WOMEN IN MEDICAL MICROBIOLOGY: REFLECTIONS ON CONTRIBUTIONS

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More than half the people involved in health care are and always have been women. For centuries before there were medical schools to formally train and accredit women as physicians, women have been healers and caregivers in society. Today, it is evident that women portraying different roles play a vital role in our health care system.

In this article, we attempt to chronicle some of the notable contributions of women in the field of medical microbiology. These extraordinary professionals include not only women physicians, but also researchers, therapists and technologists, each of whom is integral to the health care diagnostic system. These contributions form a continuum of female achievement - a heritage women in medical microbiology can proudly call their own.

Lady Mary Wortley Montague (1689-1762) was an English aristocrat and wife of the then appointed ambassador to Turkey. It was in her endeavour to understand local customs that she learnt of the Turkish practice of inoculating healthy children with the attenuated strain of smallpox (variolation). Lady Mary introduced this custom in the British nobility with eventual filtering down of the practice to the working classes.[1] Though Edward Jenner would eventually be given credit for the smallpox vaccine, it was really Lady Mary who pioneered this custom in the British nobility with eventual filtering down of the practice to the working classes.[1] Though Edward Jenner would eventually be given credit for the smallpox vaccine, it was really Lady Mary who pioneered the approach. As smallpox vaccination gained widespread acceptance eventually leading to eradication of the disease, millions of people owe their lives to Lady Mary Wortley Montague and her struggle to popularize smallpox inoculation.

The name Lancefield is associated throughout the world with grouping and typing of streptococci. Few, however, know that the rightful owner of the name was a pioneering American microbiologist Dr. Rebecca Craighill Lancefield (1895-1981). Using the serum precipitation method, Lancefield classified streptococci into groups according to the carbohydrate antigens in their cell wall.[2] She further went on to type group A streptococci, demonstrating that different serotypes were the result of antigenic variation of a cell surface M protein.[3] Though Lancefield received several honours for her outstanding research - she never developed much sympathy for the feminist point of view and preferred those accolades that came without reference to her gender.

Dr. Anna Wessel Williams (1863-1954) was a leading physician who worked closely with scientist William Park to develop an antitoxin for diphtheria. She isolated a strain of Corynebacterium diphtheriae from a case of tonsillar diphtheria which proved to be a crucial discovery in the development of an antitoxin for the disease.[4] Williams and Park shared the credit for the discovery, and named it the Park-Williams strain. This discovery was virtually responsible for eliminating diphtheria in the western world.

Dr. Margaret Pittman (1902-1995), hailed as a “woman scientist ahead of her time,” was considered an authority on the subject of Haemophilus influenzae and Bordetella pertussis. Pittman discovered that Haemophilus influenzae existed in two forms - encapsulated and unencapsulated. She further discovered six different varieties of the encapsulated H. influenzae (Pittman’s classification types a - f) and observed that only type b caused serious forms of the disease.[5] The licensing of a polysaccharide vaccine for H. influenzae type b for use in preschool children was a long term outcome of Pittman’s early research on this pathogen. In 1944, Pittman found that she could infect mice with pertussis by injecting Bordetella pertussis into the mouse brain. She then used this knowledge to test the potency of a pertussis vaccine. Pittman developed a vaccine potency standard based on a “50% dose” - the dose of vaccine that would result in the survival of 50% of mice infected with a certain number of Bordetella pertussis. Manufacturers began using this “mouse protection test” to determine the potency of the pertussis vaccine.[6]

Barbara McClintock (1902-1992) was a pioneering American scientist and one of the world’s most distinguished cytogenetists. Her work led her to theorise that genes are transposable on and between chromosomes. McClintock drew this inference by observing changing patterns of coloration in maize kernels over generations of controlled crosses.[7] These came to be known as “mobile genetic elements” or “jumping genes” or “transposons”. McClintock was awarded the Nobel Prize in Physiology or Medicine in 1983. Today, transposons are recognized as mechanisms for transfer of genes conferring antimicrobial drug resistance from one bacterium to another.

By the mid 20th century, DNA was known as the
substance capable of storing practically all the information needed to create a living being. What was not yet known was what the elusive DNA molecule looked like or how it performed this amazing hereditary function. While the now familiar double helical structure of DNA was subsequently deciphered by Watson, Crick and Wilkins - there was one other person whose essential contribution to this discovery was not to be recognized. Rosalind Elsie Franklin (1920-1958) was a British biophysicist and crystallographer who made a landmark contribution to the understanding of the structure of DNA. Her images of the X-ray diffraction of DNA formed the framework of Watson and Crick’s hypothesis of the double helical structure of DNA. Unfortunately, Franklin’s life and career were abruptly cut short by ovarian cancer.[8] After her death, Watson and Crick publicly proclaimed that they could not have discovered the structure of DNA without her work. However, because the Nobel Prize is not awarded posthumously, Rosalind Franklin could not be cited for her vital role in the discovery of the physical basis of genetic heredity.

Yvonne Barr (1932-), a British virologist is jointly credited with the discovery of the Epstein-Barr virus (EBV). EBV is named after Michael Epstein and Barr who first isolated the virus from a patient with lymphoma.[9] Commonly known to cause infectious mononucleosis, EBV has also been linked with Burkitt’s lymphoma and nasopharyngeal carcinoma.

A biochemist and pioneer in drug development, Gertrude Elion (1918-1999) developed several new drugs during the span of her career. Her most notable discoveries include Azathioprine - the immunosuppressive agent used widely in organ transplantation, 6-mercaptopurine - the first treatment for leukaemia, acyclovir - the first effective antiviral medication, pyrimethamine for malaria, trimethoprim for urinary and respiratory tract infections and allopurinol for gout. Elion used innovative research methods that would later lead to the development of the drug azidothymidine - the first antiretroviral agent.[10] “The idea was to do research, find new avenues to conquer and new mountains to climb!” she is quoted as saying while accepting the Nobel Prize in Physiology or Medicine in 1988.

On the lines of drug discovery, scientists Rachel Brown and Elizabeth Hazen are credited with the discovery of the polyene antifungal agent - Nystatin. They purified and isolated the active ingredient from the soil bacterium Streptomyces noursei. Hazen and Brown named the ingredient nystatin, after the New York State Department of Health where the discovery was made.[11]

If the discovery of nystatin is a fine example of the contribution of women to microbiology - a related story is that of outstanding mycologist Alma Whiffen Barksdale (1916-1981). Whiffen is recognized for her discovery of the antibiotic cycloheximide or actidione[12]. Derived from the fungus Streptomyces griseus, the compound is used in laboratories worldwide for isolating pathogenic fungi.

The discovery of penicillin changed the world of modern medicine. While Fleming accidentally discovered it and Florey and Chain extracted and purified the compound - it was Dorothy Hodgkin who identified the beta lactam structure central to the antibiotic using protein crystallography. This marked the beginning of synthesis of chemically modified penicillins which expanded the spectrum and applications of the drug. Hodgkin later went on to discover the structure of vitamin B12, for which she was awarded the Nobel Prize in Chemistry in 1964.[13]

Rosalyn Sussman Yalow (1921-) grew up at a time when women were given little access to scientific training. Yet, with talent and fortune, Yalow earned a Ph.D. in physics and went on to become a premier medical physicist. In 1977 she was awarded the Nobel Prize in Physiology or Medicine for the development of radioimmunoassay (RIA).[14] RIA was a novel technique of quantifying minute amounts of biological substances in body fluids using radioactive-labelled material. Yalow invented this technique to measure insulin levels in patients with diabetes mellitus.[15] It has since then been applied to several substances such as toxins, hormones, vitamins and enzymes - all previously too small to detect.

A true leader and a shining example of women in Science - Dr. Anita Roberts (1942-2006) was a molecular biologist who made pioneering observations of the protein TGF-β. Dr. Roberts isolated the protein from bovine kidney tissue and discovered that it plays a central role in wound and fracture healing.[16] She subsequently delineated its role in carcinogenesis and this research is the basis of new therapeutic approaches in breast cancer.

Esther Zimmer Lederberg (1922-2006) was an American microbiologist and pioneer of bacterial genetics. She was the first to isolate the lambda bacteriophage, a DNA virus, from Escherichia coli K-12.[17] Her other notable contributions include delineating the relationship between transduction and lambda phage lysogeny, development of the replica plating technique and discovery of bacterial fertility factor F.[18]

In recent times, Dr Claire M Fraser Liggett, Director of The Institute of Genomic Research at Washington DC and her team have been at the forefront of the genomic revolution. In 1995, Dr Fraser and her team reported the first complete genomic sequence of a free-living organism Haemophilus influenzae.[19] Dr Claire has also been a pioneer in the field of microbial forensics and played a significant role during the investigation of the rogue mails in 2001 which were laden with spores of Bacillus anthracis.[20]

Summary of notable contributions by women in medical
microbiology are presented in Table 1

### Indian Women in Medical Microbiology

Among the 16 signatories signalling the birth of the Indian Association of Medical Microbiologists (IAMM) in 1976 and later the President of IAMM in 1988 - Dr. Kunti Prakash was a remarkable woman microbiologist from India. Her work on antibodies to C-carbohydrate antigen of group A streptococci in India and efforts to control rheumatic fever put India on the world map and led to the recognition of Lady Harding Medical College as a WHO Collaborative Centre for *Streptococcus*.[21]

Dr. Prema Bhat was an eminent Indian microbiologist who did pioneering work on enteric bacterial infections and intestinal anthrax.[22,23] She collaborated with international laboratories for a landmark study on juvenile diarrhoea caused by *Edwardsiella tarda*.[24] During the span of her illustrious career, she was also instrumental in serogrouping of EPEC - 5 - 14 and establishing in vitro culture of *P. falciparum* in her laboratory.

Another inspiring microbiologist from India - Dr. Ruth Myers - was a colleague of Dr. Prema Bhat and their joint collaboration led to profiling the standard methods and procedures used in the laboratory to characterize and identify family *Enterobacteriaceae*.[25] In addition, Dr. Myers is also recognized for her work on ornithosis in India and identification of the agent *Bedsonia* in the blood of grey herons.[26]

Dr. Grace Koshi is known for her work in mycology - in documenting the first case of eumycotic mycetoma outside Latin America caused by *Acremonium recifei*. [27] Her other accomplishments include use of enzymes for typing of group A beta haemolytic streptococci and study of the protean manifestations of actinomycosis.[28,29]

In the present times, women seem so at home in the health care setting that it is easy to forget that their mere presence represents centuries of effort to prove that ability and not biology should determine opportunity. If women can now aspire to leadership positions in the medical world, it is due to the achievements of thousands of outstanding women who preceded them. While certainly not exhaustive, we hope that revisiting the accomplishments and contributions of these chosen women in microbiology will inspire a new generation of medical pioneers.

### Table 1: Notable contributions by women in medical microbiology

<table>
<thead>
<tr>
<th>Scientist</th>
<th>Year</th>
<th>Place</th>
<th>Accomplishment</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lady Mary Montague</td>
<td>1689-1762</td>
<td>Great Britain / Turkey</td>
<td>Introduced practice of variolation against small pox</td>
<td>1</td>
</tr>
<tr>
<td>Rebecca Lancefield</td>
<td>1895-1981</td>
<td>USA</td>
<td>Grouping of Streptococci</td>
<td>2,3</td>
</tr>
<tr>
<td>Anna Williams</td>
<td>1863-1954</td>
<td>USA</td>
<td>Antitoxin for Diphtheria</td>
<td>4</td>
</tr>
<tr>
<td>Margaret Pittman</td>
<td>1902-1995</td>
<td>USA</td>
<td>Typing of <em>Haemophilus influenzae</em></td>
<td>5,6</td>
</tr>
<tr>
<td>Barbara McClintock</td>
<td>1902-1992</td>
<td>USA</td>
<td>Discovery of Transposons</td>
<td>7</td>
</tr>
<tr>
<td>Rosalind Franklin</td>
<td>1920-1958</td>
<td>Great Britain</td>
<td>Crystallographic structure of DNA</td>
<td>8</td>
</tr>
<tr>
<td>Yvonne Barr</td>
<td>1932-</td>
<td>Great Britain</td>
<td>Epstein-Barr virus</td>
<td>9</td>
</tr>
<tr>
<td>Gertrude Elion</td>
<td>1918-1999</td>
<td>USA</td>
<td>Azathioprine, Allopurinol, Acyclovir, Pyrimethamine</td>
<td>10</td>
</tr>
<tr>
<td>Rachel Brown/ Hazel</td>
<td>1898-1980/</td>
<td>USA</td>
<td>Discovery of Nystatin</td>
<td>11</td>
</tr>
<tr>
<td>Alma Whiffen</td>
<td>1916-1981</td>
<td>USA</td>
<td>Discovery of Cycloheximide</td>
<td>12</td>
</tr>
<tr>
<td>Dorothy Hodgkin</td>
<td>1910-1994</td>
<td>USA</td>
<td>Structure of Penicillin</td>
<td>13</td>
</tr>
<tr>
<td>Rosalyn Yalow</td>
<td>1921-</td>
<td>USA</td>
<td>Radioimmunoassay (RIA)</td>
<td>14,15</td>
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<tr>
<td>Anita Roberts</td>
<td>1942 - 2006</td>
<td>USA</td>
<td>Role of TGF-β</td>
<td>16</td>
</tr>
<tr>
<td>Esther Lederberg</td>
<td>1922-2006</td>
<td>USA</td>
<td>Discovery of Lambda Phage</td>
<td>17,18</td>
</tr>
<tr>
<td>Claire Fraser Liggett</td>
<td>1955-</td>
<td>USA</td>
<td>Sequencing of <em>H influenzae</em> genome</td>
<td>19,20</td>
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<tr>
<td>Kunti Prakash</td>
<td>1934-2001</td>
<td>India</td>
<td>Immunity in Streptococcal infections</td>
<td>21</td>
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<tr>
<td>Prema Bhat</td>
<td>India</td>
<td></td>
<td>Enteric bacterial infections</td>
<td>22,23,24</td>
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<tr>
<td>Ruth Myers</td>
<td>India</td>
<td></td>
<td>Ornithosis in India</td>
<td>25,26</td>
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<td>Grace Koshi</td>
<td>India</td>
<td></td>
<td>Mycetoma, Actinomycosis</td>
<td>27,28,29</td>
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</tbody>
</table>

References

6. Pittman M, Cox C. Pertussis Vaccine Testing for Freedom-

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