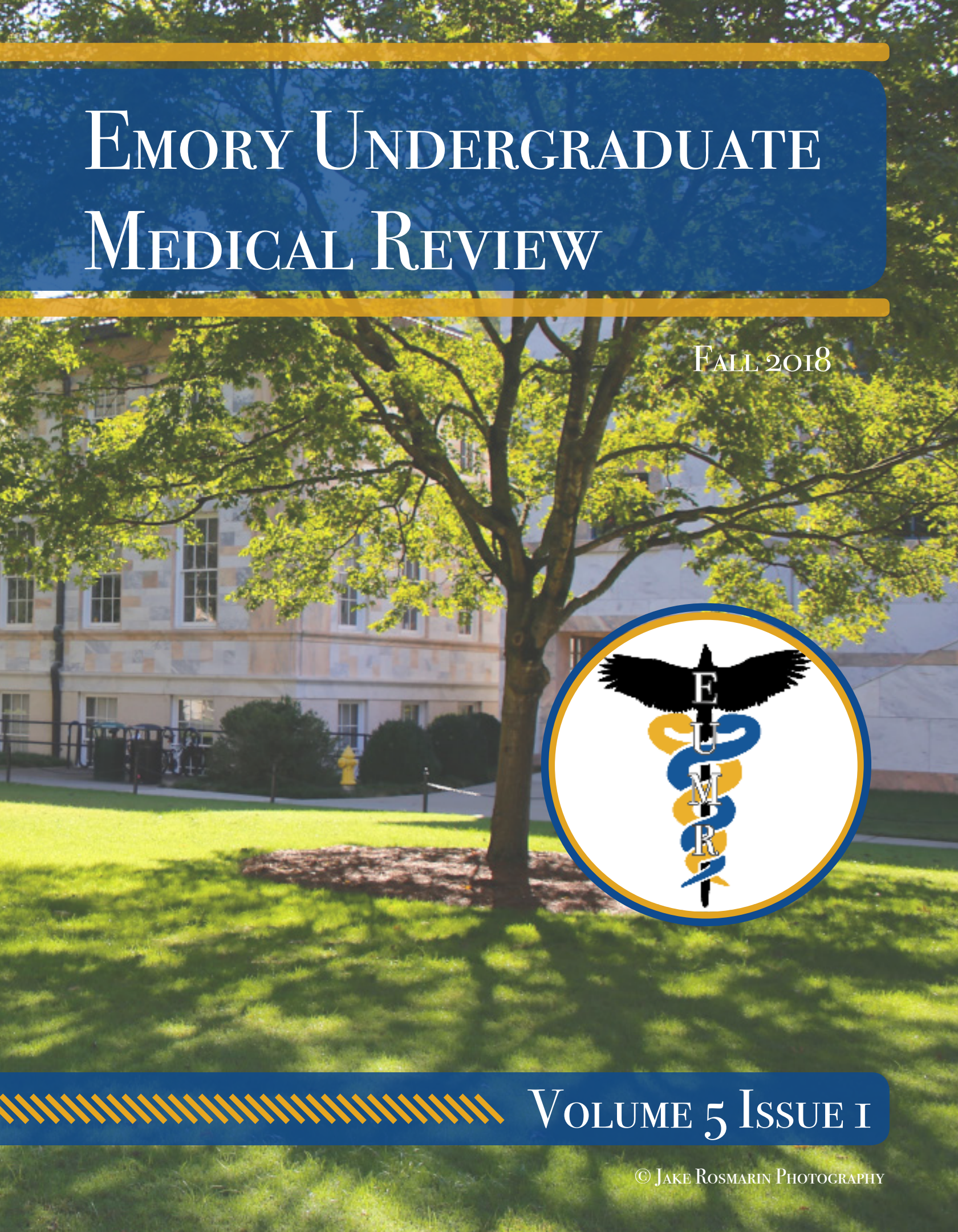
Emory Undergraduate Medical Review

Fall 2018



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About EUMR

Mission Statement:

The Emory Undergraduate Medical Review is for Emory undergraduates interested in medical or health related careers to engage in scholarly discourse with their peers and medical professionals. EUMR publishes semesterly hard-copy and online-copy journals in addition to shorter blog posts throughout each semester. Each semesterly issue primarily features reviews on interesting and cutting-edge topics in medicine, while medical opinion articles are also welcomed. All semester pieces are reviewed by doctors and researchers from around the country who are featured on our Advisory Board. Blog posts are more succinct and accessible pieces in recurring areas including ethics, biotechnology, public health, nutrition, and more. EUMR also endeavors to put on educational events relevant to students interested in medical or health careers.

Our Advisor

Dr. Michael Crutcher, PhD

Emory

Dr. Michael Crutcher is one of the many distinguished faculty members in Emory's Neuroscience and Behavioral Biology Department. Having received his PhD in Physiology from Johns Hopkins University, he joined the Department of Neurology and of the Neuroscience Ph.D. program at Emory in 1991. His research is primarily focused on the neural mechanisms of visually guided reaching movements in monkeys.

Dr. Crutcher has taught many NBB courses over the years such as: freshman seminar courses (NBB 190) on Brain Enhancement, Curiosities of Neurology and Neuroscience, and Neuroethics as well as Perspectives in Neuroscience and Behavioral Biology (NBB 401 SWR), Biology of Movement Control (NBB 370), Neuroscience Research Methods (NBB 221), Functional Neuroanatomy (NBB 470), and Topics in Neuroscience and Behavioral Biology (NBB 270).

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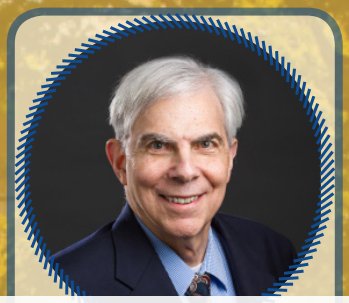

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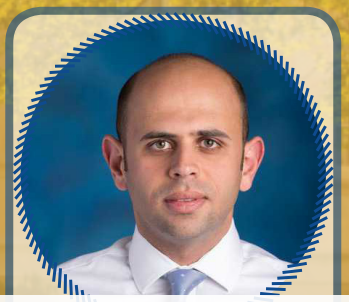

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Tracing Ancient Plagues with Contemporary Genomic Tools

Authored by: Alexa Rome
Edited by: Soumya Mandava **Reviewed by: Dr. Arri Eisen**

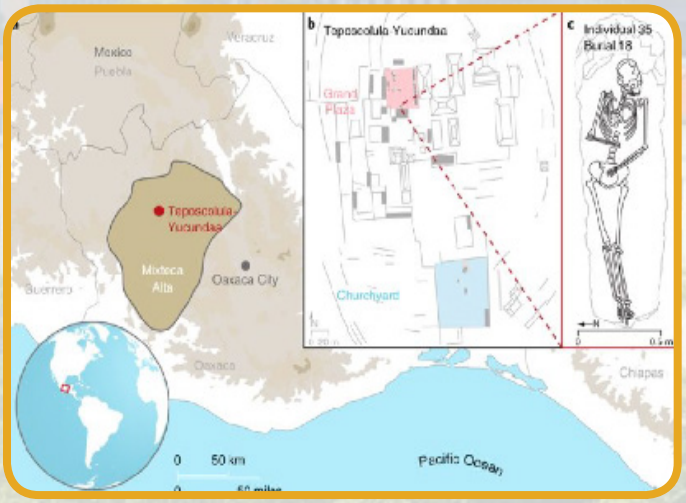
Advances in genomics and computational power are heralding in a new age of discoveries in an unexpected place: ancient history. Until now, historians have had to rely on scientifically unverifiable historical and archaeological accounts to determine the causative agents and origins of many recorded plagues. Using novel techniques to isolate ancient, usually degraded, DNA from archaeological remains, scientists are beginning to learn more about some of history's deadliest pandemics.

One such plague is the Cocoliztli Epidemic, which occurred in several waves in Mexico throughout the 16th century. This plague was responsible for the death of an estimated 8 million people, many of which were indigenous Aztec (Vågene et al., 2018). For the better part of a century, scholars have debated what pathogen could have killed so many people so quickly.

> "This plague was responsible for the deaths of an estimated 8 million people."

An interdisciplinary team of researchers discovered a cemetery associated with the epidemic through written Spanish sources, the only one of its kind known to exist. They extracted ancient DNA (aDNA), which is often degraded or contaminated, from victim's teeth. Using damage pattern analysis to confirm the sample was in fact ancient and soil sequencing to check for contamination, the researchers sequenced the extracted DNA for analysis. The team was able to find a match between the samples collected and Salmonella enterica subsp. enterica serovar Paratyphi C, an enteric fever causing pathogen (Vågene et al., 2018). Scientists and historians alike now know the cause of the mysterious plague which killed so many.

Another famous plague occurred during the reign of Justinian I and then continued between the 6th and 8th centuries CE in and around the Byzantine Empire. The Justinian Plague was one of the earliest recorded major epidemics in history. According to Procopius, an ancient historian, the Justinian Plague killed 10,000 people daily. Many sources confirm that Constantinople was overrun with bodies and that crops failed due to a lack of living farmers. Victims suffered from fever, vomiting, buboes, and in some cases, severe hallucinations (Ligon, 2006). While it was long suspected that Yersinia pestis, colloquially known as the plague, was the cause of these deaths, there was little empirical evidence to prove it. Researchers removed teeth from a grave in modern Germany wherein the individual had died from the Justinian Plague. aDNA was extracted and sequenced from the teeth, allowing researchers to reconstruct the disease genome. It was compared to known Yersinia pestis genomes and was determined to be a distant relative of the causative agent behind the Black Death



Map of graveyard where individual who died from the Cocoliztli plague was found at the archaeological site of Teposcolula-Yucundaa in Oaxaca, Mexico (Vågene et al., 2018).

(Wagner et al., 2014).

In fact, the plague arrived in Europe much earlier than previously thought. Strains of Yersinia pestis have been extracted from late Neolithic skeletons found in Southern Siberia. The late Neolithic

> "In fact, the plague arrived in Europe much earlier than previously thought."

period was characterized by rapid movement of ancient humans into and around Europe, both challenging and supplementing the local Neanderthal populations. Most of this movement came from the Eurasian steppe, a conclusion derived from the

analysis of ancient and modern genomes in these regions. Yersinia pestis thus appears to have come into Europe from steppe populations during their migration, triggering centuries of waves of the plague which hugely impacted the course of European history (Andam, Worby, Chang, & Campana, 2016; Andrades Valtueña et al., 2017)

Other plagues have been more difficult to research. The cause of the Athenian Plague is one of the most contentious cases in the field. The Athenian Plague occurred during the Peloponnesian Wars while Sparta held Athens under siege. Therefore, some, even Thucydides, suggest the outbreak was an example of early biological warfare (Papagrigorakis, Synodinos, Stathi, Skevaki, & Zachariadou, 2013). The Plague of Athens has long been a point of fascination as it took the lives of many important historical Athenian leaders such as Pericles. Historical accounts give us vague and

Mass grave of ancient plague victims in modern day Martigues, France (Drancourt et al., 2007).

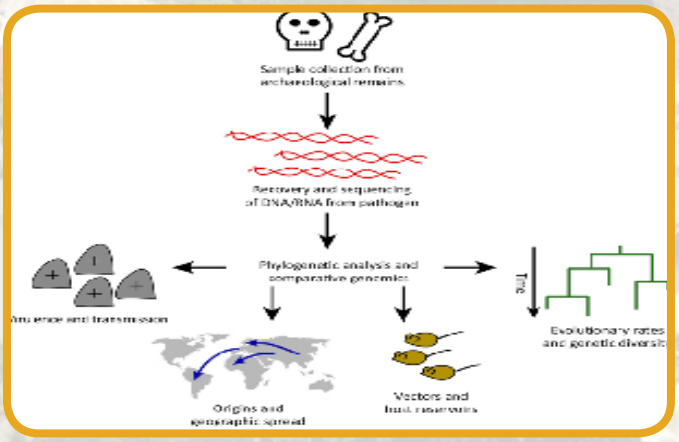
nonspecific symptoms in victims, and lack references to their exact burial sites. Some symptoms described by Thucydides, who was a victim himself, include high fever, extreme thirst, diarrhea, and restlessness (Thucydides; Smith, 1831). Historians have attributed the outbreak, which killed an estimated 25% of the Athenian population, to many different diseases: typhus, smallpox, measles, toxic shock syndrome, and even various hemorrhagic fevers (Littman, 2009; Olson, Hames, Benenson, & Genovese, 1996)

To settle this debate, bioarchaeologists have sequenced multiple samples from skeletons associated with the city during the Peloponnesian War and received mixed results. Some have found evidence of typhoid and others of smallpox (Papagrigorakis, Yapijakis, Synodinos, & Baziotopoulou-Valavani, 2006; Shapiro, Rambaut, & Gilbert, 2006; Spence). As both typhoid and smallpox were endemic in the area, some believe that they would not have caused the devastation described by ancient historians without serious mutations that increased their virulence. Without historical sources connecting researchers to cemeteries associated with the plague, scientists are unable to definitively determine its cause.

Developments in genomics and computational analysis have allowed scientists to have a deeper understanding of our past. However, some believe that studying ancient diseases may come with a deadly price. Most researchers publish the genomic information of ancient diseases freely online for other

"Some believe that resurrecting ancient diseases may come with a deadly price."

researchers to access. This open access is invaluable to ancient disease researchers who are often investigating similar questions. Some point out that other recent developments in biology may make it possible for terror organizations to inexpensively recreate deadly pathogens with only a few specialized tools given this genomic information. This would allow individuals to release a new epidemic at any time (van Aken, 2006). To mitigate this risk, new ethical safeguards need to be put in place. The National Science Advisory Board for Biosecurity in the United States helps establish codes of conduct when working with



Process of genomic paleopathology and resulting avenues of research (Andam et al., 2016).

pathogens. Additionally, they have worked with the US Department of Health and Human Services to evaluate individual cases to mitigate risk and assess potential benefits of the research being conducted. Another group, the National Research Council Committee on Genomics Databases for Bioterrorism Threat also provide recommendations to reduce bioterrorism risks (Council, Affairs, Studies, Sciences, & Agents, 2004; DeWitte, 2016).

Many believe that understanding the genomic history of pathogens, some of which still plague millions around the world, is extremely beneficial to

medical research. Knowing how pathogens change over time provides insight into their evolutionary history, transmission, and vectors. Ancient data can help scientists understand how diseases spread in the past and apply that information to fight the spread of modern emerging diseases such as SARS and Ebola (Andam et al., 2016). This real-world data from antiquity can also contribute to the creation of statistical models used to predict pandemics and understand how emerging diseases might change over time (Anastasiou & Mitchell, 2013; DeWitte, 2016). While its applications and ethical dilemmas are still being debated, there is significant value in using genomics to understand our history. Historians, archaeologists, and biologists are beginning to have a more complete and nuanced understanding of ancient disease's role in ancient society that will continue to impact our view on the past for years to come.

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Palliative Care: A Growing Field of Comfort and Compassion

Authored by: Soumya Mandava
Edited by: Preethi Reddi **Reviewed by: Dr. Lynn O'Neill**

Dr. Cicely Saunders was initially a nurse and social worker, but later decided to pursue medicine in order to better address the needs of her terminally ill patients (History of Palliative Care, 2016). While working with one young man, she asked what he wanted out of the individuals who cared for him during his last days. He responded, "For someone to look as if they are trying to understand me." This small request, that someone simply put in the effort, stuck with Dr. Saunders as she began thinking of ways to provide this care for all her patients (What is palliative care, 2018). It was at this time that she coined the idea of 'total pain', wherein an individual is assessed not only for physical symptoms, but also for external stresses (Saunders, 2001). In order to account for all factors, Dr. Saunders began implementing treatment plans that involved regular administration of medications to prevent pain rather than focusing solely on mitigation. Her treatment plans also included individualized, specific support for both patients and their families (What is palliative care, 2018). The efficacy of her service spread to nearby hospitals that were beginning to understand the importance of providing this care for terminal and end-of-life patients (Baines, 2011). Dr. Saunders's treatment plans grew into a field of medicine known as palliative care that...

Dr. O'Malley, a palliative care physician, with Zoe Meinen, a 6-year old with a terminal brain tumor. (Bohonak, 2016)

Nearly three decades later in 1990, was recognized by the World Health Organization as its own specialty. The World Health Organization defined palliative care as the prevention, relief, and treatment of physical, psychosocial, and spiritual pain in order to improve the quality of life in patients with life-threatening illnesses (WHO Definition of Palliative Care, 2012). Since then, the field has spread further, with palliative care now provided in about 75% of hospitals in America with more than 300 beds (Palliative Care, Yesterday and Today, 2017). As it becomes increasingly available around the world, it is important that we - as individuals who may one day require or have a loved one who requires these services - understand what exactly palliative care provides, its ethical implications, and its relation to spirituality and religiosity.

Palliative care is a medical specialty that provides relief from pain and other illness-related symptoms, alongside offering support for the emotional, spiritual, social, cultural, and personal needs of patients and their loved ones (Martin, 2017). It focuses on providing a better quality of life, which is defined by the patient's desires and goals for their health plan.

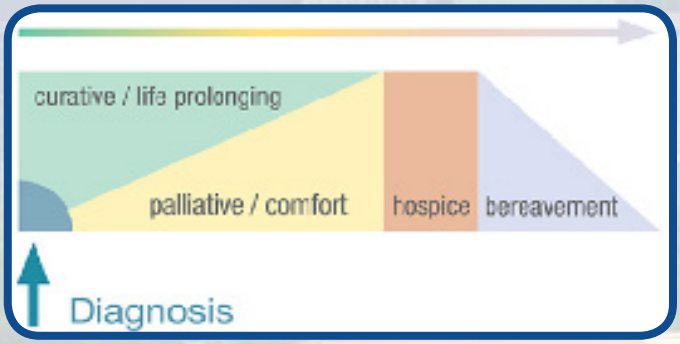
Contrary to popular belief, this care can be started at any phase of a serious illness, as early as diagnosis or they may choose to wait until a later stage.

"Contrary to popular belief, palliative care can be started at any phase of an illness."

Hospice, a form of end-of-life care within the umbrella of palliative care, is more specifically for individuals no longer seeking treatment or for those approaching their last few months of life (Martin, 2017).

In order to provide physical relief, palliative care clinicians first need to understand an individual's pain, a subjective symptom that varies from patient to patient. To effectively assess the nature of a patient's pain and other suffering, clinicians discuss its onset and temporal pattern, intensity, location, aggravating and relieving factors, previous treatments, and physical and social effects (Perron and Schonwetter, 2001). After using this information to characterize pain as either Step 1: Mild, Step 2: Mild to Moderate, or Step 3: Moderate to Severe, physicians prescribe the appropriate medications (World Health Organization, 1991). The most common classes of

medications prescribed to palliative care patients for pain are opioid and nonopioid analgesics (confer pain relief). Other symptoms such as shortness of breath, anxiety, depression, constipation, nausea/vomiting, decreased appetite, insomnia, and decreased energy are addressed with a combination of pharmacologic and nonpharmacologic approaches. Palliative care services in hospitals and clinics typically have an interdisciplinary team comprised some combination of nurses, doctors, advanced practice providers (nurse practitioners and physician assistants), chaplains,



Palliative Care in the Continuum of Illness (Reed, n.d.).

social workers, psychologists, and pharmacists. Utilizing their professional training and strengths, different team members help address different aspects of a patient's suffering. For instance, the chaplain may explore spiritual and existential distress that the patient is experiencing and the social worker would assess the financial stressors, while the clinician (MD, NP, or PA) would focus on treating the physical symptoms.

Opioids are a mainstay of pain management in palliative care. However, it is becoming increasingly common to see marijuana used concurrently with opioids in patients with serious illness. In certain areas around the world, both of these drugs are prescribed

"Individuals who rated their quality of life as "good" increased from 19% to 70%.

to patients as analgesics. A 2017 study observed 1000 patients who were prescribed medical cannabis for a 6-month period. The data showed that a little over 50% of patients previously reported unimaginable pain (8-10 on a scale of 0-10), but after the testing period, only 5% still reported pain within that range. Similarly, the percentage of individuals who rated their quality of life as "good" increased from 19% to 70% (Burns, 2017). There are similar studies detailing the benefits of opioid usage; most of them studying the efficacy of immediate-release or sustained-release and investigating different routes of administration – oral, rectal, or transdermal (Opioids in palliative care, 2012). There are, however, certain studies that warn against the concomitant usage of marijuana

Services Offered through Palliative Care (Person-Focused Palliative Care Approach, 2018)

and opioids due to evidence of adverse physical and emotional effects, difficulty in operating a motor vehicle, and the higher likelihood of developing substance-abuse disorders (Reisfield, 2010). It is an ongoing multi-dimensional discussion to consider the long-term implications of drug usage, but with more evidence-based research and further clarity about societal perceptions, society and the medical field are moving closer to a communal decision.

One of the unique elements of palliative care is its cognizance of patients' spirituality and religiosity. As Dr. Saunders observed when pioneering this field, both of these aspects play a key role in a patient's treatment efficacy and quality of life. For example, a study involving 36 cancer patients showed that individuals who considered themselves to be religious also showed significantly lower levels of pain (Yates et al., 1981). A similar study involving spirituality found a significant correlation between patient spirituality and improved quality of life, wherein 84% of participants relied on religious and spiritual beliefs to cope with their cancer (Vallurupalli, 2012).

By asking about a patient's relationship with spirituality and religion, clinicians can better understand how a patient's belief system may influence a patient's attitude towards suffering and illness. In addition, clinicians can better refer patients to appropriate services (i.e. chaplain, spiritual support groups, yoga, etc.). Therefore, awareness, sensitivity, and appreciation for a patients' beliefs and values are vital components of holistic, compassionate, and patient-centered palliative care (Puchalski and O'Donnell).

Palliative care is a growing field that focuses

on providing relief and support for patients and their families. It is available to any individual diagnosed with a serious illness and for those needing end-of-life care. Palliative care utilizes many types of pharmacological and nonpharmalogical approaches to prevent and alleviate pain. In addition, it surpasses the biological needs of a patient by offering spiritual, social, cultural, emotional, and personal support.

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Gut Bacteria: A prescription for mental health?

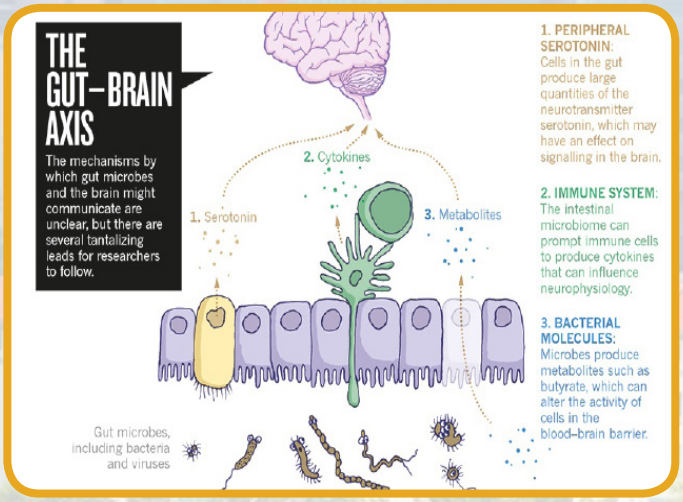
Authored by: Monjori Mukurjee
Edited by: Hannah Kelly **Reviewed by: Dr. Waqar Azeem**

The word bacteria is never met with pleasant thoughts, but the "good bacteria" in our gut may now change the way we react to the word. Recent scientific studies indicate that the diverse bacteria in our intestines, known as the gut microbiome may affect human brain chemistry. A healthy microbiome may result in reduced chances of experiencing anxiety and depression (Cryan, 2014). But how did researchers even start thinking about the connection between the gut and the brain? A dense enteric nervous system often called the "second brain" resides in the gut (Cytowic, 2017) and governs the gastrointestinal tract along with the central nervous system. The flow of information between these two systems has been shown to be bidirectional. The gut microbiome's possible role in interacting with this bidirectional system would change the way we 'think' about our microbiome (Furness et al., 2014, p.39). In the age of fecal transplants where new microbiota are introduced into the microbiome of patients, it is important to fully grasp the potential interactions between the brain and gut microbiota that may impact mental health in terms of anxiety and depression.

Because the important symbiotic relationship with the gut microbiome begins soon after birth, it has a defining impact on the development and function of many immune and metabolic systems, important to health, including both digestive and mental health (Neufeld et al., 2011, p.492).These bacteria express a variety of genes capable of producing chemicals that influence neurological functioning.

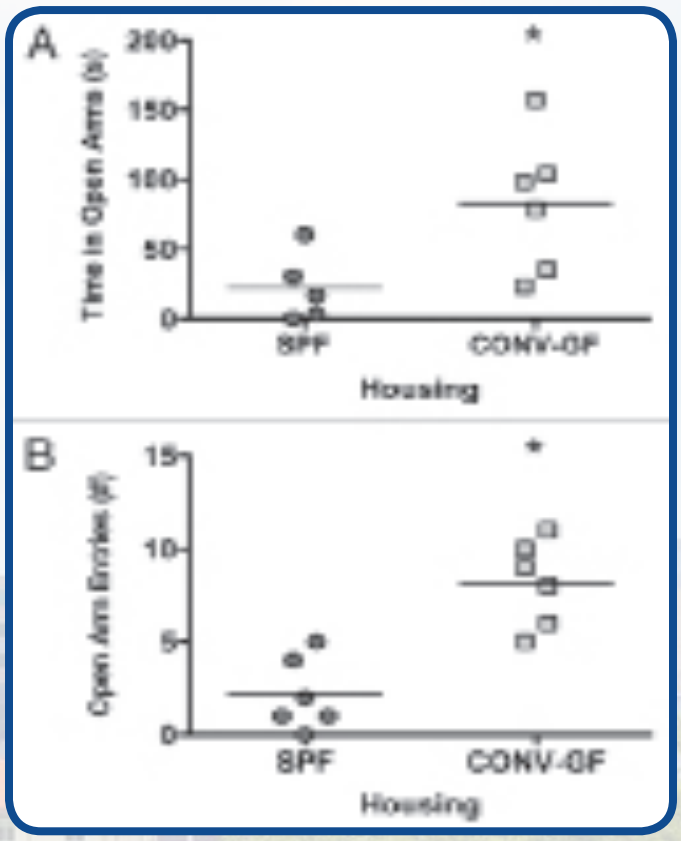
> "In fact, bacteria (that are a part of the microbiome) produce some of the same molecules as those used in brain signaling, such as dopamine, serotonin and gamma-aminobutyric acid (GABA)" (Cryan & Dinan, 2014, p.28).

Furthermore, these bacteria also produce many of the fats that make up the brain (Cryan, 2014, p.28). Recent research has also shown that the intestinal microbiome regulates the set point for hypothalamic-pituitary-adrenal (HPA) axis activity. This carries significant implications in thinking about the relationship between the microbiome and the brain, because the HPA is responsible for regulating important hormonal activities (Neufeld et al., 2011, p.492).



The interaction of the enteric nervous system with the central nervous system through the cells of the large intestine (Smith, 2015).

Neufeld and colleagues investigated the relationship between the gut microbiome and anxiety by subjecting two groups of mice to an elevated plus maze (EPM) that tests anxiety. Time spent in the open arms of the maze indicates less anxiety and a willingness to explore. The study found that mice in the germ free (GF) condition (less microbiota) spent significantly more time in the open arm condition and entered the open arm sector of the maze significantly more than the specific pathogen-free (SPF) condition. Neufeld et al. attribute these findings to connections between the central nervous system and the gut. Moreover, introduction of SPF mice stool into the GF condition, which establishes normal gut microbiota in the GF condition, still resulted in mice demonstrating increased time in the open arms of the EPM and an increased number of entries into the EPM. This finding prompted the hypothesis that there is a critical window in early postnatal development after which the reintroduction of microbiota does not normalize the behavioral phenotype shown by GF mice (Neufeld et al., 2011, p.492-494).



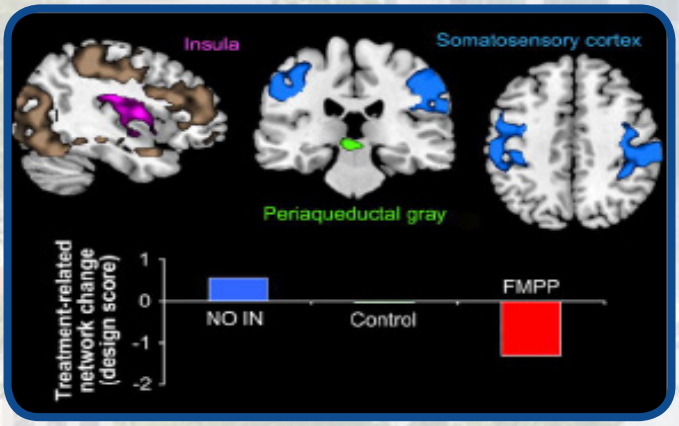
This figure shows the differences between time spent in the open arm sector of the maze (A) and number of entries into the open arm sector of the maze (B) for the Specific Pathogen Free (SPF) condition and the conventionalized GF mice (CONV-GF) after microbiota from SPF had been into the GF condition (Neufeld et al., 2011, p.492-494).

While this study implicates the microbiome in increased anxiety-like behavior, another study examining the effect of probiotic formulation on rats and human subjects observed that the probiotic administration condition reduced anxiety-like behavior in rats and significantly lowered psychological distress in human volunteers ($p < 0.05$) (measured by Hopkins Symptom Checklist Scale-90, Hospital Anxiety and Depression scale and by the Coping Checklist). The administration of probiotics also reduced the urinary free cortisol (UFC) level, suggesting reduction of stress. Massoudi et al., concluded that

> "L. Helveticus R0052 and B. longum R0175 taken in combination display anxiolytic-like activity in rats and beneficial psychological effects in healthy human volunteers" (Massoudi et al., 2011, p.755).

Thus, the administration of these particular bacteria may have brought about the differences in results seen between the two studies.

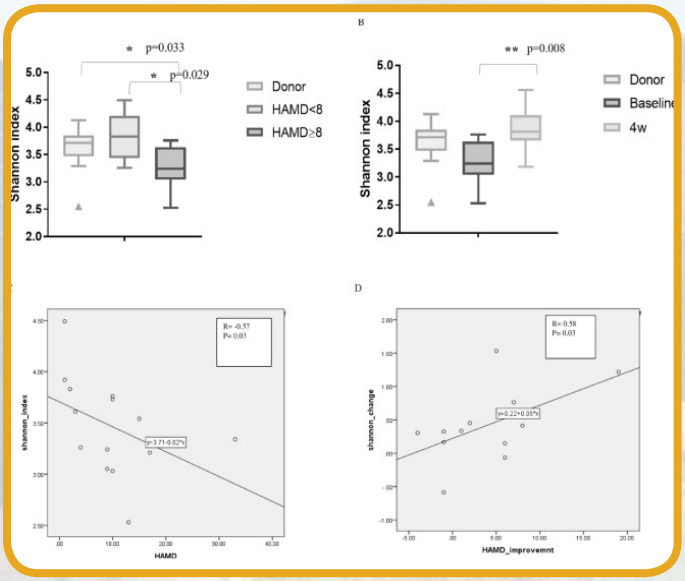
Another study examined how consumption of fermented milk product with probiotic (FMPP) affects brain modulation activity during a standardized emotional faces attention task. Healthy women with no gastrointestinal or mental health problems were divided into an experimental group that consumed the FMPP, a group that consumed non fermented milk, and a group that consumed neither. Stool analysis was conducted to assess whether the bacteria consumed were present in the gut, and those subjects who had consumed antibiotics were excluded. The study concluded that the FMPP treatment affected activity of brain regions that control central processing of emotion and sensation (Tillsh et al., 2013, p/ 1394-1401). rain maps primarily looked at the primary interoceptive and somatosensory regions, and a cluster in the midbrain region centered on the periaqueductal gray (PAG)showed reduced activity in the FMPP treated group (Tillsch et al., 2013, p. 1394-1401).



A distributed network of brain regions with shaded regions showing decreased activity in the FMPP group during the emotional faces attention task , the change in network strength with intervention is depicted graphically (Tillsch et al., 2013, p. 1394-1401).

As mentioned before, exploration of the effect of microbiome on mental health became especially relevant after the rise in popularity of fecal transplants for treatment of inflammatory digestive diseases. This model also provides a more direct understanding of what is constituted in the microbiome since the bacteria in the stool being transplanted can be studied, and the change in microbiota before and after transplantation establishes a more direct causality. One such study followed 17 patients with either Irritable Bowel Syndrome (IBS), Functional Diarrhea (FDr) or Functional Constipation (FC) who underwent fecal microbiota transplantation (FMT) for the treatment of gastrointestinal symptoms. Psychiatric symptoms were also observed based on changes in the Hamilton Rating Scale for Depression (HAM-D)

and subscale of sleep-related items, Hamilton Rating Scale for Anxiety (HAM-A) and Quick Inventory for Depressive Symptoms (QIDS) between baseline and 4 weeks after FMT. It is important to note that the study included a small sample size with no control group and was observational in nature. The results suggested that regardless of improvement in gastrointestinal condition, patients may show improvement in mood after the fecal transplant (Kurokawa, 2018, p.506-512).



*The relationship between microbial diversity and depression scores according to the (A) Shannon index at baseline of donors (n = 14), HAM-D < 8 patients (n = 5), and HAM-D ≥ 8 patients (n = 9). (B) Shannon index at baseline of donors (n = 14), baseline and 4 weeks in HAM-D ≥ 8 patients (n = 9). (C) Correlation between HAM-D total scores and Shannon index at baseline of all patients (n = 14). (D) Correlation between HAM-D total score improvement and Shannon index change before and after FMT (n = 14). **p < 0.01, *p < 0.05. HAM-D - Hamilton rating scale for depression (Kurokawa, 2018, p.506-512).*

Thus, a lack of consensus remains about the long term effect of gut microbiome fluctuations on mental health. However, there is a clear link between the gut microbiome and symptoms of anxiety and depression, possibly because of the role that the gut microbiota play in establishing the HPA. Further research exploring specific bacteria as in the studies by Tillsch and Massaudi may lead to information about the specificity of the genes expressed by the different species of bacteria and the pathways on which they act. This would therefore have important implications for prescriptions for anxiety and depression and also change how the medical field thinks about FMTs.

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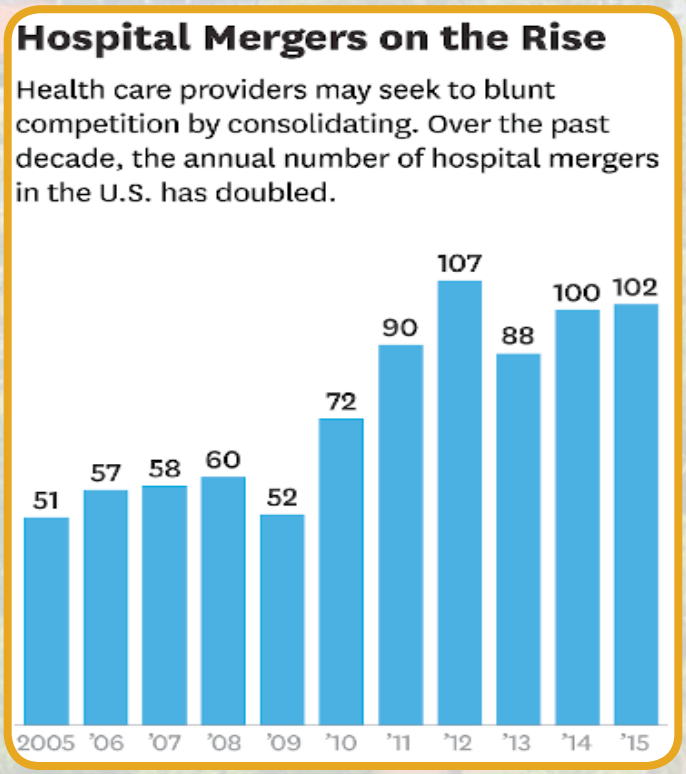
The Growing Effect of Hospital Consolidations

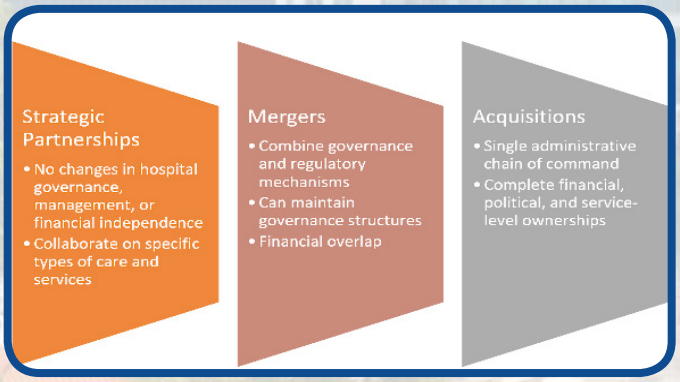
Authored by: Nivedita Potapragada
Edited by: Sharvil Patel **Reviewed by: Dr. Ian McCarthy**

In the first quarter of 2018 alone, over 30 hospital networks nationwide have consolidated into larger service groups. Especially over the past decade, hospitals are becoming increasingly consolidated through partnerships, mergers, and acquisitions. As these large hospitals networks and partnerships are beginning to emerge, more standardized forms of physician payment, patient treatment, and medical practice are being developed and formalized. What does this mean for patients and their health? The data indicates that the cost of hospital treatments seems to be increasing without necessarily improving patient outcomes after hospital consolidations.



The number of hospital mergers is shown here. This figure does not include acquisitions or other types of consolidations, but does show the rapid increase in the last 6-7 years compared to previous years of hospital mergers.

The main types of medical network combinations are mergers, acquisitions, and strategic partnerships. From just April to June of 2018, the United States had 255 healthcare merger and acquisitions deals related to hospitals and clinics. In our own backyard, Emory Healthcare and Dekalb Medical recently finalized a strategic partnership that would allow them to pull from a common pool of physicians, resources, clinics just a few months ago. The basic premise of these hospital mergers is that multiple hospitals, especially those specialized in different fields, combine to provide service under one administrative banner. Even outside of health care, there are a few main trends found in mergers, acquisitions, and partnerships (MAPs).



Shows the differences between time spent in the open arm sector of the maze (A) and number of entries into the open arm sector of the maze (B) for the Specific Pathogen Free (SPF) condition and the conventionalized GF mice (CONV-GF) after microbiota from SPF had been into the GF condition (Neufeld et al., 2011, p.492-494).

One important reason for pursuing a MAP consolidation is that health care organizations are seeking to reduce costs, especially administrative financial burdens. The driver of many of these health care integrations are profit-related, since the organizations involved are trying to expand into new areas or sectors without increasing the number of resources (staff, physical buildings, etc.) that they need to treat more people. When hospitals integrate, they are generally looking to better reach certain patient populations and manage health at a larger scale for a given community or population. By combining similarly sized hospitals, their administration can reduce the amount that they spend on administrative costs for each patient and manage population health for more people. As a result, integrating hospitals ideally provide patients in a given community with better care because they understand the prevalent

diseases and resources needed in the local area to better respond to patient needs.

> "As a result, integrating hospitals ideally provide patients in a given community with better care because they understand the prevalent diseases and resources needed in the local area..."

Another factor driving MAP integrations is to combine specialized clinics so that one hospital system provides patients with access to many different specialists without having to leave its network. The most common way of creating this network is for a large hospital to acquire smaller, specialized clinics. Physicians who are experts in one field become a part of the larger network. As a result, patients have greater access to any types of services that they might need in a health care setting without having to move out of an individual health care or hospital network. Additionally, this integration would allow physicians to share information more freely about patient history and testing, reducing the need for unnecessary duplicate tests and more streamlined diagnosis. Theoretically speaking, MAP consolidations would therefore allow patients easier access to specialized care and more personalized attention from their larger network of physicians.

However, two major concerns from health care policymakers and economists is the impact of hospital consolidation on costs and quality of care for patients. Although hospitals integrating may offer reduced administrative costs and better care coordination for patients, these outcomes need to be measured.

In terms of costs, mergers are associated with a 2.5% reduction in operating expense per admission at acquired hospitals, which was obtained from a six-year analysis of hospital consolidations nationwide after the Affordable Care Act was passed in 2010. These savings total to an average merger-related annual savings of $5.8 million for each hospital involved in a merger, which can vary depending on the size and location of the hospital. However, recent research also suggests that prices for health care services following recent hospital mergers have generally increased by 5-10%, and up to 40% in some markets. The most likely explanation for this increase in price is because larger hospital networks have more market power, so can negotiate to be paid more in the insurance market. However, if hospitals merge their facilities, staff, and resources, they tend to show smaller price increases for patients. Overall, the data suggests that while administrative costs that hospitals pay have decreased, the personal cost of care for patients and insurers has drastically increased as a result of hospital consolidations.

Changes in quality of care are slightly more ambiguous and depend more upon the type of quality and patient population being measured. Hospital mergers seem to show decreases in 30-day readmission and mortality rates according to a RWJF report from 2006, but not in a statistically significant manner. Additionally, the post-merger disease-specific mortality rates for patients can drastically vary depending on the specializations and existing resources of the hospitals that are being consolidated. Certain populations have different quality outcomes, especially Medicare patients tending to show quality declines but other populations showing improvements in quality. When examined at a national level, mergers do not seem to have consistent effects on quality of care, so further investigation is needed into the factors that impact quality measures.

> "...prices for health care services following recent hospital mergers have generally increased by 5-10%, and up to 40% in some markets."

In the end, hospital consolidations are a rapidly growing part of how our health care system functions. The critical question is to understand the cost-benefit impacts of consolidations – when do the costs to patients and insurers outweigh any potential improvements in quality? Based on results from the past eight years, it seems that hospital consolidations are not offering patients significantly helpful improvements in their health to account for the rapidly increasing costs. In creating health care policy, we need to consider how to control health care costs after consolidations and also holding hospitals accountable for constantly improving patient outcomes.

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Awake Craniotomy: Marvels in Neurosurgery

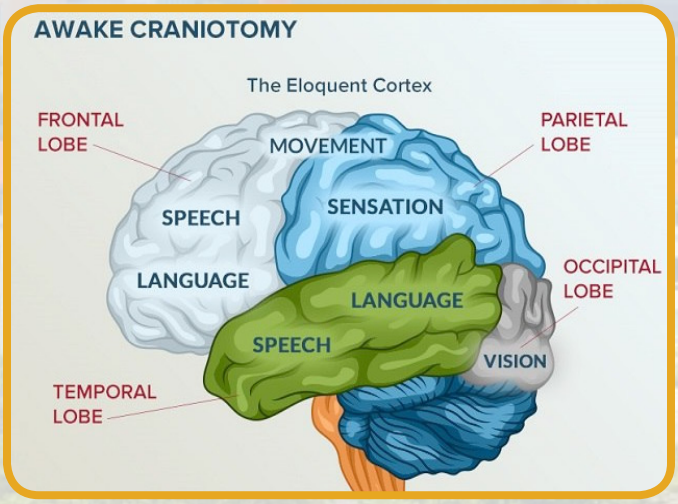
Authored by: Nathan Jacob & Daisy Li
Edited by: Soumya Mandava **Reviewed by: Dr. Lawrence Marks**

One of the most common fears patients have about surgery is waking up in the middle of the procedure. A procedure for brain surgery, known as awake craniotomy, however, allows patients to be fully conscious and cooperate with surgeons, thereby helping to better the success rates of high-risk brain tumor operations. With previous approaches to craniotomies, surgeons risked cutting into important receptive and command areas of the brain and, as a result, compromising the patient's quality of life. Awake craniotomy has given hope to patients with high-risk tumors. As neurosurgeon Dr. Henry Marsh simply put it, "All that's different about it is that fact that the patient is awake, and what you are doing is safer than what you do when the patient is asleep" (Boland, et. al., 2017).

Awake craniotomy is based on our understanding of cerebral localization, a concept introduced in the nineteenth century. In an article published in 1861, Dr. Paul Broca reported a case study suggesting that aphasia, the loss of speech that can follow strokes, may be associated with damage to a specific region of the left frontal cortex, and in 1874, Dr. Carl Wernicke suggested that another area of the left cortex, this in the temporal lobe, is responsible for speech comprehension. And in 1870, Drs. Gustav Fritsch and Eduard Hitzig performed an experiment in which they produced movement in dogs by stimulating their brain. Their experiment established two important facts: first, that fine motor skills are associated with specific regions of the cerebral cortex, and second that limb movements occur when stimulating the contralateral precentral gyrus of the cortex (Bulsara, et al., 2005). These studies and others in the nineteenth century eventually brought about the modern principle of cerebral localization: that specific mental and behavioral functions depend on neural activity in specific regions of the cerebral cortex.

In the twentieth century, modern awake craniotomies built upon this principle by developing procedures to ensure successful brain surgeries that avoid damaging functional important parts of the brain. In a paper published in 1954, Dr. Wilder Penfield expanded the fundamental concept of cerebral localization through his surgical work, in which he performed awake craniotomies on patients with seizure disorders. In a companion paper published in the same year, Dr. André Pasquet outlined important anesthetic techniques related to awake craniotomy. Modern awake craniotomies began with Penfield and Pasquet's findings.

Anesthetic techniques in awake craniotomy have improved continuously since the middle of the last century. In 1953, Paul Janssen created



The eloquent cortex, an area of the brain responsible for language, motor, and sensory functions, is mapped through cerebral localization according to its function (Syrek, 2016).

Innovar, a sedative that was marketed originally for neuroleptanesthesia (Bulsara, et al., 2005). With Innovar, patients were drowsy but could follow commands under the effects of anesthesia. However, this sedative can produce numerous side effects, such as dysphoria (distressed state) and hypertension (abnormally high blood pressure). In the 1990s, this sedative was improved as propofol, a reformulated sedative associated with fewer side effects and hypnotic properties (Bulsara, et al., 2005). Today's modern craniotomies use propofol and a short-acting synthetic opioid analgesic drug, Remifentanil, to allow better pain relief. The anaesthetic techniques of awake craniotomy are not the only area of improvement. Intraoperative magnetic resonance imaging (iMRI) is a modern method that contributes to the high success rate

for awake craniotomy. It utilizes powerful magnets, radio waves, and a computer to generate an image of the patient's brain, typically before surgery, which helps guide the surgeon in removing the brain tumor.

Awake craniotomies generally follow an "asleep-awake-asleep" procedure (Ghazanwy, et al., 2014). As the name suggests, patients are kept unconscious under general anesthesia for the first part of the operation, when the surgeon opens the skull. Brain scans done before the surgery locate the general area where the tumor is located, but the surgeon will not be able to fully determine the anatomy of the tumor before opening the skull.

Once the brain is exposed, the patient is gently brought out of general anesthesia (the actual surgical opening is locally anesthetized). Because the brain itself does not have nerve endings, the patient would not be in pain during the operation (Davies, 2016). On one side of the drapes, the surgeon is armed with an electrical probe to stimulate different regions of the brain, while on the other side, the patient interacts with a neuropsychologist, who reports, in real time, to the surgeon about changes in the patient's behavior (Knausgaard, 2015). The neuropsychologist's task is to engage the patient in conversation, word games, and visual puzzles, all the while looking for signs of speech slurring or hesitation in case the electrical probe disturbs a sensitive area of the brain. These regions, now mapped more precisely for the patient, will be excluded from any resections. In some cases, if the tumor is located near motor control centers, the surgeon may ask the patient to move certain limbs or their face. In rare cases, musicians have even been asked to play their instruments in the middle of surgery to ensure that their playing ability remains intact (Jethani, 2016).

"In rare cases, musicians have even been asked to play their instruments in the middle of surgery to ensure that their playing ability remains intact."

For a life-changing procedure, how successful is awake craniotomy and what are the risks associated with it? Looking past the fear of waking up in the middle of surgery, the statistics for awake craniotomy are fairly positive. When comparing the mortality rates of the procedure between young and elderly patients, the elderly patients did not exhibit a significantly greater mortality rate. Considering that these elderly patients tend to exhibit more high-grade brain tumors, the statistics speaks for the effectiveness of the procedure (Grossman, et al., 2012). It also allows for a more complete removal of the tumor tissue while still preserving neurological function, and patients can return to their daily activities in a shorter amount of time, typically around 1.7 days of postoperative care. This is compared to the typical 9 days of hospital care required of asleep craniotomy procedures (Zhang, et al., 2018).

During awake craniotomy, patients are asked to engage in various activities (such as playing the violin) in order to assist the neurosurgeon in the mapping of the cortex (Jethani, 2016).

One challenge to most awake craniotomies is the use of the asleep-awake-asleep format. Anesthesiologists have to ensure that the patients are calm and pain-free, but remain clear-minded and conscious during the awake phase so that accurate brain-mapping can occur. Therefore, nearly all drugs are usually stopped during the awake phase, with the exception of fentanyl and a few other agents to suppress pain (Zhang, et al., 2018). Appropriate dosage and timing of these drugs are imperative to the success of the operation and the comfort of the patient.

Other challenges are also present, including the possible production of seizures. Brain mapping requires the use of electrical stimulation, which can trigger seizures when the stimulation occurs around the cortical, subcortical, frontal lobes of the brain (Ghazanwy, et al., 2014). The incidence rate is not high, seen only in around 3-16% of patients; but can be higher in patients with a history of seizures (Zhang, et al., 2018). To minimize this risk, surgeons

are encouraged to avoid stimulating the same area twice in succession and to wash the region of the brain with cold crystalloid solution to diminish the likelihood of electrically-induced seizures (Ibid.).

Studies have also been conducted to assess the patient's experience of awake craniotomy. A study conducted by the Santa Maria della Misericordia Hospital in 2004 involved 21 patients who underwent awake craniotomy (Attari, et al., 2013). Twelve patients had stimulation in the motor cortex and 9 patients had stimulation in Broca's and Wernicke's areas, brain regions responsible for speech production and speech perception, respectively (Attari, et al., 2013). Before the surgery, many patients reported feelings of anxiety. When the awake craniotomy was underway, the patients either understood or felt the opening of the skull with some describing it as "a simple noise in my head" or feeling of "the bone shattering" (Attari, et al., 2013). After the surgery, all of the patients were tired but surprised by feeling well with no side effects. Weeks later, there were no adverse effects and the patients recovered well. In general, 70% of the patients indicated "complete satisfaction" with the results of the surgery and 81% responded that they would undergo the surgery again if needed (Ghazanwy, et al., 2014). These are high marks for a stressful, high-stakes surgery such as awake craniotomy and the outcome suggests that although side effects are present, the procedure is still accepted by patients and results in few traumatic experiences.

"When the awake craniotomy was underway, the patients either understood or felt the opening of the skull with some describing it as 'a simple noise in my head' or feeling 'the bone shattering'. "

Awake craniotomy has improved upon an important goal in neurosurgery: to maximize the success of brain surgery and patient comfort during the surgery. The "asleep-awake-asleep" procedure allows neurosurgeons to complete brain surgery with increased accuracy and improved results compared to typical craniotomies. Due to this success, patients rarely face problems or side effects after the procedure and typically have an increased life expectancy by at least 10 years. The improvements to awake craniotomy have had many sources, from introducing new medications in anesthetic techniques to advances in imaging, such as incorporating intraoperative magnetic resonance imaging. Awake craniotomy is becoming more popular due to its instant success and is proving itself as an important procedure in the field of neurosurgery.

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Combination Conundrums: Glioblastoma Multiforme Therapeutic Advancements

Authored by: Aditya Jhaveri
Edited by: Hannah Kelly **Reviewed by: Dr. Michael Crutcher**

Former Senator John Sidney McCain III passed away at 4:28 PM on August 25th, 2018. His death was caused by the healthcare field's current inability to cure glioblastoma multiforme, the most aggressive brain cancer. Unfortunately, deaths like Senator McCain's are frighteningly common in patients diagnosed with glioblastoma multiforme; however, his diagnosis placed a spotlight on the progress of research on cancer treatments and their effectiveness. The expected survival for brain cancer is grim; of those diagnosed with glioblastoma multiforme the median survival is only about 12.6 months and less than five percent of patients live more than five years (Carlsson, Brothers, & Wahlestedt, 2014). The treatment of glioblastoma multiforme has changed marginally in the last few decades, resulting in a continued poor prognosis for patients. While the painted picture of the past has been bleak, the present offers hope and a marked shift from previous thinking and practices. Exciting breakthroughs in combination therapy research towards novel treatments for glioblastoma multiforme carry promise for the future of cancer survival.

"Glioblastoma multiforme (GBM) is the most lethal and most aggressive primary brain tumor"

Glioblastoma multiforme (GBM) is the most lethal and most aggressive primary brain tumor. This brain cancer is a specific type of glioma with tumors originating in glia—cells that provide support and protection to neurons—or their precursors; additionally, these gliomas are multiforme, meaning a singular tumor shows heterogeneity in gross, microscopic, and genetic characteristics (Holland, 2000). High therapeutic resistance of GBM stems from the complexity and variation of the tumor, complicating treatment strategies. Moreover, options for dealing with GBMs are limited because formalized studies on targeted therapy are lacking. Thus, standard medical care of brain cancer begins with maximal surgical removal of the tumor and is followed by a combination of radiation therapy and temozolomide (TMZ) chemotherapy.

Complications arise in each step of the process

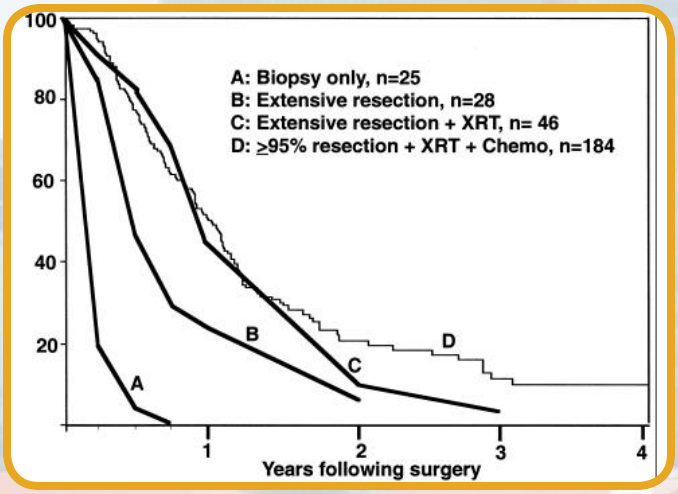

Figure 1: Survival for patients with glioblastoma multiforme is poor. Kaplan-Meier plot data shows the highest survival rates in patients with resection, radiotherapy, and chemotherapy (Holland, 2000).

of treating brain cancers. Surgical removal, while necessary, poses particular consequences because the tumor location in the brain creates possibilities of additional harm or significant disability from surgery. In addition, most brain tumors diffuse into surrounding regions and have residual cancer cells that allow for therapeutic evasion and recurrence. (Lara-Velazquez et al., 2017). Radiotherapy also comes with side-effects at the location of interest, including fatigue and skin changes (Stubbe & Valero, 2013). Furthermore, radiotherapy may help in moderation, but the harms may exceed any potential benefits when administered in excess or without specificity. Temozolomide chemotherapy, moreover, proves to be cytotoxic with its functionality as an alkylating agent (adds alkyl groups) that marks cells for apoptosis. Adding to such complications, many GBMs exhibit resistance to TMZ and render such treatment ineffective. Additionally, other chemotherapeutic options and drug delivery methods to affect the tumor encounter difficulty crossing the blood-brain barrier (blocks substances from entering the brain) or crossing the blood-tumor barrier (vascular structure surrounding the tumor). These significant treatment issues to GBM are the reason for the lack of improvement in survival rates for the last three decades (Vleeschouwer, 2017).

Fortunately, survival for glioblastoma patients is "moving in a more promising direction"

"These significant treatment issues to GBM are the reason for the lack of improvement in survival rates for the last three decades (Vleeschouwer, 2017).

with novel treatment strategies. (Tyler, DiMeco, Grossman, & Pradilla, 2014). One of those new options in treatment is the progress being made in combination therapeutics. Furthermore, a major therapeutic advancement in recent research is the use of biomarkers and different genetic characteristics to modulate treatment options for a patient. Such precision oncology focuses on profiling a tumor to develop targeted treatments of individual drugs or in combination with each other. The rationale behind employing drugs together stems from the current failure of treatment options and because additional specification offers the potential for synergistic antitumor efficacy of cancer therapeutics (Candolfi et al., 2009). Synergism refers to the process of two or more entities combining to create an effect greater than each individual component; when this process occurs with treating cancer, the chemotherapeutic toxicity can be mitigated, since drug concentration can be decreased from the dose that is required separately. Overall, combination therapies can be categorized as either cytotoxic (harmful to cells) or immunotherapeutic (stimulate the immune system). Clinical trials increasingly have been investigating different variations of combination therapies to develop novel medical options for patients.

The potential combination of different DNA repair protein inhibitors alongside temozolomide or other chemotherapeutic agents stands at the forefront of

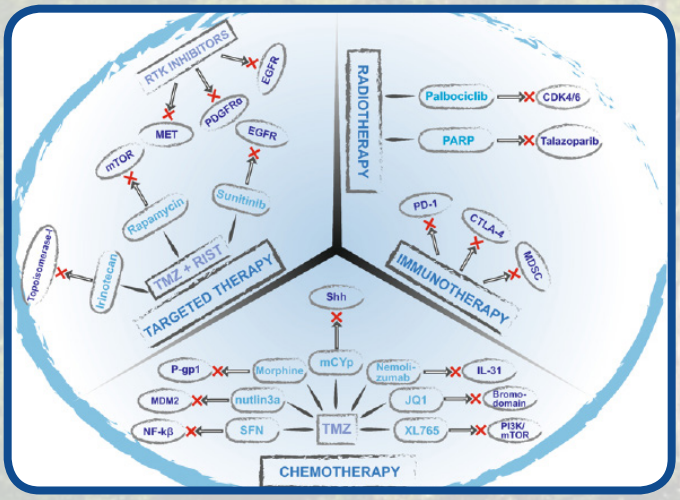

Figure 2: Combination therapies represent a possibility of using precision oncology to create better patient outcomes (Ghosh, Nandi, & Bhattacharjee, 2018)

research on treating glioblastoma multiforme. Cancers often display defects in the DNA damage response pathway (DDR) with the heightened ability of cancer cells to repair damage induced by chemotherapeutic agents (designed to kill those cells) creating resistance (Gavande et al., 2016). If GBMs exhibit resistance to chemotherapy because any attempt to trigger apoptosis is prevented, the cancer will continue to grow or recur after maximal surgical removal. Targeting those DNA repair proteins, however, may increase the effectiveness of chemotherapy and will provide individualized care since different GBMs respond to treatments differently. Current research explores this theory by examining different types of DNA damage (single-strand breaks, double-strand breaks, base damages, etc.) to explore the pathways involved in repair and identify potential inhibitory proteins to improve patient outcomes (Atkins, Ng, Stylli, Hovens & Kaye, 2015). As research continues, advancements in knowledge of drug specificity towards tumor regions, mechanisms of DNA repair proteins, and increased synergistic effects will hopefully surface.

More recent developments in immunotherapy have also shown promise. In combination with standard treatments and other combination

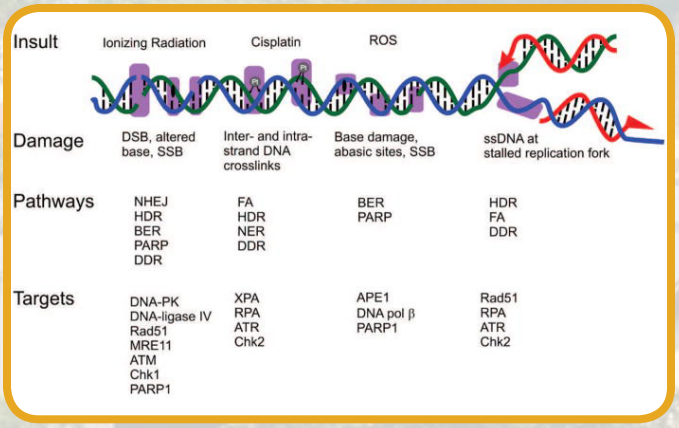

Figure 3: There are many potential DNA repair response pathway proteins that could be involved with repairing damage created by chemotherapeutic agents in glioblastoma multiforme (Gavande et al., 2016)

therapies, immunomodulation has promise in treating glioblastoma multiforme. The potential for immunotherapy treatment began with anecdotal studies of neurologists and neurosurgeons observing that brain cancer patients with postoperative infection surprisingly survived longer. They hypothesized that the immune system plays a large role in survival of cancer patients and the elevated immune response after surgery benefited patients. An experimental study confirmed this with patients surviving an average of 15 months longer if they contracted a

postoperative infection (De Bonis et al., 2011). The immune system involvement with tumor growth and regression stems from the disrupted regulation of the cell cycle in cancer cells. Immunostimulation with monoclonal antibodies, vaccinations, and immune-simulated gene therapy all present methods of potential tumor regression and treatment (Ghosh, Nandi, & Bhattacharjee, 2018). Immunotherapy thus offers another method of targeted treatment that can increase patient options in a way that promotes the body's own mechanisms of self-defense.

As the search for the cure to cancer continues, precision-oncology has surfaced as a mechanism for treating glioblastoma multiforme. Brain cancer

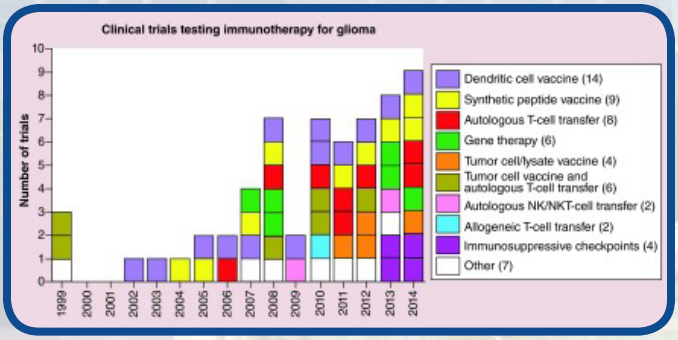

Figure 4: Clinical trials for immunotherapy in brain cancers are increasing in number showcasing the possibility for more treatment options in the near future for GBM patients (Calinescu et al., 2015)

overall has limited options for medical care, and GBM expression of resistance and recurrence places a considerable barrier to beneficial patient outcomes. However, as increased research into combination therapies of DNA repair protein inhibitors, chemotherapeutic agents, and immunotherapy continues, the potential for precision oncology to improve quality of life with decreased toxicity and overall survival of patients brings hope.

"The brain, the masterpiece of creation, is almost unknown to us." - Nicolaus Steno in 1669

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Robotic Prostatectomy: The Future of Technological Medicine

Authored by: Alex Sandberg
Edited by: Jonathan Regenold **Reviewed by: Dr. Mohammed Shahait**

The prostate is a male reproductive organ that produces a portion of a male's semen and transports the seminal fluid to the urethra located between the bladder and penis. While the prostate is critical to male fertility, the organ is not necessary for survival. Prostate cancer affects approximately 30,000 middle-aged American men annually, though there are several modes of treatment for prostate cancer, many men diagnosed with prostate cancer choose to have their prostates removed as a course of treatment. Radical prostatectomies are one of the most common operations that are being done using robotic-assisted approach. As a result, there have been dramatic developments over the past decade in the combination of approaches to operative treatment (Prostate Cancer: Statistics, 2018).

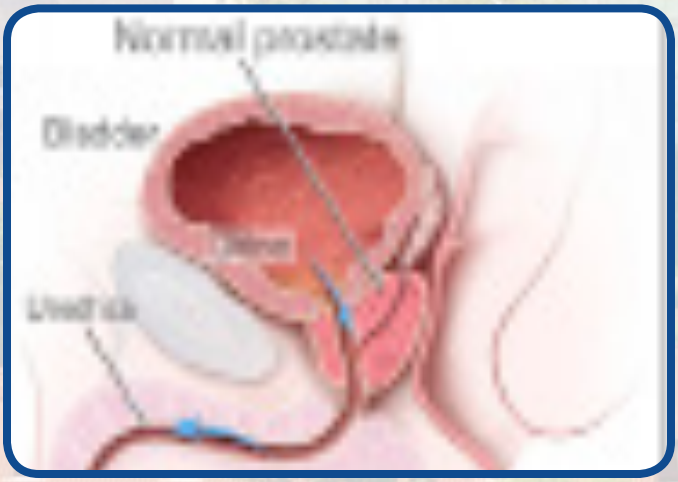

Figure 1: Outlines the anatomy of the male prostate and surrounding organs (Schroeder, 2015).

Radiation and hormonal therapy are used in different combinations as both primary and secondary treatments. Salvage radiation/hormonal therapy can be prescribed as a primary mode of treatment or after recurrence, while isolated adjuvant salvage radiation/hormonal therapy treatment is a pathway administered as a secondary treatment after surgery to prevent recurrence of the disease. Active surveillance, which involves close monitoring of patients with low grade cancer has also become a popular choice. With the advancement of surgical robotic platforms, the potential for greater postoperative success has created a meaningful debate in the urology community.

Until the last decade, the majority of the prostatectomies in the states were done using open approach. In the operation, the surgeon uses an 8 to 10 cm incision to perform a meticulous dissection of the prostate. The adoption of the surgical robotic platforms allowed urologists to develop a minimally invasive surgery to remove the prostate. The robot has three to four arms with re-attachable surgical tools that include forceps, scalpels, scissors, and etc. Using four to five tiny incisions, the surgeon introduces these instruments inside the abdominal cavity of the patient as the surgeon sits at a console station and controls the instrument (Chopra, Srivastavam, and Tewari, 2012).

Figure 2: Shows the Da Vinci system inserted into a patient with the surgeon operating the system at the adjacent console (Cancer Research UK, 2017).

The joint-wristed design used in robotic platforms, has increased the standard ranges of motion of minimally invasive equipment. The surgeon's movements are mirrored by the robot and can be displayed on the monitors in the operating room. Additionally, the 3D image presents an optimal focused view for the urologist on a minimally invasive scale (Chopra, Srivastavam, and Tewari, 2012). The console eliminates tremor and possible human random motion through the manipulators. The entire station is located in proximity to the armed robot, so the surgeon can gain access to the patient if needed. However, for the most part, urologists remain at the console where all steps of the operation can be

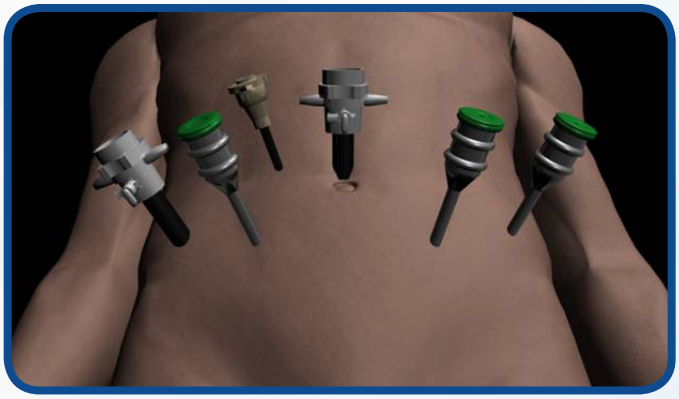

Figure 3 illustrates where the four lower robot arms make four precise incisions into the abdomen of the patient minus the attachments. The incision around the belly button is specifically designed for the prostate to be removed from ("Trocar configuration for nerve-sparing robotic prostatectomy, nd).

completed.

The introduction of robotic platforms have completely revolutionized surgery for prostate cancer. Studies have shown that patients who undergo robot-assisted radical prostatectomies had less post-recovery blood loss and shorter hospital periods (Zhao et al., 2015). The small incisions heal much more rapidly than the traditional large incision made during open surgery. As a result, surgeons generally prescribe less pain medication post-surgery, which limits risk of potential opioid abuse and addiction (Catalona, 2018). Impaired functional outcomes are often minimized due to the surgeon's ability to avoid nerves that control the urinary tract and sexual functions. Although, overall post-recovery scores show an insignificant difference in the erectile dysfunction and urinary incontinence outcomes between open and robot-assisted surgeries (Zhao et al., 2015).

In order to be effective in using the robotic approach, surgeons or residents who have been trained on the traditional approach have a learning curve and require a significant amount of training. Although with credible mentorship and time, there is considerable improvement after about twenty-forty cases (Patel et al., 2005) with more consistent favorable outcomes. Many studies conclude that the steep initial learning curve gives an advantage to younger surgeons beginning to enter the field (Tuliao and Rha, 2014).
Despite the many advantages of robotic prostatectomy, there are a handful of noted drawbacks. There is less tactile feedback in a robotic operation, simply because there is minimal physical involvement (Tozawa et. al., 2014); while open prostatectomy provides a more suitable physical access to the surgical field (Catalona, 2018). On the financial side, the cost of surgery differs among health systems, but there appears to be a correlation of higher cost with the robotic approach. The gap in cost is predicted to diminish over time, but currently there remains a clear financial burden on the healthcare system. Lastly, there is the risk of robotic malfunctioning, but cases are rare in the United States (Davies, 2015).

One of the most intriguing aspects of the robotic systems is its applicability in telemedicine. Currently, surgeons are performing the operation in the same room as the patient. With continued advancement in this field, several teams across the globe have been developing remote operation stations where surgeons can operate in different locations then where the patient resides (Stefano, 2017). Doctors from around the world will soon be able to control the surgical robot from another console, outside of a typical hospital setting. Telemedicine operations are already being conducted over the past few years, but are still being perfected as a universal option (Stefano, 2017). Continuing the momentum to improve the effectiveness of robotic surgery and various treatments will remain as the leading topic in the forthcoming years, with much more to be innovated.

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The Placebo Effect and Traditional Medicines

Authored by: Deanna Altomara
Edited by: Preethi Reddi **Reviewed by: Kim Tran**

Long before antibiotics or surgery, other types of medicine ruled the world of healing. From Chinese acupuncture to cleansing saunas to sacred ceremonies, cultures all over the world have discovered ways of maintaining health and well-being. Over time, the biomedical model that simplifies the human mind and body into quantifiable numbers and evidence-based research has yielded many life-saving advances. Yet, it has also drawn attention away from the spiritual and emotional work of healing. Increasingly dissatisfied with the insensitivity of modern medicine, many individuals are now turning to ancient wisdom for healing. Practices like acupuncture, religious ceremonies and faith healing, and talismans are finding a new niche in the American economy. As science races to understand the molecular underpinnings of illness, many doctors are left wondering—how

Experiment Tcm Plants Traditional Medicine Bean [Photograph found in Max Pixel]. (n.d.).

do traditional forms of medicine work? Is Western medicine finally catching up to traditional medicine, or is it the other way around? It is now more important than ever to understand the ethical implications of using traditional medicine in a global environment.

Ethical questions arise with the growth of ancient healing practices. Is it appropriate for Americans to try healing practices that they don't understand, from cultures they don't understand? Is it ethical to hold traditional or sacred practices to scientific scrutiny? Can findings be transferred across cultures? For example, acupuncture is an ancient Chinese practice that has gained traction in the United States. The practice involves inserting thin needles into specific points of the body to remove blockages of qi, the life force that flows through the body (Wang). Promoting healthy flow of qi is said

A Chinese chart showing common acupuncture sites Acupuncture chart with a series of points indicated on the figure of a standing Chinese man [Painting found in Wellcome Library]. (n.d.).

to ease the symptoms of many health conditions. Studies have found that acupuncture, if performed correctly, can alleviate pain. This is especially true of chronic pain conditions, such as back and neck pain and recurrent migraines. These kinds of pains are known for being particularly responsive in the placebo effect; accordingly, the success of acupuncture appears to be closely linked with a patients' expectations and beliefs (Acupuncture 2017). Traditional medicine is often founded on spiritual beliefs, but these beliefs vary across culture. Some worry that transposing these ancient practices into new populations will interfere with the success of the treatment itself. For example, many Hindus believe that the benefits of yoga are largely derived from the practice's holistic basis in spirituality and mind-body connection. They are increasingly frustrated with the Western interpretation of yoga, which is grounded in physicality rather than spirituality (Adler 2012).

No matter the culture, belief plays a significant role in traditional medicine. Some researchers theorize the success of faith healing is largely derived from the hope and positive thinking that it inspires in patients (Pretorious 2009). In Ghana, many herbalists consider themselves a type of

doctor, while many faith-based healers consider their power to be superior to that of western medicine (Kpobi 2018). Faith-based and religious healing often works: these practices can reduce unconscious stress, which can be expressed in physical ailments. Certain African cultures believe that illness is caused by anger from the ancestral spirits, which can reflect a person's inner state of being (Kpobi 2018). By relaxing a person's inner stress, it is possible to alleviate that health problems that go along with it, which seems to parallel the placebo effect.

The placebo effect is a powerful phenomenon seen across all areas of healing and medicine. They are so omnipresent that placebo treatments are often used in clinical trials to specifically test the biological efficacy of a drug. A new era of study

Sharp, J. H. Making Sweet Grass Medicine, Blackfoot Ceremony [Painting]. Smithsonian American Art Museum.

has sparked renewed interest in placebos, how they work, and whether we can harness their power in medicine. The placebo effect stems from a complex system of neuronal receptors, chemicals, and synaptic activity. These very real biological effects can change the way an individual experiences or reacts to pain (Benedetti 2010). Placebos have been shown to reduce anxiety, and operate off expectation. Rituals enhance people's belief in a treatment, making it more effective (Okpaki 1999). When people expect a treatment will work, whether because it is scientifically-backed or a long-trusted family cure, it has a significantly greater likelihood of doing so. Expectation and trust can be developed in a variety of ways, and cultures around the globe have learned to tap into the healing power of placebos. Complex, often time-honored ceremonies create the illusion of power and omnipotence, effects that amplify the placebo effect, as the patient comes to trust the treatment (Okpaki 1999). However, this effect is not only limited to distant cultural practices, but is also a vital component in Western medicine. The experience of going to a doctor—the many forms, the purifying ritual of the waiting room, the scientific lingo, and even the white coats all promise the effectiveness of medicine. Patients place their faith in the medical establishment, improving their response to drugs and treatment.

Traditional medicine offers a wide arrayof cultural healing practices, and many of these are not understood by specific biological mechanisms. In a world rich globalization and driven by modernity, it is time to turn to traditional cultures for guidance. Medicines of all types could benefit from the incorporation of the placebo effect. With the promise of belief and expectation, treatments can be more effective. How much of traditional medicine can be explained by the placebo effect, and how much of Western medicine? How can Western medicine learn from other cultures, without exoticizing or appropriating them? While many questions remain, the rich worlds of traditional medicine and the placebo effect, as well as their intersection, remains a source of promise for future treatments.

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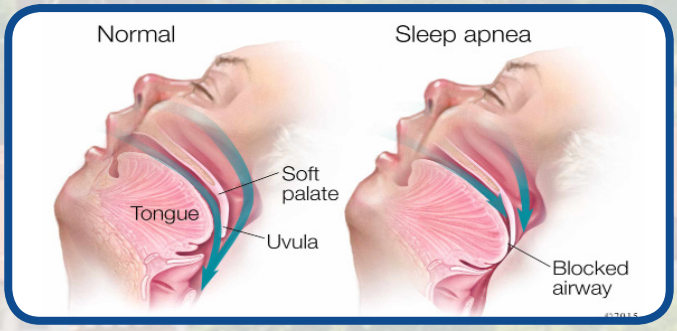
An Overview of the Complications of Sleep Apnea

Authored by: Emily Maccabee
Edited by: Jonathan Regenold **Reviewed by: Dr. Laura Otis**

Obstructive Sleep apnea, or OSA, is a common and serious sleep disorder that causes breathing to become shallow or stop completely during sleep. In some cases, this pause in breathing, called apnea, can last 10 seconds or longer, and can occur 30 or more times in an hour. Despite being a common condition, sleep apnea often goes undiagnosed because many of the symptoms occur in sleep, making it hard for individuals to pinpoint them.

It's estimated that nearly 30 million people in the United States have sleep apnea, but there are likely many more people who go undiagnosed (Gharibeh & Mehra, 2010).

This condition is prevalent and affects people worldwide, and therefore people should be educated on the seriousness of sleep apnea and symptoms that accompany it.



Differentiating between a normal versus sleep apnea patient anatomically (Mayo Clinic, 2015).

The causes of sleep apnea include obesity, large tonsils, endocrine disorders, neuromuscular disorders, heart or kidney failure, genetic syndromes, and/or premature birth. Common sleep apnea signs and symptoms are frequent loud snoring, reduced or absent breathing during the night, or gasping for air during sleep. Disrupted sleep often leads to excessive daytime sleepiness and fatigue and decreases in attention and motor skills during the day (Gharibeh & Mehra, 2010).

It's estimated that nearly 30 million people in the United States have sleep apnea, but there are likely many more people who go undiagnosed (Gharibeh & Mehra, 2010).

In order to diagnose and assess the severity of an individual's sleep apnea, physicians use a Nocturnal Polysomnography (PSG). It is conducted by connecting the patient to equipment that monitors heart, lung, and brain activity, breathing patterns, arm and leg movements, and blood oxygen levels while asleep. Whereas a physician may only recommend lifestyle changes for milder cases of sleep apnea, surgery may be necessary for more severe cases (Mayo Clinic, 2018).

Additionally, individuals with moderate to severe sleep apnea may use a device called a continuous positive airway pressure (CPAP). This machine delivers air pressure through a mask while the person is asleep. This air pressure is greater than the surrounding air, which in turn prevents apnea and snoring. This is the most common and reliable method of treating sleep apnea, but it is reported to be uncomfortable by some individuals (Mayo Clinic, 2018).

Daytime sleepiness and attention deficits, such as ADHD, are common among sleep apnea patients, with studies finding that ADHD and sleep apnea often co-occur in childhood and may persist into adulthood. The presence of both sleep apnea and ADHD negatively affect quality of life, daytime sleepiness, and psychological status. Therefore, it is becoming increasingly common for physicians to treat patients with standard ADHD treatment in order to assuage both challenges they encounter during the day, as well as improve the patient's nighttime apnea (Oguzturk, 2012).

In order to treat the daytime sleepiness, the medication Modafinal has recently been attracting attention due to its stimulating properties (Loube, et al., 2002). Conventional CNS stimulants aren't ideal for treating excessive daytime sleepiness in sleep apnea because of their interference with sleep and the danger of cardiovascular events in this at-risk population (US

Modafinil in Narcolepsy Study Group, 2000).

The correlation between sleep disorder and depression was noted in a recent study published in Innovations in Clinical Neuroscience. The paper found a higher prevalence of depression in people with obstructive sleep apnea in both clinical and community samples with many overlapping symptoms between the two conditions (Ejaz, et al., 2011). Another study, published in the Journal of Neurosciences in Rural Practice, found that 94% of patients with depression had an abnormal PSG, and over 50% had severe OSA. The study demonstrated significant overlap between sleep apnea and depression and notes that the prevalence of personality disturbances and depression is common among those suffering from OSA. Depression is considered a risk factor of OSA, due to changes in serotonin neurotransmission. Low serotonin levels can actually decrease upper respiratory tract muscle tone and disturb sleep (Shohib, 2017).

According to a recent study published in Nature and Science of Sleep, Modafinil stimulates wake-generating sites in the hypothalamus and binds competitively to dopamine transporter in the cell membrane. It is dependent on catecholaminergic signaling for wake promotion for patients who are nonresponders to Modafinil, and need to switch to extended-release formulations [i.e. Adderall] in order to provide longer duration of action(Aban, Guilleminault, 2017).Thus, it is relatively common to switch from Modafinil to Adderall to alleviate these sleeping problems. However, doctors recommend to use Afferall sparingly, and to only use it for the purpose of readjusting sleep cycles.

The brain contains serotonergic neuronal cell bodies, and studies have shown that patients with ADHD

Overall, the association between sleep apnea and depression is still being studied. Only recently have there been significant findings about such connections. Many are subject to both disorders, but there is still much more to be discovered about this realm of neuroscience.

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Robotic Prostatectomy: The Future of Technological Medicine

Authored by: Jin Yoo
Edited by: Sharvil Patel **Reviewed by: Dr. Michael Crutcher**

Prior to exploring a foreign country, tourists typically plan out an outline of renowned restaurants, popular attractions, and historical sites to visit, but a new trend has emerged. Imagine taking a flight with the sole purpose of receiving medical care for anything from cosmetic surgeries and mentally enriching meditations to cancer therapies; this is a reality in South Korea, home to a growing business in medical tourism. While some tourists seek holistic travel programs that provide health care treatments from a plethora of participating hospitals and traditional Korean medical centers, plastic surgery has seen the most significant growth and expansion of all the sectors; some of which are highlighted in Figure 1 below.

The various tourist attractions for medical treatments, ranging in beauty treatments, traditional medicine, and meditation. (Wellness Korea, 2018)

Raw statistics verify this obsession with plastic surgery in South Korea. This cultural phenomenon may be related to various social elements: the South Korean vanity capital economy is worth $4.5 trillion, larger than Germany's economy; high school students receive plastic surgery procedures as graduation gifts; professional resumes now require photo IDs; and obesity rates of >25% BMI are a mere 6.1% in men and 4.6% in women (Shen, 2015; Han, et.al 2018). But where does this all stem from?

With 20 procedures per 1000 people, South Korea ranks first as the largest international count of surgeries per capita, totaling one million a year (Shen, 2015; Jacobs and Zheng, 2018).

According to Han et al. (2018) of Mayo Clinic, the 1997 economic recession had a key role in the development of this culture. Competition in South Korea, a highly populated country with an insecure labor market, exceeded beyond the borders of mere intellectual qualifications and social compatibilities, targeting superficial characteristics such as body weight and appearance. Appearance management has become part of the checklist in employment securement, with an emphasis on lookism and stigmatization of features outside Korea's strict beauty standards. Naturally, this led to industrialization in the sector of plastic surgery, with an estimated count of over two thousand surgeons in a 2016 study conducted by the International Society of Aesthetic Plastic Surgery (ISAPS, 2016).

However, this cultural phenomenon has not been limited to South Koreans; the industry also targets foreign patients with an annual increase in count with 364,189 in 2016. Since 2009, medical tourism in South Korea has gained political and economic support, with projections that the medical tourism industry will net 33 billion dollars by 2019. In addition, the Korean government created the world's first national licensing system, the International Meditour Coordinators (IMC), in 2013. These professionals must undergo a series of examinations, training, and qualification hurdles to provide their services in international patient travel and mediation. There are various positions that have been created including medical tourism promoter/marketer, medical tour coordinator, and clinic service coordinator (Seo and Park, 2018).

The country's investment in the sector of medical tourism has not been in vain. South Korea

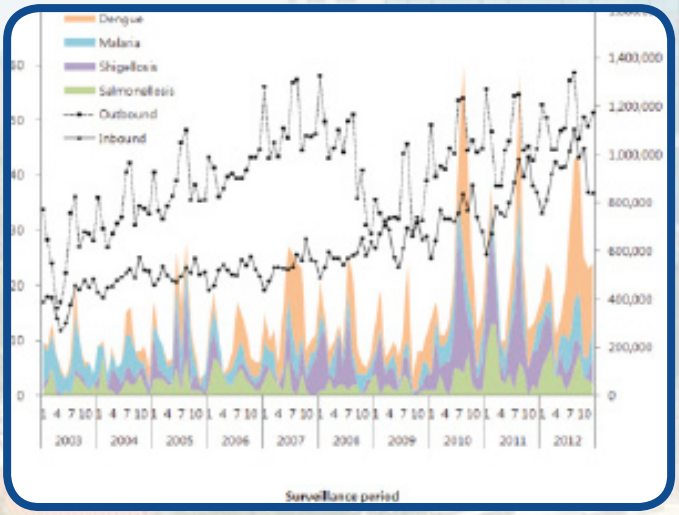
Factors considered in South Korea's medical tourism governmental sector development (Rokni, 2017)

boasts various strengths in their medical system, with higher five-year survival rates than USA, Canada, and Japan for a range of cancers including thyroid, lung, breast, and pancreatic carcinomas. According to the Organisation for Economic Co-operation and Development (OECD), there are 11.5 hospital beds for every 1000 people in Korea, higher than the US's 2.8, and as of 2013, there are over 100,000 physicians and 260,000 practicing nurses for a country with a population of 50 million. Relative to the other OECD countries, South Korea has the lowest cost in procedures, including C-sections and appendectomies, while maintaining quality. Indeed, South Korea's general medical costs composed 20-30% of the United States' and Japan's (International Federation of Health Plans, 2011). These low costs may be attributed to the significant developments in the country's medical technology, industry, and treatments. As a result, patients travel from countries such as Japan, China, and Russia to access both traditional and biomedical forms of healing for the low cost of treatment, high accessibility through government aid, and quality of care that Korea provides (Health and Medical Tourism in Korea, 2018).

The booming sector has undeniably helped South Korea's economy, but the country has also faced sociological and biological repercussions. Yet,

With international travel rampant, incidences of infectious diseases has risen, particularly in the ratio of imported cases out of overall counts, from 4.1% to 30.3% within a decade (Choe, et. al, 2017).

South Korea not only faces issues with incoming communicable diseases, but also in their development of cross-cultural communication. Despite the plethora of resources and economic support from the government, there are demands from international patients for all the professionals in the medical tourism sector to seek higher levels of cultural competence. In-depth interviews of Korean authorities concluded that there was a lack of cross cultural communication in the country, a barrier that could be resolved with human resource management policies and regulations for cultural expertise (Rokni, et. al, 2017; Seo and Park, 2018).



The increase in cases of infectious diseases (Choe, 2017)

Medical tourism is a booming field in South Korea. The various economic and cultural attributions that have led to its development have also resulted in sociological and biomedical challenges that the country must resolve. Yet despite the healthcare professionals' prominent roles in the field's development, medical tourism is ultimately consumer driven. Consequently, the future of South Korea's medical tourism health model parallels that of any other country's – the outcome lies in the hands of the patient.

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