Who cares about multidisciplinary care?
A lesson exemplified through the diagnosis of Hirschsprung's disease

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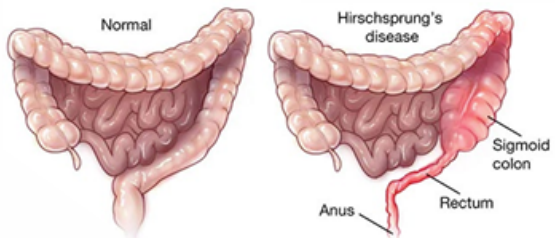
An Obvious Diagnosis: A Dilated Colon

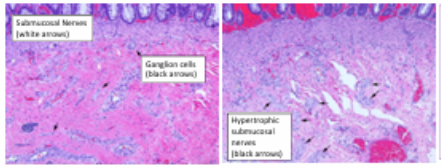
- In 1886, **Dr. Harald Hirschsprung (1830-1916),** a Danish physician, described two cases of pediatric constipation resulting in megacolon and eventual death.
- On autopsy, Dr. Hirschsprung noted:
  1. *Extremely sick and dilated intestinal loops (megacolon)*
  2. *A normal appearing rectum*
  3. *An uncertain understanding of the disease pathology of these sick children*
- The description of **congenital aganglionic megacolon** by Dr. Hirschsprung began a complicated unraveling of the disease by pathologists, radiologists and surgeons.



Normal large intestine vs. an intestine with Hirschsprung's disease, *(image courtesy of the Mayo Clinic. https://www.mayoclinic.org/diseases-conditions/hirschsprungs-disease/symptoms-causes/syc-20351556*

Microscopic Investigation

- Pathologists were deceived by the variable ascending length of aganglionic intestine from the rectum. Aganglionic sections can be cm's, to the entire colon.
- Several clinicians—**Drs. Tittel (1901), Tiffin (1940), Whitehouse & Kernohan (1948)**—found evidence of aganglionic distal bowel present in megacolon patients.
- These works, now regarded as impactful, were isolated cases and the community suspected that an aganglion colon was a *secondary* disease effect, not the cause. Pathologists couldn't decipher the real cause without looking at the bigger picture!



Normal rectal biopsy vs. Hirschsprung rectal biopsy *(Kapur RP, Hirschsprung disease. PathologyOutlines.com).*

What are colonic ganglionic cells?

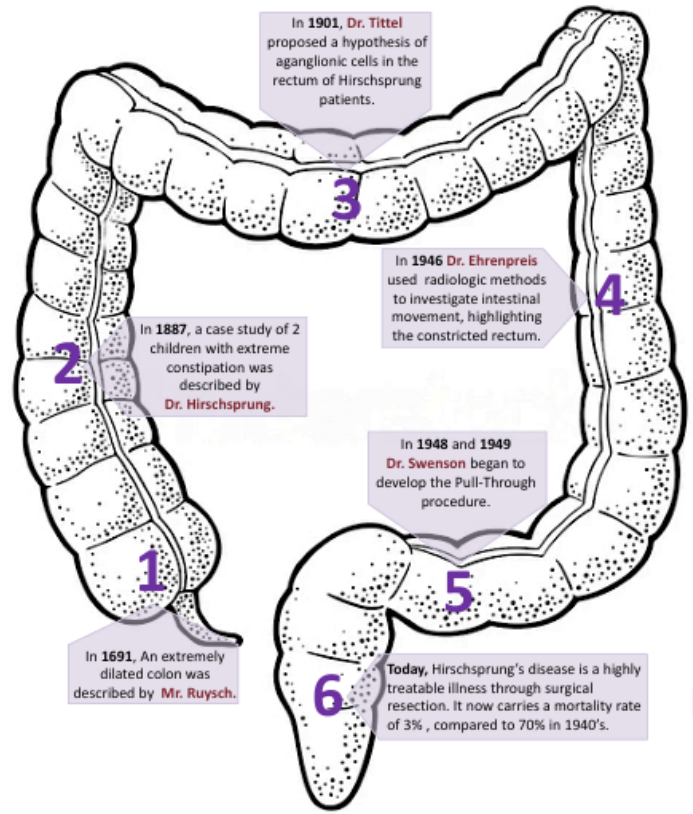
Ganglion cells are nerve cells in the colon which help with relaxation of the intestine walls.

Without ganglion cells the intestine can't open, causing stool backup and dilation.

Sources and Methods

- **Primary sources** from medical journals between 1948 – 2004 authored by Dr. Orvar Swenson Dr. Tiffin, Drs. Whitehouse & Kernohan and Dr. Ehrenpreis.
- **Secondary sources** were collected from physicians reflecting on the diagnosis of Hirschsprung's disease, ideology and pathologic diagnosis timeline.

Hirschsprung's Disease: A Timeline

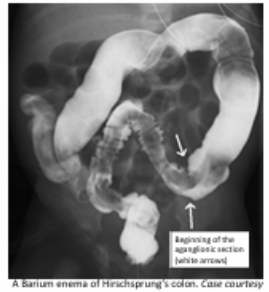


Radiographic Investigation

- In 1946, **Dr. Ehrenpreis** used barium enemas and aligned with pathologists that the primary issue in Hirschsprung's was a functional obstruction, which developed a megacolon secondary to blockage.

> *Thus, the disturbed evacuation cannot be explained by morphological-mechanical factors and should, therefore, be denoted as primary, neurogenic or purely functional.*

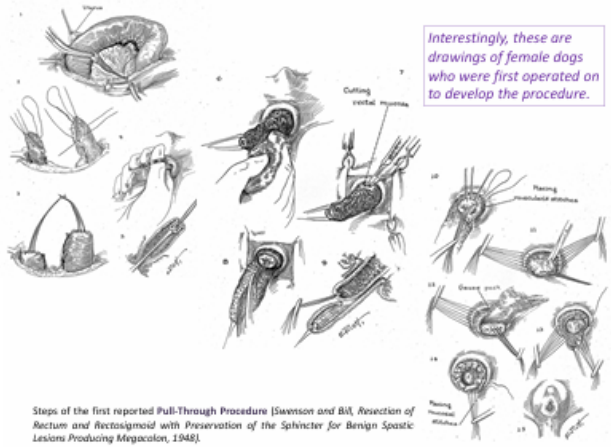
- Although this work was correct in classifying it as a functional obstruction, radiologic imaging did nothing to elucidate the neuroanatomical substrate.



A Barium enema of Hirschsprung's colon. *Case courtesy of Hani Makky Al Salam, Radiopaedia.org, rID: 7570*

Macroscopic Investigation

- **Dr. Swenson's** approach began with manometry of colostomy patient identifying weakened contractions in the unresected rectosigmoid area, elucidating the impact of aganglionic rectal pathology and radiology findings, which was ultimately causing extreme colonic dilatation secondarily.
- Dr. Swenson developed the **"Pull-Through procedure"** (*seen below*), utilizing barium enemas and intra-operative biopsies to identify ganglionic/aganglionic region to guide resection.
- Dr. Swenson was criticized by fellow physicians, including Dr. Gross, the Chief of Surgery. Dr. Gross tried to halt the surgery and take over patient care, an adamant mother ensured their child received the Swenson procedure, which was ultimately successful.



Interestingly, these are drawings of female dogs who were first operated on to develop the procedure.

Steps of the first reported **Pull-Through Procedure** (*Swenson and Bill, Resection of Rectum and Rectosigmoid with Preservation of the Sphincter for Benign Spastic Lesions Producing Megacolon, 1948).*

Why Collaborative Medicine Matters

1. In Hirschsprung's disease, surgeons were blind without pathology, pathology was disregarded until surgeons look pioneering steps. Often seen as opposing—*micro- vs. macroscopic, deceased vs. living, feeling vs. seeing*—it's clear that these disciplines must work together.
2. This diagnostic story sheds light on each discipline's strength in their area of expertise, but often needs collaboration with other specialties to clarify a patient's diagnosis/treatment.
3. When researching this topic, I often asked *"If there was increased collaboration between disciplines, would this diagnosis have taken so long?"*. The collaborative necessity of modern medicine is best reflected through historical appraisal, as to not repeat past mistakes.

I now challenge you; if you are pondering a medical quandary, reach out to a colleague in a distant specialty for their unique opinion.

Selected References

Select journal articles authored by Dr. Orvar Swenson in *Pediatrics, Surgery, American Journal of Surgery* and *the Journal of Pediatric Surgery*. Additionally, works by Drs. K Tittel, Tiffin, Whitehouse & Kernohan and Ehrenpreis were reviewed for this presentation.

The Medical Journal: Genesis of a Genre

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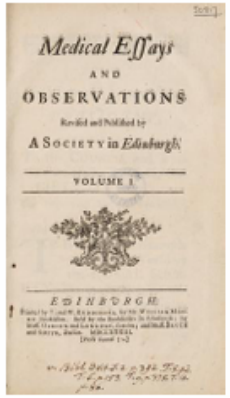
Introduction to Medical Literature

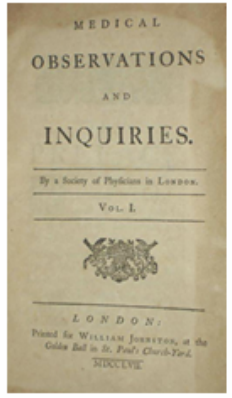
Prior to the 18th century: New medical findings were disseminated through the publication of textbooks and occasional reports in general scientific journals.

- Journals of scientific societies primarily focused on astronomy, physics, and mathematics, thus limiting their journals' relevance, popularity, and usefulness among physicians.
- Textbook authorship required talent and time commitment available to few physicians.
- The era's constantly evolving nosology, pharmacology, and practical applications were slowly communicated.
- Many discoveries were lost, as these venues were inaccessible to most practitioners.

18th Century: a new genre of literature—the medical journal—was born of physicians, for physicians, to disseminate medical findings more effectively.



Medical Essays and Observations, Volume 1
A Society in Edinburgh, 1733.



Medical Observations and Inquiries, Volume 1
A Society of Physicians in London, 1757.

The publication of short essays and medical cases, of which the earliest and most influential were the ***Medical Essays and Observations*** (1733) and ***Medical Observations and Inquiries*** (1757), established the framework for future medical journals and changed the communication of medical knowledge for centuries.

Methodology

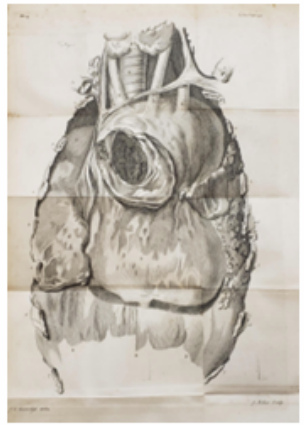
Qualitative and comparative analysis of 18th century medical journals, with special attention to:

- **Medical Essays and Observations**, Vol. 1, Ed. 2 (1737)
- **Medical Observations and Inquiries**, Vol. 1, Ed. 3 (1763)

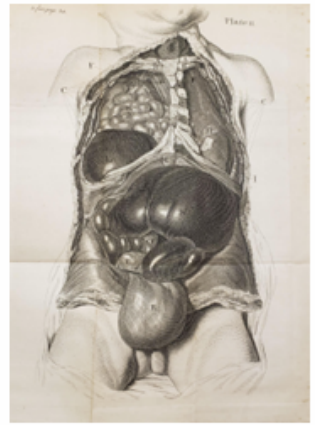
The Role of Medical Societies

The Edinburgh Medical Society (1731)

- Founded by Scottish anatomy professor **Alexander Monro *primus*** (1697-1767).
- Fourteen physician-members met with medical students monthly to discuss remarkable and unusual medical cases from Edinburgh and its surrounding hamlets.
- The society and its medical students published case reports from the British Isles.
- Five volumes titled ***Medical Essays and Observations*** between 1733 and 1744.
- First medical journal in Britain.
- First journal to implement anonymized peer review.



The History of an Aneurysm of the Aorta, with some Remarks on Aneurysms in general.
Dr. William Hunter



An account of a child, whose Abdominal Viscera were chiefly found within the cavity of the Thorax.
Dr. George Macaulay

A Society of Physicians in London (1752)

- Founded by Edinburgh medical school graduates **John Fothergill** (1712-1780) and **William Hunter** (1718-1783).
- London's diverse metropolitan population, extensive global commerce, and political connection with British colonies promoted international collaboration.
- Corresponded with doctors from Iran, Philadelphia, the East India Trading Company, and elsewhere.
- Published articles describing previously unknown symptomatology, pharmacology, nosology, and best practices.
- Six volumes of ***Medical Observations and Inquiries*** between 1757 and 1784.

Impact and Significance

Authorship: Brevity encouraged specialists to compose articles solely involving their niche topic.

- Authors had the freedom to share their personal opinions and discuss treatments that were effective, and those that were not.

Globalization: Physicians in British settlements treated exotic pathologies daily but had little means of publishing their findings independently.

- Corresponding with the **Society of Physicians in London** was an efficient method by which their findings could be shared worldwide.
- Cases that rarely presented in Europe lacked comprehensive accounts of disease onset, progression, and viable treatment plans.

Peer review: Anonymized to ensure the publication of high-quality articles without diluting the exactness, nor the importance, of the chronicled observations.

Knowledge Transfer: Medical essays rapidly updated epidemiological trends, notable disease prognoses, and promising treatment plans despite the lack of a complete, conceptual understanding.

Treatments: New medicinal compounds, treatment procedures, and surgical techniques were shared among, and introduced in, global metropolitan centers.

A meeting of the Edinburgh Medical Society in the Society's Council Chamber, 1788.
Engraving by N.C. Branwhite, 1895, after S. Medley, 1800.

The Lancet, Volume 1
Thomas Wakley, 1823.

★ **DID YOU KNOW?** **Thomas Wakley** (1795-1862) accused the medical profession of widespread corruption and nepotism. Wakley saw his journal—***The Lancet***—as a tool to incise the "boil" that was the medical community. However, Wakley plagiarized the lectures of **Sir Astley Cooper** (1768-1841) in its first volume (1823). Currently regarded as the second most prestigious medical journal in the world (after *The New England Journal of Medicine*), ***The Lancet*** has nearly 2 million registered online readers.

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The Building of Trauma-Informed Care in Medicine

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Introduction

The 1998 CDC-Kaiser Permanente Adverse Childhood Experiences (ACE) Study is one of the largest investigations to date demonstrating the long-lasting effects of childhood trauma. Surprisingly the data showed that ACEs are quite common in the general population.[3] In response to this, studies have recommended Trauma Informed Care (TIC) as a universal precaution in clinical practice.[4] TIC is a treatment framework that involves a comprehensive understanding of the effects of psychological trauma, which helps shift the question from "what is wrong with you?" to "what has happened to you?"[1] A deeper understanding of the origins of TIC and the struggles endured by its proponents may help foster greater empathy towards trauma victims.

Figure 1. Ann Burgess (left) & Lynda Holmstrom (right),1972

Purpose

Knowledge of the civil origins of TIC may serve as a powerful tool to foster empathy towards patients with past trauma, and ultimately lead to enhanced patient care.

Methodology & Sources

Qualitative research was conducted using primary research articles, newspaper archives, and physician questionnaires from the early 1970s to the present.

The Building of TIC: A Brief History

Until recently, PTSD was predominantly understood in the context of military trauma, and much less was understood about the pervasiveness of trauma within the civilian domain.[2] Below is a brief history of TIC through the lens of the women's movement.

Gaining Knowledge

- Literature surrounding rape largely focused on victim blaming.[5]
- In 1974, Ann Burgess and Lynda Holmstrom develop theory of Rape Trauma Syndrome.[6]
- RTS highlighted similarities between symptoms experienced by rape victims and war veterans, leading to official recognition of PTSD in the DSM-III (1980).[7]

Breaking Taboo

- Erin Pizzey founds 1st domestic violence shelter in London England.[8]
- Erin published a book that shared detailed case histories of the women at her shelter, and criticized legal, social, and medical services for their ambivalence towards the issue, generating immense publicity among Londoners.
- In 1979, UN adopted an international bill of rights for women (CEDAW), which improved female life expectancy & mortality rates worldwide.[9]

Creating a Treatment Framework

- In 1998, the Women, Co-Occurring Disorders and Violence Study was initiated to develop and evaluate trauma-specific principles for clinicians.[10]
- In 2014, SAMHSA released a guide to implement TIC in clinical settings for all forms of trauma.[1]
- Supporting evidence for TIC grows as its practice is disseminated into more clinics and schools worldwide.[11]

Discussion

- Work is needed in reducing the stigmatization of victims of abuse among medical professionals.
- 2019 Study: a non-TIC approach led to patient self-blame and discouraged trust in the healthcare system.[12]
- Medical education on DV and subsequent training on responding to disclosures of DV in a trauma informed way is necessary.
- TIC training has been tested and received positive outcomes in a 2018 study at the University of California.[13]
- Implementing TIC requires a shift in culture.
- Barriers to implementation include lack of formal training and awareness of the issue.[14]
- SAMHSA describes and emphasizes the need for reform at the organizational policy level if change in culture is to be achieved.

Conclusion

- TIC deserves a fundamental role in medical education.
- Broader acceptance and understanding of trauma will drive the changes needed within medicine.

Figure 2. Chiswick Women's Aid. 1971

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From Sharpened Stones to Cystoscopes: How the Evolution of Medical Equipment Defined the Field of Urology

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Introduction

Urology is a diverse area of medicine involving the treatment of diseases within both male and female urinary tracts as well as the male organs that are required for reproduction. It is widely accepted that urology became recognized as a distinct surgical specialty in France in 1890 after the French Revolution. At this time, Félix Guyon, the first Professor of Urology, opened the novel department of Urology at the University of Paris.

Figure 1. Felix Guyon (1908).

Prior to the Revolution, many urologic procedures were performed by roaming lithotomists, also referred to as "stone cutters". These stone cutters often spanned multiple familial generations, with the knowledge of how to perform the operations passed down from father to child.

Figure 2. The lithotomy procedure being performed by Stone Cutters (1707).

As medical training became standardized, urology gained prominence in the medical world. The American Urological Association was formed in 1902, followed shortly by the publication of the Journal of Urology in 1917. While these landmark achievements were important to the history of urology, urology was actually a separate field within medicine thousands of years before the French Revolution. I argue that it was the development of new technical equipment, along with the shaping of scientific knowledge, that allowed urology to flourish as a separate medical specialty.

Methods

Primary and secondary resources such as peer-reviewed publications, medical archives, journal articles and historical photographs were used to generate this presentation.

Historical Narrative

Dating back to 2400 BC, Egyptians used unique approaches for the treatment of urologic conditions. Egyptian boys entering the priesthood were routinely circumcised as a ritual initiation. The Ebers papyrus shows that surgeries were performed with specialized knives and bleeding was treated with a remedy of honey, cuttlebone, and various fruits. As practitioners honed their skills, they began using bronze catheters to treat urinary retention which continued to evolve as they were reshaped into tools like Erasistratus' S-shaped catheter following the conquests of Alexander the Great.

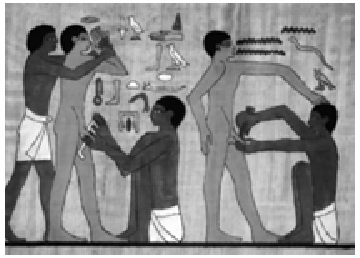

Figure 3. Circumcision practiced in early Egypt (date unknown).

Figure 4. One of the first models of the cystoscope (1879).

In the 1800s, many instruments were created to visualize spaces within the human body. One of these inventions was the cystoscope, designed by Max Nitze in 1877. The cystoscope improved the visualization of the urethra and bladder, although it was not deemed ready for clinical use at the time. Nitze moved to Vienna and worked with Josef Leiter to improve the model, eventually using it on a patient in 1879 in front of the Royal Imperial Society of Physicians in Vienna. Years later, Edison's incandescent light bulb was added to the cystoscope's design, making it more effective and affordable. This cystoscope has since been modernized, but it remains not only invaluable but very similar to its earliest version.

In 1895, Wilhelm Conrad Roentgen, a German physicist, discovered X-rays, famously taking an image of his wife's hand, which visualized her bones as well as her wedding ring. Urologists were suddenly able to preoperatively visualize renal calculi and other conditions which increased the effectiveness of many surgical procedures. Cystography was made possible by the implementation of X-rays into urologic practice, and this allowed for increased diagnostic accuracy.

Discussion

Through the innovation and improvement of medical equipment that has occurred over many centuries, the field of urology separated from general surgery and carved its own path in the world of medicine. It's important to note not just the impact of the tools that were developed, but also how these tools conferred authority upon practitioners, which further defined this specialty. Advancements in technology continue to be closely associated with urology. Robotic surgery is becoming increasingly common, as it allows for more intricate procedures and improved patient outcomes. The da Vinci surgical system, which was approved for urologic procedures in 2018, is considered the current gold standard in robotic-assisted surgery. However, many other robotic systems are being created, and it will be interesting to witness the trajectory of urology as it continually evolves.

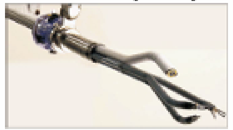

Figure 5. The da Vinci Single-Port surgical system (2018).

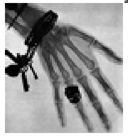

Figure 6. The first X-ray of Anna Bertha Ludwig's hand (wife of Roentgen).

Acknowledgements

Many thanks to Dr. Shauna Devine, the Schulich of Medicine and Dentistry, and the History of Medicine department for their assistance in developing this project.

Bibliography

Neither 'rushed', nor 'new': Situating the COVID-19 mRNA vaccine within a history of mRNA-based vaccine approaches for infectious diseases

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Schulich MEDICINE & DENTISTRY

Western

Introduction

Question: Drawing from current public skepticism around the COVID-19 mRNA vaccines, why are these vaccines characterized as 'new' and 'rushed'?

Argument: While **understandable**, the public's misconceptions can be **addressed** using two historical case studies: a preclinical trial for influenza in mice in 1993, which demonstrated the **effectiveness** of the mRNA platform; and a phase I clinical trial for rabies in humans in 2013, which demonstrated their **safety**.

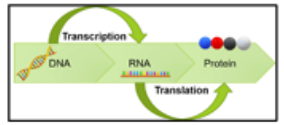

Figure 1: The Central Dogma
This flow chart outlines the relationship between DNA, RNA (or mRNA) and protein. *Adapted from biologydictionary.net/central-dogma/*

What is mRNA or 'messenger RNA'? It can best be understood using the central dogma: DNA → mRNA → protein. By connecting genetic material (DNA) with functional products (protein), it lets genetic information make its impact on cells (see Figure 1).

Why is mRNA a medicine? The first idea of using mRNA as a drug to treat disease was in 1988 by Robert Malone. Unlike DNA, mRNA does not insert into the genome, and therefore is not likely to cause cancer.

Problems with mRNA as a medicine? Unstable (short half-life), toxic delivery vehicles (liposomes or lipid nanoparticles), and can trigger unintended inflammatory responses.

Methodology and Sources

Qualitative and comparative analysis of the published scientific literature surrounding two specific mRNA vaccine clinical trials. These specific trials are:

1. **1993 influenza mRNA vaccine preclinical trial in mice**, which established mRNA's effectiveness
2. **2013 rabies mRNA vaccine phase I clinical trial in humans**, which established mRNA's safety

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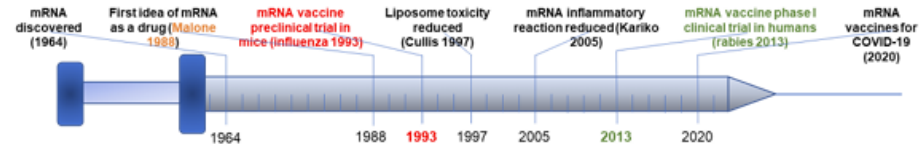

1. Influenza vaccine preclinical trial in mice (1993)

This preclinical trial in mice helped confirm the **effectiveness** of mRNA vaccines. It made three main scientific discoveries that demonstrated how to maximize the efficacy of this vaccine platform.

- **Efficacy issue: how can mRNA be efficiently delivered into cells?**
- **Solution:** Encasing the mRNA in a **liposome** (a lipid coat) prevents mRNA's degradation by stabilizing its charge (the (+) liposome binds to (-) mRNA) and fusing with the cell membranes to deliver the mRNA. Once inside, the mRNA is transcribed into protein which enters the antigen processing pathway (see Figure 2). When mRNA was injected without a liposome, no immune response occurred.

- **Efficacy issue: will the protein from the mRNA lead to an immune response?**
- **Solution:** Given that immune responses are restricted by the MHC haplotype of the organism (MHC is a molecule involved in **epitope presentation**, see Figure 2), most vaccines need to be engineered to optimize MHC-protein interactions. However, this was not the case with mRNA vaccines! It turned out that mice with three different MHC haplotypes all responded to the influenza protein encoded by the mRNA, suggesting that mRNA does not need to be reverse-engineered to fit the MHC complex. This advantage is unique to the mRNA vaccine platform.

- **Efficacy issue: what are the best injection methods and locations?**
- **Solution:** The injection method used (needle-free vs needle) and the site of injection (subcutaneous vs intramuscular vs intraperitoneal) impact how the liposome-mRNA mixture is uptaken by cells. If the liposome-mRNA mixture is damaged along the way or is not taken up by antigen-presenting cells, then no immune response will occur (see Figure 2). **Needle-free injections** subcutaneously or intramuscularly maximized mRNA uptake.

Taken together, these discoveries helped increase the effectiveness of vaccines delivered using the mRNA platform, laying the groundwork for future mRNA vaccines.

2. Rabies vaccine phase I clinical trial in humans (2013)

This phase I clinical trial in humans helped confirm the **safety** of mRNA vaccines. It was based on two preceding scientific discoveries depicted in the timeline shown above (Kariko 2005 and Cullis 1997).

- **Safety issue: how can an immune overreaction be prevented following mRNA injection?**
- **Solution:** An immune overreaction occurred with a previous mRNA vaccine, which led to cytokine storms that killed some of the recipient mice. To render the mRNA unidentifiable to the immune system, the mRNA base uridine was modified into **pseudouridine**. This dampened the immune response against the mRNA, allowing for an immune response against the protein (Kariko, *Immunity*, 2005).

- **Safety issue: how can the toxicity of the liposome-vehicle be minimized?**
- **Solution:** The liposome vehicle's (+) charge is toxic to human cells, most of which are (-). By using an **ionizable lipid**, the (+) charge is neutralized once in the alkaline environment of the blood, thereby minimizing liposome toxicity (Cullis, *European Patent* Office, 1997).

- **Safety issue: what is the vaccine safety profile in humans?**
- **Solution:** This **clinical trial was in phase I**, which is the stage that focuses on vaccine safety in humans. It showed that the mRNA vaccine was well-tolerated and indicated no risk of autoimmunity or nervous system toxicity in 101 human recipients.

Taken together, this clinical trial confirmed the safety of mRNA vaccines in humans.

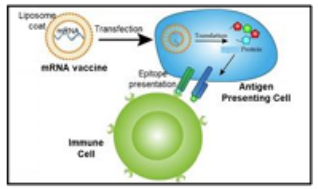

Figure 2: The antigen processing pathway
This diagram demonstrates how liposome-encased mRNAs are delivered into cells, where they trigger an immune response to their encoded protein. *Adapted from Park J.W., Int J Biol Sci, 2021.*

★ FUN FACT! ★
Robert Malone, the researcher who first created the idea of mRNA-based therapeutics, is now an **anti-vaxxer** – his LinkedIn and Twitter accounts were suspended since he was spreading so much misinformation. This is especially surprising since he was the first researcher to try to create an mRNA vaccine against common cold **coronaviruses** in 2000 (though he didn't receive funding), and that he was the first person to envision modifying mRNA and liposomes to maximize the vaccine's effectiveness.

Discussion: public skepticism considered

In revisiting the question posed in the introduction, there are many possible reasons for the public's **skepticism**, which may explain why there is a disconnect between historical cases and the public's misconceptions.

1. Science (mis)communication
The articles published by ***Nature's*** news website and ***The New York Times*** on the history of mRNA vaccines both failed to mention the influenza and rabies mRNA vaccines. Instead, both articles focus on the incremental nature of **basic science research**, which may unintentionally suggest that the mRNA vaccine is not based on **clinical research**.

2. Information "silos"
It could be argued that **researchers**, the **media**, and the **lay public** form non-overlapping information "silos", meaning that they don't share their ideas and discoveries with one another (see Figure 3). However, important external events – like the COVID-19 pandemic – bring these "silos" together.

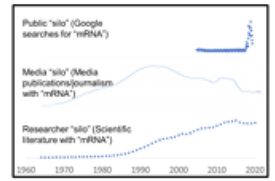

Figure 3: Information "silos"
Using the frequency of "mRNA" on different media sources, this graph supports the hypothesis that different information "silos" fail to communicate with one another. The media "silo" lost interest in mRNA in the 1990's, and the public gained interest around 2018, all while the scientific community has continuously been engaged with mRNA research since its discovery in 1964. *This graph was created using data from Google Trends and PubMed.*

3. Distrust of Big Pharma … "we've been bitten before"
For example, the ongoing opioid epidemic was fueled by pharmaceutical companies lobbying governments and downplaying the dangers of their products to maximize profits. Perhaps people fear that the COVID-19 mRNA vaccines are a similar phenomenon.
Example: Pfizer – one of two main mRNA vaccine-producers – was complicit in lobbying the government to relax regulations surrounding opioids.

4. Healthy Skepticism
In all areas of science, some skepticism is **normal**, since evidence can sometimes be incorrect. In fact, there is even a term for when previously established medical practice is supplanted by superior and contradictory evidence: **medical reversal!**
Example: The oral polio vaccine was replaced by the injected polio vaccine -- despite decades of use – due to fears of vaccine-derived polio.

Conclusion

- Public concerns that the mRNA vaccines are 'new' and 'rushed' are **understandable but may not be valid** when considering the two historical cases.
- It is understandable to be afraid of something perceived as new, but the two case studies discussed show the efficacy and safety of the mRNA vaccines, thus addressing public concerns.
- Historical clinical cases can better inform science communication, since they are **more relatable and convincing** than basic science research.

Leprosy or Lies? Stigma, Society, and the Truth in Arthur Conan Doyle's "The Adventure of the Blanched Soldier" (1926)

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Schulich MEDICINE & DENTISTRY

Western

Introduction

- *The Adventure of the Blanched Soldier* (1926, set in 1903) **examines how fear and stigma influence medical decisions.**
- Godfrey Emsworth is **wrongly assumed to have leprosy** and hidden away (3).
- The story **contrasts fear-driven assumptions with Sherlock Holmes's rational approach.**
- Doyle's narrative reveals how stigma and misdiagnosis shaped real-world medical and social responses.

Figure 1. Sherlock Holmes investigates Godfrey Emsworth's supposed illness in *The Adventure of the Blanched Soldier* (1926), contrasting rationality with fear-driven assumptions (1).

Historical Context

- Visible diseases like leprosy carried deep social stigma.
- **Leprosy as an "Imperial Danger":** Linked to colonial anxieties (India, South Africa, West Indies) (4).
- **Medical Misdiagnosis:** Doctors relied on visual symptoms, confusing leprosy with psoriasis, syphilis, and vitiligo (5).
- **Fear-driven isolation** → Patients confined to colonial asylums to maintain purity.
- **1903:** Leprosy fears reflected colonial anxieties. Diagnosis relied on visual symptoms and outdated medical ideas.
- **1926:** Medicine was challenging old diagnostic methods, explaining Holmes's emphasis on logic over fear.

Textual Analysis

Fear-Driven Misdiagnosis

- Godfrey returns from **South Africa** with **blotchy skin** → His father **assumes leprosy** and isolates him.
- Diagnosis is **based on fear**, not medical consultation.
- Reflects how **stigma influenced disease responses** in history.

Stigma & Social Isolation

- **Leprosy as a metaphor for exclusion** → Godfrey is hidden to avoid scandal.
- **Erving Goffman's "spoiled identity"**: Stigmatized individuals become defined by their condition (6).
- *Godfrey: "I am no longer a man. I am a ghost."* (3) → Highlights psychological impact of exclusion.

Holmes's Rational Approach

- **Rejects assumptions** → Investigates beyond visible symptoms.
- **Uses deductive reasoning → Rules out leprosy, correctly identifies ichthyosis.**
- **Contrasts fear vs. logic** → Shows how misdiagnosis stems from stigma, not science.

Figure 2. 19th-century photograph of a man with leprosy (Hansen's disease), showing facial and hand deformities (2).

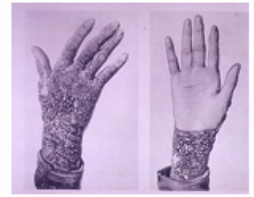

Figure 3. Medical illustration of ichthyosis, a non-contagious genetic skin condition that does not cause nerve damage, unlike leprosy (9).

Broader Implications

HIV/AIDS & Stigma (1980s-90s)

- **Visible symptoms** → led to fear, **isolation, and moral judgment** (7).
- **Parallels with leprosy stigma** → Disease seen as **moral & social contamination,** not just a medical issue.

Medical Bias & Dermatology Today

- **Non-white patients misdiagnosed more often** → Skin conditions look different on darker skin but training is Eurocentric (8).
- **Superficial diagnosis** → Leads to delayed or incorrect treatment.

Literature as a Lens for Exposing Bias

- The story does not openly critique medical bias but highlights how **fear distorts diagnosis**.
- Medicine must be **evidence-based**, not fear-driven.

Conclusion

- **Assumptions lead to harm** → Godfrey's isolation shows the dangers of fear-driven medicine.
- Holmes models a **better approach** → rational diagnosis over panic and stigma.
- The story **remains relevant** → modern medicine still grapples with bias in diagnosis.

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From Head to Tool: Mapping Dermatomes Through the Ages

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Introduction

> "...[H]e was suffering from the loss of sensation in the two small fingers and half of the middle finger of his left hand···The doctors had failed in their treatment because they did not know that the nerves supplying sensation to the upper limb have specific roots: with my anatomical knowledge I was able to attend to the spine and so restore sensation to the hand"
> - Galen of Pergamum (AD 130-210)

- Late 19th century: basis of the dermatome discovered
- **Dermatome**: an area of skin innervated by a single dorsal nerve root
- **Dermatome map**: sensory distribution of multiple dermatomes
- Key diagnostic tool in the **neurological sensory exam**
- Localise neurologic injuries such as **spinal root lesions**, identifying regions of referred pain and anesthesia

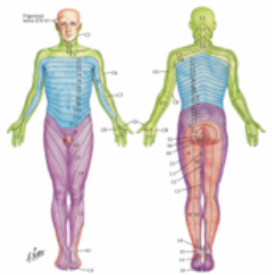

Figure 1. Dermatome map from Netter's Anatomy Textbook 7th Edition (2019).

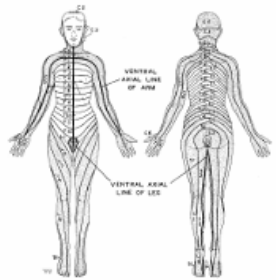

Figure 2. The original dermatome map by Keegan and Garrett (1948) from which Netter's schematic is based on.

- Modern textbooks often do not or poorly reference the maps
- Moreover, there is no universally standard dermatome map, so maps presented vary from textbook to textbook
- Interpretation of dermatome maps require an understanding that they are more complex than the static diagram often presented

Methodology

Through qualitative analysis of scientific journal articles, reviews, and textbooks on dermatome maps from the 19th & 20th centuries:

- Examine key findings that contribute to the evolving interpretation of dermatome maps
- Explore theories for conflicting dermatome maps and its relevance to clinical practice

Historical Narrative

Figure 3. Neurologists Dr. Henry Head (1861-1940) on the left and Dr. Alfred W. Campbell (1868-1937) on the right.

Early Understanding of Dermatomes

- Dermatomes believed to consist of **discrete bodily regions** where sensation from one location corresponded to one nerve root
- Map represents **typical distribution**
- However, factors such as age, body size, and skin stretching can lead to **variations** between people
- Adjacent dermatomes **overlap** (greater in limbs than in trunk)

Sensory Modalities

- Each modality of somatic sensation has a unique map
- Dermatome sizes vary by sensory modality; typically from largest to smallest: **pain > temperature > tactile sensation**

Figure 5. Setup (left) of Kirk and Denny-Brown's study in 1970. Lesions of neighboring dorsal root ganglia (middle) or spinal roots (right) resulted in larger and smaller sizes of the non-lesioned dermatome of interest (red) respectively.

First Dermatome Map

- Published in 1900 by neurologists **Dr. Henry Head** (1861-1940) and **Dr. Alfred W. Campbell** (1868-1937) based on findings from patients with **shingles**
- Based on 450 photographs and drawings of observed cases and 21 post-mortem dissections
- Segmental areas represent observed eruption of shingles on skin, each corresponding to a disturbed nerve root as labeled

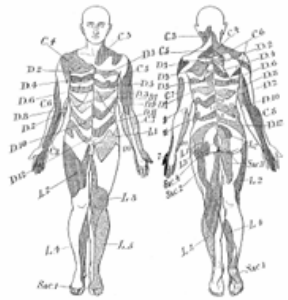

Figure 4. The first published dermatome map by Head and Campbell (1900).

Static to Dynamic

- Lesion studies in monkey model
- **Physiological changes** in dermatome pathways affect neighboring dermatome sizes
- Functional dermatome pathways help maintain the size of neighboring dermatomes
- Dermatome size can **expand** if dorsal root ganglia from neighboring dermatome pathways are inhibited
- Dermatome size can **contract** if neighboring spinal roots are lesioned

Discussion

Reasons for Conflicting Maps

- Methodology: different **lesion locations** (eg. spinal roots, dorsal root ganglia, mixed fibers), correlating **cutaneous vs deep fascial pain**
- Anatomy: differing presentations due to clinical pathology vs experimental nerve lesions, sensation from one bodily location can in fact correspond to **more than one nerve root** (up to 5)

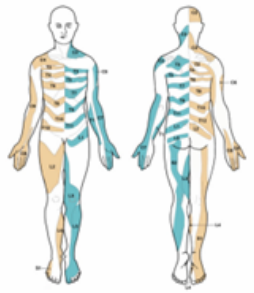

Figure 6. Evidence based dermatome map by Lee et al., 2008. Large blank areas represent dermatome overlap.

Modern Dermatome Map

- In 2008, Lee et al., constructed a **dermatome map based on evidence** from high quality spinal root lesion studies

Clinical Significance of Conflicting Dermatome Maps

- Despite representing typical distribution of dermatomes, dermatome maps can **vary in individuals** due to individual differences
- Consideration of **appropriate maps** for sensory modality
- Sensory signals from one location can be sent to **many spinal roots**
- Dermatome sizes and location can **shift within a patient** depending on lesion location, time after initial lesion, and compensatory signals from neighboring dermatome pathways

Acknowledgements

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From Cancer-Causing to Tumour-Suppressing: A Pivotal Shift in the Understanding of the p53 Protein in Cancer

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Introduction

- The *TP53* gene encodes for p53, a protein that plays an important role in recognizing DNA damage and driving damaged cells to self-destruct (**Fig. 1**).[1]
- Without properly functioning p53, cells with abnormal, damaged DNA may continue to proliferate, such as cancer cells.[1]

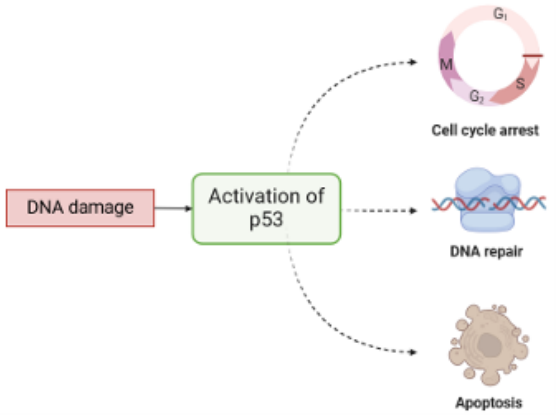

Figure 1. Various functions of the p53 protein in response to DNA damage.

- p53 is currently recognized as a "tumour suppressor". **However, when p53 was first discovered, it was mischaracterized as "cancer-causing".**
  - ➢ This (mis)understanding was shifted in the late 1980s, when researchers realized that the p53 protein has, in fact, the opposite function.

The Shift from Cancer-Causing to Tumour-Suppressing

1979: A new protein (p53) was independently discovered by many researchers studying cancer.

1983: The first p53 workshop was held.
- Took place at The Marie Curie Research Institute in the UK.
- It was at this workshop that the name "p53" was officially assigned to this new protein.

Mid-1980's: p53 was generally accepted as an oncogene.
- There was growing evidence that p53 was a new "cancer-causing" protein.
- The evidence in favour of this association between p53 and cancer was quite strong, with studies consistently showing that cancerous cells had elevated levels of p53 while non-cancerous cells did not.[2]

Late 1980's: THE PIVOTAL SHIFT

- A key paper from the Levine Lab (**Fig. 2**) at Princeton University found that, contradictory to previous work, the p53 clone they were working with could not transform cells into cancerous cells.[3]
- The researchers compared the DNA sequences of p53 clones and proposed that previous studies were conducted with mutated versions of p53 rather than the normal, non-mutated p53 that would be found in healthy cells (**Fig. 3**).

Figure 2. Arnold Jay Levine, an American molecular biologist. Photo from https://www.ias.edu/sns/alevine

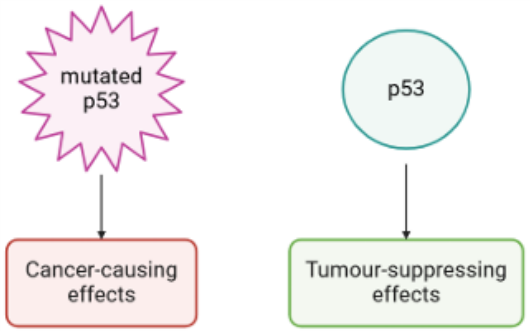

Figure 3. Mutated p53 (left) vs. wildtype p53 (right).

- With this newfound understanding, subsequent research on p53 quickly established that this protein contributes to preventing cancer rather than causing it.

Impact

- This understanding of p53 as a tumour suppressor was instrumental for cancer research.
  - ➢ p53 mutations have been identified as being the hallmark of many cancers.
  - ➢ Targeted cancer treatments have been developed to restore normal p53 function.
- This pivotal shift in our understanding of the p53 protein also underscores the importance of questioning prevailing beliefs and remaining open to unexpected discoveries.

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