

Great Lives at Manguinhos

by José Rodrigues Coura

HENRIQUE DE BEAUREPAIRE ROHAN ARAGÃO

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Henrique de Beaurepaire Rohan Aragão was one of the most wide-ranging and creative of the great pioneering researchers at the "Manguinhos School" founded by Oswaldo Cruz at the beginning of this century in Rio de Janeiro. A fourth-generation Brazilian, Henrique Aragão was born on 21 December 1879 in the former Rua da Praia, in a house that was later knocked down during the construction of an avenue in the city of Niterói, at that time capital of the State of Rio de Janeiro. The son of Dr Francisco Pires de Carvalho Aragão and Dona Elisa de Beaurepaire Rohan Aragão, hailed on his father's side from one of Brazil's oldest sugar families. According to his own son Mário Aragão, this explained "his conservative, and therefore nationalist, outlook on life". On his mother's side, his Brazilian grandfather, Marechal Henrique de Beaurepaire Rohan, was considered one of the nation's pioneer map-makers, and was also a provincial governor, a road-builder and the compiler of the "Dictionary of Brazilian Terms", still a work of reference for philologists of the Brazilian language.

Henrique Aragão went to school at the Dr João Kopke Institute and then at the National Grammar Day School (today Pedro II College), completing his pre-university studies in 1898. At 19 he entered the Rio de Janeiro Faculty of Medicine, graduating in 1904. In 1903, when still in his fifth year of medical studies, he was accepted by the Manguinhos Institute as an intern, after being introduced to Oswaldo Cruz by his colleague and friend Waldemar Schiller, who already worked at the Institute. It was here that Henrique Aragão did his doctoral thesis, entitled "Serotherapeutic assay for diseases produced by non-culturable germs". The thesis was approved by the Faculty of Medicine with distinction in 1905.

Soon afterwards he married Dona Maria Amélia Dória de Aragão, and together they had six children: Luiza, Vera, Henrique, Mário (himself a dedicated researcher at Manguinhos, recently retired, but still active), Luiz and Maria. A model husband and father, he nonetheless always maintained a certain personal reserve, which sometimes made him appear dry and

severe, although in reality this behaviour reflected his standing as a great thinker.

A tireless worker, Henrique Aragão was one of the most productive researchers at Manguinhos. Soon after receiving his doctorate he was appointed Assistant at the Institute by Oswaldo Cruz himself, and by 1906 he had already published his first study, in collaboration with Henrique da Rocha Lima, on a "new technique for diagnosis of the plague", a disease which he caught in a laboratory accident, and the effects of which he felt for the rest of his life. From that time until his death on 25 February 1956 he produced 176 publications, averaging almost four a year non-stop for 50 years. In 1929 alone, with the resurgence of yellow fever in Rio de Janeiro, he published an extraordinary number of studies - 20 in all - about the virus, its maintenance in nature, its reservoirs, possibilities for control and



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the production of a vaccine against the disease, using the Rhesus monkey and other species as experimental models. He carried out in-depth studies in at least 25 different areas of bacteriology, protozoology, acarology and virology. He is generally regarded as the founding father of virological and protozoological research at the Oswaldo Cruz Institute.

In 1907, at just 28 years of age, and two years after his appointment as Assistant at the Oswaldo Cruz Institute, Aragão published his first study on the asexual cycle of *Haemoproteus columbae* in the lung capillary endothelia of doves. According to Prof. PCC Garnham, this discovery was a precursor to the identification of the plasmodial exoerythrocytic cycle, described 27 years later in avian malaria by Raffaele, and 41 years later in human malaria by Garnham himself, in collaboration with Shortt and others. It was Garnham's study that overturned the theory of plasmodial penetration of red blood cells which had remained unchallenged for 50 years since its first coinage by the great Schaudinn.

Aragão became famous for his descriptions of the smallpox, chicken pox and milk pox viruses. His work on the smallpox virus was carried out in collaboration with one of the people who inspired him most, von Prowazek. At the invitation of Oswaldo Cruz, the German researcher spent six months at Manguinhos, during which time he collaborated directly with Aragão. On returning to Europe in February 1909, von Prowazek invited the latter to go there to further his studies. In Germany, Aragão worked at the Zoological Institute in Munich under the direction of Hertwig and the supervision of Goldschmidt. He also studied at the Marine Hydrobiology Station in Villefranche, before returning to Brazil in September 1910.

Aragão also carried out research of great economic importance on avian haemogregarines and chicken spirochetosis, leading to the production of a vaccine against spirochetosis in which he used formaldehyde as a sterilizer for the first time. This model would later be used for a variety of antibacterial and antiviral vaccines, such as the inactivated antityphoid and antipolio vaccines. With his solid grounding in biology and social affairs, Aragão frequently focused on problems that were important in economic and public health terms, in addition to other problems of a more purely scientific interest.

He did noteworthy research on ticks, publishing more than 20 studies in which he described several new species and systematized their classification. Nine of these studies were carried out in collaboration with the great specialist Flávio da Fonseca, who published the last two articles in this co-authored series in 1961, six years after Aragão's death. Throughout his life, starting in 1908 when he published his first study on "Brazilian ticks", Aragão was fascinated by the

subject, devoting himself to it with particular intensity after his retirement in 1950.

Aragão also worked alongside a wide range of noted specialists on the publication of studies that complemented his own work. First he collaborated with Henrique da Rocha Lima on plague diagnosis; then with Prowazek on smallpox; with Arthur Neiva on Lacertidae parasites (*Plasmodios* sp.); with Gaspar Viana on the pathology of *Granuloma venereum* and *Treponema minimum* isolated from ulcerous lesions; with Ezequiel Dias on Anaplasmas; with Costa Lima on several yellow fever studies; with J Carlos Penido on the transmission of leprosy to Didelphidae; again with Penido and other collaborators on the biology of Rodrigo de Freitas Lake and on the breeding of fresh water prawns and lobsters; and finally with Jesuino Maciel on a study of *Pneumocystis carinii* as a cause of plasmodiocytarian interstitial pneumonia in children, published in January 1956 in *Revista Medicina e Cirurgia de São Paulo*, the last study authored by Aragão before his death.

In addition to his important work on *Haemoproteus columbae*, on smallpox, and on transmission and vaccination with respect to yellow fever and chicken spirochetosis, another of Aragão's major contributions to international science was his work on rabbit myxomatosis, a disease discovered by Sanarelli in Uruguay in 1909, and confirmed by Aragão in Brazil in 1911. In his various investigations, Aragão was struck by the myxoma virus's potent lethality against rabbits and its rapid transmission via fleas. He therefore made contact with the Australian government, through Commonwealth channels, and suggested that the virus should be used for biological control of the rabbit epidemic that was decimating Australian agriculture. His idea was provisionally accepted, and so he sent samples of the virus to the Australian health authorities. Their initial experiments raised a series of doubts; but later on, in the great epidemic of 1950, Aragão's suggestion was taken up. The idea was initially a spectacular success, although subsequent modifications of the virus reduced its potency. Citing this as evidence in support of his theory of parasite-host adaptation, the famous Australian Nobel Prize winner, MacFarlane Burnet, remarked that the entire affair had been "a unique opportunity for epidemiologists, since we could observe it from ring-side seats."

In 1922 Aragão made an important new discovery, that was subsequently confirmed during the cutaneous leishmaniasis epidemic in Santa Teresa and Laranjeiras in 1927: namely, the transmission of leishmaniasis via *Phlebotomus (Lutzomyia) intermedius*. As well as making a very precise description of certain aspects of the disease and of its epidemiology, Aragão demonstrated experimentally that transmission

occurred via the insect, a finding that was confirmed in the field several years later by another researcher. Also in the area of protozoology, Aragão published important studies on amoebiasis; babesiasis; *Polytomella agilis*; malaria and the development of gametocytes of *Plasmodium falciparum*; and schizogony and gametogony in trypanosomes.

Despite his apparently distant manner, my research suggests that Henrique Aragão was a man of strong feelings, who felt a deep affection for his friends and who had a powerful sense of justice and patriotism. This is clear from the many obituaries and valedictions he wrote in memory of figures such as S von Prowazek, José de Castro Teixeira, Astrogildo Machado, Evandro Chagas and "Carlos Chagas, the Director of Manguinhos". His valediction for Carlos Chagas - with whom he did not see eye to eye in scientific terms - revealed Aragão's true greatness and his tremendous spirit of justice. He also wrote historical notes about the creation of the Oswaldo Cruz Institute and lectured about Oswaldo Cruz and the Manguinhos School. He was deeply concerned about endemic diseases and the need for prevention in rural areas, and was responsible for setting up various preventative services - against schistosomiasis in Pernambuco; Chagas' disease in Bambuí, Minas Gerais; yaws in Rio de Janeiro; and malaria in São Bento, in the Baixada Fluminense. The latter service later became the Malaria Prophylaxis Institute and moved to Belo Horizonte, where it now goes by the new name of the René Rachou Research Centre, although it still draws inspiration from its original motto: "The humanitarian function of Manguinhos must never be forgotten".

Aragão was Director of the Oswaldo Cruz Institute for seven years (1942-1949), and was responsible for sweeping changes that breathed new life into the institution. He quintupled its budget, and built several new facilities: the 26th Pavilion for the new Evandro Chagas Hospital; the Carlos Chagas Pavilion to house the Pathology and Hygiene Divisions and the Endocrinology and Hematology Sections; the Courses Pavilion, which now contains the Course Coordination Office and the Department of Tropical Medicine; the Pavilion for Biological Research; the Refectory, which today is shared with the FIOCRUZ Staff Association (ASFOC); the Chemistry Pavilion; the new Animal House; and the Pavilion for production of yellow fever vaccine, named after the minister Mario Pinotti, with whom Aragão continued to collaborate very closely - free of charge - even after his retirement. In addition to the Bambuí preventative service and the rest of the prophylactic programs mentioned above, Aragão also set up the Protozoology Section and the Medicinal Plants Garden at the Institute, and the Marine Hydrobiology Station on the Island of Pinheiro.

He pioneered Brazil's first penicillin factory (set up at the Institute in March 1943), and he was the prime mover behind a series of major studies: on ecology (of Brazilian scrublands, of the marshy Pantanal in state of Mato Grosso, and of Ilhéus in state of Bahia); on silvatic yellow fever (in Passos, Minas Gerais); and on malaria in bromelias (in Brusque, Santa Catarina).

Aragão devoted almost his entire career to the Oswaldo Cruz Institute, from his student days in 1903 right up to the week before his death - 53 years in all. He was absent only from 1937 to 1938, when he went to São Paulo to run the Special Yellow Fever Service. He was a member of the Rio Janeiro State Economic Council, the Federal Capital Technical Council, the Affordable Housing Foundation, and the UNESCO affiliated Brazilian Institute of Education, Science and Culture. He was president of the Brazilian National Health Council and of the International Leprology Centre. He belonged to fifteen scientific societies, nine of them in Brazil and six abroad - in France, Belgium, Argentina, Britain and the United States. He represented the Oswaldo Cruz Institute at several international congresses and was the president of the organizing committee for the V International Microbiology Congress in 1950.

Aragão was awarded the Nocht Medal by the Institute of Tropical Medicine in Hamburg for his work on tropical medicine, and the Order of the German Red Cross for his contribution to science.

As a professor, Aragão gave innumerable courses at the Oswaldo Cruz Institute, and also taught the Rockefeller Foundation's Malaria Course and the Health and Education Ministry's Public Health Course. Despite his formal manner, he was a great motivator of young people and left a vast number of followers and admirers. He is generally considered to have been Manguinhos's greatest researcher, alongside Adolpho Lutz, and the best Director of the Institute since the pioneering days of Oswaldo Cruz and Carlos Chagas. He always remained faithful to the motto coined by his mentor, the man who set up the Manguinhos School, Oswaldo Cruz himself: "There is nothing that can't be achieved by hard work". Five years after his retirement, he was spied one day bent over his microscope, as he might have been spied half a century before. It was this sight that prompted Felipe Nery-Guimarães, the man who watched him that day, "to muse that - sometimes - Man Conquers Time..." (1955, *Mem Inst Oswaldo Cruz*, 53: 144-145).

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Examples of references

Journal article:

Chagas C 1909. Nova tripanosomiase humana. Estudos sobre a morfologia e o ciclo evolutivo do *Schizotrypanum cruzi* n. g., n. sp., agente etiológico de nova entidade morbida do homem. *Mem Inst Oswaldo Cruz* 1: 159-218.

Chagas C, Villela E 1922. Forma cardiaca da tripanosomiase americana. *Mem Inst Oswaldo Cruz* 14: 15-61.

Book or Thesis:

Morel CM 1983. *Genes and antigens of parasites. A laboratory manual*. 2nd ed. Fundação Oswaldo Cruz, Rio de Janeiro, xxii + 580 pp.

Chapter in book:

Cruz OG 1911. The prophylaxis of malaria in central and southern Brasil, p. 390-398. In R Ross, *The prevention of malaria*. John Murray, London.

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