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Leopold Kirschner, Edward Sayers, and Neil Bruère: the initial descriptions of leptospirosis in New Zealand

Elizabeth Whitcombe,[1] Michael J. Maze,[1,2] John A. Crump[1]

1. Centre for International Health, University of Otago, Dunedin, New Zealand
2. Department of Medicine, University of Otago, Christchurch, New Zealand

Leptospirosis is a zoonotic bacterial infection causing a febrile illness in humans that may be associated with jaundice, renal failure, haemorrhage, pneumonitis, haemodynamic collapse, and death.[1] Leptospirosis is estimated to cause 1.03 million illnesses and 59,000 deaths worldwide annually.[2] While leptospirosis was first diagnosed in Australia in 1933, among sugar cane workers in tropical north Queensland in association with heavy rain and rodent abundance,[3] leptospirosis was widely assumed to be absent from New Zealand as recently as the 1940s. That leptospirosis is recognised as a major occupational health problem and an economically important livestock disease in New Zealand today[4] reflects pioneering work by three remarkable people. Each applying knowledge and experience gained abroad, these three confirmed the presence of the pathogen in New Zealand, identified the initial human and livestock infections, collated epidemiologic data to reveal the scale of occupational disease, and did fundamental work on environmental persistence of the organism.

Dr Edward G. Sayers: identification of human leptospirosis

In October 1949, a 24-year-old share-milker was admitted to Auckland Hospital with a five-day history of abrupt onset fever with headache, neck stiffness, myalgia, and generalised weakness followed by haemoptysis and 'dark' urine. The fever persisted, and by day six the patient was deeply jaundiced with red and white blood cells in the urine. A presumptive diagnosis was made of leptospirosis by Dr – later Sir – Edward G. Sayers, future Dean of the Otago Medical School. Dr Sayers was well acquainted with leptospirosis outside of New Zealand, having trained at the London School of Hygiene and Tropical Medicine, and served in the tropical Pacific as a medical missionary and as a medical officer during World War Two.[5] The patient appears to have been treated conservatively; penicillin may have been given, with uncertain effect. By day 10 of the illness, the patient was apyrexial and his blood count was normal, but he was still deeply jaundiced with abnormal liver function tests. On day 19, blood was taken for *Leptospira* agglutination titres with a plan to send sera abroad to confirm the diagnosis; it was then found that a reference laboratory for leptospirosis under the direction of Dr Leopold Kirschner had lately been established in the Department of Microbiology, Otago Medical School. The sample was accordingly despatched to Dunedin.[6]

Dr Leopold Kirschner: leptospirosis diagnostics, detection of infected animals, and environmental persistence

Dr Kirschner's serological report confirmed the clinical diagnosis: a strongly positive agglutination reaction to *L. icterohaemorrhagiae,* at titres of 1:1,600. Since this was the first case of leptospirosis to be reported from New Zealand, Kirschner forwarded samples to an established leptospirosis reference laboratory in San Francisco, where the findings were confirmed.[6]

Recruited by Dr – later Sir – Charles Hercus, Dr Kirschner was a distinguished member of a remarkable group of émigrés from Central Europe who contributed greatly to the intellectual and cultural life of New Zealand in the years leading up to and after World War Two. Born in 1889 in what is now Poland, Kirschner went to Vienna as a young man where he studied medicine; he completed his medical studies after serving in the Austro-Hungarian medical corps in World War One.[7] Post-war Vienna was marred by violence and virulent anti-Semitism and Kirschner followed his professor, Robert Doerr, an eminent experimental pathologist, to Amsterdam for further studies at the Koninklijk Instituut voor de Tropen (KIT), the Dutch Royal Tropical Institute. Europe's first leptospirosis reference laboratory was established at KIT in 1923. From KIT in the early 1930s, Kirschner joined the Institut Pasteur at Bandung, Java, then part of the Dutch East Indies where he did seminal research on the role of the environment as a source of spirochaete infections.[8] Kirschner's work in Java was cut short by the Japanese invasion in 1942. He and wife Alice, a gifted violinist from Vienna, survived internment with courage, resilience and ingenuity, protecting many other prisoners in the process.[7]

Upon arrival in New Zealand, Dr Kirscher was immediately sceptical of the claim that the country was free of leptospirosis. After all, a wide range of land mammals that could serve as hosts had been introduced, and efforts to prevent rats being imported on ships had been weak.[6] Drawing on his experience in Amsterdam and Java and his deep knowledge of leptospirosis, Kirschner surmised that a substantial proportion of disease presenting in rural New Zealand as 'pyrexia' was likely to be leptospirosis.[9] Under Kirschner's direction, the *Leptospira* Reference Laboratory at the University of Otago Medical School employed darkfield microscopy on clinical specimens as his initial test for leptospirosis. He also performed successful *Leptospira* culture of animal and patient samples using a modification of what he called Gardner medium comprised of 2% inactivated guinea pig serum mixed with glass-distilled water.[6,10] Kirschner maintained live *Leptospira* cultures of strains obtained both locally and from overseas for serology on both animal and human serum by microscopic and macroscopic agglutination testing. It was with this technique that Kirschner successfully confirmed the first cases of leptospirosis in New Zealand,[6] and inferred the likely infecting serovars to postulate transmission pathways. In 1951, Kirschner tested the sera and tissue from trapped rats and sera from 100 pigs, collected from the Dunedin abattoir.

Approximately 5% of these samples proved positive by agglutination testing.[6] Kirschner then circulated his experimental and clinical observations in the form of a memo to the superintendents of all New Zealand hospitals. The circular was written to raise awareness of the likelihood of leptospirosis – notably from *Leptospira pomona* – presenting, in appropriate circumstances, as acute pyrexia, and of the recently established *Leptospira* Reference Laboratory at the University of Otago Medical School.[6]

Mr A. Neil Bruère: livestock outbreaks and occupational disease

Dr Thomas F. Miller, superintendent at Greymouth Hospital, was prepared by Dr Kirschner's circular when 'R H', a 46-year-old dairy farmer, was admitted to his hospital on 23 November 1951 with a seven-day history of sudden onset rigors, severe headache and nausea, followed by intense myalgia in the lower back and limbs and a four-day history of marked subconjunctival haemorrhage. Mr A. Neil Bruère, later Professor and Emeritus Professor at Massey University, had recently been appointed as the government veterinary surgeon to serve the West Coast from Karamea to Haast. Bruère was similarly well prepared, having freshly graduated from the Faculty of Veterinary Science, University of Sydney, and was well-versed in livestock-associated leptospirosis from his teachers based on the experience in Australia.[11,12] Five days before the onset of R H's symptoms, Mr Bruère had visited his farm and found him skinning calves that had died from 'red-water fever'.[13] Now informed by the patient's wife of R H's acute admission to hospital, Mr Bruère corroborated Dr Miller's suspicion of leptospirosis. Serum was promptly despatched to Dr Kirschner's laboratory. On 26 November 1951, three days after R H's admission, agglutination titres were reported as strongly positive for *L. pomona*.

On 3 December 1951, day 10 of his illness, R H was discharged, but complained of fatigue when seen two weeks later. Meanwhile, R H's nine-year-old son had been admitted to hospital on 2 December with similar symptoms to his father. A week later, a 33-year-old farmer, a neighbour of R H who had lent a hand on the latter's farm on 30 November and again on 3 December, was also admitted to hospital with symptoms indicative of leptospirosis. Dr Kirschner confirmed the diagnosis on the basis of high agglutination titres to *L. pomona* in both instances. In all, 12 cases were reported – in meticulous detail – by Kirschner, Miller, and Garlick in their landmark paper of 1952,[9] supporting Dr Kirschner's conviction that leptospirosis was by no means uncommon in rural New Zealand.

Reflections on early leptospirosis work in New Zealand

The initial descriptions of leptospirosis in New Zealand provided a powerful illustration of the importance of cooperation between medical, veterinary, and public health services to identify and control zoonotic disease threats. 'One Health,' the collaborative, multisectoral, and transdisciplinary approach with the goal of achieving optimal health outcomes recognising the interconnection between people, animals, plants, and their shared environment, has its roots in the 1800s[14] and is presently enjoying a resurgence. Notably, cooperation between medical, veterinary, and public health services was critical, not only to the identification and control of leptospirosis in New Zealand, but also to the control and elimination of many zoonotic infectious diseases in the country.[15]

By 1955, 262 patients had been diagnosed with leptospirosis confirmed by serology at Dr Kirschner's laboratory, 200 (76%) of them dairy farmers or members of farmer's families. The occurrence of leptospirosis could now be mapped throughout rural New Zealand, representing a major contribution to medical and veterinary epidemiology.[16] In the laboratory, factors favouring or counteracting *Leptospira* were explored, including the demonstration of the anti-leptospiral effect of milk.[17] Procedures for the identification and characterisation of *Leptospira* were described in a definitive paper of 1959.[18] Dr Kirschner's systematic work also established a sound basis from which to pursue modern molecular characteristics of leptospirosis.

Dr Kirschner also left an important legacy in microbiology and leptospirosis in New Zealand and Australia. He recruited Terry Maguire out of high school as a laboratory assistant. Inspired through Kirschner's mentorship, Maguire pursued an MSc in microbiology at the University of Otago, then his PhD at Yale University, returning to Otago to pursue a subsequent career as a virologist. Among other things, Dr Maguire went on to make seminal discoveries on arboviruses of New Zealand.[19] Dr Solomon Faine, now Professor Emeritus of Microbiology at Monash University, completed his MD under Dr Kirschner's supervision at the University of Otago in 1958.[20] Through his subsequent career, Faine made many contributions to the biology of *Leptospira*, including the recognition of *L. fainei* for which he is justly celebrated.[21] The late Professor Roger Marshall[22] took his Diploma in Microbiology at the University of Otago in 1963, when Dr Kirschner had retired but was still very much a presence, often sought after to clarify and advise. Professor Marshall with Professor David Blackmore[23] formed the core of the world-class leptospirosis research group at Massey University. Marshall and colleagues paid an eloquent tribute to the master in identifying *L. kirschneri*.[24]

The events surrounding the discovery of leptospirosis in New Zealand in the late 1940s and early 1950s provide a number of lessons for public health today. First, dogma can be wrong, and often it takes fresh thinking informed by broad experience to change ideas. The 'One Health' approach, while by no means a recent invention, is a useful means to reinvigorate the essential links between human, animal, and environmental health that have been so central to zoonotic disease control in New Zealand. Finally, Kirschner, Sayers, and Bruère are testimony to thought leaders leaving a legacy of inspiration well beyond their generation.

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Correspondence to: Professor John A. Crump, Centre for International Health, University of Otago, PO Box 56, Dunedin 9054, New Zealand; e-mail: john.crump@otago.ac.nz