

► **The Speckled Monster:
A Historical Tale of
Battling Smallpox**

JENNIFER LEE CARRELL

Dutton Books, New York, 2003,
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Hong Kong. Spring 2003. People are running around the streets of the city, shrouded in surgical masks and afraid to speak to or touch anyone. The fear of severe acute respiratory syndrome (SARS) is every-

where. Doctors don't know how to treat their patients and, in the worst cases, can only make them comfortable as the afflicted slip into death. The infectious agent has yet to be isolated. Not only are the people suffering, but so is the economy. Nobody wants to accept goods from the island city, and visitors have become almost nonexistent, with the possible exception of scientists from the Centers for Disease Control and Prevention and the World Health Organization.

Now add to this very real problem the thought that someone is skulking through the streets of Hong Kong in the middle of the night, slicing open wounds in the arms and legs of healthy people, only to introduce fluid from infected individuals. This man, who doesn't even have formal medical training, is furtively moving about the city, infecting people with the pestilence, defying the legal authorities in the process. All the while, the man is telling people, "Trust me, I know what I'm doing."

What do you do? Do you gather some friends and form a lynch mob, or do you put your faith in someone who is daring enough to try something that most physicians would never dream of? Although the people of Hong Kong never had to worry about these questions, they were real to the people of Boston in the early 1700s, when the city and its citizens were being ravaged by smallpox.

In *The Speckled Monster*, Jennifer Lee Carrell follows the lives of two strong-willed individuals—Lady Mary Wortley Montagu and Zabdiel Boylston—who witnessed the ravages of smallpox firsthand and decided that they had to go against the social mores of the times to change medical history.

Montagu was an upper middle class Englishwoman who was whisked away by a politically ambitious husband to exotic Constantinople in the time of the Ottoman Empire, where she first learned of a strange medical practice espoused by the local Arab population. Half a world away, Boylston was a Boston apothecary who followed in his father's medical footsteps but without the benefit of a formal medical education. Boylston too heard the strange rumblings about an odd medical practice, but in his case, the information came by way of a local member of the Royal Society of London and interviews with members of the local slave population who had been raised in places like Africa and the Caribbean.

Unbeknownst to each other, the two mavericks explored the folk medicine called inoculation, and they risked the lives of their children by purposefully infecting their offspring with fluid scraped from the purulent pocks. The hope? That by giving people a light case of smallpox, they would make them immune to future exposure. As Carrell recounts the story, the anxiety, conflict, and emotion of the scenes are palpable. Throughout the episodes, Montagu and Boylston are plagued with a mixture of doubt and determination as they watch their children slide into fever, which is followed by the eruption of the telltale spots, only to experience relief as the infection finally subsides.

In both cities, the public reaction is nearly identical. In the broad light of day, Boylston and Montagu are decried as monsters, purposefully spreading the filth among the people. But at night, the scene changes, and both are sought by friends and foes alike, desperate to avoid the pestilence that is taking their loved ones. But with time and success, the process of inoculation—and the

people who espouse it—eventually are accepted by the public at large, and more tepidly by the medical community.

Reading more like a historical fiction novel than a textbook, *The Speckled Monster* is Carrell's attempt to put a human face on the scourge of smallpox, in the days before Pasteur and Jenner. "Where history reports dialogue indirectly or leaves it merely suggested," Carrell writes in her introduction, "I have returned it to full conversational life—while keeping as close to what was actually said as possible, often by borrowing known words from similar situations." Throughout, the author provides copious notes and sources that offer the reader further insight and give the text credibility.

— REVIEWED BY RANDALL C. WILLIS

DNA Microarrays: A Molecular Cloning Manual

EDITED BY DAVID BOWTELL
AND JOSEPH SAMBROOK

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ISBN 0-87969-625-7



DNA Microarrays: A Molecular Cloning Manual provides the reader with a wealth of information about how to manufacture microarrays, design and carry out microarray experiments, and

analyze microarray data. The editors have lined up an impressive cast of authors who are in many cases the world experts on the particular aspect of microarray technology that they describe. The book is divided into eight sections, each of which offers an introduction; a detailed protocol chapter, often including photographs of experiments and a troubleshooting guide; information panels that provide additional details; and references, including a list of relevant Web

resources. Appendices include recipes for common buffers and stock solutions used in microarray experiments, as well as safety recommendations.

In the opening sections of the book, the authors provide the information necessary to set up an in-house microarray facility, with Section 1 focusing on the acquisition and handling of clone collections and Section 2 dedicated to the technology of printing glass microarrays. An extensive list of arrayer manufacturers is provided. Another part describes the issue of quality control of printed slides, a very important—yet often overlooked—aspect of microarray manufacturing.

Section 3 is dedicated to RNA isolation, labeling, and hybridization. This extensive and well-organized section offers many detailed protocols for RNA extraction from mammalian cells and tissues, plants, bacteria, and yeast. Qualitative and quantitative assessment of RNA is addressed, although no mention is made in this section of recent microcapillary technology (e.g., that developed by Agilent Technologies), which is now used routinely by many microarray laboratories for RNA assessment. RNA amplification is also covered in this section, although it is mainly focused on T7-based linear amplification and does not mention alternative methods such as the PCR-based amplification developed by BD Biosciences Clontech. In addition, this section lacks a discussion of the biases introduced by RNA amplification. The section describing hybridizations and washes is very detailed, and the troubleshooting guide, which

includes photographs of problematic arrays, is highly informative because it offers practical solutions to most of the problems encountered in microarray hybridization. Section 4 offers a short overview of membrane-based arrays as an alternative to glass arrays and a short comparison of the two types.

Section 5 is dedicated to tissue microdissection, including laser capture microdissection. The presence of this section in a microarray book is unexpected. However, many researchers now consider the combination of this technology with microarray profiling to be an important step toward obtaining more meaningful microarray data. This section is extensive and extremely detailed, although it does not address the necessity of RNA amplification after microdissection and the expression biases associated with profiling amplified genetic material.

Section 6 covers the application of spotted arrays to comparative genomic hybridization (CGH), SNP genotyping, and DNA-protein interaction mapping. Regrettably, there is no mention of integration of DNA copy number analysis with expression analysis. Part 2 of this section, which describes SNP genotyping and mutation detection, is very instructive, and the material has not been covered in previous books on microarrays. However, the inclusion of a 38-page section providing primer sequences and locations of SNPs is questionable; it would have been best included as supplementary material on a website.

In Section 7, the authors offer an intro-

duction to microarray bioinformatics. Because microarray data analysis is a major bottleneck encountered by researchers using microarrays, this section could have been more thorough. Parts 1–3, describing experimental design, image analysis, and normalization—three issues frequently overlooked by microarray researchers—are both comprehensive and invaluable. However, the three subsequent sections on data analysis offer only a snapshot of the microarray data analysis tools currently available and do not mention simple statistical tools to determine the significance of microarray data, such as significance analysis of microarrays (SAM), a free software package developed by Stanford University (Palo Alto, CA) and used in many microarray publications. Mention of more sophisticated data analysis approaches, such as class prediction algorithms, is also lacking. Similarly, a section on microarray data validation is missing. Finally, Section 8 focuses on tissue microarrays, a downstream technology to expression arrays, and is very comprehensive.

Overall, this is an excellent book, which will prove invaluable to any researcher involved in microarray analysis. It offers a comprehensive overview of the microarray technology as well as its satellite techniques, such as LCM, CGH arrays, and tissue arrays, and is the most comprehensive and up-to-date manual currently available on DNA microarrays.

—REVIEWED BY PASCALE F. MACGREGOR ■

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