

# Transcript of JS' Ockham's Razor talk: a tale of two organs

**Robyn Williams:** Today's talk is rather shocking. I found it so, you may as well, especially if you're of a certain age, like me. It's about dementia and its causes. You'll probably be aware that there are two main schools accounting for dementia and Alzheimer's: One blames plaques, deposits accumulating with age, affecting the nerves. The other school blames little leaks of blood from capillaries in the brain. And it's that cause we hear about today. Yes, both the vascular and the plaque stories may combine to cause problems in the brain, but, as Professor Jonathan Stone suggests, it's our powerful pump that is the big threat. Who'd have thought? Professor Stone is Director of the Bosch Institute for Medical Research at the University of Sydney.

**Jonathan Stone:** The beat of our heart is symbolic of life, of energy, of courage and determination. Yet scientists are beginning to take seriously – and this is the message of this talk – evidence that, if we live to old age, the heart destroys us. And it does so in a terrible way, pummelling the brain beat after beat until its small blood vessels burst, and lesions, tens of thousands of them, erode its circuitry, until the brain shrinks around the debris, its function failing. Slowly, relentlessly – this evidence goes - the beat of the heart destroys the memory, the intellect and the personality of the person it had so long served to keep alive.

For scientists working on dementia, this is a challenging statement. Many workers in the field still accept - or at least hope – that the cause of age-related dementia – of Alzheimer's disease – will be less inevitable, less grounded in the unchangeable nature of our organs; that dementia will be a treatable disease, not a fate; that it is caused by a toxic protein, or an invading organism, something you can design a drug against, or a vaccine; something you can face square on and overcome.

But science doesn't respond to meet human hopes. Once we wanted the earth to be the centre of God's universe; that is what Cardinal Bellarmino fought for, when he confronted Galileo. Once we wanted humans to be distinctively divine - not the evolutionary relatives of fish. That is what the Bishop of Oxford fought for, when he confronted Darwinism. None of us want the end of our beautiful Earth, mercifully still a billion years away, to be its fiery consumption by the dying sun.

Those of us who have studied the ageing of the brain, seeking understanding and ways of protecting it, our search made urgent by the ravages wrought by dementia in the lives of our elders – we did not want to learn that the heart, whose beat is essential to life, becomes the destroyer of the brain, and with it, of all quality of life. But that may be the truth to which we must accustom ourselves, as we have to the cosmic insignificance of planet earth, to the evolution of species, to black holes and exploding stars.

There are five players in this tragedy. Everybody knows two of them – the heart and brain, the most vital of the vital organs. Two others are less familiar – the great distributing vessels that receive the surge of blood created by each beat of the heart; and the small vessels of the brain. And the fifth is time, which we think we know. All are crucial to our story.

**The heart** is a pump. It beats 60 or 70 times a minute, which seems just fine. But that adds up to 35m beats each year and 2-3 billion in a lifetime. If you are 70 and want to live another 10 or 20 years, you are asking a 70 year old pump to beat another 500 million times. For the majority of us, the heart will do this; until, paradoxically, it becomes an engine of death.

**The brain** is the most complex and mysterious of organs. The heartbeat may be a sign of life; the brain's activity is the core of life. When my brain dies, I will be gone, even if my heart is still beating. The best that could then be done with my surviving organs would be for them to help keep someone else's brain alive.

In your head and mine, the brain sits motionless, except for a slight shudder with every heartbeat. But it is crammed with highly active circuitry, which needs serious energy, from oxygen and glucose in the blood. To deliver that blood, the brain's vessels must be kept wide open – an engineer would say that its circulation must be low resistance. And because of that low resistance, the pulse penetrates into the smallest vessels of the brain, so that it experiences a pulse of pressure with every heartbeat.

So we come to the third player in this drama, the **aorta**. With each beat of the heart, the powerful muscle of the left ventricle ejects a squirt of blood, typically 70 ml – it would take five to fill a soft drink can. Each spurt is driven into the aorta, a great artery with two jobs. First, it pipes the blood to the head and arms and down the torso and into the legs and the intestines and every other tissue that needs it. Second – and this is key to our story – the aorta buffers the pressure wave created by each heartbeat. The wall of the aorta contains a large component of elastin, a protein which – as its name implies – can stretch and regain its shape. With this elasticity, the aorta is distended by about 15% in diameter as the left ventricle drives blood into it; and contracts back as the ventricle relaxes between beats. The effect is a superb bit of evolved engineering, for the elasticity of the aorta softens the pulse and makes the flow of blood into the brain (and other tissues) less pulsatile, more continuous.

**The fourth player – small vessels of the brain:** Blood reaches the brain through two pairs of arteries. The carotid arteries stretch upwards from the aorta through the soft tissues at the side of the neck; you can feel the pulse in these arteries easily, just behind your larynx. The other pair of brain arteries run up the back of the neck, where you cannot feel them, because they run through the bone of vertebral column. When they reach the brain, these four arteries branch and branch again, threading small vessels through every last millimetre of brain tissue. These are the fine vessels which are kept dilated – low resistance – allowing blood, and the pulse, into the brain.

#### **Finally, our fifth player, time:**

Time has many meanings; here I mean time as in lifetime, from youth to age. We know that the biggest risk factor for dementia is age; put sardonically, the surest way to avoid dementia is to die young. But, if we insist on staying alive, what happens as we age?

- First, of course, the heart keeps beating, and the wall of the aorta keeps stretching and relaxing. As the number of stretch/relax cycles builds up, the elastin in the wall of the aorta starts to fail - a nick here, a fracture there. Engineers call this stress failure; every material known to engineers is subject to it. The damage is cumulative and, as the elastin stops working, the stress of the pulse comes up against the stiff, collagen component of the aorta's wall. In common parlance, the wall of the aorta hardens, slowly, relentlessly.

- The hardened aorta does not distend as much when the ventricle injects blood into it; and the peak pressure reached as the heart contracts increases steadily. This peak, measured by the familiar pressure cuff, is maybe 110 mm Hg in the young. By the time we are 70 years old, our cardiologist will be satisfied with anything under 150mm.

- The hardened aorta does not contract as much between pulses, and the fall in pressure between successive beats becomes deeper. So the peak-to-trough pressure of the pulse – its intensity – increases with age.

· With blood spurting into them with increasing intensity, the brain's blood vessels are damaged. The sharper blood flow tears the endothelial cells that line the vessels, causing the formation of clots and of small aneurysms, swellings that burst. And then we have bleeding into the brain, caused by the internal trauma of the pulse. This bleeding, from first one small vessel, then many, then thousands, creates the neuropathology which Alois Alzheimer reported, over a century ago.

· Now, when a large brain artery bleeds we get symptoms – unconsciousness, paralysis - and the incident is called a stroke. Most bleeds, it turns out however, are from smaller vessels and do not cause symptoms; they are said to be clinically silent. Most adults have had a few such bleeds, so routinely that a few are normal. But their numbers increase with age and, when enough accumulate, we notice a loss of brain function; often memory first, then awareness of where we are, then what's called executive function, eventually personality and consciousness. That's the course of dementia; the pulse destroys the brain

I would use the last few minutes of this talk to deal with several related issues. First, if this understanding of dementia is correct, then a previously unsuspected determinant of longevity has been identified – the beat of the heart into a stiffening aorta limits our life, by destroying the brain and, incidentally, another very vascular and vital organ, the kidney.

Second, a big idea like this needs corroboration and testing. Because dementias occur so late in human life, ideas of their cause are difficult to test in the science laboratory. But in the harsh laboratory of human life, the corroborating evidence is strong. The risk factors for dementia overlap extensively with the risk factors for stroke and cardiovascular disease. Trauma to the head – in boxers, footballers, in anyone who gets more than a few whacks on the head – seems to sum with the trauma of the pulse, and accelerates the onset of dementia. The genetic modulators of dementia all have vascular actions. And finally, as more and more of us live longer and longer, dementia and kidney failure are becoming increasingly common causes of death. No data set is ever complete, but the data supporting the vascular basis of the dementia we call Alzheimer's are very considerable. In the terms pioneered by William of Ockham, the idea explains a very diverse body of observations, with a minimum of assumptions.

Third, the idea provides a rationale for prevention – anything in diet or exercise or weight control that protects our cardiovascular system is already known to protect against dementia. Now we know why.

Fourth, this understanding of dementia is unusual as a discovery. It is not the outcome of intense, reductionist work in any one discipline, but a synthesis of work done over decades by cardiologists, neuropathologists, engineers, geneticists, neuroscientists and more. Further, many of key steps were taken by researchers in this country. This is a very Australian story of discovery.

Finally, since clinically silent bleeding into the brain – the proximate cause of this dementia – occurs from a young age, so young that all but the youngest listeners will have at least a scattered few sites of bleeding, we can seek ways of protecting the brain, to minimise the damage caused when small bleeds do occur, and we can thereby delay the onset of symptoms. This field of investigation is called neuroprotection; it is the field in which I work and a fascinating and hopeful story. But a story for another day.

**Robyn Williams:** And one we shall hear quite soon, I hope, to give some guidance about avoiding those tiny strokes, such as maintaining a lower blood pressure and getting plenty of exercise. Jonathan

Stone is Professor of Neurobiology at the University of Sydney. Next week *Ockham's Razor* comes from Perth where Peter Newman insists that it is not the Wild West anymore. Before I go: *Catalyst*, our TV science program, has moved. It's now on Tuesdays at 8.00pm, starting this coming week, February 3 on ABC Television.

## Guests

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Professor of Neurobiology  
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## Credits

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