

Baruch Blumberg

(1925–2011)

Geneticist whose discovery led to a vaccine for hepatitis B.

In the 2,000 years since Hippocrates described the skin-yellowing condition he termed *ikterus*, no single event has been more pivotal to the understanding and prevention of viral hepatitis than the discovery of the 'Australia antigen' by Baruch (Barry) Blumberg. This antigen, which Blumberg found in the blood of an Australian Aborigine, turned out to be the surface antigen of hepatitis B virus. The finding ultimately led to a test to screen blood donors for the virus and to a hepatitis vaccine.

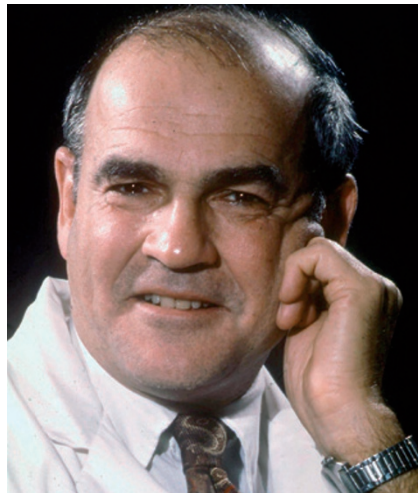
Although the outcome of Blumberg's research was monumental, his findings were initially serendipitous. In the late 1950s, while working at the US National Institutes of Health (NIH) in Bethesda, Maryland, he showed that cholesterol-transporting proteins called β -lipoproteins exist in varied forms in different populations as a result of genetic polymorphisms. In 1963, while heading the new Geographic Medicine and Genetics Section of the NIH, Blumberg and his co-workers unexpectedly found a precipitate in agar that did not take up the blue stain for lipids but stained red for protein. Blumberg had been using serum samples from haemophiliacs who had received multiple blood transfusions to provide antibodies that would react in agar with diverse proteins. The initially designated 'red antigen' was the result of an antibody in the serum of a haemophiliac from New York interacting with an antigen in the serum of an Australian Aborigine, and was later named the Australia antigen. Others might have dismissed this obscure finding as an irrelevant curio. But Blumberg's hypothesis-generating mind was set in motion.

After finding that the antigen was 100 times more prevalent in patients with leukaemia than in healthy blood donors, Blumberg proposed that it was inherited and that it predisposed carriers to leukaemia. Although this speculation was later disproved, it led to critically important studies on patients with Down's syndrome, who were known to have an inherited predisposition to leukaemia.

In 1964, shortly after Blumberg moved from the NIH to the Fox Chase Cancer Center in Philadelphia, Pennsylvania, he and his colleague Tom London discovered that although the Australia antigen was found at high prevalence in Down's patients as a group, it was not present in newborns. Rather than being inherited, the presence of the antigen in the blood of a Down's patient seemed to correlate with their living in a mental-health

institution. This was the first clue that the Australia antigen might be related to an infectious agent. The specific infection was identified as hepatitis B when two Down's syndrome patients and an investigator in Blumberg's lab were found to carry the antigen only after developing acute hepatitis.

The US company Abbott Laboratories developed a test to screen blood donors for the antigen, which dramatically reduced



the incidence of hepatitis B associated with blood transfusions. The test also identified pregnant women who carried the virus and led to measures that reduced mother-to-infant transmission by 90%.

In the late 1960s, Blumberg and Irving Millman, also at Fox Chase, postulated that the small, non-infectious Australia antigen particle could be separated from the virus and serve as a vaccine. A hepatitis B vaccine — initially produced from the plasma of infected individuals but now manufactured through genetic engineering — was developed by Maurice Hilleman at Merck and has prevented millions of hepatitis B infections. It was also the first cancer vaccine, as hepatitis B virus is a leading cause of liver cancer. For his discoveries, Blumberg received the Nobel Prize in Physiology or Medicine in 1976.

Born in New York City, Blumberg's early schooling was at the Orthodox Yeshiva of Flatbush, which perhaps accounted for his scholarly and deliberative, Talmudic approach to problems in science. After high school, he enlisted in the navy in 1943. A few years later, he pursued a degree in physics at Union College in upstate New

York and then graduate work at Columbia University in New York City. At Columbia, he first studied mathematics but then transferred to become a medical student at the College of Physicians and Surgeons.

It was at medical school that Blumberg's fascination with population genetics and disease took hold. He spent several months in northern Suriname in South America. A richly heterogeneous population had been brought to the country centuries earlier to work in the sugar plantations and Blumberg was struck by the enormous variation in how these people responded to disease. Yet his life took a few more twists and turns before the Australia antigen transformed it. After completing a medical residency at Bellevue Hospital in New York and a clinical fellowship in arthritis at the Columbia-Presbyterian Medical Center, he moved to Britain. He pursued a PhD in the Department of Biochemistry at the University of Oxford on the physical and biochemical characteristics of hyaluronic acid — a key component of connective, epithelial and neural tissues.

Barry's life after he received the Nobel prize was just as varied. He travelled in China, India and Africa to investigate liver cancer and promote the hepatitis B vaccine. In 1989 he was elected Master of Balliol College, Oxford, where, as he put it, he enjoyed "no power, but a great deal of influence". After five years at Balliol, he took a teaching position in medical anthropology at Stanford University in California. There he attended a NASA conference, became captivated by the possibilities of extraterrestrial life, and within months was appointed director of the NASA Astrobiology Institute, a post he held for five years. It was shortly after a return visit to NASA for a keynote lecture that Barry succumbed to a heart attack. He died with his boots on at age 85 on 5 April.

Barry was complex and brilliant, imaginative and adventurous, tenacious and dedicated, a deeply philosophical man of eclectic interests and myriad accomplishments — a Nobel man. ■

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