Focal Point

Castellani: centrifuging CSF

Discoveries in medicine sit at the intersection of novel ideas, new technologies, and social or political developments. One such milestone was the demonstration, in 1903, of the presence of trypanosomes in the CSF of patients with sleeping sickness by Italian microbiologist Aldo Castellani (1874–1971).[1]

Castellani's discovery was made in Uganda, whither he had been sent on the recommendation of Scottish parasitologist Patrick Manson (1844–1922) as a member of the Royal Society's Sleeping Sickness Commission. Castellani's ability to access human CSF rested on the development, 10 years earlier, of the lumbar puncture by German physician Heinrich Quincke (1842–1922), to which he applied centrifugation to precipitate and isolate microorganisms from the CSF of patients with sleeping sickness.

Castellani initially identified the wrong microorganism. A Portuguese team had reported the presence of a diplococcus in CSF taken from patients with sleeping sickness. In 1902, Castellani reported to the Royal Society that he had found a different diplococcus in 17 of 19 cases. Manson supported this finding in the 1903 edition of his book *Tropical Disease*,[2] but the Royal Society's committee were unconvinced, and sent microbiologist David Bruce out to supervise his work.

By the time Bruce arrived, Castellani had seen trypanosomes in the CSF of patients with sleeping sickness, but considered them to be contaminants. Bruce, on the other hand, had previously identified a trypanosome as the causative agent in the animal disease *nagana*, and was therefore predisposed to regard their presence as significant. Subsequent work by the Commission firmly established them as the causative agent of sleeping sickness, and identified the tsetse fly as the agent of transmission.[3]

In the fourth *Report* of the Commission, co-authored by Bruce, Castellani was ascribed credit for his novel technique of centrifuging CSF, and for the first observation of trypanosomes, but not the interpretation, the credit for which Castellani continued to claim for the rest of his long and eventful life.[4]

Mark Weatherall

1 Kennedy P. The Fatal Sleep. Africa's killer disease that went undiscovered for centuries. Luath Press Ltd, 2007.

2 Manson P. Tropical Diseases: a manual of the diseases of warm climates, revised enlarged edn. Cassell & Co, 1903.

3 Boyd J. The Castellani-Bruce Controversy. *Notes Rec R Soc Lond* 1970; **28:** 93–110.

4 Keynes M. Dr Aldo Castellani and Mussolini. *J Med Biogr* 1994; **2:** 184.

Lifeline



Siddharth Srivastava did his medical studies at Johns Hopkins School of Medicine (Baltimore, MD, USA), trained in child neurology and neurodevelopmental disabilities at Johns Hopkins Hospital and the Kennedy Krieger Institute (Baltimore), and completed a fellowship in neurogenetics at Boston Children's Hospital (Boston, MA, USA). He is associate professor of neurology at Harvard Medical School and a paediatric neurologist at Boston Children's Hospital, specialising in neurogenetics and neurodevelopmental disabilities. His research focuses on investigating genetic causes of intellectual disability and cerebral palsy.

Who inspires you?
I have three small children whose wonder and excitement inspire me every day to make sure the work I am doing contributes to the greater good of society, so that they grow up in a better world.

If you had not entered your current profession, what would you have liked to do?
If I had not become a physician, I would have become an engineer or computer scientist. I love the art of computer programming, which I liken to solving puzzles in fun, creative, and interesting ways.

Who was your most influential teacher, and why?
My fourth-grade elementary school science teacher, Mrs Babb, was inspirational. To this day, I remember the fun, meaningful, and memorable activities we did—owl pellet dissections, insect collections, Logo Turtle programming—that instilled in me a love of mathematics and science through the lens of learning, tinkering, and problem-solving.

What is your favourite book or film, and why?
I love the film *Home Alone*! To me, the movie embodies elements of mischief, adventure, excitement, and hope, and it makes the case that children can do anything if they put their minds to it.

What is your idea of a perfect day?
My idea of a perfect day is making pancakes for breakfast, going to the park with my wife and kids, and curling up with a good book along with some hot chocolate.

How would you improve the public's understanding of research?
I am passionate about rare disease research and advocating for children with neurodevelopmental disabilities. I hope that more researchers will talk about their work in school classrooms, teaching even the youngest learners.

What was your first experiment as a child?
When I was in first grade, I tried to invent invisible ink by mixing varying combinations of grass, dirt, paint, flour, and window glass cleaner. Needless to say, the experiment wasn't very successful, but it did inspire in me a lifelong love of experimentation and refusal to be deterred by failure.