

HEALTH

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DIALLING DOWN INFLAMMATION

A discovery by an Australian couple 35 years ago is driving fresh research into this common issue, writes Jill Margo.

Several years ago, I was chatting to a doctor at a party and casually asked what was new in medicine. "The role of the endothelium," he said. "It's crucial to everything."

Before he could explain, someone else joined us and the subject was lost.

That mysterious comment now makes sense. The endothelium is the inner lining in all blood vessels in the body. It looks like cellophane and for years was seen simply as an inert barrier.

No one was interested in it.

Today, there is great interest because it is regarded as a vital border that orchestrates inflammation throughout the body.

Inflammation has become a buzz word of 21st-century medical research and the public is about to hear much more about it.

For a start, on Monday, superstar doctor Michael Mosley is giving a free public lecture on it, hosted by Sydney's Centenary Institute.

Inflammation was once thought to be a simple healing process. In response to an injury or infection, an area of the body

became inflamed. It became red, warm, sore, swollen and, if around a joint, it could make moving difficult.

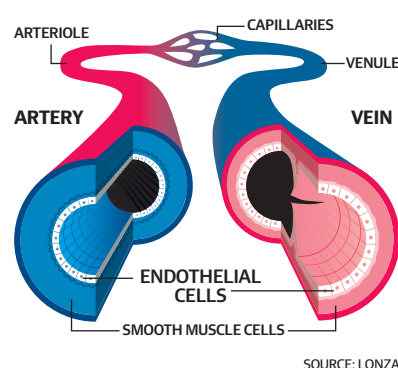
This was a temporary process and once healed, the area returned to normal. That's now called good inflammation.

But now there's a bad form too.

It smoulders for decades, deep in the

Endothelium explorers: Professor Jennifer Gamble and Professor Mathew Vadas are pioneers in the field.

The dynamic endothelium



body, and during this time it does serious damage.

Uncontrolled and erosive, it is now viewed as the driver of most chronic disease, including Alzheimer's, asthma, cancer, diabetes, psoriasis, stroke and diseases of the heart, liver, bowel and blood. More recently, it's also been considered a driver of ageing.

Because of all this, all eyes are on the endothelium. Figuring out how it works, what it lets through and how it can be managed are hot topics in medical research.

About 35 years ago, an Australian couple made a discovery that, in large part, led to a new understanding of the endothelium. This husband and wife team took a brief sabbatical in Seattle because it had technology capable of isolating and growing the endothelial cells.

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Professor Mathew Vadas

Rather than following the orthodoxy, they took a risk. "We were both in biology, but in different departments, and we combined our skills," says Professor Jennifer Gamble, now head of the vascular biology program at the Centenary Institute. "I brought a basic science approach and Mathew brought a clinical one. It was synergistic, not competitive. We had this crazy hypothesis which turned out to work and it reset the field."

They showed that the endothelium was not inert but was highly charged and dynamic. With this, they became the first in the world to demonstrate the endothelium's involvement in inflammation.

"I think we opened a gate to a new understanding which, combined with what else was going on around the world at the time, helped to develop our deep knowledge of inflammation," she says.

Their passion for this research has endured and today Professor Mathew Vadas is executive director of the Centenary Institute which, like so many other institutes, has now adopted inflammation as its shibboleth.

So how does the endothelium work? Previously, if a person hurt a thumb, it

wasn't known how the body knew to send help to the thumb and not to the big toe.

Now, it's known that the endothelium opens the border at the site of injury, so helpful cells can pass from the blood into the tissue. It directs the type of cells that get across, how many cross and for how long. Once the injury is repaired, it closes off.

"The body can tolerate short, acute bursts of inflammation," says Vadas.

But smouldering inflammation is much more complex and once it takes hold in one area, it gradually goes beyond and affects other areas too.

"People with chronic inflammatory disease, such as arthritic disease, get many more diseases of ageing unrelated to their arthritis, and they get them earlier. They have a chronic inflammatory insult."

Vadas says inflammation reaches into every aspect of medicine. "Those with underlying inflammation age more quickly, become frailer sooner and get dementia earlier."

He says it is implicated in many conditions people wouldn't suspect, such as heart failure. "The heart muscle is infiltrated by inflammatory cells that exacerbate the process."

So, if smouldering inflammation is so harmful, can anti-inflammatory drugs that are bought over the counter help?

Vadas says research suggests they only deal with one aspect of a multifactorial complex process and while they may have short-term effects, that reverses.

Each type of inflammatory condition requires specific medication. Rheumatoid arthritis, for example, requires a drug that targets it.

"While seven of the top 10 selling drugs today are attacking inflammation from various corners, we have not scratched the surface of the complexity of the mechanisms that cause inflammation and the various ways to combat it with new drugs," he says.

So, how can young and middle-aged people protect themselves against inflammation?

Vadas says regular exercise appears to be one of best ways to reduce it. During exercise, muscles release factors that limit or inhibit the inflammatory process.

Altering the gut biome with fibres that are less digestible will probably become another intervention but it is early days for understanding this possibility.

There are also suggestions that the balance of carbohydrate to protein to fat may be an important determinant too.

"It appears that carbohydrate may not be bad for you. In fact, in animal models, it is very helpful and some human trials suggest this too."

This weekend, the World Congress on Inflammation is being held in Sydney, with the Centenary Institute as a major sponsor and Gamble as its co-chair.

With inflammation driven by many cell types, Gamble says protection could come with the next generation of drugs designed to dampen chronic inflammation.

"But the kind of inquiry-driven research needed to understand the process and then develop the next line of drugs is not being readily funded," she says. **W**

Jill Margo is an adjunct associate professor at the University of NSW Sydney.



SUPPORT FOR SURVIVORS

Men's health Australia is poised to lead the world in a new way of managing prostate cancer, writes Jill Margo.

The power behind prostate cancer was revealed in Canberra this week. Prime Minister Scott Morrison talked about being tested and how his father had survived more than a decade since his diagnosis.

Federal health minister Greg Hunt disclosed he had a family history of the disease, too, and Opposition Leader Anthony Albanese said because he'd had a high reading on a test he was now being tested every three months.

All were talking before the annual Parliamentary Big Aussie Barbie, run by the Prostate Cancer Foundation of Australia (PCFA).

Given that one in seven Australian men will be diagnosed with this cancer, many more politicians could have joined them.

Australia is poised to transform the way this cancer is managed.

If it pulls it off, it will be the first country to do so.

This new push is being led by Professor Jeff Dunn, recently appointed chief executive of the PCFA, who has been working on it for about 15 years.

He already has support from all clinical groups associated with prostate cancer and at the barbecue on Wednesday he formally received bipartisan political support too.

So, what is it?



It's a radical approach aimed at ensuring that men with this cancer not only live long, but live well too.

Dunn says it is not enough to treat this cancer as just a physical disease. The heavy emotional, social and personal payload it carries requires serious attention too.

The new push involves routinely screening patients for distress and offering those in need quality help.

"This is the new frontier in innovative care. It's not just defeating prostate cancer, but restoring hope in a future free from both physical and psychological pain," he says.

Before and after treatment, up to one in four men experience anxiety and up to one in five report depression.

Australian men diagnosed with this cancer are at a 70 per cent increased risk of suicide compared with their peers.

Dunn believes such distress should be measured as the 6th Vital Sign after temperature, blood pressure, pulse, respiration and pain. This is the consensus view of international psychologists who

specialise in cancer, and a view which he helped form.

His plan is ground-breaking because survival rates are now so high that men are living with the fallout for decades. More than 200,000 Australian men live with it and as the population ages and grows the pool of survivors will continue to grow.

On Wednesday, Hunt launched *The PCFA Position Statement for Distress Screening and Psychosocial Care for Men with Prostate Cancer*, which describes the plan.

It, and a monograph launched with it, are products of the Centre for Research Excellence in Prostate Cancer Survivorship, funded by the government through the National Health and Medical Research Council. The monograph provides a model for psychosocial care.

The real challenge for Dunn now is to roll out the plan and see if he can change practice and make attention to psychological wellbeing part of standard care. **W**

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