\frac{\partial L}{\partial x_i} - \frac{d}{dt} \left(\frac{\partial L}{\partial \dot{x}_i} \right) = 0, \quad i = \{1, 2\}$$

$$\ddot{x}_1 = 2x_2 + U_1$$

$$\ddot{x}_2 = -2x_1 + U_2$$

$$U = \frac{1}{2} (x_1^2 + x_2^2) + \frac{(1-\mu)}{\sqrt{x_2^2 + (\mu - x_1)^2}} + \frac{\mu}{\sqrt{x_2^2 + (x_1 + 1 - \mu)^2}}$$

$$U_i = \frac{\partial U}{\partial x_i}, \quad i = \{1, 2\}$$

The first term on the right hand side of both equations represents the Coriolis force and the second term is the effective potential which contains the centrifugal and gravitational forces.

2. Path of Minimal Force

We now wish to find a path connecting two points in phase space, i.e. we want to find a path connecting two points in real space with the velocity vector specified at both ends. More specifically, we will find the path that minimizes the square of the non-gravitational force needed to move between the two points. The equations of motion including a non-gravitational force are

$$Dw_1 = \ddot{x}_1 - 2\dot{x}_2 - U_1$$

$$Dw_2 = \ddot{x}_2 + 2\dot{x}_1 - U_2$$

Where D is a unitless constant specifying the magnitude of the applied force and w_1 and w_2 are the applied forces in the x_1 and x_2 directions, respectively. To find a minimal path we need to find the minimum of the functional

$$F = D^2 \int_{t_0}^{t_1} (w_1^2 + w_2^2) dt$$

The minimum will occur if the function satisfies¹

$$\frac{\partial F}{\partial x_i} - \frac{d}{dt} \left(\frac{\partial F}{\partial \dot{x}_i} \right) + \frac{d^2}{dt^2} \left(\frac{\partial F}{\partial \ddot{x}_i} \right) = 0, \quad i = \{1, 2\}, \quad F = w_1^2 + w_2^2$$

This yields two fourth order ordinary differential equations (ODE) for x_1 and x_2

$$\begin{aligned} & -(\ddot{x}_1 - 2\dot{x}_2 - U_1)U_{11} - (\ddot{x}_2 + 2\dot{x}_1 - U_2)U_{12} - 2(x_2^{(3)} + 2\ddot{x}_1 - U_{22}\dot{x}_2 - U_{12}\dot{x}_1) \\ & + x_1^{(4)} - 2x_2^{(3)} - (U_{111}\dot{x}_1 + U_{112}\dot{x}_2)\dot{x}_1 - U_{11}\ddot{x}_1 - (U_{112}\dot{x}_1 + U_{122}\dot{x}_2)\dot{x}_2 - U_{12}\ddot{x}_2 = 0 \\ & -(\ddot{x}_1 - 2\dot{x}_2 - U_1)U_{21} - (\ddot{x}_2 + 2\dot{x}_1 - U_2)U_{22} - 2(x_1^{(3)} - 2\ddot{x}_2 - U_{12}\dot{x}_2 - U_{11}\dot{x}_1) \\ & + x_2^{(4)} + 2x_1^{(3)} - (U_{112}\dot{x}_1 + U_{122}\dot{x}_2)\dot{x}_1 - U_{12}\ddot{x}_1 - (U_{122}\dot{x}_1 + U_{222}\dot{x}_2)\dot{x}_2 - U_{22}\ddot{x}_2 = 0 \end{aligned}$$

2.1 The Hamiltonian

The fourth order ODE's for x_1 and x_2 can be converted into a system of eight coupled first order ODE's by the following substitutions

$$Dw_1 = \ddot{x}_1 - 2\dot{x}_2 - U_1$$

$$Dw_2 = \ddot{x}_2 + 2\dot{x}_1 - U_2$$

$$p_1 = 2w_2 - \dot{w}_1$$

$$p_2 = -2w_1 - \dot{w}_2$$

$$\dot{x}_1 = v_1, \quad \dot{x}_2 = v_2$$

Yielding the equations of motion

$$\dot{p}_1 = -V_{11}w_1 - V_{12}w_2$$

$$\dot{p}_2 = -V_{12}w_1 - V_{22}w_2$$

$$\dot{w}_1 = 2w_2 - p_1$$

$$\dot{w}_2 = -2w_1 - p_2$$

$$\dot{v}_1 = 2v_2 + V_1 + Dw_1$$

$$\dot{v}_2 = -2v_1 + V_2 + Dw_2$$

$$\dot{x}_1 = v_1, \quad \dot{x}_2 = v_2$$

Upon inspection, these equations can be viewed as canonically conjugate variables with Hamiltonian

$$H = \frac{1}{2}D(w_1^2 + w_2^2) + (2v_2 + U_1)w_1 + (-2v_1 + U_2)w_2 + p_1v_1 + p_2v_2$$

2.2 The Optimal Path to the Moon

The problem of finding the optimal path to the Moon, or more generally, that between any two bodies whose proximity relative to their mass allows outside gravitational influences to be neglected, has recently been revisited by the work of Belbruno and others⁴. While the Hohmann transfer, or in the case of an Earth-Moon type system, a modified Hohmann transfer, can be shown to be the most efficient path for two discrete impulses⁶, Belbruno's work demonstrated that other paths are vastly more efficient if one allows for continuous burn trajectories. The paths we will find have at least one major qualitative difference from Belbruno's work; Belbruno found paths which leave the plane of motion, while our paths do not.

The problem is split into two sections; first we find the path from an earth orbit to L1, and then we find the path from L1 to a moon orbit. We assume that the path connecting these two orbits will travel through L1, which is justified as L1 is the point of least energy connecting the Earth-Moon system. The chaotic behavior of the system with respect to small changes in initial conditions makes the shooting method somewhat intractable. The assumption that any solution which minimized the functional (so $\delta J = 0$) would travel through L1 allows us to split the problem into two parts. We find a path from a near Earth orbit to L1. Independently, we find a path from L1 to the moon.

We then 'glue' these paths together to form the path of minimum force. The first part of the problem was solved by time-reversing the equations of motion for a particle, starting at L1. As L1 is unstable, just inside L1 the gravitational force of the earth tends to dominate the influence of the random force. Therefore, after time-reversing the equations of motion, a path from L1 to a near earth orbit was easily found. Using the same technique we were able to find a path from L1 to the moon, since the moon's sphere of influence extends infinitesimally close to L1.

The actual solutions depend critically on two parameters: the mass parameter μ and the force constant D. We used the mass parameter of the Earth-Moon system and found various paths for different values of D. The smaller the applied force, the longer it will take to reach the desired final condition.

The total amount of impulse necessary to achieve this path is drastically less than that required for a Hohmann transfer. Additionally, the maximum instantaneous thrust is far smaller. For a Hohmann-type transfer, the total Delta-v is about 5.5 km/s. By numerically integrating the magnitude of the applied force over the path we find that the total Delta-v is about 2.27km/s for the D=1 path. The maximum instantaneous thrust varies in the paths shown below but is many orders of magnitude smaller than the maximum instantaneous thrust required by a lunar injection. This is particularly relevant in light of recent developments in engine technology which would allow small, low-thrust engines to be used, such as an Ion engine.

3. Random Forces⁷

We now want to find the most probable path in the PCR3BP under the influence of a random force. We use the standard model of a stochastic force which has no correlation between distinct times (i.e. $\delta(t - t') = 0$ if $t \neq t'$) and has Gaussian distribution. The modified equations of motion are

$$\begin{aligned} \dot{v}_1 &= 2v_2 + U_1 + \sqrt{D}\eta_1 \\ \dot{v}_2 &= -2v_1 + U_2 + \sqrt{D}\eta_2 \\ \dot{x}_1 &= v_1, \quad \dot{x}_2 = v_2 \end{aligned}$$

where D is a unitless diffusion constant. This set of coupled Langevin equations is described by the following Fokker-Planck equation^{2,3}

$$\frac{\partial P}{\partial t} = \frac{1}{2}\sigma^2 D \left(\frac{\partial^2 P}{\partial v_1^2} + \frac{\partial^2 P}{\partial v_2^2} \right) - \frac{\partial}{\partial v_1} (2v_2 + U_1) P - \frac{\partial}{\partial x_1} v_1 P + \frac{\partial}{\partial v_2} (2v_1 - U_2) P - \frac{\partial}{\partial x_2} v_2 P$$

where σ is just a placeholder for ease of calculation. We then use the ansatz $P = e^{-\frac{\Phi}{\sigma^2}}$ which leads to the "Riccati" form of the Fokker-Planck equation³

$$-\frac{\partial \Phi}{\partial t} = -\frac{1}{2}\sigma^2 D \left(\frac{\partial^2 \Phi}{\partial v_1^2} + \frac{\partial^2 \Phi}{\partial v_2^2} \right) + \frac{1}{2} D \left[\left(\frac{\partial \Phi}{\partial v_1} \right)^2 + \left(\frac{\partial \Phi}{\partial v_2} \right)^2 \right] + \frac{\partial \Phi}{\partial v_1} (2v_2 + U_1) + \frac{\partial \Phi}{\partial x_1} v_1 - \frac{\partial \Phi}{\partial v_2} (2v_1 - U_2) + \frac{\partial \Phi}{\partial x_2} v_2 + 2\sigma^2$$

We make an approximation for small diffusion constant D by expanding $\Phi = S + \sigma^2 S1 + \dots$ and dropping all terms of order σ^2 or higher

$$-\frac{\partial S}{\partial t} = \frac{1}{2} D \left[\left(\frac{\partial S}{\partial v_1} \right)^2 + \left(\frac{\partial S}{\partial v_2} \right)^2 \right] + \frac{\partial S}{\partial v_1} (2v_2 + U_1) + \frac{\partial S}{\partial x_1} v_1 - \frac{\partial S}{\partial v_2} (2v_1 - U_2) + \frac{\partial S}{\partial x_2} v_2$$

This is a Hamilton-Jacobi equation, and we restate it in a more familiar form below:

$$H = \frac{1}{2} D (w_1^2 + w_2^2) + (2v_2 + U_1) w_1 + (-2v_1 + U_2) w_2 + p_1 v_1 + p_2 v_2$$

This is the same Hamiltonian that we found for the path of minimal force in section 2. Therefore, we can conclude that under the influence of random forces a particles in the PCR3BP will tend to take the path which minimizes the square of the applied force, assuming the diffusion constant is small. The fact that the most likely path of a particle under a small random force is the same as the path which minimizes the square of the applied force is a non-obvious result which can be generalized to many other dynamical systems.³

These equations could also be used to model the path of particles or planetesimals in the early solar system, since frequent collisions with small particles would have the same effect of random forces being placed on the particle.

Acknowledgements

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- This section follows the work of S. Rajeev.³

Figure 1a : D=6

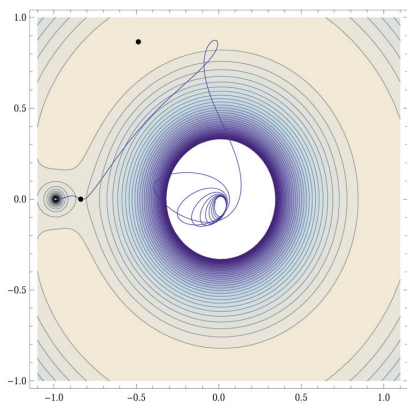


Figure 1b : D=1

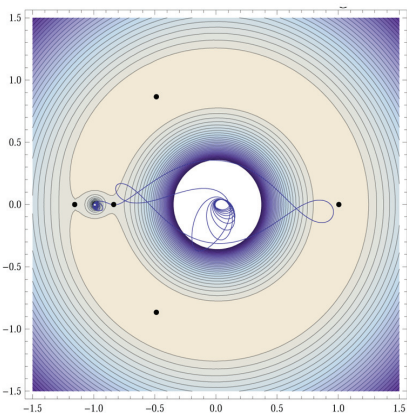
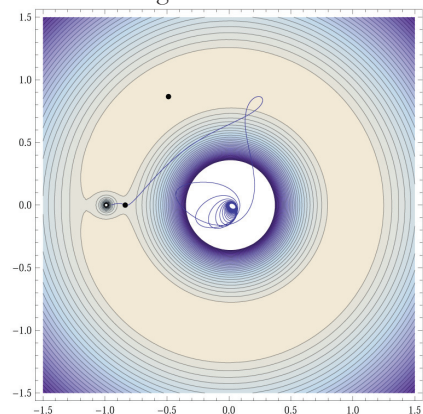


Figure 1c : D=5



| D | $\nabla V(m/s)$ | T(days) | $F_{max}/m(N)$ |
|---|-----------------|---------|----------------|
| 1 | 2.27 | 60 | .02 |
| 5 | .9 | 36 | .03 |
| 6 | .8 | 33 | .03 |

Figure 1 (a-c). Paths for various values of D are shown. The Delta V and time appear to go down for higher values of D, but the instantaneous thrust needed increases.

The Strongest Hand and the Longest Sword: Colonial Politics, Trade, and the Courts in the Golden Age of Piracy (1695-1726)

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“What will not thirst of gold lead men to attempt, when they are conscious that there is no sufficient power to check them?” When Governor Jeremiah Basse of New Jersey posed this question to William Popple of the Board of Trade in 1696, the English colonies in America were plagued by the anarchies of war, political impotence, and the pirates of all nations who threatened their coastal trade. New Jersey, known at the time as the proprietary colonies of West and East Jersey, had no official fortifications, courts, or even a government with which to “not only protect the people but repress injuries and violence.”¹ At a time when England was engaged in cyclical conflict with France during the Nine Years’ War (1688-1697) and later against France and Spain in the War of the Spanish Succession (1701-1713), the plight of New Jersey was certainly not uncommon to the rest of England’s colonies in America. Merchants of the proprietary and chartered colonies alike suffered from the leadership of ineffective and unscrupulous governors, rampant illegal trade, privateering, and a lack of jurisdictional power to combat pirates and those who harbored them on land.

In this context of England as an imperial power being stretched to its limits in the late seventeenth century, acts of maritime predation became increasingly frequent and a significant blight on mercantile trade between England and her American colonies. The profession of piracy became an attractive alternative for the seamen of the merchant shipping industry and the Royal Navy who received meager pay for their hard labor and were subjected to the vicissitudes of a dangerous life at sea.² Pirates, in contrast to naval or merchant seamen, performed less work and enjoyed the benefits of higher pay in the form of shares of plunder and the absence of a captain with unrestrained authority. Some historians argue that the autocratic presence of the captain on board merchant vessels drove many seamen to acts of mutiny and piracy.³

The pirates of the late seventeenth century benefited particularly from wartime chaos and a limited amount of direct Parliamentary governance as they engaged in illegal trade and plundering of colonial and English prizes. In the proprietary colonies of New Jersey, Connecticut, and Pennsylvania pirates

preyed parasitically on the richly laden merchant vessels traveling along the trade routes to and from the port of New York. Lying between Maryland with its sinewy creeks and rivers and New York, Pennsylvania in particular was described as “a most commodious centre for illegal trade” by the Commissioners of Customs.⁴ Skilled tradesmen and merchant seamen fled the southern colonies to Pennsylvania and the Jerseys where the jurisdiction of other colonial courts and governors was unable to halt the expansion of piracy and illegal trade with Scottish and Dutch merchants.⁵ It was the successful banditry of these hostis humani generis that prompted the Crown, the Lords Justices, and the Parliamentary Board of Trade to craft new statutes and courts capable of eradicating the menace of piracy in the early eighteenth century. In this fashion, the increasing frequency of acts of maritime predation contributed to the growing spirit of political independence in the colonies and necessitated an expansion of power for the institutions of colonial government.

This paper examines piracy during its golden age of the early eighteenth century from an angle that is scarcely employed in other works of maritime history. Historian Marcus Rediker and economist Peter Leeson have interpreted pirate behavior in the context of an insular pirate society at sea governed by unique customs and decision-making processes. But as maritime historian Daniel Vickers has noted, by limiting the focus of maritime history to interactions at sea, the field is deprived of the perspective necessary to explicate change over time.⁶ Rather, we must cross-analyze the heterogeneous perspectives of mariner, merchant, and government official to explain how piracy affected the workings of England’s growing mercantile empire. Borrowing from the fields of legal and economic history, this study will present pirates not as precursors to the proletariat or as burgeoning capitalists, but rather as a third party whose actions contributed to the political rift emerging between England and her American colonies as early as the late seventeenth century.

The Status Quo before 1700 and the establishment of the Vice-Admiralty Courts

Colonel Quarry of Virginia, writing in 1700 to the Council

of Trade and Plantations proclaimed that “all the news of America is the swarming of pirates not only on these coasts, but all the West Indies over, which doth ruin trade ten times worse than a war.” After failing to solicit the aid of Governor Penn in enlisting men for his cause, Quarry paid mercenaries to help him apprehend suspected pirates in Virginia. Disappointed by the inability of the colonial governments to effectively suppress piracy, Quarry was hoping to receive a reward of 10 £ for each pirate he apprehended to offset the costs he incurred as a loyal subject of the Crown.⁷

Quarry’s case illustrates the fear merchants had of the pirates, now newly unemployed from their former privateering professions. Colonial trade with England began to recover as demand for textiles, lumber, and tobacco increased after the signing of the Peace of Ryswick (1697) with France. Unfortunately for the “sly and crafty” merchants in centers of commodity trading,⁸ their ability to profit from this excess demand for goods in the West Indies and England was tempered by reports of the successes of pirate captains in capturing merchant vessels.

Word spread quickly of the private commission given to Captain Thomas Tew in 1694 by deposed Governor Benjamin Fletcher of New York and his descent into piracy off the coast of East Africa, as well as of the illicit deals linking Fletcher and his Council to members of Captain Avery’s crew.⁹ Deputy Governor Markham of Pennsylvania was known to have granted legal protection to Avery’s crew and “had a great present made to him and his family by them.”¹⁰ Captain William Kidd’s capture of the *Quedab Merchant* in 1698 after the Earl of Bellomont had commissioned him to hunt down Tew was no less scandalous. The subsequent political backlash that Bellomont preempted occurred mainly because Kidd’s “Pyracies so alarmed our Merchants that some Motions were made in Parliament, to enquire into the Commission that was given him, and the Persons who fitted him out.”¹¹

It was out of the sensationalized reports and rumors about the corruption of the Crown’s officials and the barbarous plundering of ships by specific pirates that the Board of Trade and Plantations and the Commissioners of Customs took legal action. The passage of the Act of Trade in 1696 directly followed Avery and Tew’s capture of the Mogul Emperor’s *Gunj-i-Sumaae*, in an attempt by the Board of Trade and customs officials to limit the illegal trade of East Indian goods originating from suspected pirate crews.¹² This new Act of Trade underlined the embargo on colonial trade with European powers other than England and included a provision for the establishment of vice-admiralty courts.¹³ The provision, however, was subject to much debate and scrutiny by the colonial assemblies and the governors and their respective councils up until the passage of the Act for the More Effectual Suppression of Piracy in 1700.

Shortly after the passage of the Act of Trade, Lieutenant Governor Stoughton of New York and Governor Basse of New Jersey requested greater admiralty power in their respective provinces. Under the axiom “the strongest hand and the longest sword will be the best title to estates,” Basse went so far as to assert that the prudent establishment of vice-admiralty courts in all English colonies under civil law would be the best course of action to protect the Crown’s revenues from illegal trade

and piratical activity.¹⁴ But still some governors argued in favor of increased naval presence in their province instead of new legislation or increased fortifications, as was encouraged by Parliament during war with France.¹⁵ The pleas of governors and the Board of Trade’s recommendations for increases in naval patrol of colonial coasts and merchant convoys continued into the 1720’s, when piracy began to wane.

Central to the debate surrounding the provision for vice-admiralty courts was the question of whether the King actually had the legal authority to impose courts upon the proprietary as well as the royally chartered colonies. The original Parliamentary Act (1361) for convictions of piracy under civil law in the Admiralty Court of Edward III was amended by the 1536 Offences at Sea Act (28 Henry VIII, c.15) to place all piracy convictions under common law. The 1536 mandate made pirate conviction subject to a jury of twelve subjects and accomplice testimony at the Court of Admiralty in England; all accused of piracy in the colonies were transported to England for trial.¹⁶ Although it was easier to convict pirates with the inclusion of accomplice testimony (which was not admissible under the 1361 Act) the Offences at Sea Act was inefficient and costly to both the colonies and the Crown. The Offences at Sea Act encouraged the unwarranted release of pirates to defray the transportation costs associated with the Royal Navy escort assigned to take the convict back to England.

Although the Lords Justices confirmed the legality of vice-admiralty courts in all colonies and royal nominations of attorney-generals, some colonies opposed the imposition of civil law procedure on the grounds that this constituted a violation of their rights as English citizens.¹⁷ Rhode Island created its own vice-admiralty court through the Assembly and Council under the auspices of a need to try privateers and prizes at the conclusion of the Nine Years’ War.¹⁸ Bellomont viewed this act as Rhode Island’s attempt to legitimate its high frequency of releases of known pirates from conviction. After the Board of Trade later realized in 1700 that Connecticut had also instituted its own Court, the Lords of Trade concluded that the King must first approbate governors and council and assembly leaders before they could enforce the Acts of Trade through vice-admiralty courts.¹⁹ In further exercises of political defiance, the Council and Assembly of Maryland attempted to hinder the passage of the 1700 Act for the More Effectual Suppression of Piracy by attaching copies of private acts to correspondences regarding the official Act.²⁰

These attempts of the chartered colonial powers to preclude the jurisdiction of the High Court of Admiralty in their provinces illustrate the contentious nature of vice-admiralty courts in the colonies. The original provision of the 1696 Act of Trade was not expounded into law until four years later. One possible reason for this is that the Council of Trade’s recommendation to the King in 1697 for “a law enacted here to extend uniformly through all your Plantations” was judged sufficient for combating the evils of piracy.²¹ The Jamaica Act (1681) was a statute similar to the Offences at Sea Act but still required either a full confession or eyewitness testimony. Copies of the Jamaica Act were distributed to the Governors for them to encourage the passage of a similar act in the other colonial assemblies. Common law proceedings before a sympathetic or

fearful jury made it ever more unlikely that a pirate tried in the colonies would be convicted or hanged.

Vice-admiralty courts were a matter of political conflict from 1697-1704, for their powers were still largely undefined during this period.²² The ability to use capital punishment against pirates convicted in the courts was still in question from 1697-1698.²³ A lack of regulation of court fees for the trying of seizures and forfeitures in the courts caused prosecuting fees to be too high. These high court fees, which continued into the eighteenth century, discouraged merchant seamen from bringing suit against abusive captains and limited the capacity of alleged pirates to prepare an adequate legal defense.²⁴ But regardless of these deficiencies and the recalcitrance of the colonies, the Council of Trade saw the vice-admiralty courts as a great success by the time they were formalized in the Act for the More Effectual Suppression of Piracy. The Lords of Trade even went so far as to declare that they “have proved of great encouragement to legal trade.”²⁵ The validity of this statement, however, was tested in the following two decades, during the height of pirate hegemony in colonial waters.

Pirates as Barriers or Facilitators of Trade?

Blackbeard “struck three lighted Matches under his Hat, which appearing on each Side of his Face, his Eyes naturally looking fierce and wild, made him altogether such a Figure, that Imagination cannot form an Idea of a Fury, from Hell, to look more frightful.”²⁶ Captain Teach, alias Blackbeard, was among the most infamous pirates of the Golden Age of Piracy. His actions at Charleston and North Carolina provide a useful case study for analysis of how the Crown and the powers of colonial government responded to severe interruptions of trade by pirates.

The debaucheries of Captain Teach and his crew on the coastline of the southern colonies in 1718 were committed at a time in which the vice-admiralty courts alone were proving insufficient to discourage acts of piracy. Noting the expansion of the pirate ranks to numbers estimated from 1,800 to 2,400 between 1716 and 1718, George I issued a series of “proclamations” or pardons in 1717 and 1718.²⁷ Under these series of pardons, murder committed during any act of piracy was forgiven and pirates could retain a portion of their own goods but not those proven to have been unlawfully seized; individuals could also bring charges against pardoned pirates who caused them property damages of any kind.²⁸ The King’s proclamations also provided for an incentive structure for the apprehension of pirates that had been called for earlier (as in the case of Col. Quarry in 1700). 100 £ was awarded for the capture of a pirate captain and 20 £ for privates, with amounts ranging between 20 £ and 100 £ awarded for the capture of officers.²⁹

The continual changes made to the expiration date before which all piratical acts were pardoned indicated the hope of the Crown and the colonial Governors to accommodate a greater number of ex-pirates.³⁰ But changes to the original proclamation (1717) also showed that issuing pardons was a flawed method for eliminating the pirate threat to merchant trade. Fighting in the War of the Quadruple Alliance (1718-1720) had already begun when Governor Lawes of Jamaica

wrote to the Council of Trade and Plantations requesting a constant patrol of three well-armed Royal Navy vessels. Pardons did nothing to impede the efforts of Spanish and French privateers from frightening merchants into keeping their cargoes at port.³¹

The hostage situation that Teach and his crew created at the port of Charleston further fomented discontent among the colonial merchants. All shipping was at a standstill for the week that Blackbeard and his crew lay off the bar of Charleston. Blackbeard held hostage the crew and passengers aboard two pinks and a Brigantine until the party he sent to town returned with the chest of valuable medicine he demanded.³² Charleston, which possessed “no autonomous mercantile community” of its own, was hit especially hard by Teach’s actions. Given that Charleston was a drop-off point for merchant shipping from Britain and the West Indies, successful trade depended heavily on the swiftness of transactions and traffic within the harbor.³³ Accounts of Blackbeard at Charleston expressed the merchants’ frustration with an inept and crippled South Carolina government in the aftermath of the Yamasee War against the Native Americans in the western part of the province. These accounts blamed the government for incorrectly believing that the pardons would be effective and for misjudging the deceitful nature of pirates, many of whom had returned to their old ways after accepting His Majesty’s clemency. One assemblyman even argued that “most of those that took up with the Proclamation are now return’d to the same employment which has rather proved an encouragement than anything else, there now being three for one there was before the Proclamation was put out.”³⁴ This argument would seem valid, given that Blackbeard and his crew, along with Major Bonnet reportedly received certificates of pardon from Governor Charles Eden of North Carolina before returning to commit further acts of piracy.³⁵

The immediate effect of piracy was a reduction in the commodities available to consumers because merchants were less willing to ship their goods to Britain and the colonies of the British Empire. This in turn increased transaction costs for the merchants who shipped the commodities because they now had to pay for insurance on their vessels and cargoes. Costs also rose indirectly for the Crown; Britain’s profit from colonial trade was diminished by the costs it incurred to supply convoys for vulnerable merchant vessels.³⁶ The failure of legal means to sufficiently eliminate piracy as a threat to trade in the colonies necessitated an eventual expansion in the ranks of the Royal Navy patrolling colonial waters.³⁷ But the very forces employed by Britain to clear the seas for free trade with her colonies also contributed to the discontent of merchants on both sides of the Atlantic.

Indeed, the merchants of the American colonies suspected that the Royal Navy, being in colonial waters on the pretense of expelling piracy and pressing merchant seamen, conducted its own trade with the cargoes seized as illegal goods from pirates. Governor Lawes reported to the Council of Trade and Plantations that local merchants claimed that the Royal Navy had become a barrier to trade by carrying stolen cargoes on board His Majesty’s Ships.³⁸ Lawes even went so far as to attribute the loss of virtually all trade at Port Royal to “the men of warr’s transporting goods and merchandize which otherwise

would be done by vessels belonging to the Island.” Lawes saw this disruption of normal trading patterns as a blight on the livelihood of the merchant seamen “who now have no bread for want of employment, which is the chief occasion of so many of them going a pyrating.”³⁹ Piracy may have been the impetus for this disruption of trade caused by private naval trading, but it also catalyzed the active, albeit marginally successful, legal actions originating from the complaints of disgruntled colonial merchants.

The Role of the Governors and Justices of the Vice-Admiralty

In many ways the governors of colonial America were fountainheads of the spirit of independence that began to distinguish British citizens from their colonial counterparts. As the previous examples of the improprieties of Governors Fletcher and Markham illustrate, the interests of some colonial governors often ran counter to the interests of the Crown and the powers that appointed and commissioned them. It would seem from Defoe’s account of Captain Teach’s notorious end at Ocracoke Island in 1718 that Governor Eden was also on friendly terms with a pirate; Eden reportedly staged a mock vice-admiralty court trial and gave Teach the rights to a stolen ship on the pretense that it was of Spanish origin.⁴⁰ Judging from the harsh words spoken about these governors by Commissioners of Customs and other governors who actively pursued measures to discourage practices of illegal trade and piracy, it is apparent that some governors were polarizing figures in colonial politics.⁴¹

Other governors, in contrast, were paragons of loyalty to King and Parliament and vigorously expanded their jurisdictional authority towards suppressing piracy and illegal trade in their own provinces and elsewhere. The Council of Trade and Plantations congratulated Governor Francis Nicholson on numerous occasions for his efforts in eradicating pirates during his tenure as Governor of Maryland.⁴² The former privateer Governor Woodes Rogers of the Bahamas led a successful campaign against pirate Captain Vane and the crew of Major Stede Bonnet even after Vane threatened to burn down Rogers’ personal guard-ship. Rogers’s dependability as a pirate-hunter became so well known that Governor Johnson of South Carolina attempted to enlist Rogers’s aid to combat Blackbeard at Charleston.⁴³

But Governors Nicholson and Rogers did not stretch the limits of their royal commissions to the extent that Governor Alexander Spotswood of Virginia did. Traders in the James River area who owned sloops that Blackbeard pillaged “sent a Deputation to Virginia, to lay the Affair before the Governor of that Colony, and to solicit an armed Force from the Men of War lying there, to take or destroy this Pyrate.” Before the Men of War under the command of Lieutenant Maynard set out on November 11, 1718 in search of Blackbeard, Spotswood swiftly “called an Assembly, in which it was resolved to publish a Proclamation offering certain Rewards to any Person or Persons, who, within a Year after that Time, should take or destroy any Pyrate.”⁴⁴ The news of Maynard’s victorious campaign and killing of Blackbeard enhanced Spotswood’s reputation as being a decisive and impressive leader in the war against piracy. His reputation as the man who brought down Blackbeard and his

crew became so pronounced that in 1724 he feared that he may become a victim of pirate vengeance. He therefore requested to be transported back to London in a man-of-war.⁴⁵

Some governors were in a unique position of higher authority after the passage of the Act for the More Effectual Suppression of Piracy in 1700 commissioned them as vice-admirals. Until it was deemed legal for the King to institute vice-admiralty courts in the colonies, governors’ commissions only empowered them to appoint officials designated by the Lords Justices in England as justices of the vice-admiralty. The Crown saw fit to promptly grant vice-admiralty commissions to governors who had shown dedication to the cause of combating piracy, such as the Earl of Bellomont in 1697. However, the Lords of the Admiralty were at first reluctant to make vice-admirals of the governors of proprietary colonies.⁴⁶ Whereas Bellomont received a full commission of vice-admiralty so that he would have the authority to try pirates known to be hiding in the proprietary colonies of West and East Jersey, the Lords of Admiralty feared that the agents of the proprietary colonies would use the authority of the vice-admiralty to grant legal protection to pirates and contraband traders.

The Act for the More Effectual Suppression of Piracy also created new positions within the vice-admiralty courts that came to be known as justices or Judges of Admiralty. These individuals presided over an increasing number of cases involving acts of maritime predation during the height of piracy in colonial America. But by the 1720’s, the common law courts of the colonies had moved to supplant the powers of the Judges of Admiralty in favor of a jury system that was lenient on illegal traders. The recalcitrance of these Judges of Common Law was especially prevalent in New England, where the need for vice-admiralty courts to try and punish pirates had diminished by 1720 from previous levels.⁴⁷ As early as 1719, warnings from justices of the vice-admirals to the Council of Trade and Plantations and the Commissioners of Customs reflected the attempts of the common law courts to encroach on the jurisdiction of the vice-admirals in Boston in order to shield illegal trade and to keep the wages of merchant seamen low.⁴⁸ To this end, the flourishing merchants of New England used their authority within the colonial assemblies “to assure a ready supply of cheap, docile labor.”⁴⁹

The influence of the common law courts on vice-admiralty jurisdiction would not reach its zenith until several decades after the Act for the More Effectual Suppression of Piracy. By the 1760’s, when Britain enacted greater restrictions on colonial trade with the Revenue Act (1764) and the Stamp Act (1765), the jurisdictional authority of England’s American colonies had shifted dramatically from the vestigial legal proclamations of the late seventeenth century.⁵⁰ The interests of the colonial merchants and traders who had originally opposed the institution of the vice-admiralty courts were protected by the growing hindrance of the common law courts to cases of smuggling.⁵¹ As the Commissioners of Customs were under greater pressure following Britain’s fiscally damaging Seven Years’ War (1756-1763) they encouraged a careful revision of the powers of the vice-admiralty courts in response to the New England colonists’ efforts to evade new and aggressive tax collecting.⁵² Indirectly, these events led to the consolidation of powers traditionally held

separately by the Court of the Exchequer and the High Court of Admiralty in Britain.

Parliament created an alternative admiralty court system in the colonies under section forty-one of the Revenue Act, requiring that all cases involving violations of trade, customs, and revenue laws be tried in an autonomous system of imperial courts.⁵³ The vice-admiralty courts that were initially created in the American colonies to give the Crown's officials the ability to efficiently condemn pirates gained the ability to regulate economic relations between Britain and her colonies. Any prosecutions for the violation of Stamp Act provisions could be tried in either the provincial common law courts or the provincial vice-admiralty courts. As a result, the vice-admiralty courts became akin to a revenue court, with verdicts subject to the decision of a single judge.⁵⁴ Throughout this process, the colonial protestation that "the courts of vice-admiralty were infringing on English liberty by taking away trials by jury" was omnipresent.⁵⁵ Such complaints, which existed from the inception of the vice-admiralty courts in 1700, were echoed in the rhetoric of the Declaration of Independence during the throes of the American Revolution: approximately fifty years following the end of the golden age of piracy.

The relationships linking the complex institutions of governance in England and those in her colonies during the period of pirate predominance from the late seventeenth century to the mid-1720's were fraught with contentious officials, disorganization and often polarizing differences in legal opinion. A decline in piracy, facilitated in part by the dramatic increase in the ranks of the Royal Navy between 1725 and 1727, virtually eliminated the prime focus of the original vice-admiralty courts established at major colonial ports at the turn of the eighteenth century. The original expansion of jurisdictional power initiated by the High Court of Admiralty, the Council of Trade and Plantations, and King and Parliament in these courts was prompted by the parasitical persistence of piracy as a barrier to profitable trade between Crown and colonies. A policy of extending the "strongest hand" and wielding the "longest sword" had succeeded to small extent with the paltry convoy system that the Royal Navy provided and the ineffective proclamations of George I not only in limiting the success of pirates but also in breeding discontent among the merchants and colonial assemblies. The merchants and assemblies over time felt as if the traditional rights as English citizens to which they were entitled had been eroded. The imposition of civil law, impotent and dubious governors, and overzealous customs officials contributed to the growing rift between England and her colonial subjects in the decades following the Golden Age of Piracy. Certainly, it was in no small part a product of an illustrious pirate legacy that as early as 1719, officials acting under the authority of the King endured "intolerable oppressions occasioned by an utter aversion the great part of the people" in the colonies "entertain against all powers not derived from themselves."⁵⁶

References

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2. Marcus Rediker, *Between the Devil and the Deep Blue Sea: Merchant Seamen, Pirates, and the Anglo-American Maritime World, 1700-1750* (Cambridge: Cambridge University Press, 1987), 107.
3. For more on the abuses endured by merchant seamen at the hands of captains and quartermasters see *Ibid.*, 212-226.
4. Commissioners of Customs to the Lords of the Treasury, CSPC, Nov. 16, 1696, Item 396, vol. 15 (1696-1697), 212-215.
5. [Maryland] Governor Nicholson to Council of Trade and Plantations, CSPC, March 27, 1697, Item 862, vol. 15 (1696-1697), 420-421.
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10. Robert Snead to Sir John Houblon, CSPC, Sept. 20, 1697, Item 1331, vol. 15 (1697-1698), 613.
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16. Peter T. Leeson, *The Invisible Hook: The Hidden Economics of Pirates* (Princeton: Princeton University Press, 2009), 143-144.
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19. [Whitehall] Answer of the Council of Trade and Plantations to the Order of the House of Commons, CSPC, March 6, 1700, Item 244, vol. 18 (1700), 132.
20. Council of Trade and Plantations to Governor Nicholson, CSPC, Aug. 21, 1700, Item 728, vol. 18 (1700), 490-491.
21. [Whitehall] Council of Trade and Plantations to the King, CSPC, Dec. 9, 1697, Item 94, vol. 16 (1697-1698), 60; Circular: Council of Trade and Plantations to the Governors, CSPC, March 21, 1698, Item 309, vol. 16 (1697-1698), 140.
22. In Bradley P. Nutting, "The Madagascar Connection: Parliament and Piracy, 1690-1701," *The American Journal of Legal History* 22, no. 3 (July 1978): 204, 208 Nutting argues that the Jamaica Act (1681) was not only effective in reducing piracy in Jamaica, but that by the end of the Nine Years' War the need for vice-admiralty courts to suppress piracy had been greatly reduced.
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28. Mr. Attorney and Mr. Solicitor General to the Council of Trade and Plantations, CSPC, Nov. 14, 1717, Item 201, vol. 30 (1717-1718), 104-105.
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30. Boston News-Letter, April 13-20, 1719, p.2.
31. [Jamaica] Sir N. Lawes to the Council of Trade and Plantations, CSPC, Aug. 29, 1717, Item 54, vol. 30, (1717-1718), 17-18.
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36. John L. Anderson, "Piracy and World History: An Economic Prospective on Maritime Predation," *Journal of World History* 6, no. 2 (1995): 178-180.
37. Marcus Rediker, "Under the Banner of King Death': The Social World of Anglo-American Pirates, 1716-1726," *William and Mary Quarterly* 3rd ser., 38 no. 2 (April 1981): 226. Sailors in the Royal Navy increased from 6,298 in 1725 to 20,697 in 1727 as part of a steady increase in those employed by the Navy beginning in 1724. Rediker questions whether this dramatic increase was predicated mainly on an increasing frequency of pirate activity.
38. Leeson, *The Invisible Hook: The Hidden Economics of Pirates*, 147.
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40. Defoe, GHP, 75-76. Defoe later adds information to the appendix in Volume II to suggest Eden's innocence in any dealings with Capt. Teach. The colonial records on the subject of any impropriety on Eden's part are curiously silent.
41. For complaints about the actions of these governors see London] Jeremiah Basse to William Popple, CSPC, July 26, 1697, Item 1203, vol. 15 (1696-1697), 563-565; A collection of papers handed in by Edward Randolph in reference to the enforcement of the Acts of Trade and Navigation in the Colonies, CSPC, July 31, 1696, Item 120, vol. 15 (1696-1697), 58; Commissioners of Customs to the Lords of the Treasury, CSPC, Nov. 16, 1696, Item 396, vol. 15 (1696-1697), 212-215; Robert Snead to Sir John Houblon, CSPC, Sept. 20, 1697, Item 1331, vol. 15 (1697-1698), 613.
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47. Mr. West to the Council of Trade and Plantations, CSPC, June 20, 1720, Item 117, vol. 32 (1720-1721), 53-55; Boston] James Menzies, Judge of Admiralty in New England, to H.M. Commissioners of Customs, CSPC, July 25, 1720, Item 153i, vol. 32 (1720-1721), 69.
48. [Boston] James Smith to Josiah Burchett, CSPC, Feb. 18, 1719, Item 52 iv, vol. 31 (1719-1720), 27.
49. Rediker, *Between the Devil and the Deep Blue Sea*, 258.
50. For examples of colonial assembly laws before the passage of the 1696 Act of Trade see Boston Legislature, "At a General Court for Their Majesties colony of the Massachusetts Bay in New-England, sitting at Boston, upon adjournment, December. 22th. 1691," printed by Samuel Green, 1691; New York Legislature, *An Act for Restraining and Punishing Privateers and Pyrates*, 1692, printed by William Bradford, 1693. Appointing officers to colonial courts and imposing custom duties separate from those of the 1660 Act of Trade on commodities crucial to the trade of the respective colonies were common strategies employed before the founding of vice-admiralty courts.

51. This was particularly true of Massachusetts after the passage of the Molasses Act of 1733.
52. Andrews, introduction to *Records of the Vice-Admiralty Court of Rhode Island 1716-1752*, 76.
53. Oliver M. Dickerson, *The Navigation Acts and the American Revolution*, (Philadelphia: University of Pennsylvania Press, 1951), 183, 212.
54. Carl Ubbelholde, *The Vice-Admiralty Courts and the American Revolution* (Chapel Hill: University of North Carolina Press, 1960), 74-77.
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Designing Artificial Skin for Wound Healing: An Intersection of Biology and Tissue Engineering

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Over the years, physicians have developed means of treating all types of skin wounds, from small cuts to life-threatening burns. Most of these options rely on the natural ability of the body to repair damaged skin. Unfortunately, this innate physiological ability to repair is somewhat coarse and unrefined, most likely due to the evolutionary need to mend wounds as quickly as possible.

The body has little ability to repair large wounds or extensive burns. Therefore, skin grafting techniques from a variety of sources have been employed. Such methods, though proven somewhat adequate, are riddled with complications, economic hindrances and other shortcomings.

The door has opened for the design of artificial skin substitutes by biomedical tissue engineers. While Engineers up until now, have had limited success in creating artificial skin for such wound, they appear to be on the right track. They are studying the underlying physiology of natural wound healing to better understand the mechanisms of this process. Engineers have also set lofty goals; to eventually achieve complete tissue regeneration rather than just repair. That is, they hope to deploy skin constructs that will allow skin to return to its exact healthy and functional state as it was prior to injury.

To this end, engineers are studying biological models of tissue repair, as well as the few examples of perfect regeneration in nature. Additionally, tissue engineers have teamed up with biological researchers to look at how stem cells and gene therapy can be implemented. Therefore skin tissue engineering today is a series of paralleled efforts combining the worlds of engineering, biology, anatomy, pathology and genomics to develop an artificial skin substitute for wound healing and regeneration.

Function and Anatomy of Skin

Human cutaneous tissue, or skin, is the largest organ in the human body and provides significant protection from damaging environmental elements. Skin acts as a barrier of defense from ultraviolet radiation, rapid heat loss or addition, abrasive or mechanical stresses, toxic substances and bacterial/viral infestation. Moreover, skin is involved in the prevention of internal water loss and thermoregulation, control of body

temperature.^{1,2,4} This is actuated by means of sweating and control of the exposed surface area.¹¹

To understand the physiology of the skin as an organ, it is necessary to understand the anatomy of the skin. The skin is composed of three well defined layers as shown in Figure 1. The outermost layer is the epidermis, which is further divided into 5 sub-layers or strata. This layer is relatively thin and is completely composed of cells, the most prevalent of which are keratinocytes. Keratinocytes are epithelial cells, which are produced in the basal layer of the epidermis (deepest layer) and differentiate into specific cell types as they rise to the surface of the tissue. The outermost layer of keratinocytes is predominantly composed of dead cells that eventually erode off the surface of the human body.⁶ Due to the relative location of the epidermis, this layer plays the most important role as the protective barrier of the skin.

The next layer directly below the basal layer is the dermis. This layer is composed mostly of connective tissue and makes up the bulk of the skin's mass. The most common type of cell in this region is the fibroblast, which generates the proteins of the extracellular matrix (ECM) and collagen. Both of these compounds are crucial to the structural integrity and strength of the skin. Elastin proteins, which allow elasticity, and glycosaminoglycans (GAG's) also populate this layer. The base of hair follicles and sweat glands stretch down from the surface into the dermal layer.⁶

The deepest layer of the skin is the hypodermis, or subcutaneous layer. Adipose (fat) cells are the predominant cell type in this region.⁶ Therefore, this region is extremely well vascularized. Nutrients, such as oxygen and vitamins, enzymes, cofactors and leukocytes (immune cells) all reach the dermis and epidermis by means of vessels in the hypodermis.¹ Furthermore, the hypodermis is responsible for the thermoregulatory actions of the skin.

Physiology of Wound Healing

The biology of wound healing occurs in a stepwise fashion that must be understood for proper repair and regeneration to take place. The first of these steps is the formation of a clot,

The Skin

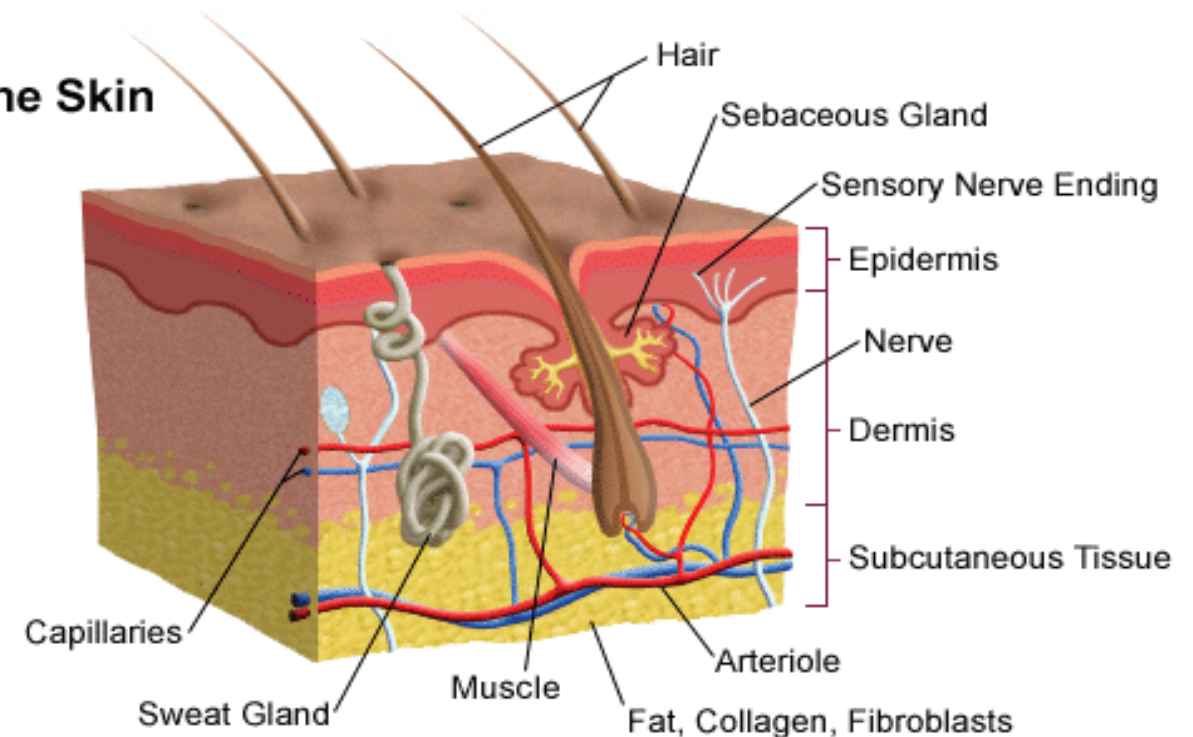


Figure 1. Schematic of the cutaneous anatomy. (Stanford University Medical Center)

a process called thrombosis. A fibrous protein called fibrin, in conjunction with blood platelets, is responsible for this pathway. Thrombosis is an evolved pathway that prevents excessive bleeding/hemorrhaging. This control of blood loss is called hemostasis.⁴

After thrombosis occurs, inflammatory mediator cells rush into the wound site to kill any bacteria, and remove debris. Fibroblasts and capillaries also invade the clotted region to form contractile granulation tissue that draws the wound margins (edges) together.¹¹ An oxygen gradient is important to the physiology of this step. At the margins, diffusion causes a higher content of oxygen, which activates fibroblasts to produce collagen, and stimulates angiogenesis, the growth of new blood vessels. At the center, the oxygen content is much lower, which causes macrophages, a type of leukocyte, to release specific cytokines for chemotaxis.² This means that these healing cells release certain molecules that draw other cells toward them, like a molecular magnet. In this case, dividing and growing cells are drawn to the region.

The last step occurs when fibroblasts and endothelial cells migrate to perform fibroplasia and further angiogenesis, respectively. Fibroplasia is characterized by fibroblasts laying down collagen and ECM, the components that make up a cell's outer structure and foundation, into the tissue site. However, this process becomes excessive, and excess collagen is produced. Gradually, the excess collagen is remodeled in the following months to form a scar, which is different in texture and quality from normal skin tissue.

Current Skin Grafting Options

Today, major burns and wounds are most often treated with autologous skin grafts. This treatment involves obtaining from the tissue bed, an area of skin from another part of the same patient's body.¹² This graft is placed on the wound, allowing it to establish blood supply by vascularizing with the inherent wounded tissue. However, there are some major problems with such a therapy. This process can be extremely painful for the patient because other portions of skin have to be removed, thus creating new wounds. Additionally, it cannot be performed on patients with extensive wounds, such as serious burn victims, because there is not enough tissue available for transplantation and it is a risky procedure due to the already compromised, unstable condition of such patients.¹

A similar option to autologous grafting is to obtain a healthy skin sample from another individual with identical genetics, such as an identical twin. Obviously, this option is only available to a small percentage of the human population. Grafts from other non-identical individuals are called allogeneic grafts. Yet, such donation is prone to an immune rejection, similar to that of other organ transplants. This has led to the idea that skin could be removed from cadavers for allogeneic grafting. The advantage is that cadaver skin does not harm anyone else, and can be obtained at any time. Also, since it can be prepared before an injury, it can be properly treated to remove its antigenicity, and thus decrease the chances of rejection. Skin prepared in this manner for "off-the-shelf" use is sold under the name Alloderm.¹⁰ The last option is xenogeneic grafts, which are obtained from other species. Clearly, this method also causes no human injury, but lacks aesthetic matching and is more likely to

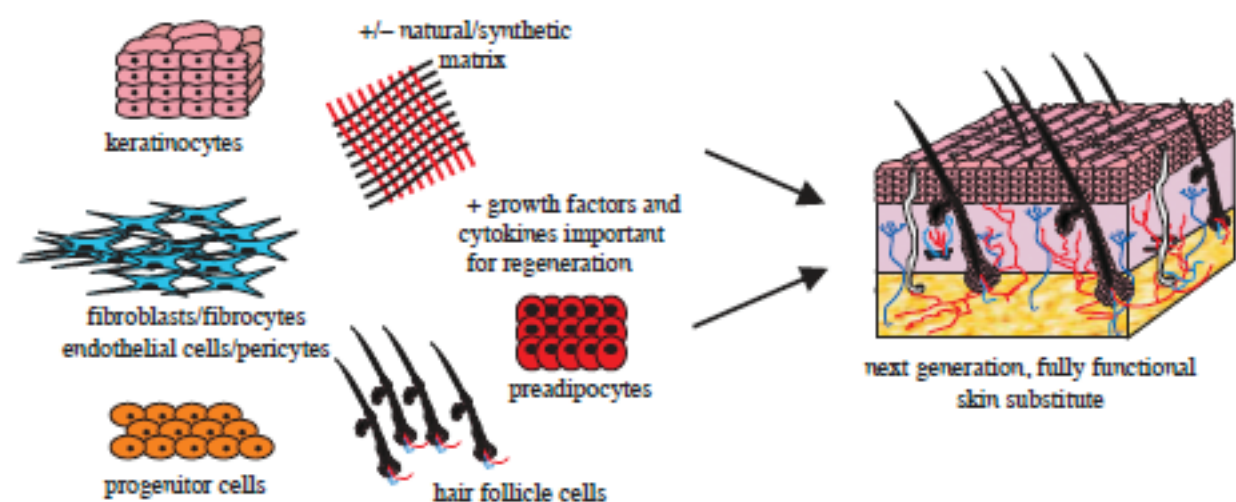


Figure 2. Schematic of the theory to use combined efforts of engineered scaffolding matrices, specific growth factors and cytokines (perhaps from gene delivery), necessary individualized cell types, and both kinds of stem cells (progenitors and hair follicle cells). (Metcalfe & Ferguson 2007, 413)

be rejected by patients.

Role for Tissue Engineering in Wound Healing

Tissue engineers are faced with the challenge of designing an artificial skin substitute to replace (or possibly complement) the aforementioned skin grafts. Currently, efforts are being made to aid in the wound repair process, but no true skin substitute exists today, and many strides must be made before this is achieved.

The first efforts were focused on adding cells and tissue to the wound site, but these were met with limited success. In order for adequate repair mechanisms to occur, a proper cellular "scaffold" is necessary for cells to bind and act as a template for growth.² Cell adhesion to environmental surfaces is important to tissue development. Many of the wound healing processes rely on mechanotransduction signals to function correctly, meaning that they need specific physical contact with their surroundings to be effective. To facilitate cell binding, many scaffolds incorporate collagen into their structure, which has been shown to increase cell-to-matrix affinity. Results have shown increases in neurogenesis, the growth of neural cells, and better skin fibroblast migration and activation.²

Studies have shown that a porous design is required for such scaffolds. Typically, the size of such pores is on the order of magnitude of 100 μ m. Without compromising structural quality, the pores are meant to leave space for migrating and differentiating cells (maturing into a specific cell type) to move through and occupy. This is especially important because intercellular communication and interaction are imperative parts of the repair pathways. Moreover, sufficient space is necessary for nutrient molecules to be able to pass through to support cells.²

Many attempts have been made to use natural biopolymers to produce such scaffolding. Using natural compounds has many important benefits, including biocompatibility and the lack of an immune response. One such natural scaffolding is composed entirely of collagen. Collagen is the most significant

structural protein in vertebrates because it exists as the major protein of the ECM. As previously indicated, collagen improves cell adhesion, migration and differentiation for many cell types involved. Moreover, it is inherently biodegradable so it dissolves as tissue repair progresses.¹

Another natural material that has been tested is fibroin, or silk. This material supports cell adhesion, proliferation and differentiation, and has been highly investigated for its use in other areas of tissue engineering, specifically in skeletal tissue. Therefore, it is certainly a candidate for skin scaffolds as well.²

Lastly, fibrin glue has been studied as a scaffold because it is already being used as an adhesive in plastic surgery to slow hemorrhaging. It helps achieve hemostasis while also acting as a scaffold polymer. Furthermore, research has shown that natural fibrin clots in wound healing build their own provisional matrices that promote blood vessel growth. This is because fibrin is known to augment the production of vascular endothelial growth factor (VEGF), which supports angiogenesis. Fibrin is also known to support keratinocyte and fibroblast growth, which clearly is a positive outcome for such therapy.²

Synthetic polymers are also being investigated because they provide the option to incorporate various cell types, including stem cells, growth factors and genetic plasmids for gene delivery/modification. These scaffolds are produced using extremely precise laser technology so that they contain many of the desired features. They are porous and made from biomaterials that are structurally sound and biodegradable. Scaffolds must be inert and biocompatible to avoid harming the fragile tissue of the wound. Additionally, many are designed to mirror the layered anatomy of normal skin. This is known as biomimetics - mimicking natural processes with synthetic materials. To meet this end, multidimensional matrices are layered on top of each other in a bilayered fashion. The deeper of the two layers often has fibroblast cell sheets to promote repair. Due to the complex nature of these highly designed scaffolds, they are often referred to as smart matrices.¹ Clinical

outcomes are still limited and significant enhancements and research are to be made in this area of scaffold technology.

Current Skin Substitute Technology

The most highly evolved skin replacement option currently available is called Graftskin (Apligraf). It is bilayered and uses epidermal and dermal fibroblast cells seeded on a collagen matrix to foster growth.⁹ These cells come from neonatal foreskin removed and discarded from circumcision. Prior to treatment, Graftskin can be preserved for approximately six months cryogenically. This graft is claimed to act as a living skin patch, and in this manner, is used for non-healing sores. It is FDA approved for treatment of venous and diabetic ulcers, which are chronic wounds. However, FDA approval for major burns is still pending. Clinical trials underway have shown that it is effective in treating burn wounds when applied with meshed autografts. Hence, its use in wound healing may be coming soon.²

Another popular substitute is Epicel (Genzyme Tissue Repair). An autologous biopsy is performed to obtain autologous epidermal cells. From these cells, a sheet of keratinocytes cells are grown.⁹ Since these cells are obtained from a patient's biopsy, they cannot be prepared ahead of time, like Graftskin. Because these cells are obtained from the host's own body, they will most likely not be rejected during grafting. This product is currently FDA approved for full-thickness burns.²

Dermagraft is a synthetic product that also implements neonatal dermal cells, in particular, neonatal dermal fibroblasts.⁹ It can also be cryopreserved to ensure sufficient shelf-life. The graft is slightly transparent, thus allowing caretakers to easily monitor healing progress. Dermagraft is also the only FDA approved product for the treatment of foot ulcers. Nevertheless, clinical trials have shown that this technology is especially applicable as a bridge to autologous transplantation. That is, Dermagraft worked well in treating a wound until adequate autografts could be placed. Research has also shown that compared to cadaver allografts, Dermagraft caused less hemorrhaging and was more easily removed when used as a bridge to autografting.²

Like Graftskin, Integra is also a bilayer system. It has a porous matrix of fibers composed of cross-linked collagen and GAG, a carbohydrate that is important to many connective tissues. Yet, this substitute is acellular, lacking the fibroblasts and keratinocytes of the other matrices.⁹ Part of the scaffold itself is made of silicone and operates to maintain moisture content in the wounded area. If the wound desiccates, successful tissue repair is inhibited and restrained. With this technology, after sufficient new blood vessel growth has occurred, the silicone layer is removed (since it is not biodegradable), and an epidermal autograft is placed on top of the new formation. Essentially, Integra uses this technology to form a biopolymer dermal analogy layer, and then uses autograft tissue to make the epidermal layer. This product is thus an intuitively strong option; however, many physicians see the need to have two different operations as an immediate disadvantage to other treatments. Integra is FDA approved for full-thickness burns as well.² A summary of

these four results has been produced below.

Problems with Current Skin Substitute Technology

There is clearly significant room for improvement in the area of artificial skin substitutes. One of the most recognized of such shortcomings is the ability for substitutes to vascularize. Without adequate blood flow, tissue repair will lag or fail altogether due to lack of oxygen and proper cellular nutrition. Recent research has demonstrated that successful revascularization in autografts is caused by the anastomosing of host and graft blood vessels. This means that the ends of the graft vessels fuse with the ends of the vessels in the wound site to establish blood flow to the new tissue. Thus, tissue engineers have been trying to design artificial skin grafts that have prefabricated blood vessels. If this can be accomplished, blood vessel development in the graft will be assumed much more easily.¹

Another problem with many of the technologies is they take too long to procure cells for the grafts. It can often take 2 to 3 weeks to culture the cells necessary for transplant. For instance, with Epicel technology, cells that are obtained from autologous biopsy have to be grown, which can often take extended periods of time. During this time, natural wound healing is occurring, and there are regions of the wound that are left untreated. It is quite evident that this is disadvantageous when compared to other therapies. Therefore, methods for growing tissue need to be developed to hasten this process or cells need to be obtained from other sources.¹

Another significant insufficiency is the lack of complexity of the current skin substitutes. The outcomes of these products do not produce results that mirror actual skin, which has many layers and a diverse anatomy. Specifically, most of the products lack sweat and sebaceous glands as well as hair follicles. They also lack melanocytes, the cells that determine skin pigmentation, and fail to achieve thermoregulation. Likewise, Langerhans cells, a cell type essential to the skin's immune control, are lacking. Therefore, current skin substitutes suffer in providing all the functional characteristics of the skin. This has been the reason that stem cell therapy has received more and more attention in this field, as will be discussed.¹

Though this may not be as high on the priority list for inclusion in skin substitutes at this time, the issue of scarring will become more important to tissue engineers down the road as the science approaches perfection. Outside of aesthetic considerations, scar tissue retains poor functional quality compared to normal skin tissue. Moreover, sweat glands and hair follicles do not grow on scar tissue.¹

Scarless Tissue Regeneration

Parallel studies are examining scarring mechanisms so tissue engineers can eventually build artificial skin grafts that will not scar. One means for analyzing tissue regeneration that does not scar is to examine fetal wounds.⁷ Through the first third of human gestational development, wound repair completely lacks scarring and fibrosis. Clearly, this has sparked large amounts of interest in the world of regenerative medicine. Scientists are trying to distinguish the differences between fetal and adult wound healing that account for the altered regeneration.

One important discovery is that fetal tissue lacks fibrin

clots.¹ Another deviation in fetuses is that there are significantly less inflammatory molecules that migrate to the wound.

This is known because decreased levels of growth factors released by platelets and leukocytes are found in fetal wounds.⁷ Additionally, larger amounts of skin restructuring molecules are found in fetuses. These molecules are important to the proper construction and shaping of newly formed skin in the wounded area.¹ Already, successful changes in the levels of these specific growth factors obtained in adult wounds have been shown to greatly diminish scarring.¹³

Other models, though limited in number, are being studied because of their ability to fully regenerate themselves naturally to pre-injury conditions. Such examples include the rabbit ear, deer antler and *Xenopus* and salamander limb regeneration. In mice, scientists have even found a specific strain of genetically altered mice (called MRL/MpJ) that regenerate punctures in their ears perfectly after around thirty days.¹⁴ Genomic level mapping has been applied to study the genes involved in this regeneration. However, no specific genes have been elucidated as predictors for this regenerative process, which points towards inflammatory responses as the culprit.⁹ Hopefully, tissue engineers will eventually learn enough information from studying such regeneration processes to replicate their actions and apply them to wound healing treatments or artificial skin technologies.

Gene Delivery

While perfect skin has yet to be perfectly recreated by skin substitutes, genetic modifications of existing cells presents itself within the means of today's technological capacity. Ideally, such alterations would induce cells to produce (or not produce) different growth factors, such as those involved in scarring. Providing larger amounts of fibroblast and endothelial growth factors has been shown to enhance vascularization as well. Using DNA array technologies that are able to analyze thousands of gene expression profiles, biologists have ascertained specific, isolated genes to be the targets of such gene delivery. Moreover,

genetically modified skin substitutes present themselves as ways to deliver therapeutics both locally and systemically.⁵

Means for more effective and efficient gene delivery to cells, especially stem cells, need to be engineered before this therapy becomes a complete solution. Biomaterials need to be developed that will allow targeted delivery in terms of both spatial and temporal control.⁸ This is vital since certain expression is only desirable in certain locations of the wound (for example specific layers or only at wound margins) and at certain times, since wound healing is a highly sequential process.⁵ If this can be actualized, skin substitutes will be able to achieve a much higher level of competence.

Stem Cells

In discussing the failures of current skin substitutes, it was noted that there was a lack of complexity in the outcomes, owing to a lack of properly differentiated cells to form the natural anatomy of skin. Therefore, stem cell therapy seems to be a likely option for artificial skin grafts if they are to become real, true skin. The idea is that undifferentiated stem cells could be multipotent, meaning that they could differentiate or mature into any one of a variety of cells. Most stem cell research has shown that such multipotent cells will differentiate into their correct cell type if they are placed into that cell type's normal environment.³ That is, if one inserts a totipotent stem cell (one that can turn into any kind of cell) into muscle, it will become a muscle cell, and if you put it in endothelial tissue, it will become endothelial tissue.

Hence, when stem cells are placed onto a wound site, given the correct environmental conditions, all the parts of natural skin will be formed. Clearly, this is only theoretical at this point in time, but the groundwork for the concept is in place. Embryonic stem cells would most likely be needed to have the cells be completely undifferentiated and totipotent. Until recently, embryonic stem cells have been avoided for ethical and political reasons, so this arena of stem cell therapy research has

fallen behind. Perhaps though, given the right conditions and correct stem cell types, dermal and epidermal progenitor (skin cell precursor) stem cells could be used instead. However, this would require correct identification and purification of such cells from skin samples, which is a very difficult and expensive procedure. Stem cell researchers are looking for specific biomarkers on such stem cells that they could use to tag them for such purposes.³

Another source of stem cells, specific only to dermal tissue, that has been identified is the root of hair follicles. These multipotent stem cells make up an area called the hair follicle bulge. Not only are these cells used to build the cells necessary for generating hair follicles, but they also are known to play a role in natural wound healing; they migrate to the surface of the wound to aid in the regrowth of epithelial cells.³

Conclusions

Wound healing is a dynamic physiological process that appears to be evolutionarily inadequate since humans have difficulty surviving severe wounds such as extensive burns, and repair incorrectly by forming scars. Over the last few decades, skin grafts have sufficed as surgical treatment for such injuries. Nevertheless, shortcomings in such therapy have opened the door for tissue engineers to design artificial skin grafts that would allow proper tissue regeneration.

Ultimately, the goal of skin tissue engineering is to rapidly produce a construct that offers complete skin renewal. Yet, this renewal must include all functional components, including hair follicles, sweat and sebaceous glands, sensory glands and all functional layers (epidermis, dermis and hypodermis). This newly formed skin must be able to maintain moisture content in the skin, while remaining impermeable to water. It must also constantly divide and proliferate for proper skin renewal after healing is complete. Similarly, it must have all the necessary vascular and nerve networks that normal skin has, while proposing itself without antigens that may result in immunocompromisation. Lastly, it should be able to incorporate itself without scarring, and blend perfectly into the surrounding skin.

Considering the existing technology of skin substitutes, there is much work to be done before all of this can be achieved. However, the ever-advancing nature of science should yield developments in the understanding of many of the supporting biological processes as well as enhanced technological techniques and materials for building proper scaffolding, delivering specific genes and culturing/manipulating stem cells. With such efforts, it is reasonable to believe that the perfect artificial skin substitute can be built, and wound healing can be treated much differently than it is today.

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| Skin Substitute | FDA Approved for Burn Treatment (Y/N) | Requires Autologous Supply of Cells (Y/N) | Advantages |
|--------------------------------|---------------------------------------|---|--|
| Graftskin (Apligraf) | No | No | Preserved Cryogenically; Advanced Bilayer Structure |
| Epicel (Genzyme Tissue Repair) | Yes | Yes | No host rejection |
| Dermagraft | No | No | Preserved Cryogenically; Transparent for Physician Monitoring |
| Integra | Yes | No (but does require autograft) | Contains collagen; Silicon maintains moisture content in wound |

Table 1. Chart of current skin substitutes.

Joshua Kinsler, Ph.D.

Assistant Professor, Department of Economics

jur: What type of research do you do?

Kinsler: Education, the relationship between education and economics, and empirical findings based on students' data and other research data.

jur: In your research you reached the conclusion that teachers have a certain influence on students, but this influence is not long-lasting. Could you please explain that a little bit?

Kinsler: Sure, some scholars believe teachers' influence on students disappears immediately, while others believe that a teacher can impose life-long influence on the student body. However, based on my research, I found that a teacher's effect on the achievements of a student is rather short-lived. For instance, you do not remember what your 3rd grade teacher had taught you back in elementary school, even though he or she exerted a positive effect on you.

jur: Your research seems related to President Obama's education agenda. What do you think about President Obama's education plan, which links student-teacher performance?

Kinsler: That's a good question. This plan can be very good in theory, but there are some other factors we need to take into consideration. There are a lot of things going on in the student's life. It's hard to distinguish a teacher's performance from others when unpredictable things come up. What if the teacher just had a very bad year but he or she is an excellent educator? Maybe if the system can observe teachers for a long time, Obama's

education plan will be more accurate. Another thing is that this plan compares teachers and gives teachers the incentive to become more selfish and less cooperative because they all want their students to perform the best on standardized tests. Thus the system creates a less collaborative education system with fewer teachers willing to share their thoughts and skills. But I did not say the plan was a bad idea in general.

jur: What is the current project you are working on?

Kinsler: I am writing a paper on college students' major choices. Theoretically, math and science graduates get a higher income than other majors. The government is encouraging more science majors by giving out a great number of grants and scholarships. But why are there a lot of students not taking math and science in college?

jur: How did you get involved in research?

Kinsler: I got involved in research in graduate school. So the last three years of graduate school turned me from a knowledge observer to a knowledge generator. I began to create knowledge. The transition can be tough but exciting.

jur: What do you like about working in the research field? Why is research important?

Kinsler: I enjoy teaching as much as researching. Of course, research is more intellectually challenging. My motivation is not just to publish my work. I would like to practice my ability to

influence policymakers. Maybe someday, lawmakers will take a look at my research and discuss my idea before they write something into national policies. Research is important to me because I want to be important.

jur: What drew you to the University of Rochester?

Kinsler: Because they hired me. (*Laughs*). Historically, Rochester has a very strong economics department. Our program was ranked top 20 in the nation for the past [few] decades. Graduate students here are very dedicated and hard-working.

jur: What would you recommend for students getting involved in research?

Kinsler: Talk to your professors about the field you are interested in, and see where you can go from there.

jur: Is your research topic related to your career choice?

Kinsler: Yes. I just ran into a student of mine from a few years ago yesterday. He told me how the skills and knowledge I taught him benefited him [in his graduate studies]. It was a very heart-warming moment.

The Voting Patterns of Freshmen Congressmen: Party Conformity or Party Rebellion?

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Department of Political Science

Political scientists have often assumed that freshmen members of Congress begin their careers in an “ignorant and bewildered” state, unsure of what to do and where to begin.¹ However, the amount of actual research performed on the topic of congressional freshmen is extremely limited—often restricted to a case study of a few individuals² or mentioned as an afterthought in an article addressing the general workings of Congress.^{3,4} Nonetheless, differences between junior members of Congress and more senior members do exist. Scholars have noted discrepancies between the two, ranging from the perception of the congressional apprentice process,⁵ to the specific use of party as a vehicle to formulate informed roll call votes.⁶

Especially relevant to our study is a noticeable difference between the voting behaviors of freshmen and their incumbent colleagues. Some research has shown that freshmen members tend to look to their party and party leaders for voting cues until they become accustomed to their new job, only later assuming a more comfortable, self-reliant position similar to that of the more senior members of Congress. For example, Herbert Asher found strong evidence that freshmen align quickly with more experienced members of their party as a means of seeking guidance.⁷ If Asher’s claims are true, we expect to find that freshmen align more frequently with their party majority and/or party leaders than other members of Congress. If we find that the opposite is true, we suspect that freshmen either enter Congress with confidence in their individual decision-making skills, or that they look to other resources for guidance, such as their staff or their constituency. This leads us to ask the question: do freshmen members of Congress vote more along party lines than their more experienced colleagues? If such a relationship exists, it will be quantitatively manifested in the roll-call voting patterns of freshmen. If we detect this trend, there will be a point in time when freshmen begin to vote more independently like their more experienced colleagues, resulting in the pattern’s ending. Therefore, our next question is: how long does this trend persist?

Undoubtedly, there are numerous factors that may have an

influence on freshmen voting behavior. As Bullock suggests, party influence and re-election strategy may play a pivotal role in the decision-making process.⁸ How accountable is a member of Congress to his or her party for the purposes of being re-elected? Do Democrats demand more party alliance than Republicans and/or does this pressure depend on whether the party is in power? John Kingdon examined this theory and found that in instances where a particular party controlled both the executive and legislative branches, the party’s freshmen conformed more frequently to the majority position than the freshmen of the minority party.⁹ If Kingdon’s theory is accurate, a shift in partisan freshmen voting behavior after a change in presidential administrations might indicate such a phenomenon.

In order to compare freshmen voting behavior to that of their senior colleagues, we analyze House and Senate roll call votes as recorded by Keith Poole at VoteView.org. Specifically, we review the years 1992-2007 (103rd through 110th Congresses) and code every member of Congress as either a freshman or a non-freshman. We also determine how the majority of Democrats and Republicans voted on each individual measure. By doing so, we are able to calculate the percentage of times freshmen and non-freshmen legislators voted with their party. Rather than only calculating these percentages for the majority party, we additionally examine each congressman’s agreement with his or her party leader and party whip. The additional examination of the frequency that each member agrees with his or her party leader and party whip is of great importance to this study. This is because it is widely believed that the party leadership may often “influence their party colleagues, because of their accumulated years of expertise, their public exposure, and their influence on vital House prerogatives.”¹⁰ Furthermore, comparing how often freshmen and non-freshmen tend to vote against these influential partisan leaders provides interesting information about how freshmen may formulate a stance on a specific bill. These calculations that measure members’ tendencies to vote along party lines allow us to compare the partisan voting trends of freshmen to their more experienced colleagues. Moreover, these measures also provide an efficient way to examine the voting trends of individual freshmen and

detect any sharp changes in their patterns that are indicative of a “break-in” period.

Our data indicate that there are indeed differences between the voting tendencies of freshmen and non-freshmen members of Congress. Freshmen members vote along party lines more often than their more experienced colleagues. Additionally, we find significant evidence that a “break-in” period exists, in that after a period of time freshmen begin to vote less often with their party.

BACKGROUND/PREVIOUS RESEARCH

Freshmen versus Non-Freshmen

The first and perhaps most obvious influence on freshman voting behavior has historically been attributed to the prominent role of party leaders and senior members in the Senate and the House. In particular, the Senate, consisting of a smaller body of people, allows for the party leader to take on a more personal role and therefore influence the voting tendencies of the members more effectively. Factors such as leadership style and personal appeal can play a large role in affecting member votes.¹¹

The primary method of analysis which researchers have used to examine the freshman versus non-freshman relationship is the case study. Interestingly, several of these studies seem to come to opposite conclusions. In his book, *The Congressional Party: A Case Study*, David Truman found that junior members formed a distinctive grouping around party leadership, and hypothesized that these members would tend to stay close to the party’s position: “Presumably many of the newcomers... seem to have [been in] special need of cues in their voting.”¹² In this case, Truman’s research supports our hypothesis that freshmen members are likely to follow the lead of senior party members.

In a more recent study, Edward Sidlow asserted that younger members have relatively strong policy preferences and therefore are generally independent from the senior party members. Sidlow’s study followed Congressman Joe Schwarz as he progressed through the different phases of a first-year legislator. Although Sidlow does not draw many conclusions in regard to Schwarz’s voting cues, he does mention the role of party leadership in Schwarz’s decision-making processes: “[Schwarz] always does listen to what the leadership wants...but he is absolutely not afraid to oppose the leadership. But if he feels strongly about something, he won’t budge...regardless of what the leadership or anyone else might want.”¹³ In this way, Sidlow indicates his belief that younger members of Congress are not dependent on their party leadership.

Despite Sidlow’s findings, we concur with Truman in believing that there is indeed a reliance on party members, possibly the result of an intrinsic tendency to defer to one’s elders, rather than a conscious decision to ignore one’s own opinions. This subtlety may not be highlighted in a direct interview or case study, as it may be difficult for a Congressman to recognize or admit his or her dependence on party voting cues. In fact, some political scientists affirm that “legislators are unlikely to admit that they pay attention to party influence. They are more likely to claim that they are good legislators who follow the wishes of the people back home,” which may be why Congressmen such as Schwarz are reluctant to indicate party as a major factor in the formulation of their votes.¹⁴

Therefore, we determined the need to conduct a quantitative study on the actual roll-call voting patterns of these younger members. Drawing from Truman’s research, as well as our own belief that party leaders play an instructive role in the voting process of freshmen members, we come to our first hypothesis:

H1: first-year legislators are more likely to vote with the majority of their party and party leaders.

The Learning Curve of Congressional Freshmen

If it is the case that differences exist between freshmen and junior members of Congress, then there must also exist a time frame during which these younger members acquire the skills necessary to become experienced legislators. Herbert Asher examined this idea in a study of the freshmen members of the 91st Congress. His hypothesis was that certain legislative norms were transferred to new members in the early months of their careers via a socialization process. In these interviews with Asher, the incumbent and freshmen responses were unified and indicated a general agreement on what represents the most important norms. By norms, Asher refers to informal rules or laws that govern the legislative process, specialization, reciprocity of votes, house rules, and committee attendance/participation.¹⁵ These norms may have been transferred in what Asher refers to as the congressional “apprentice” process, which is the concept that general guidelines regarding legislative behavior are gradually absorbed by younger members through observing the older members of Congress.¹⁶ In Asher’s study, freshmen members expressed a stronger belief in the importance of this process than did the older members of Congress.¹⁷ This notion of temporary apprenticeship ties into our belief that a certain period of time is required for these younger members to become acclimated to their new positions. Once this period of time has passed, we expect freshmen to abandon this voting bloc. Therefore, our second hypothesis is:

H2: After a period of time, these freshmen legislators will develop more independent voting patterns and will break away from the party and party leaders more often.

Differences across Parties in Freshman Voting Patterns

A possible factor that could lead a member to abandon this “freshman voting bloc” is whether the member’s party has control of both branches of government—executive and legislative. John Kingdon examined patterns of congressional voting behavior and discovered that party leadership is especially influential in cases where the same party controls Congress and the presidency. Kingdon found that among Republicans (the majority party at the time of his study), the youngest congressmen ignored party leadership only 41% of the time, compared to Northern Democrats who rejected their party leadership 74% of the time.¹⁸ Therefore, in cases where a freshman’s party controls both branches of government, the freshman is expected to vote along party lines more often than freshman members of the minority party. This is seemingly because the party exerts more influence during such periods of high control, and younger members are less likely to oppose this influence.

Despite his findings regarding majority party control, Kingdon found that newer legislators were much more independent of leadership than usually suspected. He attributes this independence to strong constituency and policy orientation.¹⁹ In fact, according to Kingdon, the general influence of party leaders may have little effect on a member's overall voting habits. If true, this would conflict with our hypotheses and offer an opposing viewpoint about the voting habits of first-year members of Congress. However, we believe Kingdon's findings do not constitute a challenge to our theory for two main reasons. The first is in regards to the time frame of his study; Kingdon himself admits that the influence of party leaders may have changed since the time this study was conducted. Due to rule changes in the 1970s, the Speaker has gained more control and influence in the House, while the committee chairs have lost some of that power.²⁰ The second reason is that he did not conduct a large-scale quantitative study; he simply interviewed a group of congressmen in session during the year 1969 and based his conclusions on their comments. Our research and background knowledge led us to believe that Kingdon was wrong about the relative independence of freshmen, but that he was correct in asserting that party influence is stronger during periods of congressional and presidential unity. Our final hypothesis reflects this belief:

H3: When one party controls both the executive and legislative branches, freshmen of the controlling party will vote along party lines more often than those of the minority party.

OUR CASE STUDY

As a supplement to our quantitative analysis, we conducted our own case study in an effort to better understand possible differences between freshmen and incumbent members of Congress. We interviewed a newly elected Republican member of the House, Congressman Chris Lee, in order to gain a better sense of the setting in which congressmen vote and the possible influences upon freshmen members. Congressman Lee affirmed that there are times where he finds himself initially unsure about how to vote on specific legislation when it is first presented to him. In fact, he attempts to meet with every interest and constituency group possible in an effort to familiarize himself with the countless issues that different legislative proposals bring. Additionally, he explained that in his cases of uncertainty, he has a myriad of advisors he can turn to, including his legislative director, a Republican think-tank, his party leaders, and his district. This affirms our belief that party leaders have a role in freshmen voting decisions. Congressman Lee also informed us that despite being a freshman, he has already had plenty of opportunities to learn House rules and gain advice regarding a multitude of issues from the twelve senior members on his advisory working group. This supports our prediction that freshmen will look to more senior members for advice.

When asked if he could detect a difference in voting tendencies between freshmen with more legislative experience and freshmen without much legislative experience, Congressman Lee said that he observes no difference. He did mention, however, that more experienced legislators coming

into the House as freshmen were more likely to be familiar with the intricacies of the issues debated in Congress than those who entered with no experience. When asked about the influence of party stance and party leaders on these issues during roll call votes, Congressman Lee indicated that at least in his party, the party leader and the whips do not pressure congressmen to vote a certain way; they simply announce their stance and then allow the congressmen to vote as they wish. He emphasized the fact that the party leader recognizes that congressmen have district obligations outweighing party obligations and therefore will not pressure the congressmen to vote a certain way. These claims are similar to those of Representative Schwarz in Sidlow's case study, and as mentioned earlier, our findings indicate that party leaders play a more important role in freshmen voting decisions than individual congressmen may assume.

DATA/METHODS

Our empirical analysis is based on a dataset consisting of congressional roll call votes compiled by Keith Poole. Specifically, we utilize the set of data spanning from the 103rd Congress to the 110th Congress. We select this period because of the various ideological compositions of these congresses. In some instances, the same party controls the presidency and congress, while in others each party controls a part of the legislative government. By examining this period of varying ideological control, we are able to observe the effect that a change in party control has on freshmen voting. In fact, major congressional party shifts occur twice during this period: the first with the Democratic control of Congress after the 1992 election changing hands to the Republicans in the election of 1994, and the second with the Democrats regaining complete control in 2006. Furthermore, during this time period, the presidency was held by both the Democratic Party and the Republican Party.

Our examination relies upon three characteristics of each vote placed in the House and Senate. These three characteristics are the way the majority of each party votes, the vote of each party's leader, and the vote of each party's whip. Consequently, an examination of a vote consists of identifying three important features. These features are important because they act as our basis for calculating each legislator's tendency towards party conformity.

Measuring party conformity consists of calculating the percentage of the number of times individual members voted with their party majority, party leader, and party whip throughout the length of a Congress. By eliminating any member who did not submit a vote in at least 87.5% of the votes in a given term, we substantially limit the variance of agreement among members.²¹ Coding each member as a freshman or a non-freshman then allows us to compare these percentages between the two groups. Additionally, we code each freshman member by his or her party in order to locate any partisan differences in voting behavior among freshmen.

Finally, after coding each member into their respective group, we calculate the mean of the agreement percentages among all of the members of each group. Using an independent samples t-test for equality of means,²² we measure the difference between the mean agreement percentages of each group (freshmen v. non-freshmen; Republican freshmen v. Democratic freshmen).

Any significant differences between the groups indicate that there are "real" (non-chance) differences in conformity to one's party and party leaders. Nonetheless, these tests allow us only to compare voting behavior across each Congress, limiting our ability to make judgments about each individual legislator's "break-in" period.

Locating a "break-in" period involves examining individual congressmen's voting tendencies and looking for any points in time where significant change occurs. To test for such a phenomenon, we track each freshman of the 103rd Congress as he or she progressed through the 105th Congress.²³ Any significant change amongst the collective freshmen percentage of times voting with both the party majority and party whip allows us to identify a time frame in which voting with one's party may change. To examine this effectively, we measure the average change of freshmen (among those reelected) between the 103rd Congress and 104th Congress, 103rd and 105th, and 104th and 105th.

FINDINGS: House Results

Table 1 presents a comparison of the percentage of times freshmen and non-freshmen vote with their party majority, party leader, and party whip. This comparison allows us to determine whether or not there are substantial differences in voting trends between the two groups. Each Congress under examination yields the same result: freshmen vote alongside their party at higher rates than their more experienced colleagues. The difference between the two is significant in five of the eight periods measured, suggesting a meaningful tendency among House freshmen to vote more frequently along party lines than non-freshmen. This difference between the two groups averages 2.3%,²⁴ and because members of Congress cast an average of more than a thousand roll call votes per term, a small percentage such as this is substantial. Considering this, when examining the length of an entire Congress, our results suggest that freshmen House members cast around 25-35 more votes along party lines than their more experienced colleagues do.

Knowing that incumbents are frequently reelected to their positions and that freshmen vote more often with their party than their older (reelected) counterparts, freshmen members as a group must decrease their tendency to vote with their party at some point during their careers.²⁵ Table 2 shows the result of a test pointed at finding when freshmen members begin to decrease their likelihood to vote alongside their party. Consistent with Hypothesis 2, we find that as freshmen members gain experience in the House, they begin to vote less often with their party. However, our findings indicate that this relationship does not strongly exist in a Congressman's first or second term in office. Rather, the most significant decrease in party conformity occurs during these members' third terms.

Table 3 indicates that there are significant differences between the voting trends of Republican and Democratic freshmen in the House. Each Congress that we examined yields strikingly similar results: the freshmen of the party in control of Congress voted significantly more often with their party, party leaders, and party whip. This difference between the freshmen of the two parties averaged at 5.3%.²⁶ Interestingly, we find the strongest difference (among party, party leader, and party whip) to be the freshmen

tendency to vote with the party leader, possibly indicating the leader's heightened role in a freshman's vote formulation, especially among freshmen in the current majority. Newly elected legislators in the majority are likely pressured to conform to a majority voting bloc, and thus, often vote alongside their party.

Additionally, our results indicate that this tendency of conformity among freshmen has more to do with which party controls Congress rather than the presidency. In this study, when different parties control Congress and the presidency, those freshmen of the majority in Congress align with their party in much greater frequencies than those freshmen of the Congressional minority. For example, freshmen Republicans voted with their party indicators an average of 6.9% more often than Democratic freshmen during the period from 1995-1997 (104th Congress), which consisted of a Republican majority in Congress and a Democratic President.

FINDINGS: Senate Results

Similar to freshmen in the House, we find that freshmen senators have a tendency to vote more often with their party, party leaders, and party whip than their more experienced colleagues. In fact, at 2.4%, the average difference between freshmen and non-freshmen agreement percentages is roughly the same in the Senate as in the House. However, according to Table 4 only one of these percentages is significant, which may lead one to think that these differences do not indicate a meaningful result.²⁷ Nonetheless, the differences in agreement among the tested senators do exist, and there is much academic debate about whether tests of significance are necessary in a situation such as this. We contend that because these differences between freshmen and non-freshmen senators are substantial and mostly consistent through the Congresses under examination, these results compiled for the Senate do have meaning and importance.

Table 5 presents the average change in freshmen senators' agreement percentages across time. We find that freshmen senators vote significantly more often along party lines in their third and fourth years in office than in their first two years. Such a trend suggests that they may rely more on their party as time passes. However, the freshmen senators under examination began to decrease their tendency to vote along party lines in their fifth and sixth years. These results, although somewhat consistent with our hypothesis, are not as convincing in proving our "break in" theory as the results from the House.²⁸ Furthermore, we likely do not formulate representative projections about the freshmen of the Senate using these results due to the small number of freshmen senators examined in this portion of our study.

The comparisons made between Democratic freshmen and Republican freshmen shown in Table 6 do not demonstrate any significant differences between the voting trends of the two senatorial groups. This is likely due to the small number of freshman senators elected to each Congress. However, the randomness of differences between the two groups suggests that if a significantly higher number of freshmen were elected to a given Congress, little would change in the results.

CONCLUSIONS

In this study, we offer a quantitative analysis examining the voting trends of freshmen Congressional members, significantly adding to the minimal amount of existing information about this group of legislators. Our results indicate that freshmen members of Congress more frequently cast votes along party lines than their more experienced colleagues. Additionally, a “break-in” period seems to exist. As freshmen members gain experience in Congress, they begin to vote along party lines at lower rates. Furthermore, freshmen members of the majority party in the House are more likely to vote with their party majority and party leaders than freshmen members of the minority party.

Why do these differences in partisan voting trends exist between freshmen and non-freshmen Congressmen? The most obvious reason is experience. Freshmen members, especially of the House, tend to lack the national political experience that would allow them to confidently formulate an independent roll call vote. By interviewing Congressman Chris Lee, we affirm this belief that a lack of experience leaves freshmen Congressmen feeling that they don’t have the necessary knowledge of every intricacy of every issue, leaving them to turn to other sources for help. As much as freshmen legislators may be reluctant to admit it, their party and party leaders are likely significant sources of guidance for them as they formulate their roll call votes.

Attempting to gain political power is another possible reason for freshmen voting more often along party lines. Freshmen may see opportunity in agreeing with the leading members of their party, as these powerful members make committee assignments within their party. The party leaders often aim to place members who push their parties’ platform in strong committee assignments, leading us to believe that freshmen may vote alongside their party in order to gain one of these lucrative positions.

Future researchers may want to further analyze the variance in the voting trends of freshmen, examining which freshmen members are more likely to vote along party lines. We find that party is a strong indicator. However, margin of victory, national party campaign contributions, previous political experience and education may play a role in how often a freshman tends to vote alongside their party. Additionally, the strength of the partisanship of a freshmen’s state caucus could factor in how likely that freshmen is to cast votes in a partisan manner.

We present a strong groundwork for understanding the partisan voting tendencies of freshmen Congressmen. However, future research could clarify this tendency further, giving us information about which freshmen members are likely to rebel against their party and which are likely to conform. Our analysis answers foundational questions about freshmen members of Congress, while suggesting that there is still much to learn about this interesting group of legislators.

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21. 87.5% was chosen as a cut-off point because it eliminated enough members to effectively lower the variance across the groups, while leaving enough members in the data set to appropriately test our hypotheses.
22. Equal variances assumed.
23. The 103rd Congress was chosen because of its large freshmen class.
24. This average is an average of all results reported in Table 1, noting the average difference in the percentage of times freshmen and non-freshmen members vote along party lines.
25. This measure is the average of each percentage found in the mean difference portion of Table 3. It is a mean of means.
26. The small number of freshmen senators elected per Congress likely is the cause of this lack of significance.
27. In fact, most senators enter office with some legislative experience, so they should require a very short (or no) learning period.

Supplementary Figures

TABLE 1. The Difference in Means of Percentage of Times Voting With Party: Freshmen vs. Non-Freshmen (House)

| Congress | 103rd | 104th | 105th | 106th | 107th | 108th | 109th | 110th |
|----------------|-------|-------|-------|-------|-------|-------|-------|-------|
| Party Majority | 3.5** | 5.0** | 1.5 | 2.0 | 3.4* | 2.5** | 0.5 | 2.2** |
| Party Leader | 2.0* | 6.6** | 0.7 | 0.07 | 4.0** | 2.1* | 0 | 2.7** |
| Party Whip | 2.5** | 3.7** | 0.4 | 1.4 | 2.9* | 2.3** | 0.4 | 2.1* |
| N Freshmen | 108 | 86 | 69 | 40 | 41 | 49 | 40 | 53 |

Note: Differences calculated by subtracting non-freshmen agreement from freshmen agreement. *p<.05; **p<.01

TABLE 2. Average Freshmen Agreement Changes Across Time: 103rd Congress through 105th (House)

| Freshmen Alignment Influences | Change 103rd to 104th | Change 104th to 105th | Change 103rd to 105th |
|-------------------------------|-----------------------|-----------------------|-----------------------|
| Party Majority | 0.4 | 1.0 | 0.8 |
| Party Leader | -1.7 | 3.1 | 0.9 |

Note: Changes are calculated by subtracting average freshmen agreements. The latter agreement Percentage of the two Congresses in each set is always subtracted from that of the former year.

TABLE 3. The Difference in Means of the Percentage of Times Voting With Party: Freshmen Republicans vs. Freshmen Democrats (House)

| Congress | Number of Freshmen | | Mean Differences between Republicans and Democrats | | |
|-----------|--------------------|-----------|--|---------|--------|
| | N of Dems | N of Reps | Party | Leader | Whip |
| 103rd [d] | 61 | 47 | 0.4 | 5.2** | 2.8** |
| 104th [r] | 13 | 73 | -3.7** | -12.4** | -4.6** |
| 105th [r] | 38 | 31 | -6.4** | -15.9** | -9.7** |
| 106th [r] | 23 | 17 | -2.7 | -9.6** | -2.1 |
| 107th [x] | 13 | 28 | -4.3** | -10.6** | -4.4** |
| 108th [r] | 18 | 31 | -4.1** | -2.9** | 2.7** |
| 109th [r] | 16 | 24 | -4.3** | -5.9** | -3.0* |
| 110th [d] | 40 | 13 | 2.3 | 3.7** | 3.7** |

Note: Differences calculated by subtracting freshmen Republican agreement percentages from freshmen Democrat agreement percentages. Party in control of Congress is noted in parentheses (d=dem control, r=rep control, x=split control). *p<.05; **p<.01

TABLE 4. The Difference in Means of The Percentage of Times Voting With Party: Freshmen vs. Non-Freshmen (Senate)

| Congress | 103rd | 104th | 105th | 106th | 107th | 108th | 109th | 110th |
|----------------|-------|-------|-------|-------|-------|-------|-------|-------|
| Party Majority | -0.1 | 2.8 | 2.8 | 0.2 | 0.5 | 3 | 6.8 | 5.7 |
| Party Leader | -0.6 | 2.6 | 2.5 | 0 | 0.4 | 3.2 | 1.9 | 4.3 |
| Party Whip | -1.8 | 5.1* | 2.8 | 0.1 | 1.4 | 3.3 | 2.9 | 7.6 |
| N Freshmen | 14 | 11 | 15 | 6 | 11 | 11 | 9 | 7 |

Note: Differences calculated by subtracting non-freshmen agreement from freshmen agreement. *p<.05; **p<.01

TABLE 5. Average Freshmen Agreement Changes Across Time: 103rd Congress through 105th (Senate)

| Freshmen Alignment Influences | Change 103rd to 104th | Change 104th to 105th |
|-------------------------------|-----------------------|-----------------------|
| Party Majority | -3.2 | 1.2 |
| Party Leader | -3.0 | 1.8 |

Note: Changes are calculated by subtracting average freshmen agreements. The latter agreement percentage of the two Congresses in each set is always subtracted from that of the former year.

TABLE 6. The Difference in Means of the Percentage of Times Voting With Party: Freshmen Republicans vs. Freshmen Democrats (Senate)

| Congress | Number of Freshmen | | Mean Differences between Republicans and Democrats | | |
|-----------|--------------------|-----------|--|--------|------|
| | N of Dems | N of Reps | Party | Leader | Whip |
| 103rd [d] | 8 | 6 | 3.3 | 3.8 | 4.3 |
| 104th [r] | 0 | 11 | n/a | n/a | n/a |
| 105th [r] | 6 | 9 | 0.8 | -0.1 | -4.4 |
| 106th [r] | 3 | 3 | 3.4 | 1.5 | 2.2 |
| 107th [x] | 9 | 2 | 0.2 | 0.2 | 2.8 |
| 108th [r] | 2 | 9 | -3.2 | -3.0 | -3.4 |
| 109th [r] | 2 | 7 | -17.7** | 3 | 1.8 |
| 110th [d] | 6 | 1 | 5.3 | 4.1 | 15.6 |

Note: Differences calculated by subtracting freshmen Republican agreement percentages from freshmen Democrat agreement percentages. * $p < .05$; ** $p < .01$

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Presence of Depression in Indian Blind Students

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Many depression studies have been conducted with blind geriatric patients, but most studies have not focused on younger subjects. For example, in the study "Association between visual impairment and depression in the elderly", blindness was found to be positively correlated with depression.¹ In "*Detection of depression in patients with low vision*," a wider range of individuals with visual handicaps was studied.² However, this study did not consider adolescents and young adults. Since such groups have not been tested for depression, it remains undetected and untreated. In hopes of filling this void, these blind students were interviewed and assessed by both qualitative and quantitative observations.

Purpose & Approach

The main purpose of this cross-sectional study was to explore the relationship between visual impairment and depression in Indian blind students. It was hypothesized that blindness would result in a high incidence of depression. A total of 164 students, 23 females and 141 males ages 13 to 25, were administered the Beck's Depression Inventory (BDI – II), Barthel's Index, and a supplementary questionnaire that assessed basic demographics, the extent of the students' interactions with others and specific questions dealing with activities of daily living. The participants of this study were from the all-boy school St. Louis Institute for the Deaf and the Blind in urban Chennai, India and the coeducational Askwith School for the Visually Handicapped in rural Tirunelveli, India. Depression was the primary dependent variable in this study. The variables of mean age, gender, degree of blindness, age of onset, rural or urban school, their independence and the involvement of family members were tested as possible predictors factors that cause of depression. This research did not only consider depression

but also the many other implications of being visually impaired and was conducted in hopes of learning more about this particular population.

Observations

The attitude the students held regarding various aspects of their lives were often shaped by their visual impairment. Gender differences, school attended, and degree of family involvement are a few factors that visibly impacted their outlooks on life. Despite their disability, their overall stance on life did not appear to differ substantially from those who are not impaired. There were both optimistic and pessimistic students but most were neutral in their approach, seemingly accustomed to their way of life. Many reported that they had gone through phases of despair at some point in their lives as a direct result of their handicap.

Certain responses to the query of whether blindness obstructed the students from the future they wished to have were particularly telling. Strikingly, one male student from Chennai claimed that he was pleased to be blind. When questioned further, he thoughtfully replied that if he had vision, he would have been wasting time watching television and surfing the Internet. However, due to his blindness, he was able to concentrate completely on his education. Responses like his were inspiring and unusual but introduced a new perspective to understanding the lives of blind individuals. This was an exception to most cases since very few members of this sample were satisfied to his extent by their visual impairments.

A comparison of students in the urban Chennai and the more rural Tirunelveli revealed that those in Chennai were more confident and driven than those in Tirunelveli. Of the students in Tirunelveli, the male students appeared dramatically more optimistic than the females. These



Student and staff of the Askwith School for the Visually Handicapped in rural Tirunelveli, India, taken August 2009.

differences could be attributed to the influences of the regional culture in which they were raised. The education and opportunities available to those in the city are greater than those available to students in more rural locations. Government funding is generally higher for the city students as well, which may explain some differences in the availability of services. The belief that females are inferior to males still exists in rural parts of the country; therefore, they are generally more oppressed than males. This observation is limited, however, since female data from the all-male school in Chennai could not be collected. The female students in the rural school seemed unsure of their future and felt that they were not likely to go beyond high school. Even those who were planning on attending a college believed that due to their visual limitations, they would most likely be restricted to becoming a teacher at a blind school. A fairly large number of students in both schools stated that they wished to pursue a career in music or teaching. However, the responses in Chennai were much more varied than those in Tirunelveli. In Chennai, many students stated an interest in engineering and felt that they had more options. They often specified the degree they wished to attain. Even the younger students had a positive outlook regarding their future. Many students in Tirunelveli did not even have a response to the question and the few who did were geared toward teaching. They explained that they did not really know what else they could do given their condition. Signs of depression seen in these students could be attributed to their uncertain academic future and lack of choice.

When asked whether they believed they were a burden to their families, students generally responded that at this point in their lives, they felt like a burden regardless of their life goals. Those in Chennai were more certain that, although they considered themselves to be a burden presently, they would cease to be in the future when they could begin to financially support their family. The

students in Tirunelveli did not have such high hopes of attaining higher education and felt that their occupational options were limited to low paying fields.

Most of the students acknowledged that their lives would have been significantly different if not for their visual impairment. They would have had more opportunities and would not have been completely closed off from fields they may have otherwise explored. During a group discussion, one student expressed a desire to pursue medicine but was immediately teased by his friends on how impractical his ambition was. Many of the older students explained that they would have been in college if they had vision. Some of the students were already in their early twenties and still in school. These were mostly students who became blind later on in life and had to adjust to the onset of the handicap. Therefore, they had to learn the basic necessities of living as a blind person and were placed in lower grade levels.

Typically, the students interacted well, closely bonded and protective of one another. There were normal skirmishes (clarify what a normal skirmish is), but in general the students were very close. The older students at the school helped to look after and assist the younger children and newly impaired students. In Tirunelveli for example, the older girls helped care for the nursery students. Also, most of the students grew up with each other. In Chennai, most of them had known each other since the first grade and in Tirunelveli many started nursery school together. Since most of them lived on the school campus from such young ages, they reported that they felt safer and happier at school than at home. For them, the school was their home and sanctuary. The students felt most comfortable when they fit in with others and could understand what their peers were going through. At school, the students could relate to one another easily



Visually impaired students from Tirunelveli, India.



Top Left: The large gated premises in the Tirunelveli school allow safety and enclosure. Top Right: The main office of the blind school in Tirunelveli, India. Bottom Right: Two visually impaired female students from Tirunelveli, India.



since they were unified by blindness. However, when away from the school, they felt isolated from the sighted society. Several of the students mentioned that they did not blend in with other kids in their neighborhood and reported looking forward to coming back to school.

The schools instituted a mealtime system where the partially sighted students would distribute the food to the completely blind students. They were responsible for their own dishes and stored them in their own designated locations. When walking from one destination to another, many times a student who was affected with partial blindness would lead the group while the others would hold on to one another. In this way, they could get to places safely and in groups. Newer students were assisted in this manner as well. Once a student was adjusted to the environment, they said that they confidently walked alone.

The classroom setting for younger students was commonly in a U-formation with the teacher in the front and center. This way, the teacher was able to reach each of the students easily and assist in learning the basics of the subject. The U-formations proved accessible for blind teachers as well. For older students, the tables were in rows since they were more independent and did not need continual assistance. For most of the class, a teacher would dictate from textbooks and the students would copy it in Braille into their own notebooks. They would then study these notes. For math they used small plastic or metal pieces with raised dots on the surface that represented different numbers when placed in different positions.

The students were very well behaved in their classes. Since they had to base their learning on what they heard, they could not afford to fool around as they would be unable to write notes. Most of them focused on what the teacher was instructing and would ask questions or request

repetition. Even when the teacher had to leave the class, the students remained seated and conversed responsibly. This could be explained by how their safety depended on being responsible and aware of their surroundings. If they acted foolishly and did not pay attention to guidelines, the consequences could be detrimental.

Teachers were exceptionally friendly toward the students. They were very approachable and supportive of the students. This was surprising since most schools in India are generally very strict; punishments are severe and students have many assignments that they must complete. However, in the blind schools, the teachers were more lenient and assistive rather than austere and demanding. This may have been because they wanted to make the students' experiences in school positive and ensure that they did not go through more stress than necessary. The teachers themselves were often blind and were thus very understanding. In many cases, they were even former students of the same school.

The degree of influence and involvement that the families had with the blind students varied as well. While many students claimed that their parents were very supportive, there were other instances where this was not the case. One individual who did not live at the school



A typical classroom for grades nine and higher in Tirunelveli, India. For lower grade levels, the tables tended to be organized in a U-shape, with fewer students, to optimize student-teacher interaction.

was both blind and mentally challenged. He said that whenever his family left the house, they would lock him up alone at home. He was noticeably upset about his situation. There were other cases where students said the opposite and reported that their parents took more care of them than their sighted siblings. Yet most of the students said they were treated equally as their siblings. One student disclosed openly that he had been depressed and suicidal in the past. However, the support his family provided helped him overcome that stage in his life. He said that he was currently very content and that this was mainly due to the encouragement he had received at such a crucial point in his life. His family worked with him on becoming accustomed to life with blindness as a blind person, and he eventually learned how to cope with his blindness.

Many of the students reported that their parents are blood related, often first or second cousins. This close genetic relation between parents may have resulted in the blindness of their offspring. Some siblings attended the school together. Marrying close relatives is becoming less common in India but does still exist. In the uneducated and poor regions, these marriages occur more frequently. This may be due to a lack of awareness

of the risks associated with intrafamilial marriage.

Most of the adult family members worked in low-income jobs. The effect of this was more apparent in the rural school. Many family members could not afford to visit the student on a regular basis due to their financial limitations and many students were shabbily dressed. Even personal talking watches were rare in this school. To tell time, the students often depended on the rare student who had a watch or asked a teacher. Most of the students in Chennai had these watches. One student who did not have one said that he would get one only when his parents could afford it. The students had few possessions outside of their basic essentials and they carried very little pocket money.

In India clothing is generally washed by hand on a daily basis and hung up to dry during the day. In Chennai, the students were responsible for washing their own clothing. When asked how they could identify their own clothing, they replied that either they left their clothes hanging in their own rooms to dry or had a specific spot that they would always use. This way, they would not confuse their clothing with those of others. To match colors they would either have their clothing marked in some way or have a sighted person help them.

The students could identify who had passed them in the hallways only by their smell and sounds. It was surprising when the students could detect the unfamiliar scent of sunscreen and immediately ask who it was. Similarly, the students could determine if a passerby was female from the smell of jasmine flowers that are worn on the head almost everyday by Indian women. In the male-only school, they would quickly assume that the flower scent was from a female teacher. Even when individuals walked into a class quietly, there were students who acknowledged their presence.

Scribing for a student during a midterm exam was an informative experience. It was interesting to see how a relatively simple task for a sighted person was so much more difficult for the blind. For multiple-choice questions, they had to remember the auditory input they received for each choice before making a decision. If they needed to clarify a section, it had to be restated for them. Keeping everything organized in the head is definitely a challenge. However, it is a system they are used to. For essay questions, they would dictate the answer and a scribe would write it. They could then ask the scribe to reread any questions they wanted to modify. If they chose to skip questions to revisit later, they had to be told which ones they had missed. For a sighted person it would be much easier to just flip through and add anything they had missed. It was not as simple for the blind. Scribing for a student was also very subjective. While some were strict and only wrote down exactly what the student gave as a response, others would give the student hints.

A mini money test was conducted with the students to see whether they could accurately identify three common Indian coins and two paper bills. The methods used by the students to aid in identifying them correctly varied. Some compared the size of the coin they recognized with one which they could not tell. recognize. They used the concept of comparing relative sizes. Those with partial vision moved to where there was more light in order to see it better. Some students smelled the money. Others dropped the coins on the table to hear the varying degrees of heaviness and were able to make conclusions based on the sounds. Similarly, some tapped the coins against the table. It was truly devastating to hear students confidently provide incorrect responses. Also surprising was how clueless some of the students were when it came to identifying money. One student was convinced that a note he held up in his hand was valued at 1 rupee. However, 1 rupee notes do not even exist; it was actually a 100 rupee note. Others, mainly the partially blind students, were extremely fast in stating their answers. Other students would openly state that they could only identify either

coins or notes but not both. Although some did not seem to care if their responses were incorrect, others were visibly disappointed with themselves if they missed just one or two.

Data Analysis

The mean age of the students in this study was 16.12 years. The participants of this study were students; therefore, this number is appropriate. In the Chennai School, students from 7th grade to 12th grade were considered to be acceptable subjects; while in the Tirunelveli School, students from 7th to 10th were studied. Since the BDI-II was designed for people 13 years of age or older, only these students were considered suitable. A smaller narrower range of grade levels was used in the rural school as because the schools only went up to tenth grade; the students moved to different schools after that.

Many more males than females were interviewed since one school was not a coeducational institute. While there were 105 male students at the school in Chennai, there were 20 female and 39 male students at the school in Tirunelveli. Due to the limited number and location of female students, conclusive results could not be made regarding females.

The average age of the onset of blindness was 1.51 years. This suggested that most of the students were blind at birth. It seemed that those students who were blind at birth were more accustomed to it than those who had become blind later in life. Most of the students who were blind at birth were directly affected by genetic defects or, in some cases, unsuccessful abortion. In some instances the mothers had attempted to abort the baby by drinking poison. There were many cases where the student was the only blind family member and so it had been due to chance. Students who lost their vision later in life usually attributed it to accidents and sports injuries. Some students said that they were born seeing but were told early on that they would lose their vision as they aged so they had been placed in these schools even when they could see well in preparation for their future.

The students were asked to designate from 1-10 how involved they felt their parents were with them (10 being extremely involved). The mean values were 9.62 and 9.59 for the father and mother's involvement, respectively; most of the students reported that their parents were very involved in their lives. In most cases, when they said that they were in touch with their parents, they meant that they would at least talk on the phone regularly and did not necessarily meet each other physically. More students in Chennai lived at their homes than those in Tirunelveli. A high number of students lived on campus and had been living there for most of their lives. For such students to be

reporting high numbers also suggests that despite being physically separated from their families, they still believe that their family cares for them and is involved in what they do.

The Beck Depression Inventory - II (BDI-II) is a 21 question survey that studies the incidence and severity of depression symptoms.³ Each question has four possible answers that range from a value of 0-3. Two of the questions have 7 options but the point value is still between 0-3. Officially, the recommended scoring cutoffs are as follows: A total score between 0-13 is considered minimal, 14-19 is considered mild, 20-28 is defined as moderate, and 29-63 is considered severe depression. This can be adjusted based on the sample however.³ The BDI-II result with a mean value of 4.62 is in the minimal range according to the recommended scoring. In this sample, the scores ranged from 0-26. A floor effect may have occurred where many individuals showed little to no depression that even those who had found it were undetectable.⁴ High levels of depression were believed to exist in the sample, but they were only detected in blind individuals.

Barthel's Index is scored on a scale of 0-100 with higher numbers correlating with higher reports of independence.⁵ Although it is used quite commonly with people suffering from severe disabilities, it is not highly sensitive. The points go up in increments of 5 and thus it is difficult to get the exact numerical response that the respondent may wish to express. Barthel's Index gave a result of 88.47 out of 100, which is relatively high. This may be considered a ceiling effect since very few people reported that they were dependent on others. They felt that the tasks assessed in Barthel's Index were uncomplicated.

Two contrasts were created to compare the three options that children with siblings chose regarding their perception of the attention that they received compared to their siblings. The first contrast (con1) compared feeling ignored with perceiving equal attention as siblings. The second contrast (con2) compared feeling ignored with perceiving more attention than siblings. The results indicate that perception of parent attention compared to siblings significantly accounts for 7.9% of the variance in depression scores, $F(2, 127) = 5.47$, $p < .01$. Specifically, feeling ignored compared to their siblings versus perceiving receiving an equal amount of attention as their siblings, predicted higher depression scores among children in this sample, $t(127) = 3.30$, $p = .001$. Moreover, perceiving more parent attention compared to siblings as opposed to perceiving an equal amount of attention also predicted higher depression scores, $t(127) = 10.73$, $p < .001$. Comparing children

who felt ignored and children who perceived more parent attention did not significantly predict depression scores. No other variable significantly accounted for variance in children's depression scores.⁴

Conclusion

Although conclusive decisions cannot be made purely from the results of this study, it could be used as a stepping-stone in the quest for a better evaluation of depression in blind students. Although several individuals showed high levels of depression, the overall sample did not. This may be a result of having such young people respond; they may not have a clear understanding of what depression involves. Perhaps in the sheltered schools they attend, depression is not present. When they enter the real world, however, they will face challenges they had not planned for. Both the BDI-II and Barthel's Index were useful tools in analyzing the impact of visual impairment on depression. The way that blind students live is very different from how typical adolescents do. The sense of unity among students and staff, the structure of school life, their optimism, their interactions with other family members and future ambition were all defining aspects of their life. Their entire perspective of life was influenced dramatically by their blindness.

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About the Journal

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