



Texas Heart Institute

Cardiovascular disease costs the US \$449 billion each year. **Dr James T Willerson**, President and Medical Director, enlightens us on the remarkable feats of the THI and reveals his thoughts on reducing the heavy burdens of this widespread, and often fatal, health issue

To begin, what brought you to this position, and to what extent do your own research interests inform your role?

For more than 20 years, I have been working as a cardiovascular disease scientist, educator and physician at the Texas Heart Institute (THI) in Houston, in several different leadership capacities. My own research is focused on vulnerable atherosclerotic plaques, non-invasive imaging procedures of the heart and blood vessels and, recently, stem cells. When I originally came to the Institute, Dr Cooley, then President, wanted me to be the Medical Director of Cardiovascular Research. When he decided to resign in 2008, he asked me to succeed him in that position.

Can you offer a short summary of the organisation's mandate?

THI has been dedicated to education and research discovery since it was founded in 1962. Our commitment is to new discovery that ultimately prevents cardiovascular disease in all of its forms, and in the interim, to relieving and improving the hearts of patients with cardiovascular disease.

Since 1962, we have been involved in training cardiologists, heart surgeons, imaging specialists in cardiovascular medicine and cardiac electrophysiology, and pathologists, and we have educated hundreds of cardiovascular specialists during this period.

It has been 50 years since the Institute was first established. What have been its greatest moments, and what challenges has it had to overcome?

Simply, it is an exhilarating challenge ensuring that THI conducts cutting-edge research and educational programmes in cardiovascular medicine, and is dedicated to applying these to the care and prevention of cardiovascular disease in humans. Each of our research discoveries and their applications to humans has been a great moment.

Also, THI is a non-profit organisation in the truest sense. Unlike most institutions that have a source of operating revenue, the Institute has primarily been supported by research grants and philanthropy and this has represented a challenge annually over the past 50 years.

Accounting for over a quarter of all deaths in the US each year, cardiovascular disease is a major health concern; however mortality from coronary heart disease (CHD) has substantially decreased in recent decades. What might account for this trend?

I believe that the decrease in mortality from CHD in the US is a result of research discoveries that have provided insights into mechanisms responsible for thrombosis in injured coronary and cerebral arteries, and led to improved treatment. For example, advancing the understanding of 'bad' low-density lipoprotein (LDL) cholesterol in patients to values well below 100 mg/dl has been a very important contribution. The development of statins to lower LDL has also been crucial. The use of aspirin, medications to control blood pressure, avoidance of smoking and use of recreational drugs, control of blood sugar in patients who are diabetic, emphasis on diet and exercise, and improved imaging techniques for blood vessels and the cardiovascular system, generally, have played a role in protecting patients and decreasing mortality risk.

However, the greatest risk factor for cardiovascular disease is a genetic one, and we must identify the genes that contribute to this risk; ultimately silencing the most dangerous ones using microRNA methodology.

THI is recognised nationally and internationally for important contributions in the battle against cardiovascular disease. Could you outline some of the successes?

The Institute has established itself as an international leader in the area of mechanical circulatory support research, ie. implanting more left ventricular assist devices (LVADs) and conducting more heart transplants than any other institution in the US. We are also making great strides in the area of myocardial regeneration, ie. the use of patients' own stem cells (autologous) and also allogeneic cells to repair damaged heart tissue.

We have conducted numerous clinical studies in patients with cardiovascular disease using a variety of stem cell types, including mesenchymal stem cells taken from the bone marrow or adipose tissue. Through the pioneering work of Dr Doris Taylor, we are now able to deplete human hearts of their cellular structure and then restore that same heart to normal function by the infusion of stem cells. With continued success, these efforts could fill a great unmet need and pave the way to a new area of transplant medicine.

More women than men die of heart disease. Why is this so, and how is THI addressing this issue?

There are presently 43 million women living with heart and vascular disease in the US. In comparison, there are 8 million women living with cancer. If you are female, you are more likely to die of heart and vascular disease than all cancers combined; and five times more likely to die of heart and vascular disease than breast cancer. Women's symptoms are also often different from those found in men. For instance, some women with heart attacks may experience pain in their ear or may simply not 'feel well'. Moreover, their responses to various procedures, including bypass surgery, are often different than in men.

Recognising this, we have created the Center for Women's Heart and Vascular Health – one of the first in the US. This new Center allows us to educate women about their heart disease risks. We are also working to develop new approaches for effectively identifying and treating cardiovascular diseases in women.

An ageing population, increasing levels of obesity, lack of physical activity and rising numbers of Americans living with diabetes, are all contributing factors to cardiovascular disease. To what extent do lifestyle factors limit the impact of research?

Part of THI's mission is to educate men, women and children about the risks for developing cardiovascular disease. We are creating educational

programmes that may be used throughout Texas to inform children and adults about risks associated with obesity, lack of physical education and diabetes. We are also recruiting young people who have been very successful in their athletic endeavours to be representatives and role models to children, women and men all over the US in this war against cardiovascular disease.

Cardiovascular disease costs the US \$449 billion each year in healthcare services, medications and lost productivity. What measures could be taken to reduce this outlay in the long term?

Prevention would be the single most effective means of reducing healthcare costs. Prevention should be the main concern initiated at very young ages and continuing throughout adulthood. There are a variety of other measures, including healthcare clinics that educate, treat simple abnormalities, and direct patients that need more complicated cardiovascular care to advanced facilities.



TEXAS HEART[®] INSTITUTE
at St. Luke's Episcopal Hospital

The heart of THI's achievements

THI, based at St Luke's Episcopal Hospital, is credited with:

- The first successful heart transplant in the US in the late 1960s
- The first use of a total artificial heart in the late 1960s
- Creating LVADs; every major LVAD in use today worldwide has been either developed or instigated through the work of THI
- Demonstrating that vulnerable atherosclerotic plaques, leading to an acute myocardial infarction or cerebrovascular action, have temperature heterogeneity
- Being the first to use patients' own stem cells to treat coronary heart disease and severe heart failure
- Being the first Food and Drug Administration (FDA)-approved clinical trial of adult stem cell therapy for severe congestive heart failure and coronary heart disease in the US
- Showing the importance of platelet-derived mediators, including thromboxane A2, serotonin, thrombin, adenosine diphosphate, platelet-activating factor, oxygen-derived free radicals and endothelin, in mediating thrombosis and dynamic vasoconstriction at sites of atherosclerotic plaque rupture or endothelial injury. This has led to treatments that individually or collectively help resolve and prevent thrombosis in patients with acute coronary syndromes
- Identifying nine genes that play a role in the development of heart attacks in families

In addition, following a national competition, the National Institutes of Health National, Heart, Lung and Blood Institute (NHLBI) has selected THI to be an adult stem cell centre for treating patients with cardiovascular disease. The Institute has also been chosen as the biorepository for all of the stem cells in cardiovascular treatment and research by the NHLBI consortium in the US.

