AN UNSUNG HERO

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Cystic fibrosis was for long considered a fatal childhood disease. One woman's contributions, as a physician and researcher, to the study of this disorder has helped improve the quality and life expectancy of patients suffering from it in significant ways. Who is this unsung hero? What do we know of her life and work?

"Today is the most best day ever in my life. They found a jean for cistikfibrosis".

Written on 25th August, 1989, this was the diary entry of an 8-year-old child, who was lucky to survive a rare genetic disorder called Cystic Fibrosis (CF). This disorder had, until the mid-1990s, claimed the lives of many children in their infancy. Their bodies would produce very thick, sticky mucus that would build up in and obstruct the tubes, ducts, and passageways in many organs, particularly the lungs and pancreas. Affected children would show symptoms like very salty skin, breathing difficulties, and digestive problems. Those suffering from a severe form of the disorder would become malnourished (despite a good appetite), weak, and susceptible to lung infections and pneumonia.

This rare congenital condition had for long baffled doctors. The medical community had attributed the deaths to coeliac disease, a chronic digestive and immune disorder, and would treat it like that. However, a pathbreaking discovery in 1938 by the pathologist Dorothy Hansine Andersen changed that (see **Fig. 1**).

The medical sleuth

In 1935, Andersen was working as a pathologist at the Babies Hospital, Columbia Presbyterian Medical Center, New York. Part of her work involved the dissection of organs and examination of body fluids to investigate the cause of death in patients.

Fig. 1. Dorothy Hansine Andersen. A physician, paediatrician, and pathologist, Andersen was the first to identify and describe CF.

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Andersen was often overwhelmed by the number of infant deaths that occurred due to lung infections and malnourishment. Then, one day, in 1938, while performing an autopsy on one such three-year-old, she observed that the airways of the child's damaged lungs were blocked by unusually thick mucus. Further probing revealed similarly thick mucus blocking the tubes leading out of the child's pancreas. She also observed that the child's pancreas was damaged and *"completely covered by a sandy, tough fibrous cyst"*. Andersen surmised that the thicker mucus had blocked the release of the corrosive enzymes that the pancreas produces for digestion. These enzymes had, therefore, acted on the pancreas itself. Further, she correlated the blocked distribution of pancreatic enzymes with increased salinity in the epithelial cells that line airways and pancreatic tubes. In healthy people, these cells secrete mucus to lubricate the airways and tubes. In those with CF, the epithelial cells produced and secreted the thicker, stickier mucus that had clogged the airways of the child and made the lungs more susceptible to infection. Andersen recognised this anomaly as a new disorder. She named it 'Cystic fibrosis of the pancreas' and shared a detailed description of it in a 50-page journal paper. In 1939, she was awarded the E. Mead Johnson Award, given by the Society for Paediatric Research, for her work on this disease.

Andersen did not think of herself only as a pathologist; she also worked directly with CF patients, mostly young children. This was something that many pathologists of the time, and especially women, did not do. In 1942, she collaborated with the researcher and clinician Paul di Sant'Agnese to devise a test to measure the amount of chloride in sweat (those with CF have higher levels of chloride in their sweat). This 'sweat test' continues to be the gold standard for diagnosing CF. Andersen and Sant'Agnese also went on to study and champion the use of penicillin as a treatment option for CF symptoms (see **Fig. 2**). In 1958, Andersen published a paper suggesting that CF was caused by a recessive mutant gene (implying that a child gets the disorder only if **both** parents carry the defective gene **and** pass it on to the child).

A trailblazer

Born in 1901 in Asheville, North Carolina, Andersen was an unassuming and enigmatic person who lived a private life. Very few records remain of her professional and personal life; even portraits of her are rare (see **Box 1**). Her biographers describe Andersen as a soft-spoken but 'ruggedly individualistic' person who did not conform to the societal norms of the day. She remained single by choice. Unlike most women of her time, Andersen was often unkempt in attire and was frequently seen with a cigarette dangling from her fingers and with ash on her clothes. She enjoyed an active lifestyle that included hiking, canoeing, and carpentry.

Professionally, Andersen stood out. In the 1900s, opportunities for women to study and work were limited. In fact, a very small number of medical

Fig. 2. Andersen with her collaborator Paul di Sant'Agnese (standing to her left). The two devised a diagnostic test for CF and championed the use of penicillin to treat CF symptoms.

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Box 1. Timeline of key events:

May 15, 1901: Born.

1914–20: Loses both parents.

1922: Graduates with a Bachelor of Arts in Zoology and Chemistry from Mount Holyoke College, Massachusetts.

1922-1926: Graduates with a medical degree from Johns Hopkins University School of Medicine, Baltimore.

1930-35: Accepts position of Instructor at the Columbia University College of Physicians and Surgeons. Completes a doctorate in Endocrinology.

1935: Accepts position of Assistant Pathologist at Babies Hospital at the Columbia-Presbyterian Medical Center, New York.

1938: Describes CF.

1942: Collaborates with Paul di Sant'Agnese to develop a diagnostic 'sweat test' for CF.

1945: Accepts position of Assistant Paediatrician at Babies Hospital at the Columbia-Presbyterian Medical Center, New York.

1949: Shows that CF is likely to be caused by an autosomal recessive gene.

1952: Appointed Chief of Pathology at Columbia-Presbyterian Hospital, New York.

1958: Full-time professor at Columbia College of Physicians and Surgeons, New York.

1962: Diagnosed with lung cancer. Undergoes surgery.

1963: Breathes her last on 3rd March.

professionals were women. Andersen was a rare genius who earned two degrees—one in medicine and the other in endocrinology. She obtained a medical degree from Johns Hopkins University School of Medicine in 1926 and taught anatomy for a year at the University of Rochester in Rochester, New York. After this, she applied for the surgical residency programme at Strong Memorial Hospital at Rochester, New York. She was denied this post. According to many historians, the denial was solely due to her gender. Undeterred, Andersen joined the department of pathology at the Columbia University College of Physicians and Surgeons as an instructor. Between 1930-35, she focused on medical research, studying endocrine glands and female reproduction with a grit and tenacity that earned the respect of her peers. It also earned her a doctorate in endocrinology. In 1935, she accepted the position of assistant pathologist at Babies Hospital at the Columbia-Presbyterian Medical Center, New York. It was here that she discovered and described the pattern of disease in CF. It was also here that she developed an interest in congenital heart malformations and started a collection of the hearts of infants who had died of inborn cardiac defects. In 1958, she was made Chief of Pathology at Columbia-Presbyterian Hospital and a full professor of pathology at the Columbia University College of Physicians and Surgeons.

Box 2. Tune in to the podcast on Lost Women of Science, Season 1:

Lost Women in Science is a non-profit organization that describes its mission as an initiative to unearth and narrate the *"hidden histories of women scientists who made ground-breaking achievements in their fields"*. Its inaugural season called 'The Pathologist in the Basement' is dedicated to Dorothy Andersen. This season has four original episodes (called 'The Question Mark', 'The Matilda Effect', 'The Case of the Missing Portrait', and 'Breakfast in the Snow') and one bonus episode (called 'The Resignation'). For more exciting details on Andersen's research, listen to this podcast here: https://www.lostwomenofscience.org/season-1. Also, do not miss the rare voice recording of Andersen's speech on CF, curated by her biographer Dr Scott Baird, that is available in episode 4 of the podcast.

Andersen was an astute pathologist and a meticulous researcher. She kept detailed records of her CF patients and devised disease management strategies for them. As a member of the medical education committee of the Cystic Fibrosis Foundation, Andersen visited medical colleges across the US, where she gave lectures to spread awareness of this disorder (see **Box 2**). Her knowledge of anatomy and cardiology was so extensive that she was invited as a consultant to the Armed Forces Institute of Pathology during World War II. She went on to use her research to develop a training program for surgeons pioneering in open-heart surgery. This was not all. Andersen also investigated and described a rare glycogen storage disease (called GSD type IV or Andersen disease) that was caused by a defective liver enzyme. Showing an autosomal recessive inheritance pattern, the symptoms of this disease first appeared during the first few months after the birth of a child and usually resulted in death within the first few years.

Andersen's habitual smoking took a toll on her health. In 1963, at the age of 62 years, she succumbed to lung cancer. For her pioneering work in CF, she was inducted into the National Women's Hall of Fame in 2002.

Key takeaways

- At a time when women had limited opportunities to study and work, Dorothy Hansine Andersen earned two degrees, qualifying to become both a physician and an endocrinologist.
- Starting out as a teaching assistant, Andersen went on to work as a paediatrician, pathologist, researcher, cardiologist, and an active member of the medical education committee.
- She was the first to identify and describe a rare congenital disorder that had claimed the lives of many children in their infancy. It was also she who named this disorder 'cystic fibrosis'.
- Andersen collaborated with Paul di Sant'Agnese to develop a 'sweat test' to diagnose CF and to advocate the use of penicillin in treating it.
- Her work helped turn a near-fatal disease in children into a manageable condition with improved quality of life and life expectancy.

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