

THE TENTH SIR JOHN QUICK BENDIGO LECTURE

# **Alois Alzheimer: Gone but not Forgotten**

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# **Alois Alzheimer: Gone but not Forgotten**

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*"I have recently been told that I am one of the millions.....  
who will be afflicted with Alzheimer's disease...  
I now begin the journey that will lead me into the sunset of my life".*

Ronald Reagan  
New York Times 6/11/98

**A**ccess Economics and the Australian Alzheimer's Association released a report in March 2003, which estimated that in Australia there is currently 162,300 people diagnosed with dementia and the current cost to the country is \$6.6 billion per year. The majority of these people are women and equate to 0.8% of the population. The report also predicts that by 2050 the number of people with dementia will rise to 580,000 or 2.3% of the population. The Victorian Burden of Disease Study released in 1999 estimated that by 2016, dementia would replace heart disease as the greatest cause of disability in the women of Victoria. It is therefore not being melodramatic when the Australian Alzheimer's Association labels this "The Dementia Epidemic." This phenomenon will take place during a period of unprecedented growth in demand for health services expenditure. The Intergenerational Report released as part of the 2002 Commonwealth Government Budget predicts that, if current trends continue, health expenditure, as a percentage of gross national product will more than double over the next four decades.

Alzheimer's disease is the most common form of dementia, however there are many other causes. The second commonest is vascular dementia, followed by Lewy body dementia and then fronto-temporal dementia or Pick's disease. Other significant causes include alcohol and head injury. The first part of this lecture will concentrate on Alzheimer's disease and in the second part will discuss the issue of dementia more broadly

Alois Alzheimer who was born on June 14th 1864 in the Bavarian town of Marktbreit (first described Alzheimer's disease). He attended a number of universities and graduated in medicine at Wurzburg in 1887. His doctoral thesis was on the wax producing glands of the ear. In 1888 he joined the staff of the Frankfurt Asylum and began his training in psychiatry and neuropathology along with a colleague Franz Nissl, later famous for his histological staining techniques. In 1908 he worked at the Psychiatric Institute with a number of famous researchers in neurology including Creutzfeldt, Jakob, and Lewy, whose names have been attached to others forms of dementia.

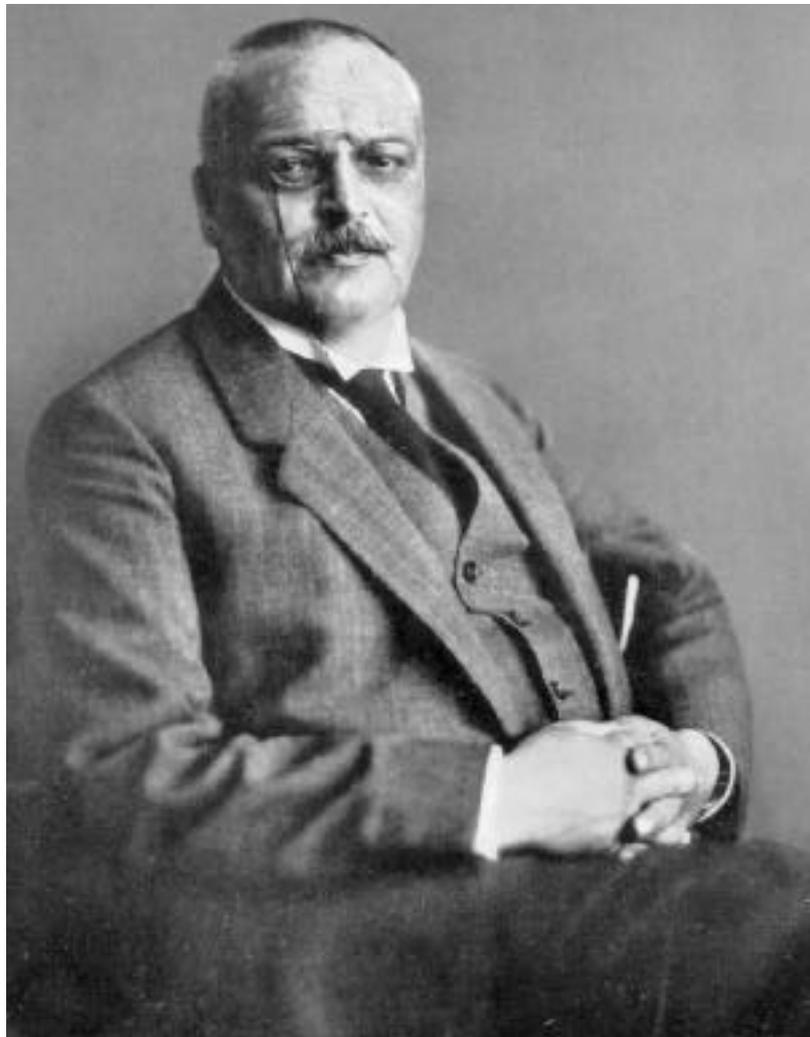
Alois Alzheimer married Cacilia Geisenheimer, the wealthy widow of a banker. It is alleged that Erb, a colleague of Alzheimer's, treated Alzheimer's wife's former husband for syphilis and that Alzheimer had accompanied them on an overseas trip. His wife died after seven years of marriage leaving Alzheimer financially independent.

Alzheimer's first description of the illness was in 1906 and he presented the story of a lady admitted to the Frankfurt Asylum in 1901 exhibiting difficulty with speech, disorientation, unpredictable behaviour, paranoia, auditory hallucinations, and pronounced psychosocial impairment, her name was Auguste D. This paper was presented at the November meeting of the South-West German Society of Aliens and entitled, "A peculiar disease of the cerebral cortex." A second report was published in 1911 and described the story of Johann F, a 55-year-old man who died of dementia. Microscopic analysis of their brains allowed Alzheimer to describe the pathological findings, which are now considered characteristic of this condition, "the plaques and tangles." The eminent German psychiatrist Emil Kraepelin proposed that the syndrome should be called "Alzheimer's disease."

Alois Alzheimer died on 19th December 1915 from acute kidney failure as a result of a serious infection of the heart. He was buried next to his wife in the Frankfurt-am-Main cemetery.

In 1992 and 1997 the original pathological material prepared by Alzheimer was found in a laboratory in Munich. Manuel Graeder from the Max Planck Institute of Psychiatry reanalyzed the material in detail and his findings were published in 1999 in the journal of Brain Pathology. Photographs of the original pathological slides from which Alzheimer made his drawings were also found and published by Graeder.

The characteristics of Alzheimer's disease have been described in literature as far back as the early Greek scholars, the saying "Whom God wishes to destroy, he first makes mad" has been attributed, with some dissent, to Euripides.



Alois Alzheimer c. 1900

The characteristic clinical features that are now used to identify the condition include a progressive loss of memory, plus two of the following; loss of speech or aphasia, loss of the ability to undertake complex tasks or apraxia, loss of the ability to recognize objects or people or agnosia and finally loss of the ability to undertake executive functions such as planning, organizing, sequencing and abstraction. These diagnostic features are important. To date, apart from a brain biopsy, there is no test available that is able to accurately diagnose Alzheimer's disease during life. The diagnosis is based on the clinical findings of the medical and psychological history, the physical examination, and some laboratory tests and importantly the course of the illness over time. Many tests such as the "minimal state" examination or more complex neuropsychological examination are repeated over time to establish the patterns typical of the cognitive changes that are seen in Alzheimer's disease and thus these can be used to support the diagnosis. As might be expected, where there is no one test that is considered the "gold standard", a myriad of tests have been developed and are used. In expert hands a clinical diagnosis, backed up by laboratory tests, is up to 90% accurate.

The person with Alzheimer's disease is usually first identified by a spouse or family member who comments on their "forgetfulness" which is often only initially of "nuisance value" and often unrecognized or not accepted by the patient. Often this is attributed to "old age," however as the disease progresses other changes such as an inability to solve common problems, reduced judgment, difficulty managing finances, difficulty performing household tasks, reduced interest in hobbies, unsafe driving, and reduced ability to care for oneself can occur. Another common presentation is the sudden occurrence of an episode of confusion when the person is under some stress. Examples of these include a trip to an unfamiliar surrounding, or an admission to hospital. The symptoms gradually accumulate as the disease progresses moving through mild, moderate to severe stages, when physical as well as mental disabilities occur. Death is usually 8 to 10 years after diagnosis but the course of the illness may vary from 3 to 30 years.

So who is likely to develop Alzheimer's disease? There are a number of risk factors that have been identified such as, age, gender, family history, head injury, high blood pressure, high blood fats, exposure to electromagnetic radiation, vitamin deficiency, and elevated homocysteine levels. To better understand possible methods of prevention and treatments it is important to understand the possible causes of Alzheimer's disease.

The cause of Alzheimer's disease has been the focus of intense research. A significant contribution has been made in this area by Australian researchers such as Colin Masters. Professor Masters was one of the early proponents of the "Amyloid Theory." Whilst much more information is still required in order to understand the biochemistry of the condition a simplified unifying hypothesis helps us understand the condition and is guiding the search for an effective treatment. The protein amyloid is formed from the breakdown of amyloid precursor protein, a normal part of the cell. Under normal circumstances this protein is broken down by  $\beta$ -secretase and is then harmlessly cleared from the brain. In Alzheimer's disease the amyloid precursor protein is broken down by either amyloid-cleaving enzyme or by  $\beta$ -secretase to form the toxic amyloid, which accumulates in the brain in "plaques." It has been postulated that these plaques are toxic and disrupt the normal functioning of the brain cells that then produce "tangles," formed from abnormal protein called, "tau." As a consequence of this cellular dysfunction certain important chemicals in brain are reduced, one being acetylcholine, important for memory. This is an oversimplification of the current knowledge and there are many areas of contention. Whilst we currently think of Alzheimer's disease as one condition it is very likely that many subgroups of this condition will be identified in years to come.

An understanding of this biochemistry has allowed researchers to investigate treatments, which may be effective in preventing or at least slowing the progress of Alzheimer's disease. Clearly the ideal would be prevention, that is, stopping the disease before it starts.

To better understand the treatment and management of people with Alzheimer's disease, the disease progression is best divided into six phases, normal but at risk, induction, pre-clinical, questionable, mild, moderate and finally severe. Clearly the ideal treatment would be the identification of those at risk and then modification of the risk factor to prevent the disease starting. At present there is no clear evidence to favor any one approach over another and some suggested interventions remain contentious. Some of the risk factor modifications suggested include, hormone replacement therapy or HRT, treatment of hypertension, control of diabetes, lowering of cholesterol levels and the independent use of cholesterol lowering drugs, dietary modification including the use of vitamins E, C, B12, and folate, moderate alcohol intake, regular physical activity, higher level mental activity, the use of anti-inflammatory drugs, increased caffeine intake, and the avoidance of aluminum ingestion. Research is underway to try and reduce the production of amyloid by controlling the enzymes that cleave the amyloid precursor

protein or to clear the amyloid by the use of vaccines. The latter is exciting but serious side effects including encephalitis have caused the trials to be ceased.

If we are unable to prevent commencement of the disease, the next alternative would be the early identification of people with Alzheimer's disease. Because there is no way of accurately identifying those most at risk of Alzheimer's disease, we wait for the development of early symptoms. There are some genetic markers, which are interesting from a research point of view but have been disappointing in practice. However, they have produced an ethical issue, which I will discuss later. The main area of interest is the E4 allele of the APOE gene. Whilst this is a marker it does not accurately distinguish between those who will develop Alzheimer's disease, and those who will not. The use of special imaging of the brain such as computerized tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET) and single-photon emission tomography (SPECT) can help, but at present only assist those in which the process has reached the point where it is noticed clinically and therefore has already caused damage to the brain.

So where are we at present? Current clinical practice lags behind the body of knowledge that describes the disease. From a treatment point of view we are only at the point of replacing the chemicals that are missing rather than effecting the underlying disease, although a new drug, memantine, recently released on to the market in Australia claims to slow down the disease in moderate to severely effected patients. There are currently three drugs available in Australia to treat the symptoms of dementia, donepezil, rivastigmine, and galantamine and one to slow the disease down, memantine. It is important to put these drugs in perspective. Whilst they do work, their results are modest. All three have been shown to improve memory by 3-4 points on a 70-point scale. Importantly they have also been shown to improve behavior and one study from Henry Brobaty in Sydney showed a saving of one hours care per day. As I will discuss later this can be very significant for carers. Currently access to these medications is restricted to those people with Alzheimer's disease and is only available for longer than six months to those people who show an improvement in memory. These restrictions clearly discriminate against those people with other forms of dementia where the drugs have been shown to be useful particularly Lewy Body diseases. It also excludes those people who show maintenance of memory rather than an improvement and importantly those whose behavior improves rather than their memory. Many carers rate an improvement in behaviour as more important than an improvement in memory.

It is important to recognize that many people use complimentary medicines in an effort to ameliorate the symptoms of dementia. Popular herbal medicines include ginkgo biloba and Brahmi. There have been a number of trials of ginkgo biloba, which have demonstrated a modest improvement, however as the debate regarding their efficacy continues a large trial is underway and results are awaited.

Currently the major goal of treatment for people with Alzheimer's disease is to support them and their carers through their life with the disease. In the rest of the paper I will use the term dementia more generally to include the other forms of dementia as well as Alzheimer's disease, as the services we need to provide are common to all. It is therefore important to review the current system of care for a person with dementia and their carers, that is our state of preparedness for managing this "epidemic." We need to examine many of our societies institutions to determine how they are preparing to provide the services that will be required. Whilst every person with dementia's journey is unique there some common themes which can be grouped into the three stages of the illness, mild, moderate and severe.

In the early stages of the illness issues such as providing a diagnosis, recognizing and treating depression, continuing driving, and organizing financial and legal affairs have to be faced. It is a common complaint that people are not told of their diagnosis and not provided with information. In a study carried out last year by the Centre for Rural Rehabilitation and Aged Care, based at the Bendigo Health Care Group, only 42% of family doctor's surgeries and Community Health Centres had information about dementia available. The Centre for Rural Rehabilitation and Aged Care in conjunction with the Alzheimer's Association has since provided all Community Health Centers and general practitioner's surgeries in our region with up to date information on dementia. A British study of people with dementia found that less than 35% of doctors had given their patients the diagnosis whilst in a similar study of cancer patients, 90% had been told. Many patients are aware that their abilities are failing and depression is a common co-existing illness. One of the most difficult issues to be faced is driving, particularly for men and particularly in rural areas. The loss of the ability to drive can adversely affect the independence and self esteem of both the patient and the carer. Currently there is no "gold-standard" of cognitive function against which to judge a person with dementia's ability to drive. Also Victoria is the only state that does not require a compulsory driving test in older age. Vicroads argue that Victoria has the lowest crash rate for older drivers of any of the jurisdictions; therefore our current systems are adequate. Identification of 'at

risk' drivers rests with themselves, their family, doctors, police and the general public. Vicroads will undertake a driving assessment or arrange for a driving assessment by an occupational therapist especially trained in this area. The Australian Society for Geriatric Medicine considers the on-road test as the accepted "gold-standard" for driver assessment.

Making adequate provision for and planning of our future should we become incapacitated is something we should all give thought to. In the Memory Clinic at Bendigo Health Care Group we see 30% of people with an enduring financial power of attorney in place, less than 10% with a medical power of attorney in place and almost none with an enduring guardianship in place. This again emphasizes the importance of an early diagnosis and provision of information to patients and their families.

At this point it is also important to provide the person and their family with an opportunity to discuss their wishes about future care and medical treatment. This can be confronting for all concerned and some patients and their families may not wish to discuss the issue. In my experience if the subject is handled with sensitivity patients and their families value the opportunity and feel relieved and thankful that the issue has been raised and discussed.

Throughout all stages of the illness people with dementia will come into contact with the health system. They will often use multiple services concurrently, and this can be a confusing and frightening experience. The provision of co-ordinated care to people with dementia and their carer's is a challenge to all health service providers. The Loddon Mallee Dementia Management Strategy developed by the Centre for Rural Rehabilitation and Aged Care brought together all those agencies in the Loddon Mallee region who provide dementia services to develop a "care pathway" so that each section of the service system could understand each others role, communicate effectively, reduce duplication, and provide better care. The Loddon Mallee Dementia Management Strategy has provided educational programs to all sectors of the system and the educational material has been made available on the Internet and on CDROM at:

<http://www.bendigohealth.com.au/Regional-Dementia-Management/default.htm>.

As the first contact may be through the family doctor, hospital, ambulance service and even police we have developed and provided standard information that will assist these services in providing consistent services to those people with dementia. In conjunction with police and ambulance we have developed information sheets that are now standard in rural ambulance and have been issued to police.

Hospitals face a particular challenge, as they have not been designed to care for older people with their disabilities and cater more for people who require short lengths of stay. With our ageing population and an increasing number of people with dementia requiring services we need to rethink the way in which our hospitals are designed and the services they provide. We need to examine the Canadian system of “Elder Friendly hospitals.” Their hospitals are accredited if they provided services that meet the needs of older people. These include such basic needs as providing someone to feed and provide fluid for those people who cannot do it themselves. They need to provide adequate signage, appropriate lighting, and disabled access, to name a few. We also need to urgently change our attitude towards older people in acute hospitals. We currently label older people who for various reasons have an extended stay in hospital with the pejorative term, “bed blocker” – as if it is in some way their fault! We have the new “disease” of “acopia,” somehow implying that it is the older persons or their family’s fault that they have presented to the hospital for care. Clearly these are not “elder friendly attitudes.” Taking a term from marketing, we need to ask, “what is the demographic of the hospital’s customer?” Clearly it is providing services to older people and our attitudes, planning and services provision needs to recognize this. It was encouraging to hear Gavin Jennings, the Victorian Minister for Aged Care, who recently said, “Health services need to realize that caring for older people is a core business.”

As people with dementia pass into the moderate to severe stages of the disease over 90% will develop the behavioral and psychological symptoms of dementia. These symptoms are very distressing to the patient and their families and can provide a challenge to all those who come into contact with or have to provide care to a person with dementia. The behavioral symptoms include: restlessness, physical aggression, screaming, agitation, wandering, culturally inappropriate behaviours, sexual disinhibition, hoarding, cursing and shadowing. The psychological symptoms include: anxiety, depressed mood, hallucinations and delusions. A person with these symptoms can cause distress to carers, family, neighbours and other residents for the hospital, hostel or nursing home. Another study carried out by the Centre for Rural Rehabilitation and Aged Care earlier this year revealed that 76% of hospitals, and 28% of hostels and nursing homes did not feel they were equipped to care for people with these symptoms. Given that 50% of people with dementia are currently cared for in health facilities and 90% of people with dementia have BPSD at some stage in the illness, there is clearly cause for concern. In order to provide a high quality of care, a range of strategies need to be employed including an appropriate environment and adequately trained staff. In a further study by the Centre for Rural

Rehabilitation and Aged Care's 94% of health services identified a deficiency in these two areas. Unfortunately a failure to have these available often leads to the excessive use of medications. Whilst medications are useful in some instances they can lead to side effects and sometimes greater harm than good.

Over the last three decades Australia has moved from a position where we had one of the highest rates of institutional care for older people and people with physical and psychological disabilities to an arguably more enlightened position where more people are cared for in a community setting. The 1985 Commonwealth's Aged Care Reform Strategy was based on the premise that most people wished to stay in their own home but also aimed to achieve cost efficiencies and cost containment. This has not been without a significant social and economic cost to families. There has been a significant transfer of responsibility of care to the individual and their family. The development of home support services have given people more choice and in many cases an improved quality of life. Therefore, critical to the care of the person with dementia is support for the carer. A range of support services are available including such services as home nursing, adult day care, and respite care. Respite care is designed to give the carer "time-out" but in its current format is under-utilised by carers of people with dementia. Our research indicates greater need for residential respite care as carers had a preference to this over in home based respite care. The latter they found did not give them the quality break they required.

The ethical issues surrounding dementia are legion and we need increased informed community debate to provide clarity. The community has largely accepted the argument that people should be provided with information regarding their health that will allow them to make informed choices; in the case of dementia there is still a reluctance to discuss the diagnosis and provide information. The ability to make end of life care plans is available to us but few avail themselves of the opportunity. There needs to be greater awareness in the community of the various enduring powers of attorney and our ability to appoint an enduring Guardian. Recently the Victorian Civil and Administrative Tribunal and the Supreme Court gave some clarity to the legal issues around end-of-life support for people with dementia. We need to debate the issue of individual standards of home care and risk. At what stage should there be an intervention by authorities as the person is judged to be "at risk?" Many older people will happily accept the risk of a fall and subsequent injury rather than move into residential care. We may also accept a lower standard of cleanliness in return for staying in their own home. At what point should society and its institutions intervene?

The discovery of gene markers has raised the possibility for people to be identified who are at greater risk of developing Alzheimer's disease. This raises serious ethical issues for families and clinicians. The current recommendations published in the Medical Journal of Australia by Peter Panegyres suggest that gene testing be restricted to people with a positive family history of early on-set dementia and clinical features suggestive of Alzheimer's disease. They also recommend that APOE testing is restricted to ethically approved research projects unless there is pre and post-test counselling.

There is increasing competition for the health and research dollar. We are assailed on a daily basis with campaigns to fund research on various diseases and lectured to by various experts on the dire consequences if we don't develop service X or fund research project Y. It is for this reason we need a greater clarity in the debate about our future health system and its priorities. If we are to have a national strategy on dementia which aims to improve the care for people with this condition and their carers we need to address issues such as the provision of early diagnosis and support, the provision of appropriate pharmacological interventions as they become available, the provision of adequate care in all levels in the health service in particular for those with the behavioural and psychological symptoms of dementia, community debate on the ethical issues and the funding of research.

Dementia is an illness that will touch us all, either as a sufferer, a carer, a family member, and friend or work colleague. It is therefore in our interests to ensure that we are prepared for the "Dementia Epidemic."



## **Associate Professor Tony Snell**

**MB ChB (Otago) MRCP (UK) MRACMA FRACP**

**T**ony was born in Scotland and his family immigrated to New Zealand where he received his primary and secondary education in Tauranga.

He graduated in Medicine from Otago University in 1970 and undertook postgraduate training in Internal and Geriatric Medicine in both New Zealand and the United Kingdom. He was appointed a lecturer in Geriatric Medicine at the University of Manchester in 1979. He was admitted as a Fellow of the Royal Australasian College of Physicians in 1980.

He moved to Bendigo with his family in 1985 and between then and 1998 held a senior management position with the Bendigo Health Care Group and its predecessors. In addition to his administrative duties he also undertook a full time clinical role establishing many visiting aged care services in the region. His current clinical role is as a consultant physician in the Memory Clinic and the Dementia Assessment Unit.

He has served on the Regional Board of La Trobe University, Bendigo and the Council of La Trobe University. He has been a Ministerial Appointment to several Government committees and was a member of the Guardianship and Administration Board.

In 1998 he was appointed an Associate Professor and Director of the Centre for Rural Rehabilitation and Aged Care, jointly sponsored by Bendigo Health Care Group and Monash University.



## Sir John Quick

**J**ohn Quick was born in Cornwall, England in 1852. In 1854 his family migrated to Australia; his father died shortly thereafter.

At age 10 he entered the workforce, undertaking various manual jobs in mines then progressed to journalism. His drive for self improvement led him to complete a law degree at the University of Melbourne (1874-77) and in 1882 he was awarded a Doctorate in Law.

At this time, Sir John Quick was in charge of the Age Parliamentary staff. He entered politics himself in 1880, winning the Legislative Assembly seat of Sandhurst (Bendigo), which he held until 1889.

Quick's public support for Australian Federation commenced with an 1882 speech to Parliament. As a delegate from the Bendigo A.N.A., he attended the 1893 Corowa Conference where he presented the famous resolution which took Federation's fate away from Parliaments, and gave it directly to the people via elections for representatives and a referendum on the draft Constitution. He wrote the Enabling Bill needed for these stages to occur and also wrote a booklet, *A Digest of Federal Constitution* (1896), to help educate the public.

Throughout the two referenda campaigns of 1898 and 1899, he addressed numerous public meetings.

Quick's work for Federation was recognised with the award of a knighthood in 1901.

He was elected unopposed as Bendigo's first Federal M.P., holding the seat until 1913.

The Sir John Quick Bendigo Lecture has been established to revive the memory of this self-made man who had the forethought and perseverance to promote Australia's union. Quick himself referred to his long devotion to Federation as a "public duty" he had to perform. Sir John Quick deserves to be recognised as a "Father" of Australian Federation.

*Written by Michele Matthews, BA(Hons) Melb, DipEd LaT*

## THE SIR JOHN QUICK BENDIGO LECTURE SERIES

The Sir John Quick Bendigo Lecture is presented annually by La Trobe University, Bendigo and the Sir John Quick Committee with the support of the City of Greater Bendigo.

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Outreach, ScreenSound Australia, Canberra