The Body's Guided Missile System of Defense

The Importance of Antibodies

By

AJ Russo

The Body's Guided Missile System of Defense: The Importance of Antibodies

by AJ Russo

2025

Ethics International Press, UK

British Library Cataloguing in Publication Data

A catalogue record for this book is available from the British Library

ISBN (Hardback): 978-1-83711-355-2

ISBN (Ebook): 978-1-83711-356-9

Table of Contents

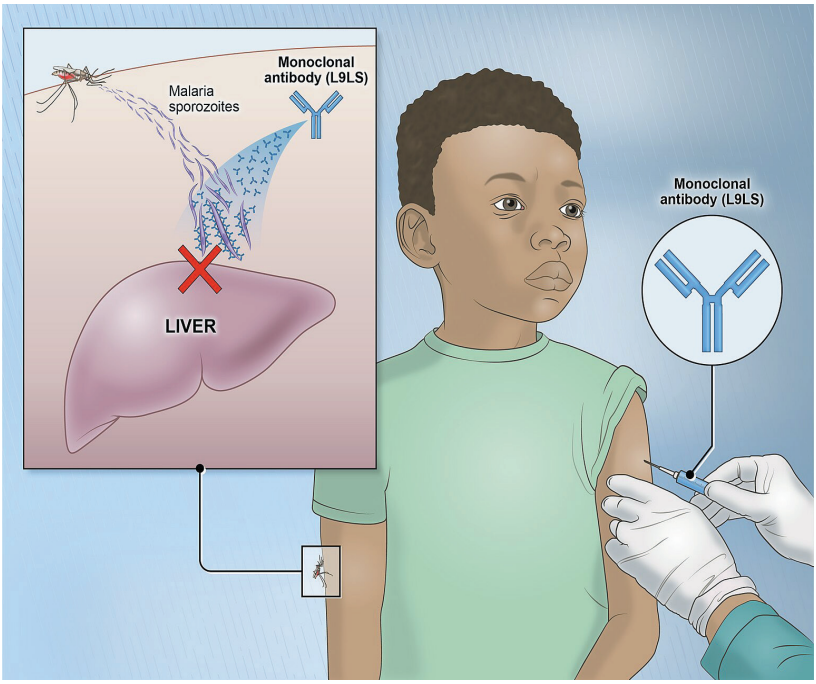
Introduction

Imagine nearly half a million children dying of a disease each year. Impossible with today's medical expertise, right? Wrong. Two hundred forty-one million children contract malaria each year, and nearly 500,000 of those die. Luckily, there are a couple of very promising therapies on the horizon. One of these, antibody therapy, is the basis for this book.

Monoclonal antibodies (mAbs) represent a promising frontier in the fight against malaria, offering a novel approach to prevention and treatment. They are engineered to target specific proteins of the malaria-causing parasite, Plas modium falciparum, thereby preventing infection.

Recent studies have shown that mAbs can provide significant protection against malaria. For instance, the monoclonal antibody CIS43LS demonstrated up to 88.2% efficacy in preventing malaria infection over six months in Mali, Africa (1). Another antibody, L9LS, has shown promise due to its ability to be administered subcutaneously, offering a more convenient delivery method than intravenous infusion (2,3).

Several clinical trials have assessed the safety and efficacy of monoclonal antibodies against malaria. A Phase 2 trial in Mali demonstrated that a single dose of CIS43LS effectively prevented malaria infection in adults during the peak malaria season (4,5). Similarly, L9LS has shown 77% efficacy in protecting children from symptomatic malaria in a recent Phase 2 trial (6). These trials highlight the potential of mAbs as a complementary strategy to existing malaria prevention measures (7,8).



Introduction Fig.1 *A single injection of an experimental monoclonal antibody called L9LS prevented malaria infection in children in Mali. L9LS binds to and neutralizes "sporozoites," the form of the malaria parasite transmitted by mosquitoes that invades the liver to initiate infection. Credit: NIH See related April 26, 2024 news release, "Experimental NIH Malaria Monoclonal Antibody Protective in Malian Children," at* www.niaid.nih.gov/news-events/experimental-nih-malaria-mo... *NIAID* https://www.flickr.com/photos/54591706@N02/53687072608/

There are challenges to the widespread use of these antibodies. The high cost of production and administration is a significant barrier, particularly in low- and middle-income countries where malaria is most prevalent (9). Efforts are underway to reduce costs and improve the accessibility of mAbs, with organizations like the Gates Foundation investing in technologies to make these treatments more affordable (10).

The development of monoclonal antibodies for malaria prevention is ongoing, with researchers focusing on optimizing the biophysical properties of these antibodies for cost-effective manufacturing and dosing, especially in pediatric populations (11). The discovery of new antibody lineages and the engineering of potent, long-lasting mAbs are crucial steps toward making these treatments viable for large-scale use (12).

Antibodies for Alzheimer's

As our life expectancy continues to rise, diseases of dementia and particularly Alzheimer's Disease have become more prevalent.

Monoclonal antibodies (mAbs) have also emerged as a promising therapeutic approach for Alzheimer's disease (AD), particularly targeting amyloid-beta (Aβ) plaques, which are believed to play a crucial role in the disease's progression.

Aducanumab and lecanemab are two mAbs that have received accelerated approval from the US FDA for treating early Alzheimer's disease in patients with confirmed β-amyloid pathology. These treatments mark a significant step forward in Alzheimer's therapeutics, offering disease-modifying properties that were previously unavailable (13,14).

Both aducanumab and lecanemab work by significantly reducing total brain Aβ, as evidenced by amyloid positron emission tomography (PET) scans. This reduction is associated with a slowing of cognitive decline, which is clinically meaningful as it extends cognitive integrity and delays the onset of severe dementia phases (15,16).

Donanemab is another promising monoclonal antibody that has shown potential in clinical trials. It has been observed to slow disease progression in amyloid-positive, early symptomatic patients over 76

weeks. Notably, about half of the participants on donanemab experienced no clinical progression at one year (17). However, the treatment does come with safety risks and limitations, and its effectiveness outside of structured research settings remains uncertain (18).

FDA-approved anti-Aβ mAbs have demonstrated statistically significant improvements in clinical outcomes, including various cognitive and functional scales such as CDR-SB and ADAS-Cog. These improvements suggest that mAbs can effectively enhance daily life activities in mild or moderate AD (19,20).

Despite their benefits, mAbs are associated with increased risks of adverse events, such as amyloid-related imaging abnormalities (ARIA), cerebral edema, and hemorrhage. These risks highlight the need for careful patient selection and monitoring during treatment (21,22).

The development of Aβ-targeting monoclonal antibodies represents the beginning of a new era in molecular therapies for Alzheimer's and related neurodegenerative disorders. While these treatments offer hope, they also underscore the complexity of Alzheimer's disease and the need for continued research to optimize their use and minimize risks (23,24).

Antibody Therapy for COVID

Antibody therapy, particularly monoclonal antibodies, has emerged as a significant tool in the fight against COVID-19, especially for individuals with compromised immune systems.

The FDA has recently authorized a new monoclonal antibody treatment, Pemgarda, specifically designed to protect immunocompromised individuals from COVID-19. This treatment is a successor to Evusheld, which was withdrawn due to its ineffectiveness against new variants (25). Pemgarda is administered as an hour-long infusion and

is expected to be available to about 6% of the U.S. population, targeting those who are severely or moderately immunocompromised (26).

Monoclonal antibodies like Pemgarda provide passive immunization, offering an additional layer of protection for those with compromised immune systems. However, they are not intended for treating active COVID-19 infections (27). The development of new variants has challenged the efficacy of previous monoclonal antibodies, such as Evusheld, which could not keep up with the evolving virus (28).

Globally, monoclonal antibodies have been a preferred therapeutic solution for vulnerable individuals, although many have lost efficacy against newer variants like Omicron (29). In France, for instance, around thirty monoclonal antibodies are authorized for various diseases, but none are currently approved for preventive use against COVID-19 (30).

The ACTIV clinical trials have been pivotal in evaluating the safety and efficacy of monoclonal antibodies. ACTIV-2 and ACTIV-3 protocols focused on outpatient and inpatient settings, respectively, assessing the ability of these therapies to reduce symptoms and improve recovery in COVID-19 patients (31). These trials have highlighted the potential of monoclonal antibodies in non-hospitalized patients with mild-to-moderate symptoms (32,33).

The development of monoclonal antibodies is rooted in a long history of immunological interventions, dating back to the first therapeutic serum for diphtheria over 125 years ago (34). Today, the production of recombinant monoclonal antibodies is scalable and cost-competitive, making them a viable option for widespread use (35).

Monoclonal Antibodies to Combat Cancer

Monoclonal antibodies (mAbs) have become a cornerstone in cancer therapy due to their ability to target cancer cells specifically.

Antibody-drug conjugates (ADCs) are a novel monoclonal antibody class with significant promise in cancer treatment. They work by linking a cytotoxic drug to an antibody, which targets specific antigens on cancer cells, thereby delivering the drug directly to the tumor site. This targeted approach enhances the antitumor efficacy while minimizing systemic toxicity (36). The FDA has approved several ADCs; many more are under clinical investigation, highlighting their growing importance in oncology (37).

Notable ADCs

1. **Gemtuzumab Ozogamicin (GO)**: This was the first ADC to receive global market approval. It targets CD33 and is used in the treatment of acute myeloid leukemia (38,39).

2. **Brentuximab Vedotin (BV)**: Approved for the treatment of Hodgkin lymphoma and systemic anaplastic large cell lymphoma, BV targets CD30 and is linked to a microtubule-disrupting agent (40,41).

3. **Trastuzumab Emtansine (T-DM1)**: This ADC targets HER2-positive breast cancer by combining trastuzumab with the cytotoxic agent DM1 (42,43).

4. **Inotuzumab Ozogamicin (InO)**: Used for relapsed or refractory B-cell acute lymphoblastic leukemia, this ADC targets CD22 (44,45).

5. **Polatuzumab Vedotin (PV)** Targets CD79b and is combined with other therapies for treating diffuse large B-cell lymphoma (46,47).

6. **Enfortumab Vedotin (EV)**: Targets Nectin-4 and is used in urothelial carcinoma (48,49).

7. **Trastuzumab Deruxtecan (T-DXd)**: Another HER2-targeting ADC, it is used for breast cancer and other HER2-expressing tumors (50,51).

These antibodies work by stimulating the immune system to attack cancer cells. Examples include anti-CTLA-4, which is in phase III trials for malignant melanoma, and other antibodies targeting immune checkpoints and co-stimulatory receptors (52).

Several monoclonal antibodies have been well-established in cancer treatment over the years. These include:

- **Rituximab (Rituxan®)**: Used for non-Hodgkin lymphoma and chronic lymphocytic leukemia (53).
- **Trastuzumab (Herceptin®)**: A key treatment for HER2-positive breast cancer (54).
- **Bevacizumab (Avastin®)**: Used for various cancers, including colorectal and lung cancer, by inhibiting angiogenesis (55).

Monoclonal antibodies to Malaria, Alzheimer's, COVID-19, and Cancer represent a fraction of the current and futuristic ways antibodies can be used for therapy. Antibodies are also a valuable tool for use as diagnostic and research tools.

This book is a comprehensive look at the biology of antibodies, how they are produced in the body and laboratory, how they are currently used in therapy, diagnosis, and research, and their possible future in medicine.

References Introduction

[1] https://www.nih.gov/news-events/news-releases/monoclonal-antibody-prevents-malaria-infection-african-adults#:~:text=One%20dose%20of%20an,malaria%20season%20in%20Mali%2C

[2] https://www.nih.gov/news-events/news-releases/monoclonal-antibody-prevents-malaria-infection-african-adults#:~:text=Dr.%20Seder%20and%20colleagues,rather%20than%20by%20intravenous

[3] https://www.bioanalysis-zone.com/new-monoclonal-antibody-treatment-for-malaria-a-breakthrough-on-the-horizon/#:~:text=L9LS%20targets%20another%20conserved,absorbed%20over%20a%20longer

[4] https://www.nih.gov/news-events/news-releases/monoclonal-antibody-prevents-malaria-infection-african-adults#:~:text=The%20Phase%202%20NIAID%2DUSTTB,a%20monoclonal%20antibody%20called

[5] https://www.iavi.org/iavi-report/monoclonal-antibodies-for-malaria-prevention-iavireport/

[6] https://www.iavi.org/iavi-report/monoclonal-antibodies-for-malaria-prevention-iavireport/

[7] https://www.nih.gov/news-events/news-releases/monoclonal-antibody-prevents-malaria-infection-african-adults#:~:text=These%20study%20results%20suggest,malaria%20from%20defined%20geographical

[8] https://www.nature.com/articles/s41591-023-02659-z

[9] https://www.iavi.org/iavi-report/monoclonal-antibodies-for-malaria-prevention-iavireport/

[10] https://www.iavi.org/iavi-report/monoclonal-antibodies-for-malaria-prevention-iavireport/

[11] https://www.nature.com/articles/s41591-023-02659-z#:~:text=1%29%20a%20potent%20and,and%20dosing%20in%20pediatric

[12] https://www.nature.com/articles/s41591-023-02659-z

[13] https://pubmed.ncbi.nlm.nih.gov/37955845/#:~:text=Two%20monoclonal%20antibodies%20%28mAbs%29%2C,have%20proven%20β%2Damyloid%20pathology

[14] https://eurjmedres.biomedcentral.com/articles/10.1186/s40001-023-01512-w#:~:text=Drugs%20aimed%20at%20slowing,lecanemab%20on%20January%2022%2C

[15] https://pubmed.ncbi.nlm.nih.gov/37955845/#:~:text=Anti%2Damyloid%20mAbs%20share%20the,by%20amyloid%20positron%20emission

[16] https://eurjmedres.biomedcentral.com/articles/10.1186/s40001-023-01512-w#:~:text=FDA%2Dapproved%20anti%2DAβ%20mabs%20perform,%28PET%20SUVr%29%20%28P%20%3C

[17] https://www.ama-assn.org/delivering-care/public-health/promising-monoclonal-antibody-joins-fight-against-alzheimer-s#:~:text=donanemab%20slowed%20clinical%20disease,disease%20patients%20over%2076

[18] https://www.ama-assn.org/delivering-care/public-health/promising-monoclonal-antibody-joins-fight-against-alzheimer-s#:~:text=The%20trial%20delivered%20clinically,safety%20risks%20and%20some

[19] https://eurjmedres.biomedcentral.com/articles/10.1186/s40001-023-01512-w#:~:text=FDA%2Dapproved%20anti%2DAβ%20mabs%20showed,including%20CDR%2DSB%20%28P%20%3D

[20] https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2023.1147757/full

[21] https://eurjmedres.biomedcentral.com/articles/10.1186/s40001-023-01512-w#:~:text=The%20FDA%2Dapproved%20anti%2Damyloid%2Dβ%20monoclonal,meta%2Danalysis%20of%20randomized%20controlled

[22] https://www.medicalnewstoday.com/articles/alzheimers-treatments-the-risk-of-monoclonal-antibodies-may-outweigh-benefits#Potential-risks-with-monoclonal-antibodies

[23] https://pubmed.ncbi.nlm.nih.gov/37955845/#:~:text=Approval%20of%20these%20agents,disease%20therapeutics%20with%20disease%2Dmodifying

[24] https://www.ama-assn.org/delivering-care/public-health/promising-monoclonal-antibody-joins-fight-against-alzheimer-s#:~:text=The%20emergence%20of%20Aβ%2Dtargeting,AD%20and%20related%20neurodegenerative

[25] https://www.healthline.com/health-news/fda-oks-new-drug-to-boost-covid-19-protection-for-immunocompromised-people#:~:text=The%20FDA%20has%20authorized,people%20be%20protected%20from

[26] https://www.healthline.com/health-news/fda-oks-new-drug-to-boost-covid-19-protection-for-immunocompromised-people#:~:text=Pemgarda%2C%20which%20is%20expected,infusion%20at%20a%20medical

[27] https://www.healthline.com/health-news/fda-oks-new-drug-to-boost-covid-19-protection-for-immunocompromised-people#What-makes-this-treatment-different-from-past-infusions

[28] https://www.healthline.com/health-news/fda-oks-new-drug-to-boost-covid-19-protection-for-immunocompromised-people#Why-was-Evusheld-not-effective

[29] https://www.pasteur.fr/en/research-journal/reports/covid-19-which-monoclonal-antibodies-should-be-used-vulnerable-individuals#:~:text=monoclonal%20antibodies%20have%20long,been%20the%20preferred%20therapeutic

[30] https://www.pasteur.fr/en/research-journal/reports/covid-19-which-monoclonal-antibodies-should-be-used-vulnerable-individuals#:~:text=Definition%20%2D%20What%20are%20monoclonal

[31] https://www.nih.gov/research-training/medical-research-initiatives/activ/covid-19-therapeutics-prioritized-testing-clinical-trials#:~:text=ACTIV%2D2%3A%20Outpatient%20Monoclonal%20Antibodies%20and%20Other

[33] https://www.nature.com/articles/s41577-021-00542-x#:~:text=In%20the%20United%20States%2C,imdevimab%20as%20a%20combination

[34] https://www.nature.com/articles/s41577-021-00542-x#:~:text=More%20than%20125%20years,actively%20immunized%20against%20diphtheria

[35] https://www.nature.com/articles/s41577-021-00542-x#:~:text=Today%2C%20the%20process%20to,is%20cost%2Dcompetitive%20with%20other

[36] https://www.nature.com/articles/s41392-021-00868-x#:~:text=The%20antitumor%20efficacy%20of,of%20antibody%20derivative%2C%20an

[37] https://www.nature.com/articles/s41392-021-00868-x#:~:text=The%20FDA%20has%20approved,ADCs%20are%20under%20clinical

[38] https://www.nature.com/articles/s41392-021-00868-x#:~:text=46%20GO%20is%20a,the%20toxin%20to%20the

[39] https://molecular-cancer.biomedcentral.com/articles/10.1186/s12943-024-01963-7#:~:text=GO%2C%20the%20pioneering%20ADC,to%20receive%20global%20market

[40] https://www.nature.com/articles/s41392-021-00868-x

[41] https://molecular-cancer.biomedcentral.com/articles/10.1186/s12943-024-01963-7#:~:text=BV%2C%20initially%20developed%20by,the%20second%20approved%20ADC

[42] https://www.nature.com/articles/s41392-021-00868-x#:~:text=Ado%2Dtrastuzumab%20emtansine%20%28also%20known,via%20a%20stable%20thioether

[43] https://molecular-cancer.biomedcentral.com/articles/10.1186/s12943-024-01963-7#:~:text=T%2DDM1%20is%20an%20ADC,DM1%29%20via%20a%20thioether

[44] https://www.nature.com/articles/s41392-021-00868-x

[45] https://molecular-cancer.biomedcentral.com/articles/10.1186/s12943-024-01963-7#:~:text=InO%20is%20an%20ADC,calicheamicin%20through%20an%20acid%2Dunstable

[46] https://www.nature.com/articles/s41392-021-00868-x

[47] https://molecular-cancer.biomedcentral.com/articles/10.1186/s12943-024-01963-7#:~:text=Polatuzumab%20vedotin

[48] https://www.nature.com/articles/s41392-021-00868

[49] https://molecular-cancer.biomedcentral.com/articles/10.1186/s12943-024-01963-7#:~:text=EV%20is%20an%20ADC,MMAE%20through%20a%20cleavable

[50] https://www.nature.com/articles/s41392-021-00868-x

[51] https://molecular-cancer.biomedcentral.com/articles/10.1186/s12943-024-01963-7#:~:text=Trastuzumab%20deruxtecan

[52] https://www.nature.com/articles/nrc2051#:~:text=Using%20mAbs%20to%20stimulate,new%20indirect%20mode%20of

[53] https://www.nature.com/articles/7310143#:~:text=Rituximab

[54] https://www.nature.com/articles/7310143#:~:text=Trastuzumab

[55] https://www.nature.com/articles/7310143#:~:text=Bevacizumab

Part I

History

Chapter 1

Overview of Early Experiments and Discoveries

Smallpox Inoculation (1714-1717)

The journey of the understanding of antibodies began in the early 18th century with efforts to combat smallpox. Lady Mary Wortley Montagu, Emanuel Timoni, and James Pylarini were pioneers in smallpox inodculation, laying the groundwork for future immunological research (1).

Chapter 1 Fig 1 *A portrait of* Lady Mary Wortley Montagu, *wife to the ambassador of the Ottoman Empire and forerunner of the variolation movement in England.*

Chapter 1 Fig 2 Ivory and box wood vaccinator, Europe, 1701-1800 Wellcome L0058083.jpg *This file comes from* Wellcome Images, *a website operated by Wellcome Trust, a global charitable foundation based in the United Kingdom. Refer to* Wellcome blog post *(*archive*).*

The history of smallpox vaccination does not necessarily start with Edward Jenner's (1749-1823) introduction of a cowpox vaccine in 1798. A procedure known as variolation was devised in China about a thousand years ago and then spread westwards to Turkey and several other Islamic countries. In variolation, material from smallpox pustules was given to an undinfected person by blowing dried smallpox scabs into their nose in the expectation that they would contract a milder form of the disease and so be protected from more dangerous infections. This method was brought to England by Lady Mary Wortley Montague (1689-1762) in 1720. It was made illegal in the United Kingdom in 1840 as it could spread the disease further while also transmitting other diseases, such as syphilis.

Serum Therapy (1890)

In 1890, Emil von Behring and Shibasaburo Kitasato demonstrated that serum from animals immunized against diphtheria could cure infected animals. This experiment was crucial in proving the therapeutic potential of antibodies (2,3).

Antitoxin Production (1894)

To treat diphtheria in humans, larger quantities of antitoxin were needed. Pharmaceutical companies began immunizing sheep and horses, significantly reducing mortality rates (4).

Paul Ehrlich's Hypothesis (1897)

Paul Ehrlich proposed that cells have side chains that bind to toxins, coining the term "antibody" and describing it as a branched molecule. This theoretical framework was foundational for future antibody research (5,6)

Advances in Antibody Characterization

Protein Nature of Antibodies (1923)

Michael Heidelberger and Oswald Avery discovered that antibodies are proteins, dispelling the mystical views surrounding them and solidifying their biochemical nature (7).

Plasma Cells and Antibody Production (1948)

Swedish immunologist Astrid Fagraeus identified plasma cells as crucial for antibody production, enhancing our understanding of the immune response (8).

Molecular Structure (1959)

Rodney Porter and Gerald Edelman independently published the molecular structure of antibodies, a discovery that earned them the Nobel Prize in Physiology or Medicine (9).

Modern Era of Antibody Research

Monoclonal Antibodies (1975)

The modern era of antibody research was revolutionized by Georges Köhler and César Milstein, who invented monoclonal antibodies. This breakthrough allowed for the production of antibodies with high specificity and uniformity (10).

Humanized Monoclonal Antibodies (1980s)

Greg Winter and colleagues at Cambridge University developed techniques to humanize mouse and rat monoclonal antibodies, making them suitable for therapeutic use in humans (11).

Phage Display Technology (1985)

Winter's development of antibody phage display enabled the discovery of antibodies to almost any target by using a library of human gene fragments inserted into bacteriophage DNA. This technology

has been instrumental in the development of numerous therapeutic antibodies (12).

Recent Innovations and Applications

High-Throughput Screening (2023)

Recent advancements include the use of the Illumina HiSeq platform for rapid screening of antibody-antigen interactions. This method significantly accelerates the discovery of high-affinity antibodies, reducing the time from months to just a few days (13).

Machine Learning in Antibody Discovery (2023)

Machine learning models trained on antibody-antigen interactions are now being used to generate new high-affinity antibody sequences, further enhancing the efficiency of antibody discovery (14).

Therapeutic Applications

Monoclonal antibodies have become one of the most important classes of biological drugs used in treating diseases such as rheumatoid arthritis, multiple sclerosis, and cancer. The development of recombinant antibodies and engineered variants like afucosylated antibodies has expanded their therapeutic potential (15,16).

Conclusion

The discovery and development of antibodies have been marked by a series of groundbreaking experiments and innovations. From early inoculation practices to modern high-throughput screening and machine learning techniques, each milestone has contributed to

our current understanding and utilization of antibodies in medicine and research.

References Chapter 1

[1] https://www.evitria.com/journal/antibodies/history-antibodies

https://www.evitria.com/journal/antibodies/history-antibodies/

[3] https://ki.se/en/research/popular-science-and-dialogue/spotlight-on/spotlight-on-covid-19/the-history-of-antibodies#

[4] https://ki.se/en/research/popular-science-and-dialogue/spotlight-on/spotlight-on-covid-19/the-history-of-antibodies#

[5] https://www.evitria.com/journal/antibodies/history-antibodies/#

[6] https://ki.se/en/research/popular-science-and-dialogue/spotlight-on/spotlight-on-covid-19/the-history-of-antibodies#

[7] https://ki.se/en/research/popular-science-and-dialogue/spotlight-on/spotlight-on-covid-19/the-history-of-antibodies#

[8] https://ki.se/en/research/popular-science-and-dialogue/spotlight-on/spotlight-on-covid-19/the-history-of-antibodies#

[9] https://ki.se/en/research/popular-science-and-dialogue/spotlight-on/spotlight-on-covid-19/the-history-of-antibodies#:

[10] https://www.evitria.com/journal/antibodies/history-antibodies/#

[11] https://www.cam.ac.uk/stories/antibodies-research-nobel-prize#

[12] https://www.cam.ac.uk/stories/antibodies-research-nobel-prize#

[13] https://www.nature.com/articles/s41551-023-01093-3#

[14] https://www.nature.com/articles/s41551-023-01093-3#

[15] https://www.evitria.com/journal/antibodies/history-antibodies/#

[16] https://www.cam.ac.uk/stories/antibodies-research-nobel-prize#

Chapter 2

Variolation and the Development of a Smallpox Vaccine

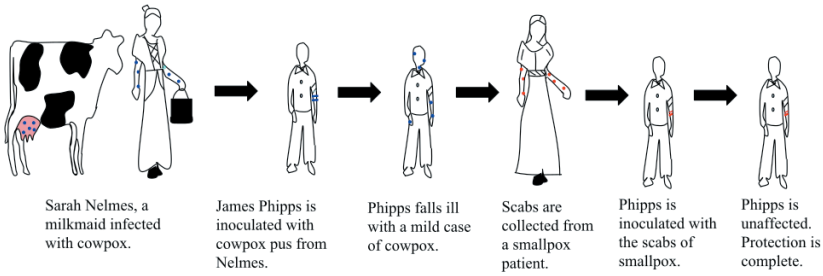
Smallpox was one of the deadliest infectious diseases known to humanity, causing millions of deaths before the advent of effective immunization strategies. The journey from variolation to the development of the smallpox vaccine marks a significant milestone in medical history.

Variolation: The Early Method of Immunization

Variolation was an early method of immunization against smallpox, practiced widely in the Ottoman Empire, England, and the U.S. colonies by the 18th century (1). This method involved deliberately infecting a person with material from smallpox sores, usually under the supervision of a physician, to elicit an immune response without causing a full-blown infection (2). Despite its risks, variolation was the only known way to prevent smallpox infection before 1796 (3).

The Birth of Vaccination

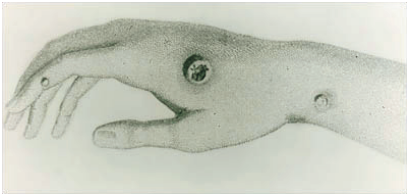
The practice of variolation was eventually replaced by vaccination, a safer and more effective immunization strategy (4). The basis for vaccination began in 1796 when the English physician Edward Jenner observed that milkmaids who had contracted cowpox did not get smallpox (5). Jenner hypothesized that inoculating a person with the cowpox virus would protect them from smallpox (6). He tested this hypothesis by inoculating an 8-year-old boy, James Phipps, with matter from a cowpox sore, which successfully rendered the boy immune to smallpox (7).



Chapter 2 Fig 1 *The process above shows the steps taken by Edward Jenner to create vaccination. Edward Jenner, the father of vaccination, created the first vaccine for smallpox. He did this by inoculating James Phipps with cowpox, a similar virus to smallpox, to create immunity, unlike variolation, which used smallpox to generate immunity to itself.* Srcyr16

The Impact of Jenner's Discovery

Edward Jenner's detailed description of his experiments convinced his colleagues and authorities that vaccination with cowpox was preferable in terms of safety compared to variolation (8). By 1803, Jenner's findings had been translated into multiple languages, and vaccination campaigns were launched in the Americas and the Far East (9). This marked the beginning of a global effort to control and eventually eradicate smallpox.



Chapter 2 Fig 2 *This shows accidental cowpox on the hand of Sarah Nelmes, from whom Jenner vaccinated James Phipps in 1796. Published in his Inquiry, 1798. From the USA NLM of the NLH (who have now, in March 2014, removed it to the vaccination page) who do not assert copyright and, in general, provide pictures under PD. This is a very old image.*

The Eradication of Smallpox

The development of the smallpox vaccine was a significant milestone in the history of medicine (4). It not only led to the eradication of smallpox but also paved the way for the development of vaccines for other diseases, such as diphtheria, measles, mumps, rubella, and influenza (1). In 1980, the World Health Organization (WHO) declared smallpox officially eradicated, marking the end of a disease that had killed millions (10,11).

Conclusion

Variolation was an important step in the history of immunization, but it was the development of the smallpox vaccine by Edward Jenner that truly revolutionized the control of infectious diseases. Jenner's work not only saved countless lives but also laid the foundation for modern vaccinology, leading to the development of vaccines for numerous other diseases and the eventual eradication of smallpox.

References Chapter 2

[1] https://www.who.int/news-room/spotlight/history-of-vaccination/history-of-smallpox-vaccination#

[2] https://historyofvaccines.org/history/edward-jenner-frs-frcpe/overview

[3] https://historyofvaccines.org/history/edward-jenner-frs-frcpe/overview

[4] https://www.who.int/news-room/spotlight/history-of-vaccination/history-of-smallpox-vaccination#

[5] https://www.who.int/news-room/spotlight/history-of-vaccination/history-of-smallpox-vaccination#

[6] https://historyofvaccines.org/history/edward-jenner-frs-frcpe/overview

[7] https://www.who.int/news-room/spotlight/history-of-vaccination/a-brief-history-of-vaccination#

[8] https://historyofvaccines.org/history/edward-jenner-frs-frcpe/overview

[9] https://historyofvaccines.org/history/edward-jenner-frs-frcpe/overview

[10] https://www.mayoclinic.org/diseases-conditions/history-disease-outbreaks-vaccine-timeline/smallpox

[11] https://www.who.int/news-room/spotlight/history-of-vaccination/history-of-smallpox-vaccination#

[12] https://www.mayoclinic.org/diseases-conditions/history-disease-outbreaks-vaccine-timeline/smallpox

[13] https://www.who.int/news-room/spotlight/history-of-vaccination/a-brief-history-of-vaccination#

[14] https://www.sciencemuseum.org.uk/objects-and-stories/medicine/smallpox-and-story-vaccination#

Chapter 3

Experiments by Emil von Behring and Shibasaburo Kitasato on Serum Therapy

In the late 19th century, Emil von Behring and Shibasaburo Kitasato conducted groundbreaking experiments that demonstrated the potential of serum therapy to combat infectious diseases like diphtheria. Their work laid the foundation for modern immunology and earned von Behring the first Nobel Prize in Physiology or Medicine in 1901. This chapter delves into the details of their experiments and the impact of their discoveries.

Key Experiments and Findings

Development of Antitoxins

Von Behring and Kitasato's initial experiments focused on developing 'antitoxins' against diphtheria and tetanus. They injected diphtheria and tetanus toxins into animals such as guinea pigs, goats, and horses. Once these animals developed immunity, they extracted antitoxins from their serum, which could then protect and cure non-immunized animals (1).