



HISTORY OF MEDICINE

Marinus van den Ende

Jan van den Ende

Marinus van den Ende was one of South Africa's most outstanding medical scientists. Jan, his eldest child, delivered the eponymous memorial lecture on 6 November 2007 on the 50th anniversary of the death of Marinus. Present also were Marinus van den Ende's widow, and his daughter Joan. Jan

was 15 years old and the van den Ende's youngest daughter Marina 5 when Marinus died in 1957. This occasion provided more detail on van den Ende's life and achievements, as previous lectures had included only brief overviews.

Origins

Marinus van den Ende was born on 9 February 1912 in the small Northern Transvaal town of Potgietersrust, now Makopane, in Limpopo province. His father, also Marinus, was a Dutch pharmacist born in 1880 who had travelled from The Hague to join two other Dutch pharmacists who had set up in Pietersburg. Subsequently he moved to Potgietersrust to start a pharmacy there.

Marinus (the elder) married a Dutch lady, Miss Ida Austermahe. They were married by proxy (as expressed in Dutch: *'met die handschoen getrouwd'*), presumably because in those days it was not considered seemly for an unmarried woman to travel alone by ship from the Netherlands to the Cape. Her husband met her in Cape Town, where they had a church wedding; they then travelled to Potgietersrust. Ida died in 1920 aged 38, when Marinus was not yet 9 years of age. Marinus had an elder brother named Hein and a younger sister, Ida. Marinus (the elder) married again and he and his new wife, who had been a Miss Kirchner, had two sons, Ireneé and Gerhard. Marinus (the elder) died in 1936.

Marinus must have had a very strict upbringing, as he was not encouraged or allowed to participate in sport as a child, but was expected to work in the vegetable garden after



Marinus van den Ende

school! He excelled academically at the small village school in Potgietersrust, matriculated at the age of 15, and proceeded to the University of Cape Town to study medicine in 1928.

Early years at UCT

A contemporary, the late Dr Bob Riemer, remembered that Marinus had arrived at Smuts Hall in khaki shirt and shorts. He spoke Dutch, German and Afrikaans, with English as his fourth language. Legend holds that his new-found fellow students promptly took him to Randalls to teach him to drink beer! As an undergraduate Marinus was known as 'Duck' by his contemporaries, because someone thought his surname was 'van den Eende'. Later in the UK he would be called 'Van', and to others he was 'Rinus'. In this way one could work out at what stage of his career different persons had met him.

Marinus graduated MB ChB in 1933, with distinctions in Anatomy, Physiology, Psychiatry and Surgery. He was an intern at New Somerset Hospital in 1934, where he earned the princely salary of £8 6s 8p!

Jan van den Ende is a pathologist and University of Cape Town graduate. His career has included chairs in Medical Microbiology at the universities of the (Orange) Free State and Natal and directorship of the former South African Institute of Medical Research, followed by a period in private pathology practice. His interests include the diagnosis, treatment and prevention of infections and tropical diseases. He is currently employed as a consultant microbiologist in the UK. He is the eldest child of the late Marinus van den Ende.

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In 1935 he joined the Pathology Department at UCT Medical School, under Professor B J Ryrie, as a junior assistant in Pathology and Forensic Pathology until 1937. Professor J H (Jannie) Louw's book *In the Shadow of Table Mountain* records that during this period van den Ende attempted to produce Hodgkin's disease in a rabbit, by injecting it with lymph node material from a patient, because he thought it might be an infectious condition.

Cambridge, UK and war experience

At the end of 1937 Marinus became the second recipient of a John Lucas Walker scholarship (Florey of penicillin fame was the first) and proceeded to Cambridge University, where he was awarded a PhD in Pathology in 1940. His dissertation was entitled 'Some observations on so-called reversed anaphylaxis and related phenomena'.

At Cambridge Marinus met Sir Henry Dale, then Director of the National Institute for Medical Research (NIMR) of the (British) Medical Research Council. This contact, and Sir Henry's appreciation of his research potential, was the turning point of his career. Dale supported his transfer to the Institute in Hampstead in 1938, where he was offered a permanent post in 1939. Thus, in the prewar milieu in the company of other like-minded and motivated researchers, he embarked on an exciting research career.

In 1939, days before the declaration of World War II, Marinus married Miss Joan Herold Barry. They had met at UCT Medical School, where Miss Barry, a BSc graduate, was working as laboratory assistant in the Bacteriology Department. In London she initially worked at the New Westminster Hospital and later at the NIMR.

Marinus initially refused the permanent post, as he intended to return to South Africa, where he believed his duty lay, but nevertheless received approval to remain in England until the end of 1939. With war becoming imminent he obtained special 'war leave' from the University of Cape Town and the Cape Hospital Board, and he and his wife remained in England for almost another 7 years. During the war they endured the harrowing doodle bugs (V2 bombs), experienced nights in bomb shelters, and served as fire wardens during the 'Blitz'!

At the NIMR Marinus worked with a team investigating aspects of infection, with particular reference to the war effort. The two major areas of involvement were 'air hygiene' and rickettsia infections.

The air hygiene studies had a particular emphasis on investigating possible risks posed by crowding in various war situations – civilian and military. Accurate air sampling equipment was designed, built and tested. Viable counts were performed in various settings, including mess areas on ships, schools, wards, etc. Various mask materials and designs were developed and tested. Van den Ende was heavily involved in evaluating the ability of various oils on floors and bedding,

to trap dust and reduce aerial bacterial counts. The emphasis in these settings was on *Staphylococcus aureus* and various streptococci – the most common and important pathogens in wound sepsis.

Rickettsia infections, particularly epidemic or louse-borne typhus, which emerges in situations of human upheaval such as war; the milder endemic or murine typhus in Europe and North Africa; and scrub typhus (Tutsugamushi fever) in the Far East, were major problems, affecting war-torn communities and combatants. Infection was debilitating, and epidemic typhus especially could be severe and even fatal. Much of the research in which van den Ende was involved revolved around the culture of rickettsiae and their quantification. In parallel, diagnostic tests, transport, storage and standardisation of inocula were studied.

As cell cultures were not yet available, laboratory animals were used to isolate or culture rickettsia, which are essentially obligate intracellular bacteria and therefore cannot be cultured on media. Intranasal inoculation of mice was used, which was very hazardous for laboratory workers. During 1941/2 a total of 12 workers at the NIMR and the Royal Army Medical Corps laboratory became infected with murine typhus, including van den Ende, despite all of them having received varying numbers of doses of killed typhus vaccine. However, most cases were mild, only three getting severe disease and none dying.

Marinus and co-workers designed an apparatus – essentially a glovebox-type extraction or exhaust cabinet with UV lighting – for the safe inoculation of experimental animals. An add-on was an electric furnace to sterilise the extracted air. No further laboratory-acquired infections occurred.

The second spin-off from the staff infections was the good evidence that although vaccination with killed rickettsiae did not prevent infection, it appeared to ameliorate the disease in infected persons.

Success by others in identifying two sulphone compounds (V147, V186) with potential therapeutic effect in experimentally infected animals heralded the need for clinical trials in humans. However, the animal work indicated that both of the drugs needed to be given fairly early after exposure (within 42 hours).

In 1943, Marinus was seconded to the Royal Army Medical Corps (RAMC) with the rank of major and travelled with an army medical team to Algiers in North Africa, where an outbreak of epidemic typhus was being experienced. Since there were insufficient cases they were moved to Naples in 1943, where there was a larger outbreak extending into 1944. Unfortunately, under the prevailing conditions the drugs did not prove effective, possibly because of late presentation of cases, and some patients developed nephrotoxicity.

Later in 1944, Marinus was seconded to the Wellcome Research Laboratories of Tyburn, to head up the large-scale production of scrub typhus vaccine. This was *in vivo* cultivation of rickettsiae on a massive scale in cottontail rats, with



harvesting of rickettsiae from infected rat lungs. The intent was to stockpile killed vaccine for Allied troops for the planned Far East counter-invasion, which never occurred because of the atom bombs dropped on Japan.

Marinus regarded the invention and application of DDT as the most important single factor in controlling epidemic typhus in war-torn Europe and the post-war period.

Return to UCT

In 1945 Marinus applied for and was appointed to the Chair of Bacteriology at UCT, which he filled in 1946 at the age of 34.

Jan was 4 years old when the family travelled on a troopship from Liverpool via the Mediterranean, Suez Canal and Mombasa to Durban, where they disembarked and completed their journey to Cape Town by train.

From 1946, Pathology and particularly Bacteriology at UCT were galvanised into increased teaching, service and research activity by the arrival of Marinus van den Ende. Professor J H Louw comments in his book: 'The year 1946 also marked the arrival of large classes of the post-war bulge into the third year'.

In 1947 the Departments of Pathology, Bacteriology and Chemical Pathology were restructured as a combined Department of Pathology, with van den Ende as overall head. The reorganisation clearly had a bacteriological, particularly a virological, emphasis. In the same year revamping of the Animal House was approved.

Van den Ende's research productivity was soon recognised and in 1948 the CSIR created the Virus Research Unit under his directorship. He was always aware of the central role of the basic sciences in medical research and eagerly acquired the support of chemists and physicists including Dr Tom Mead the chemist and Dr Alfie Polson the physicist. Dr Polson was still in action in the department in the early 1970s – a genius, particularly in the separation of molecules of different sizes. These scientists plus other researchers from the department were the core of the Virus Research Unit, the first in South Africa. Many papers were published from the Unit, including work on bacteriophages, influenza virus, poliomyelitis, Rift Valley fever, rabies and blue tongue, plus physical and chemical studies on viruses and general methods of virus research.

Jan remembers Sunday mornings spent with his father, candling inoculated fertile eggs to assess their viability. On Saturday mornings tea was had in a Nissan-type prefab on a corner adjacent to the Anatomy/Physiology block.

On the Bacteriology side, *Pseudomonas aeruginosa* and its typing was the subject of several research papers.

Professor Fred Holliman, Professor of Chemistry at UCT and a close personal friend of the van den Endes, wrote in the obituary that appeared in the Transactions of the Royal Society of South Africa:

'It was to van den Ende's personality and research ability, to a great measure that this effectiveness [of the VRU] was due. He was quick to appreciate the results obtained in one field with respect to another. He had a deep insight into the problems at hand, a genius for getting right down to the fundamentals of it, and working up from them, step by step, to a final solution. His enthusiasm was infective and he drew the best from his collaborators.

'Critical, of himself as well as others, he would only accept results fully corroborated by exhaustive re-experimentation. Quick to recognise worth in others, he was always ready to offer encouragement and, although actively engaged in a problem by his own contributors in thought and advice, he would never put his name to a paper unless he had participated in the experimental work himself. Van den Ende was a scientist, an exceptional scientist, burning with a deep love for his subject and pursuit of truth.'

In addition to his academic achievements, he was clearly a great teacher and speaker and also a highly competent administrator. His research success was particularly remarkable, as he worked in relative isolation in Cape Town, with little opportunity to interact with other distant experts.

In 1953, as recipient of the Arthur Sims Travelling Fellowship, van den Ende was able to spend several months in Melbourne, Australia, in the laboratories of (later Sir) MacFarlane Burnett, at the renowned Walter & Eliza Hall Institute. Here he worked on recombinant influenza viruses – still a topic of major current global significance. He and co-workers, particularly Perry, were able to show that redistribution of virulence can occur when dual infections by virulent and non-virulent strains of influenza A viruses are achieved. It is now known that this phenomenon is due to reassortment of RNA genome segments during dual influenza virus infections. He would have revelled in the advances in molecular biology and nucleic acid technology and their current applications in virology!

Toward the end of this visit van den Ende became ill. Shortly after his return to South Africa, he and his wife departed for the UK where an exploratory thoracotomy and mediastinal node biopsy revealed Hodgkin's disease. In the 1950s the prognosis was abysmal.

Nevertheless, on his return from the UK towards the end of 1953, van den Ende not only threw himself back into research and teaching, but became full-time Dean of the Faculty, while retaining Headship of Bacteriology. His administrative load became still heavier – with the then Principal Dr T B Davie, he was involved in negotiations leading to the Joint Medical Scheme between the University and the Province. He was also appointed as the University's representative on South African Medical and Dental Council. Stellenbosch University was starting a medical faculty and sought his advice. He tried to persuade the late Professor Fransie van Zyl, who became first Dean, that a joint venture would be preferable.



Several other activities and awards also deserve mention:

In 1948 he became Chairman of the Medical Subcommittee of the Cape Blood Transfusion Service.

In 1953 he was awarded a University of Cape Town Fellowship, becoming only the second member of Medical Faculty to obtain this recognition – the first being Professor J T Irving of Physiology in 1948.

In 1954 he was elected a Fellow of the Royal Society of South Africa.

In 1956 he became the first recipient of the Silver Medal of the South African Medical Association.

In 1956, in recognition of his high international standing, he was invited to participate in a prestigious Ciba Foundation Symposium on Viruses, in the UK.

In 1957 he was Acting Principal of the University, during Professor James's absence.

No document or obituary makes any mention of van den Ende's political views. Despite his conservative background he clearly did not support Afrikaner Nationalism but was a liberal, counting persons such as Leo Marquard (co-founder of the Liberal Party) and Leonard Thompson the historian as close personal friends. His political philosophy was probably influenced by his time at UCT and particularly Cambridge, the war effort, and the recognition of the evils of Fascism.

His political views are summed up by his angry comment soon after the 1948 election when Malan came to power: 'It will take 40 years to get them out again!' He felt particularly strongly about the moves to 'close' universities, and played a prominent role in the Wits-UCT opposition to this.

For relaxation, van den Ende's interests and activities included enjoying an afternoon at Newlands rugby grounds, particularly when UCT or Western Province was playing. At the time of his death he was President of the UCT Rugby Club. He enjoyed fishing and golf, and was an excellent amateur carpenter. He loved classical music and philosophical debate and was an active member of the 'Owl Club' up to his death.

He got on well with people at all levels, including his students.

Marinus van den Ende was clearly a great man, multi-talented and multi-faceted, a person who led, inspired and developed others. It is no wonder that he left a mark and his early death a huge gap, which prompted the establishment of this annual memorial lecture.

Mrs van den Ende, widowed very young, brought up four children, Jan, Pieter, Joan and Marina. She reinvented her life, did a postgraduate Diploma in Librarianship when Marinus was incurably ill, and eventually became Lady Warden of a University residence until her retirement.