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Carl Prausnitz Giles – family doctor and father of reagin detection

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Abstract Dr. Carl Prausnitz Giles was born in Hamburg, Germany in 1876, the son of Otto Prausnitz, a Physician in the army reserve of the King of Prussia and Edith Giles, daughter of George and Elizabeth Giles of Bonchurch, Isle of Wight, United Kingdom. Carl qualified in Medicine at the Universities of Leipzig, Kiel and Breslau. He began work at the Hamburg Hygiene Institute, undertaking diagnostic work on cholera, plague, typhoid, diphtheria and tuberculosis. Carl frequently visited his mother's home in Bonchurch and became proficient in both German and English and obtained British medical qualifications, MRCS. LRCP. The key work, for which he is mainly remembered, was the discovery of the principle responsible for the supersensitivity of his co-worker, Küstner, to cooked fish. In a classic paper published in 1921, he showed this could be transferred to non-sensitive individuals. He called it reagin, eventually shown to be IgE antibody. The test demonstrating its existence, the Prausnitz-Küstner reaction, was used for many years to demonstrate allergy in patients. In 1926, Prausnitz was appointed Professor and Director of the Institute of Hygiene in Breslau. Due to his Jewish antecedents, in 1934 he was compulsorily

retired from his Chair in Breslau and moved his family to England. In 1935 he moved to Bonchurch. At the age of 60 years he embarked on a career in General Practice in partnership with a childhood friend, Dr. Bruce Williamson. He took his mother's maiden name and became Dr. CP Giles of Ventnor, Isle of Wight. UK.

Keywords Carl Prausnitz Giles · Allergy and immunology · Hypersensitivity · History · 20th century

Otto Carl Willy Prausnitz (Fig. 1) – also known as Carl Prausnitz or Carl Prausnitz Giles – was born in Hamburg, Germany, on 11th October 1876. He was the first child of Hamburg army physician Otto Prausnitz and Edith Giles, the daughter of George Giles, a railway engineer from Bonchurch, Isle of Wight, United Kingdom.

Carl Prausnitz attended school in Hamburg starting with primary education at Höhere Bürgerschule. In 1895, he moved on to the Wilhelm-Gymnasium to study Latin, Greek, and history. Afterwards, he studied higher mathematics, physics, heat and light, electricity, and mechanics at the Technical High School in Darmstadt, Germany.

He then began his medical training at the University of Leipzig, Germany, where he spent two years taking the equivalent of the 1st and 2nd MB in Britain (anatomy, physiology, chemistry, and botany). Carl Prausnitz progressed to Kiel University in the city of Kiel, Germany, and spent a year studying clinical medicine and surgery, before moving to Breslau in May 1899 for the final period of his training. He completed his examination before the Medical Examination Commission in Breslau on 26th February 1901. The Certificate of the Staatsexamen was endorsed “good”. One year later, he submitted himself to the

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Fig. 1 Prausnitz as a young man

University of Breslau for examination as Doctor of Medicine (MD), which was awarded with the highest commendation 'summa cum laude' on 14th February 1902.

Carl Prausnitz accepted an appointment as house surgeon at the Hamburg Masonic Hospital once he had qualified. Very soon an opportunity arose to take a research post in the same city. William Philipps Dunbar, a young physician of American parentage but trained in Germany, had been appointed as Director of the Hamburg Hygiene Institute in 1893, in the wake of a devastating cholera epidemic. Prausnitz obtained a post as assistant to Dunbar in June 1901 and remained for four years. Much of the work of the Institute was directed at the prevailing infectious diseases. William Dunbar had a particular interest in hay fever from which he suffered and which he considered a reaction to some toxic factor in pollen. Dunbar and his assistants carried out many experiments in which they induced the symptoms in the eye and respiratory tract of vulnerable individuals. Prausnitz, towards the end of his life, stated that he and Dunbar had been unaware of the pioneering work of Charles Blackley in Manchester, UK, which had confirmed the relationship between grass pollen and hay-fever.

Carl Prausnitz describes how he and Dunbar were working together on a pollen antitoxin "pollantin", a preparation obtained by immunizing horses. On one occasion Prausnitz administered an injection to the professor, who fell unconscious to the floor. He describes his anxiety and powerlessness "at that time we had no adrenaline, no coramine. I just stood helplessly at his side until he recovered." Hypersensitivity to horse-serum among a number of recipients of pollantin caused Dunbar and Prausnitz to abandon their pioneer work on desensitizing for hay-fever.

Prausnitz's English connections took him to London, UK, to a post at the Royal Institute of Public Health. Here, Prausnitz was engaged in diagnostic work, chiefly involving diphtheria, typhoid, and tuberculosis. His publications in this period were con-

cerned with disinfectants; one intriguing contribution to the first volume of the Journal of the Society for the Destruction of Vermin was entitled "The destruction of rats on ships". At this time he took the opportunity to obtain a British medical qualification, the conjoint diploma of the Royal Colleges of Physicians and Surgeons (MRCS, LRCP).

After the First World War, Carl Prausnitz returned to his post in Breslau and resumed his diagnostic and teaching responsibilities. His research output increased with publications on typhus, the diagnosis of syphilis, treatment of hay-fever by desensitizing, the use of serum to counteract infections, and into the nature of bacteriophage. His most remarkable discovery was made in 1921 ([1]; for the English translation of his original work see electronic supplementary material at doi:10.1007/s40629-016-0004-9; Fig. 2). Prausnitz was aware that a colleague, Heinz Küstner, had an extreme sensitivity to cooked fish. On one occasion, he had developed an urticarial rash after dining in a restaurant. Küstner had eaten no fish but used cutlery that had been washed with knives and forks used for fish. In Prausnitz' own words:

Küstner had for many years been suffering from hypersensitivity to fish; the smallest trace of fish eaten by him caused intense sickness and diarrhoea, urticaria and asthma, one of these attacks was almost fatal. Extracts were prepared from boiled fish, which were filtered through Berkefeld filters and tested for sterility. These extracts, even in quantities corresponding to 1/100th of a milligram and less of the original fish, when injected subcutaneously to Küstner produced the signs of an attack: by intra-cutaneous injection of minute quantities of the extract typical papules were obtained within a few minutes which subsequently were surrounded by a halo, and disappeared after half an hour. The chemical properties of the antigen, its heat stability, for example, were demonstrated. It appeared desirable, however, to find a method by which similar tests could be performed without running the risk of harming the supersensitive patient by causing a possibly dangerous attack through injection. I therefore devised the method of transferring the supersensitive substrate to a non-sensitive person; this should be done in such manner that the latter should not become permanently supersensitive, as had occurred in persons having received transfusion of blood from an asthmatic person. Therefore the serum of Küstner was injected intra-cutaneously to myself, not being fish hypersensitive, in various dilutions. The following day fish extract was injected into exactly the same spots of the skin, as well as to spots not previously treated. A strong reaction appeared immediately afterwards, but only in the spots treated with Küstner's serum, both concentrated and diluted. It was therefore proved that his serum contained antibodies responsible for the reaction of supersensitiveness.



Fig. 2 Prausnitz at the time of publication of the “reagin” paper 1921

It is impossible to over-estimate the significance of this observation. Prausnitz and Küstner had demonstrated that the serum of an allergic individual contained a specific factor that, when transferred to another without that allergy, would produce the characteristic allergic response when the non-allergic individual was challenged. The factor was named “reagin” by Coca and Cooke but another 45 years were to elapse before the nature of reaginic antibody, responsible for most immediate allergic reactions, was determined by the married couple Kimishige and Teruko Ishizaka, working in the United States, and independently by Hans Bennich and S. Gunnar Johansson in Sweden. In the interim, the Prausnitz-Küstner (PK) reaction was used widely in determining the presence of antibodies. Medical students in many countries learned how to perform the PK test, although relatively few of them might know too much of the eponymous originators of the test. Since 1966, methods have become available to measure total and specific levels of IgE in the blood so that the PK test has been relegated to history.

On April 1st 1926, Carl Prausnitz was appointed to succeed his friend and mentor, Richard Pfeiffer, as Director of the Hygiene Institute in Breslau. However, after National Socialists came to power in 1933, Prausnitz became under increasing pressure, due to his Jewish antecedents. In October 1933, the Ministry of Education in Berlin granted Carl Prausnitz indefinite leave without pay; In April 1934 he was compulsorily retired from his Chair in Breslau. Not unnaturally he turned for sanctuary for his family and himself to his mother's home, England.

The stature of Carl Prausnitz at the time qualified him for an academic role of the first eminence but such a post was not immediately available to him. He was invited by Professor Hugh Maitland to his department at the University of Manchester and so, at the age of 56 found himself again a research fellow, albeit one of great distinction. He succeeded in obtaining

small grants from the Medical Research Council and the Rockefeller Foundation to cover his stipend and the costs of his research. He turned his attention to the problem of asthma in cotton spinners. Fifteen years earlier, Richard Pfeiffer had described Prausnitz as having “a complete command of method and utmost exactitude in his work”. Perhaps then it is not surprising that he should produce a paper “Investigations on respiratory dust diseases in the operatives in the cotton industry” that has been described by Professor Robin Coombs of Cambridge, UK, as “a model of research in clinical immunology” [2]. The investigation in Professor Maitland's Department had been initiated by the home office who were concerned at the ill-health, particularly respiratory disease, in card-room workers in the cotton industry. Preliminary epidemiological work into the prevalence of such problems among cotton operatives was carried out by Bradford Hill. Then, John Crighton Bramwell and Arthur William Mickle Ellis examined many cotton workers and suggested that some form of sensitization to cotton dust was playing a role in symptomatology.

Carl Prausnitz studied “strippers asthma”, suffered by the cotton workers, and noted the symptoms were worse when the patients were in close contact with the dust and improved when they moved away from it. The symptoms were often at their worst at the beginning of the week after a day or two away from work. The syndrome earned the name “Monday Fever”. Prausnitz concluded that cotton dust contained a substance, or group of substances, in the protein fraction of the dust, that was responsible for the allergic reaction in the lungs. He did not consider histamine, which Maitland had found in the dust, to be the causal toxic agent.

Prausnitz' background in industrial medicine, as well as bacteriology and immunology, qualified him to investigate this major disease and offer advice on preventive measures to minimize exposure to the sensitizing dust particles.

His report received wide coverage in the national press at the time. Headlines ranged from “Cause of Stripper's Asthma” in the Manchester Guardian to a somewhat patronizing “German solves a problem of cotton mills” in the Morning Post.

During this time, Carl, his wife Margot, and their son Christopher lived very modestly in Manchester. Carl's stipend as a research fellow was small and his salary from Breslau had ceased. He was invited to take the Chair of Hygiene at the University of Zurich, Switzerland, but he had decided that the future for Margot, Christopher, and himself lay in the UK. He therefore chose to make a change of direction that few medical men or women would feel able to make as they approached 60 years of age – a move from the comparative shelter of academia to the “coal-face” of general medical practice as a rural family doctor (Fig. 3).

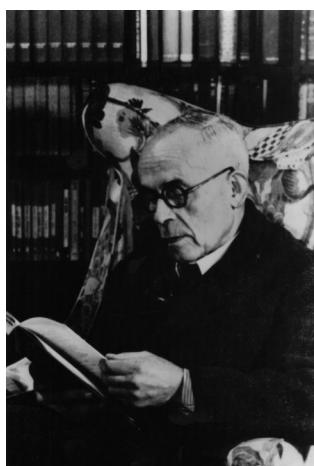


Fig. 3 Prausnitz when in general practice

The contrast between life in a city undergoing the first experience of man's extreme intolerance to man, now called ethnic cleansing, and into a small, out of the way, English village in the mid 1930s could not have been greater. Perhaps it is not surprising that Carl Prausnitz' desire to escape from National Socialism took him to Bonchurch. He had maintained links with his mother's home throughout his life. As a school-boy he had visited aunts and cousins living on the Isle of Wight during his holidays. There had been many opportunities to maintain these family relationships during his five years working at the Royal Institute of Public Health and for the Metropolitan Asylums Board.

Carl Prausnitz used to visit a general practice family called Williamson at their home in Ventnor, Isle of Wight, and was particularly friendly with a son Bruce. Bruce followed his father into general practice. In 1935, Bruce was seeking a partner to take the place of a retiring partner. Prausnitz was concluding his studies in Manchester and when he was told by his great aunt Amy of the vacancy, he decided to apply. In those pre-National Health Service days it was necessary to buy one's way into general practice and Carl had to borrow a substantial sum of money to do so. In consequence, he was never to be wealthy but his style of life was modest, even austere, in 1935 the family moved from Manchester to Kingseat, Bonchurch, Isle of Wight, which became the family house and surgery. Carl fitted out the basement as a laboratory believing that he would be able to undertake various investigations, and perhaps continue his research. In the event the clinical needs of his patients precluded laboratory research although he continued to contribute to scientific knowledge from his intellect and experience until he died.

Carl applied himself to his new responsibilities as a family doctor in the only way he knew completely. He rapidly obtained the respect of the local community although even the "back of the Wight" was not unaware of the storm clouds developing over Europe.

As the Second World War grew closer, anti-German feeling became evident and the Prausnitz' family was not spared it. On one occasion, on the tennis courts of Ventnor, a local lady declaimed in a loud voice "what are those Germans doing here?". If there was any conflict of loyalty the family did not show it. Carl formally added his mother's maiden name to his own, becoming Prausnitz Giles, and the family took the oath of allegiance to the British Crown. Carl joined the Local Volunteer Force, later known as the Home Guard, with the rank of Captain.

Carl had resolved not to return to Germany but he was persuaded to go to Berlin in 1958 to receive the Aronson award of the Robert Koch Institute. Two years later, in 1960, he accepted recognition that must have given him great satisfaction, an honorary Doctorate of Medicine from the University of Hamburg. He continued to work tirelessly for his patients in Ventnor. He always regarded himself on call and made few concessions to his advancing years. Shortly before he retired, he attended an emergency on the top of Saint Boniface Down the steep hill lying to the North of Ventnor. He climbed the 750 feet, carrying his medical bag, to attend to an injured holiday-maker. He was then 80 years old.

Carl retired officially in 1960, in his 84th year, but continued to visit his patients "my old friends" as he called them.

Although by now becoming frail, his mental faculties in no way deserted him and he read all the proofs of Cell and Coombs now classic textbook *Clinical Aspects of Immunology*. The early editions of the book include English translations of the original Prausnitz-Küstner paper of 1921, the translation being by Prausnitz himself, which is now made available again to our readers as supplementary material at doi:[10.1007/s40629-016-0004-9](https://doi.org/10.1007/s40629-016-0004-9).

What then is Carl Prausnitz' place in medical history? In an obituary, David Harley wrote "his name is assured of an honorable place in that select band of medical immortals for the discovery of the Prausnitz-Küstner test". That must be so, and the more than 100 publications on many aspects of immunology, microbiology, industrial, and preventive medicine, are testimony to an outstanding and innovative doctor. But Harley continues' perhaps he would have liked his epitaph to be "Here lies an old-fashioned country general practitioner who used to be a professor once-upon-a-time", for thus did he describe himself, such was the humility of the man.

The consequence of that decision, to become a general practitioner, undoubtedly resulted in Carl Prausnitz Giles receiving less recognition internationally than was his due. Academic and civil honors are desirable, and many seek them strenuously and envy those to whom they are given. But such vestiges are of little worth compared with the affection and respect the patients of Dr. Giles bestowed on him. For many years after his death, his former patients continued

to mourn his passing. This eminent academic had become the epitome of a family doctor. The stone at the head of his grave in Saint Boniface churchyard could bear no more apposite inscription “Beloved Physician”.

Conflict of interest A.M. Edwards declares that he and the late D.W. Hide have no competing interests.

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