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HELIO GELLI PEREIRA
23 September 1918 — 16 August 1994

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Elected F.R.S. 1973

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Dr Helio Pereira, who was known internationally for his work on the viruses of vertebrates, died on 16 August 1994 in Rio de Janeiro, Brazil. He was born on 23 September 1918 in the small town of Petropolis in the state of Rio de Janeiro, where his father Raul Pereira Geronymo had been born. His grandparents were Portuguese and came from the Azores islands to set up a modest grocery business in Petropolis. His mother's family originated from Italy. His maternal grandfather had earned his living from eel fishing but in 1893 came to Brazil and started a cabinet-making business, which grew into a prosperous furniture factory and a chain of furniture shops run by members of the family.

Helio lived for the first five years of his life in Petropolis, the site of the Imperial summer palace, which was then a small summer mountain resort near Rio de Janeiro with a permanent population largely of German, Italian and Portuguese descent. Of that period he remembered mainly the life in his mother's family. This centred on the patriarchal figure of his grandfather and comprised a close-knit family of twelve sons and daughters and their wives, husbands and children. The family followed Italian customs to a large extent but these were influenced by the more easy-going Brazilian way of life, and so the general atmosphere was light-hearted and cheerful.

Between 1924 and 1928 he attended a small primary school (Colegio Pitanga) in Rio de Janeiro and then moved to the Anglo-American School. In spite of its name, this school was run on Brazilian lines and although the standard of teaching was average there were virtually no facilities for practical work. He described his academic achievements there as undistinguished and felt that he only scraped through the final examinations. He did well enough to gain entrance to the Faculty of Medicine in Niteroi, which at that time was the capital of the State of Rio de Janeiro. The faculty was private and had poor accommodation and equipment and teaching facilities, but it had a dedicated and largely voluntary teaching
staff whose efforts partly compensated for the other deficiencies. He found the basic scientific
subjects more interesting than clinical topics and was particularly attracted to microbiology,
which was taught in a very stimulating way by Arlindo de Assis and A. Monteiro Filho. As
was the custom in Brazil at the time, half-way through his medical course he obtained
part-time work as a laboratory technician in the clinical pathology laboratory of a local
hospital. He finally obtained his medical diploma in 1941.

The next year he entered a postgraduate course in general biology at the Instituto Oswaldo
Cruz, a prestigious Brazilian medical and biological research institute, with which he was to
have many significant contacts later in life. Although the course was interrupted to some
extent by military service, he found it very interesting and for the first time in his student
career he graduated with distinction. In the next two years, 1943–44, he had a number of
part-time jobs, including clinical pathology in private and government institutions, and
assistants in departments of microbiology and neurology under Professor A. Monteiro
Filho and Professor D. Couto respectively. He did not like dispersing his efforts into a
multiplicity of largely routine activities and so he decided to break away and to apply for a
British Council Scholarship to study microbiology in the UK. His application was successful
and in 1945 he left for England to work in the Department of Microbiology of the University
of Manchester under Professor H.B. Maitland.

Maitland had been a pioneer in virology and in the growth of viruses in the so-called
Maitland cultures of chopped tissues, and Helio felt that he was very fortunate to be
introduced to virology by working under his direct supervision. He also worked for the
eminent bacterial taxonomist S.T. Cowan and he felt that the stimulating influence of these
two men contributed greatly to his later career. He spent a short time at the University of
Liverpool, where he felt he learnt a great deal from Professor A.W. Downie, F.R.S. After eight
months in Manchester he moved to London and stayed for nearly a year at the National
Institute for Medical Research (NIMR), which was then located at Hampstead, and worked
under the direction of C.H. Andrewes, F.R.S., and W.J. Elford, F.R.S. He commented,
‘although this period of postgraduate training did not lead to formal qualifications or
published papers, it was certainly one of the most satisfactory and rewarding stages of my
professional career’, and a biographer can see how this period of apprenticeship kindled his
interest in the areas of virology to which he subsequently contributed so much, and roused his
enthusiasm for tackling fundamental problems by laboratory research.

In 1946 he married Marguerite (Peggy) Scott. Peggy was the daughter of the distinguished
Scottish bacteriologist, William McDonald Scott, a senior medical officer in the laboratory
division of the Ministry of Health, the forerunner of the Public Health Laboratory Service,
which he directed with Frederick Griffith until they were killed in London by enemy action in
1941. Her mother was the daughter of Antoine Mollar, a publisher and politician, who
became a senator of the French Republic. In 1947 they left Britain for Brazil, where their
three children were born. At the government hospital where he worked as a clinical
pathologist, Helio was unable to continue to work in virology and there were no other
opportunities elsewhere in Rio de Janeiro. However, a new department for research in
rickettsiae was being set up at Instituto Oswaldo Cruz under the direction of Dr J. Travassos
who agreed to take him on as a part-time assistant. With Dr Travassos’s ‘highly competent
and stimulating’ guidance he gained experience in field and laboratory study of the organisms
and was able to demonstrate the presence of both murine typhus and tick-transmitted spotted
fever in the State of Rio de Janeiro and to develop new methods for the study of rickettsial
antigen–antibody reactions (1–6)*. However, the Institute was entering a very troubled period with frequent interference in its affairs by local politicians, and when Helio received an invitation to return to Britain to take a post under Dr (later Sir) Christopher Andrews he accepted without hesitation; in 1951 he returned with his young family to live and work at the Medical Research Council's Common Cold Research Unit on the southern outskirts of Salisbury, Wiltshire.

In Salisbury the family were allocated one of the single-storied wartime huts of which the unit consisted. Other members of staff had similar accommodation, which was warm and spacious but furnished in a spartan style. The same green-painted huts were adapted as 'flats' in which the human volunteers were isolated for the ten days of each inoculation experiment. Other huts were modified to become laboratories, animal house, office and so on, to form a largely self-contained research unit. However, it was in fact an outstation of the National Institute for Medical Research in Mill Hill and was directed by Dr Andrews, Head of Bacteriology and Virology at the Institute, who had conceived the scheme for the unit and had it implemented in 1946 in the immediate aftermath of the war. It was, and remained until it was closed in 1990, the only place in the world where volunteers were kept in isolation from each other and the outside world to study the effects of possible cold viruses on them. In some ways the unit was run like a small hospital of the time, with a medical superintendent, a nurse matron, maids, cooks, porters, cleaners, maintenance staff to look after the volunteers and their accommodation, and scientists, technical and ancillary staff to undertake the laboratory work. Helio was employed as one of the scientists to tackle a major scientific question. 'How can we culture the common cold virus in the laboratory?' The resources were ideal and unique in the world but that did not make the task an easy one.

Although the site was isolated on the edge of Salisbury, where little or no other research was done, Helio had the chance to go up to Mill Hill at frequent intervals and meet and talk science with others in Andrews's Department, visit the library, arrange to get equipment made for him and so on. He also enjoyed the progress that his family was making: the children were starting at schools in the town and from time to time they could entertain visits from relatives. In due course his wife returned to the laboratory in the local hospital, where the microbiology laboratory was also part of the Public Health Laboratory Service. He had some success in his research and in 1957 he moved to Mill Hill to enter Andrews's laboratory and his wife to take a post in the Virus Reference Laboratory of the Central Public Health Laboratory at Colindale, not far away in the northern suburbs of London. There he greatly enjoyed the opportunity to discuss his interests with able and imaginative investigators in the same department and elsewhere in the institute. This experience was enhanced by meeting the many visitors from abroad who passed through or stayed as visiting workers.

In 1961 he became Director of the World Influenza Centre, which brought contacts and collaborations with influenza workers from round the world. He remembered particularly a collaboration with N. Nardelli and A. Rinaldi on avian influenza in Italy. He also returned to Brazil and, apart from short visits, spent one year at the University of Brazil in 1960–61, and at the University of São Paulo in 1965. In 1963 he spent three months at the University of Montevideo.

In 1973 he left the National Institute for Medical Research for the Animal Virus Research Institute, Pirbright. There were apparently several reasons for this. He had become more

* Numbers in this form refer to the bibliography at the end of the text.
interested in comparative virology; there was a link with his department at NIMR going back to the days when Andrewes had been on the governing body at Pirbright; and he saw the possibility of interesting studies like those that he had been doing at Mill Hill through the World Reference Laboratory for Foot and Mouth Disease (FMD); this was an integral part of the Department of Epidemiology, which he was to head. The institute had a substantial programme of research on exotic viral diseases, ranging from basic virology to studies of pathogenesis and vaccine development, and he found 'a congenial atmosphere for research unencumbered by administrative duties'. There were practical difficulties, of course, and he had to plan his journeys carefully whenever he wanted to drive from his home in north London to the Institute in the country to the South without being trapped in the very heavy traffic in between.

In 1979 he retired from Pirbright and became a Scientific Consultant to the Instituto Oswaldo Cruz until 1985, when he became Pesquisador Titular. During this period he lived for much of the year in Rio de Janeiro, enjoying and supporting members of his Brazilian family. When the weather became too hot he liked to be back in the UK. He was able to help many young scientists by guiding and supervising research projects, most of them arising from the local health problems, though while working on these they developed new methods and discovered new viruses. His wife joined him for some long periods and she, for example, organized an important study of the viruses that caused acute respiratory illnesses in children in the city. They had significant input to a meeting in the city organized by the World Health Organisation to draft a protocol to be used in studies of this type throughout the world as part of the Organisation's Respiratory Diseases Programme. At this time Peggy was still in the UK Public Health Laboratory Service. Once she retired she planned to go to Brazil and see much more of Helio. Tragically, not long after she arrived, they were both involved in a serious road accident in which the car in which they were being driven was in collision with a bus. Peggy was killed outright and Helio was seriously injured.

He continued to be involved in scientific issues and at the age of over 70 he became an honorary visiting professor for a year at St George's Medical School, London University, and he visited the Center for Disease Control in Atlanta, Georgia, as a visiting fellow for a year to work on the characterization of some unusual viruses found in faeces collected in Brazil. Back in Brazil he was entertaining his granddaughter from England. He had proudly 'shown her off' to friends and relations, and after a morning at the beach returned to his flat, where his body was found later in the day. One suspects that he would have called that an ideal end to a remarkable and productive life.

RESEARCH CAREER

The common cold

Helio arrived at the Common Cold Research Unit at a time when the basic methodology of work in volunteers had been established and the group had tried hard to confirm various claims in the literature that colds in animals could be caught by man or that material from human colds would induce colds or some other recognizable symptoms. The unit had particularly studied claims for the propagation of cold virus in the embryonated hen's egg, but had failed to produce colds in volunteers with material from inoculated eggs. In the early 1950s came the exciting news from the USA that poliomyelitis and other viruses that had
never before been convincingly propagated in the laboratory had been grown by Enders and his collaborators in cultures of human foetal tissues. Helio became involved in this area in two ways. First he set up studies of ‘model’ respiratory viruses, to discover how to handle such systems and establish the important factors to control if a virus was to grow well. For this he used suspended chick embryo cells and fowl plague virus, an influenza virus of birds (8, 9). Secondly he used a pool of nasal washings containing a cold virus obtained from one of his colleagues, D.M. Chaproniere, for passage in organ cultures of human foetal lung. They saw no cytopathic effect but they took the medium and inoculated it into volunteers; typical colds occurred a few days later. They continued passing serially from one culture to another until all the cultures they had made from that particular embryo had been used. At each passage level tested they could produce colds with the medium. This seemed such an important and clear-cut finding that a short paper was sent to The Lancet announcing that the common cold virus could be grown in cultures of human embryo lung in roller tubes (7).

Having done this they set out to repeat and develop the method but in the succeeding four years were not able to do so. Later work showed that foetuses vary considerably in their sensitivity to these viruses and one must assume that they were the victims of chance variations in the embryos that they received. There is no doubt that they had grown a cold virus. Many years later, Sylvia Reed working at the unit took a culture fluid that had been stored at the time of the original experiments and tested it in a highly sensitive strain of fibroblasts. She found that the virus grew well and produced a cytopathic effect in the cells and typical colds in volunteers. It turned out to belong to what had been designated as rhinovirus type 9 and was subsequently used for many studies in volunteers, particularly because it was sensitive to a range of antiviral drugs. There is no doubt that the study reported in 1953 was a careful and systematic piece of work, which in retrospect can be seen to have been the first successful propagation of a common cold virus in the laboratory. However it did not seem like that at the time and Helio changed the direction of his research to work on a new virus group, the adenoviruses.

Adenoviruses

Adenoviruses were first described in human adenoid tissue cultures and associated with acute respiratory infections in young adults by researchers in the USA shortly after Helio joined the Common Cold Research Unit. As part of the unit’s objective of developing expertise in virus growth and detection in cells in culture, Helio, together with Kelly (12–14) used adenoviruses to distinguish two different types of cytopathic effect in virus-infected HeLa cells, of the sort on which infectivity titrations are based. One effect that occurred early after infection seemed to be toxic in nature; the other was related to virus replication. On his transfer to the National Institute for Medical Research in 1958 Helio was able to show that the characteristic clumping and rounding of cells early in infection was caused by a trypsin-sensitive protein that could be separated from virus in infected-cell extracts by centrifugation, and that the effect did not involve cell killing and was reversible (15, 16). In subsequent studies he showed that the cytopathic effect was neutralized by adenovirus antisera and eventually that the protein involved was the penton antigen (see below) (19–22). Only recently it has been shown that, as a virus component, the penton’s interaction with cell-surface integrins is required for the cellular uptake of infecting viruses. Because integrins are the receptors through which cells attach to extracellular matrices, interference by pentons with these interactions seems to be the basis for the early cytopathic effect.
In continuing his studies of adenovirus infections of cells in culture, Helio, in collaboration with the electron microscopist Valentine, determined the number of virus particles in an infectious unit to be between 10 and 100 (17). Together with Allison and Balfour, he was also able to establish conditions for the study of one-step growth curves of adenovirus type 5 and to determine the kinetics of replication by immunofluorescence, concluding that each infected cell produced about 50,000 viruses (18). This line of study was eventually extended with Russell and colleagues to address the times of synthesis of each of the virus proteins (33). By defining these parameters and the conditions required for virus replication a virus–cell system was established that became the basis at Mill Hill for the preparation of virus and virus proteins and for subsequent studies of virus replication, structure, and antigenicity.

Extracts of infected cells contained virus particles and large amounts of virus proteins, the 'soluble antigens' that are produced in excess during infection. In a collaboration with Allison and Farthing, Helio purified individual proteins by electrophoresis, detecting them antigenically (19), and with Klemperer he showed that similar purification could be achieved by ion-exchange chromatography (22). This procedure in particular became central to subsequent studies of the virus proteins and provided material essential for defining the distinct antigenic components of the virus. It led to the identification with Kjellen of the hexon as the type-specific neutralizing antigen as well as the group-specific antigen (36); the definition of the penton as the trypsin-sensitive protein responsible for the early cytopathic effect (23); and the identification of of the fibre antigen as the haemagglutinin, the cell receptor-binding protein (24). In addition it allowed studies with Haase and Mautner on the immunogenicity of the hexon and with Haase and colleagues in the USA of its use in vaccination trials (48, 49). Most importantly, DEAE-chromatographically purified proteins were used in Helio's studies with Valentine and Russell on hexon crystallization (38) and with Mautner on fibre crystallization (47). These were the first two proteins from an animal virus to be crystallized. Their analyses did not progress at Mill Hill, beyond initial characterization of the crystals (42), but the research that the analyses involved created a supportive environment for virus protein analysis and structure determination in which numerous studies of adenovirus, arbovirus and especially influenza virus proteins were subsequently initiated.

With the availability of purified virus proteins, Helio also collaborated with Valentine in a classic study of virus structure by electron microscopy (28). Valentine's research had already indicated that adenoviruses were probably icosahedral and this was clearly established by Horne, Brenner, Waterson & Wildy in their first experiments with negatively stained animal viruses. Helio and Valentine now showed by comparing images of purified virus proteins and virus particles that, of the 252 capsomers that form the virus capsid, 240 have six nearest neighbours and are approximately spherical with a diameter of 80 Å. The remaining 12 capsomers are at the vertices of the icosahedron and have five nearest neighbours. They consist of a trypsin-sensitive sphere 80 Å in diameter, attached to which is a fibre about 250 Å long terminated by a smaller sphere about 40 Å in diameter. Most remarkably, in some images of the intact virus the fibres could be seen projecting 250 Å from the vertices.

By agreement with colleagues in the field, the three proteins of the virion capsid were subsequently named hexon, penton and fibre (30).

A number of additional electron microscopic studies with Russell and Valentine on the effects of heat on virus structure (34), with Laver, Russell and Valentine on the isolation of an internal component from virus disrupted with acetone (37), with Laver and Wrigley on the removal of pentons from viruses at low ionic strength (41), and with Wrigley on the
consequences of incubating viruses in deoxycholate and trypsin (50), were all designed to support this description of the virus and to obtain information on its assembly and disassembly. They led to the observations that the pentons could each be isolated in association with five peripentonal hexons, that the remaining 180 capsomers could be obtained as twenty groups of nine hexons that form the twenty faces of the icosahedron, and that inside the capsid there is a nucleoprotein core. The last of these studies with Wrigley, published in 1974, was Helio’s final publication on adenovirus from the National Institute for Medical Research.

Influenza

On his return from a sabbatical in Brazil in 1961, Helio took over the position of Director of the World Health Organisation’s World Influenza Centre at Mill Hill from Alick Isaacs (F.R.S. 1966). He had had a long-term interest in influenza, having used the influenza virus, Fowl Plague virus, in the early 1950s at the Common Cold Research Unit as a model virus in establishing tissue culture systems for the replication of viruses generally, but especially those infecting the respiratory tract. By using cells derived from chicken embryos he optimized the conditions for virus production and introduced roller tube cultures of chick cells and embryonic lung cell cultures, in collaborations with Gompels (10) and Chaproniere (11) respectively, as being particularly favourable for virus propagation.

The early 1960s were the middle years of the Asian influenza pandemic. Asian influenza infections had been first detected in humans in 1957 and Helio’s work in the Centre plotted the course of the pandemic with antigenic analyses of viruses isolated in national influenza laboratories throughout the world, by using haemagglutination inhibition and strain-specific complement fixation tests. Together with Law and his wife Peggy, who as Head of Virology at the Public Health Laboratory Service at Colindale had responsibility for influenza surveillance in England and Wales, he summarized in 1964 the importance of this work in establishing requirements for changes in vaccine virus components and for updating diagnostic and reference reagents (25).

An extensive outbreak of influenza in Hong Kong in July 1968 heralded the appearance of the Hong Kong influenza viruses and was the most important epidemiological event during Helio’s directorship of the World Influenza Centre. These antigenically novel viruses resulted in a new pandemic and replaced the Asian influenza viruses. In an important paper to The Lancet in December 1968 together with Coleman and Dowdle, from the International Influenza Centre for the Americas of the National Communicable Disease Center in Atlanta, Chang from the government virus unit of the Medical and Health Department in Hong Kong, and Schild from Mill Hill, Helio reported a detailed characterization of the new virus (39). They showed that of the two virus surface antigens only the haemagglutinin was different from that of the previous Asian viruses; the neuraminidase was unchanged. They also showed that there were low but reciprocal cross-reactions between the Hong Kong haemagglutinin and the haemagglutinin of a virus previously shown, in 1963, to be responsible for influenza outbreaks in horses; the neuraminidases of the equine and the new Hong Kong viruses were unrelated. The significance given to the possible equine influenza origin of the new human influenza virus haemagglutinin was based on proposals for the generation of new pandemic viruses by the reassortment of virus genes in mixed infections.

Helio’s research in the World Influenza Centre contributed to the experimental basis of these proposals. He had developed a particular interest in avian influenza viruses that began
with a comparison of the antigenic properties of a collection of avian viruses, in which cross-reactions between animal and avian viruses were established and consideration was given to the classification of influenza viruses on the basis of their species of isolation and their antigenicity (26). Subsequent comparisons of human, porcine, equine and avian viruses led to the acceptance of host specificity as a major aspect of classification (29) and to the proposal of the existence of a reservoir of numerous antigenically different viruses in animals and birds that could, on occasion, overcome a host barrier (44). Further strain-specific complement fixation analyses established relationships between avian and human influenza viruses and these antigenic cross-reactions were eventually shown in neuraminidase inhibition tests, together with Webster (40), and in immunodiffusion tests, with Schild and Schettler (45), to be due to a common neuraminidase.

Estimates of the extent of variation within avian influenza reservoirs were also made by using isolates from poultry farms near Pavia in Italy from which sixteen different viruses were obtained from quail, ducks, turkeys, pheasants and chickens (31, 46). With colleagues from the Ministry of Agriculture laboratory at Weybridge and from the USA, six groupings of avian influenza viruses were described that subsequent amino acid sequence analyses have shown to have been correctly separated, with five out of six correctly grouped (29). Extension of these studies to influenza infections of migratory waterfowl was made in a serological survey in 1968 with Trainer, Tumova and Easterday, in which direct evidence of the infection of wild birds was obtained (35). Importantly for subsequent expeditions for virus isolation, the Canada goose (Branta canadensis) and the Snowgoose (Chen hyperborea), out of nine avian species tested, were shown to have been infected.

In parallel with these surveys of domestic and wild bird viruses, Helio and Tumova began a series of experiments on genetic interactions between animal influenza viruses, including human viruses and avian viruses. These were initially designed to investigate the reason for the relative difficulty of obtaining evidence of genetic interaction between viruses that were more widely separated in time of isolation, which had been taken as a reflection of unrelatedness. Most other studies of influenza recombination had in fact dealt with mixed infections between different human strains or between human and porcine influenza viruses. Helio and Tumova (27) showed that plaque formation by inactivated Fowl Plague virus could be reactivated by different human, porcine and avian viruses. Antigenic analyses showed that the viruses recovered were reassortants (32). Eventually, in collaboration with Easterday, Laver and Schild, Helio was able to demonstrate by haemagglutination inhibition, neuraminidase inhibition and immunodiffusion tests that one of them contained the neuraminidase of the human virus and the haemagglutinin of the avian parent (43).

These studies highlighted the possible role of avian influenza viruses in the generation of novel pandemic human viruses by recombination, a possibility that has subsequently been widely accepted. They also stimulated the search for influenza viruses in migratory birds in the 1970s and 1980s, a search that was strongly promoted by Helio and that with a variety of other studies led to the description of fifteen distinct influenza haemagglutinins and nine distinct neuraminidases, all of which have been identified in avian influenza viruses.

Foot and Mouth Disease

During his time at Mill Hill, Helio had been appointed to the governing body of the Animal Virus Research Institute at Pirbright, Surrey, where the main subject of study had been FMD virus, not only as it concerned the health of animals in the UK but as a worldwide problem.
Helio knew that FMD was a serious and continuing problem in South America and as he approached the time to retire from the Medical Research Council he 'rather tentatively' approached the then director at Pirbright, John Brooksbys, F.R.S., with the suggestion that he might spend a few years at the institute working on the epidemiology of FMD virus. The outcome was that he was made Head of the Epidemiology Section. Virus strains were sent to the section from various parts of the world and it was already known that a number of serotypes could be distinguished by complement fixation and neutralization tests and that some of the differences in strains revealed were significant because vaccines made with the 'wrong' strain did not protect in the field.

There was a feeling that epidemiology and the section in which it was done were rather boring and it was difficult to produce reproducible results—the exciting work was done in other departments. Helio dealt with this situation by introducing newer immunological methods, such as gel electrophoresis and electrofocusing to characterize and separate viral proteins, monoclonal antibodies as precise tools to augment or replace animal sera, and immunodiffusion and enzyme-linked immunosorbent assay (ELISA) tests for the detection of antigen-antibody interactions. When the results obtained with this improved technology were related to those of field epidemiology and experimental vaccination and challenge, it became apparent which of the earlier results were important, and strain typing and vaccine design were put on a firm basis (51, 52).

At this time there was a national problem with Swine Vesicular Disease, which mimicked FMD clinically but was not a risk for cattle. Nevertheless, epidemics could start up very quickly and spread if countermeasures were not taken without delay. It turned out that the virus was related closely to a Coxackievirus and could indeed infect humans. Helio built up a group of tests for the rapid diagnosis of the infection so that field workers could have an answer within a very few days of material's arriving at Pirbright. In the course of the routine work three new porcine enteroviruses were recognized and formally described (53).

In all this work he interacted closely with others working in the Institute. F. Brown, F.R.S., and his colleagues were studying the basic biology of FMD and other viruses; their molecular analysis, by T1 ribonuclease mapping and later by sequencing, was welcomed by Helio as providing new dimensions to understanding the viruses and new techniques to be exploited.

**Comparative virology**

All those who knew him agree that Helio was a gentle and modest man, self-depreciatory at times. On more than one occasion when he was referred to as an 'adenovirologist' he corrected the speaker, saying he was an 'adenovirologist type 5'. It may have been that this was his way of drawing attention to the very important biological principles that he had uncovered while concentrating, as good biologists often do, on a system that can be made to yield specific results, which can then be generalized. Nevertheless, in addition to his being a focused investigator he was also a man of broad vision, aware of the large and complicated environments in which all living things operate, and fascinated by the similarities, differences and relationships that these very complex interactions revealed. His early experience of fieldwork and the influence of Cowan and Andrewes probably led him to the mixture of natural history and virus taxonomy out of which grew his interest in comparative virology to which he contributed a great deal, particularly through the book *Viruses of vertebrates*.

As James Porterfield recalls, *Viruses of vertebrates* was a book that had a remarkable influence on virologists and the way in which they began to think of all the varied families
and species of viruses in systematic terms, as well as being a very convenient source of essential information about any organism. It was of course the brain child of Christopher Andrewes, but Helio certainly sustained and developed it as Andrewes moved further and further into retirement. James Porterfield describes how it happened.

I cannot think of Helio without thinking of *Viruses of Vertebrates*. I have copies of all five editions, and I was looking through these to see how they changed as Helio’s role increased. In the first edition which CHA [Andrewes] wrote alone, thanks are expressed to 13 virologists named in alphabetical order and including Helio and both of us [J.W. Porterfield and D.A.I. Tyrrell]. The second and third editions were ‘Andrewes and Pereira’, and there are no separate acknowledgements. CHA had by this time retired and Helio put an immense amount of work into these two editions. Peter Wildy joined him in the fourth edition, reducing the load on Helio somewhat, although he still wrote the greater part of the volume, which was read and checked by CHA throughout. By the time the fifth edition was being planned, Peggy, Os Jarrett and I were recruited to join CHA, Helio and Peter, but after Peter Wildy’s death in 1987 the volume very nearly collapsed. Helio and I met several times when he was back from Rio and we both felt that, while CHA was still alive we should do everything in our power to see that the 5th edition did not fall by the wayside. Eventually I became overall editor, and for the first time individual chapters were attributed to different people. Of the 23 chapters in VVV, as we called it during its gestation, Helio wrote 9, I wrote 6, Peggy wrote 3 before she died, and the remaining 5 came from others.

From this very brief account, Helio’s contribution over the years is apparent. He was certainly very much more than an ‘adenovirologist type 5’. As that last edition came off the press the time for such books was passing, but many must feel grateful that for so many years the books were available to refer to and to influence their thinking.

Helio also exercised his influence by his participation in committees, such as the Executive Committee of the International Commission for the Nomenclature of Viruses and as Chairman of its Vertebrate Virus subcommittee. He was also Vice Chairman of the International Committee for the Nomenclature of Viruses. These were not administrative bodies so much as scientific discussion groups at which consensus was thrashed out regarding the truths to be expressed in the names to be given to new and old organisms. In such discussions he spoke for reason and wise balance.

**Research in Brazil**

Helio left the UK and returned to Rio de Janeiro, and was in close touch with the work going on in virology. For example, there were continuing studies on the aetiology of acute respiratory disease, especially in children. He focused on diarrhoea and the role of viruses in disease in local children (54). With a team of collaborators he evaluated the use of various methods available at the time for the detection of rotaviruses, such as the application of polyacrylamide gel electrophoresis, immunoelectron microscopy and enzyme immunoassay applied to faeces (55). He was also involved as an adviser to young people wishing to make progress as virologists and with Peggy and co-workers in making an essential response to the serious problems posed by AIDS in Brazil (57–59). He exploited electrophoresis and used it to characterize the rotaviruses, developing new methods with Gomes and co-workers for the laboratory diagnosis of adenovirus infections including *in situ* hybridization on clinical specimens (56). He also detected a new faecal virus, a picobirnavirus, which had a divided RNA genome and seemed to be associated with diarrhoea (60–62). He continued work on this problem in 1990 when he went to the USA as a visiting scientist at the Center for Disease Control in Atlanta. There he was able to study the virus further and to see his diagnostic...
Helio Gelli Pereira

methods applied to samples from patients with AIDS with and without diarrhoea (63). The results of this study showed that the virus was associated with diarrhoea and in an important proportion of cases (9%).

PERSONAL CHARACTERISTICS

It is difficult to capture the personality of an individual on paper but it is important to attempt to do so in this case because he was such an integrated person that what he did at home and at work and in various parts of the world has such a consistency about it that each illuminates the other. He gives the impression that as a boy he was not thought of or expected to be particularly academic or brilliant. Yet in spite of this he clearly felt that he wanted to learn how to do laboratory work and basic science and took opportunities when they were offered. Everyone noticed his quiet and gentle manner and personal courtesy, often enhanced by the way he would sit and puff his pipe during a laboratory discussion. He was never known to attack or humiliate a colleague even when he disagreed—and probably knew that they were wrong in their views. On the other hand, if one expressed interest in what he was doing or had discovered recently, he was only too glad to explain, and talk helpfully about problems that one might have had with applying his methods. Because he was so good at it one forgot that he was an accomplished linguist. His first language was Portuguese, which he could enunciate in rich and sonorous tones; he found it easy to ‘ad lib’ as he put it, in Italian, he was very familiar with French because at the time of his medical training the best textbooks available were in that language. However, he had a complete mastery of English and was able to write the text of an article in such a way that it required very little redrafting. This probably reflected the careful and orderly way in which he thought. His scientific style was to do experiments that made a point clearly and unambiguously and then write the work up in clear English prose with a few very straightforward tables and figures. His personality was such that although he did not seek to do large-scale team science he could always find co-workers with whom he could collaborate happily. He liked to be modest about his role and interests. Better than many scientists, however, he could use a detailed study of a narrow field to uncover important general ideas and because of his broad scholarship he was able to recognize their significance outside that field.

He started his career with a medical training when most of virology was concerned with viruses as a cause of disease, and he moved forward into a period when the basic molecular biology of virus structure and replication was found to be the proper basis for understanding their relationships and classification. He took all this in his stride, yet he did not forget his early interest in disease and was willing to return to clinical studies when these were required for answering questions about the importance of an organism to human health.

He was able to build very good relationships at work. Some people found C.H. Andrews a difficult though very stimulating person to work for, but Helio never complained on this score. Helio seemed to be universally liked and appreciated by his colleagues, and particularly by junior and visiting workers. Many will recall occasions, which would probably cause administrative convulsions nowadays, when coming in to check experiments on a Saturday morning, they were invited over ‘to coffee’. We sat along the bench where experiments were done all week, and watched while Helio took coffee that had been sent to him by his mother, double-roasted to give extra flavour, and extracted by boiling it in an old sock dropped into a
litré beaker over a Bunsen. We drank from small beakers, conversing all the while on subjects ranging from how coffee was grown to the latest excitement in molecular science in a relaxed, cheerful and friendly way that his presence encouraged.

His friendship did not stop there, as an example from M. Pollock, F.R.S., shows. Pollock mentions that although he had overlapped with Helio at Mill Hill he did not really know him at all well. Nevertheless he was given much advice when he was planning to take the Pollock family on their ‘trip of a lifetime’ round South America by motorized caravan in 1961. They reached Rio de Janeiro in April and it so happened that the Pereira family were there. Helio had arranged for them to have permission to camp in the Botanical Gardens while they were in the city, but when they tried to bring their caravan ashore they were met with steadfast opposition by the Customs authorities. In spite of daily visits to the Customs office and Helio’s fluent Portuguese the vehicle was impounded as they were not willing to pay its full value in cash as the authorities demanded. Meanwhile they were accommodated at the Pereira’s flat, where they were impressed by the family’s generosity and friendliness, and the time that Helio was prepared to spend in trying to resolve their difficulties. In spite of all his advocacy they had to acknowledge defeat and take ship to Uruguay to start their land journey.

Outside the laboratory, Helio was quiet and unassuming with a gift for friendship. He stayed a young man at heart in many ways; for example he took up skiing in middle age and he still went for a swim in the sea each day when he returned to Brazil. Also in middle age he decided to learn to play the cello, which he did to such effect that he could enjoy playing piano trios with his friends in the evenings. He and his wife Peggy are also remembered for happy, friendly parties to which they invited their friends in London, and supplied them with an abundance of wonderful food, especially if one of the grannies was staying. The family group in London was obviously not as extensive as that of his boyhood but he cared deeply about each of his children and the different ways in which each of them developed.

He had firm convictions in the political field and was thoroughly out of sympathy with the dictatorial government from which Brazil suffered for so long. It was partly this that impelled him to return to Britain when invited. Yet he retained a real affection for the country and the culture in which he had been raised and he certainly returned there to support his elderly aunts and other relatives and to encourage the young scientists in his own city.

APPOINTMENTS

1948–51 Assistant in the Rickettsial Department of the Instituto Oswaldo Cruz
1943–45, 1948–51 Assistant at the Chair of Microbiology of the Faculdade Fluminense de Medicina
1951–57 Member of the Scientific Staff of the Medical Research Council serving at the Common Cold Research Unit
1957–73 Member of the Scientific Staff of the Medical Research Council serving at the National Institute for Medical Research
1964–73 Head of Division of Virology
1961–70 Director of the World Influenza Centre
1974–79 Head of Department of Epidemiology and World Reference Laboratory for Foot and Mouth Disease at the Animal Virus Research Institute, Pirbright, Surrey
honours

1973 Fellow of the Royal Society
1975 Fellow of the Institute of Biology
1987 Carlos Findlay Prize, UNESCO

Public Appointments

Member of the Governing Body of the Animal Virus Research Institute
Member of the Committee on Immunological Products Control
Member of the Council of the Society for General Microbiology
Member of the Executive Committee of the International Committee for the Nomenclature of Viruses
Chairman of the Vertebrate Virus Subcommittee of the International Commission for the Nomenclature of Viruses
Vice-Chairman of the International Committee for the Taxonomy of Viruses; Life Member 1981

Member of the WHO Expert Advisory Panel on Virus Diseases
Member of the WHO Animal Virus Characterization Board
Member of the Ad-Hoc Committee on Non-Oncogenic Viruses of INSERM
Member of the Scientific Advisory Committee of the Pan American Foot and Mouth Disease Center

Acknowledgement

The frontispiece photograph was taken in 1973 by Godfrey Argent.

Bibliography

The following publications are those referred to directly in the text. A full bibliography appears on the accompanying microfiche, numbered as in the second column. A photocopy is available from the Royal Society Library at cost.


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