

TROPONINS: THE TWENTY FIRST CENTURY GOLD STANDARD

“IF ANY PATIENT HAS CHEST PAIN AND HAS ANY LEVEL OF CARDIAC TROPONINS, THERE IS A PROBLEM. YOU SHOULD NEVER JUST SEND SUCH A PATIENT HOME.” DR GEORGE BIRO REPORTS.

PHOTOGRAPHERS: EAMON GALLAGHER + TONY LEWIS

What diseases do we Australians fear the most? According to a recent survey we want to put most dollars into research on cancer. But we are actually far more likely to suffer heart disease. Sure we know how to prevent heart attacks: choose your ancestors wisely, exercise regularly, watch your diet and weight, don't smoke, see your doctor to check your blood pressure and cholesterol... Sounds simple?

But too many of us still end up in hospital, with chest pain, frightened out of our wits; sweating, pale and clammy, praying: "Let it be just indigestion." Our partner is distraught. Should our children rush back from overseas? We implore the doctor: "It's not a heart attack, is it?"

This is a big decision for any doctor. You may need urgent treatment: aspirin or heparin to thin the blood, maybe a stent to reopen a blocked coronary artery, or even a coronary artery bypass graft (CABG, the Big Zipper).

On the other hand you may not have had a heart attack at all; chest pain often

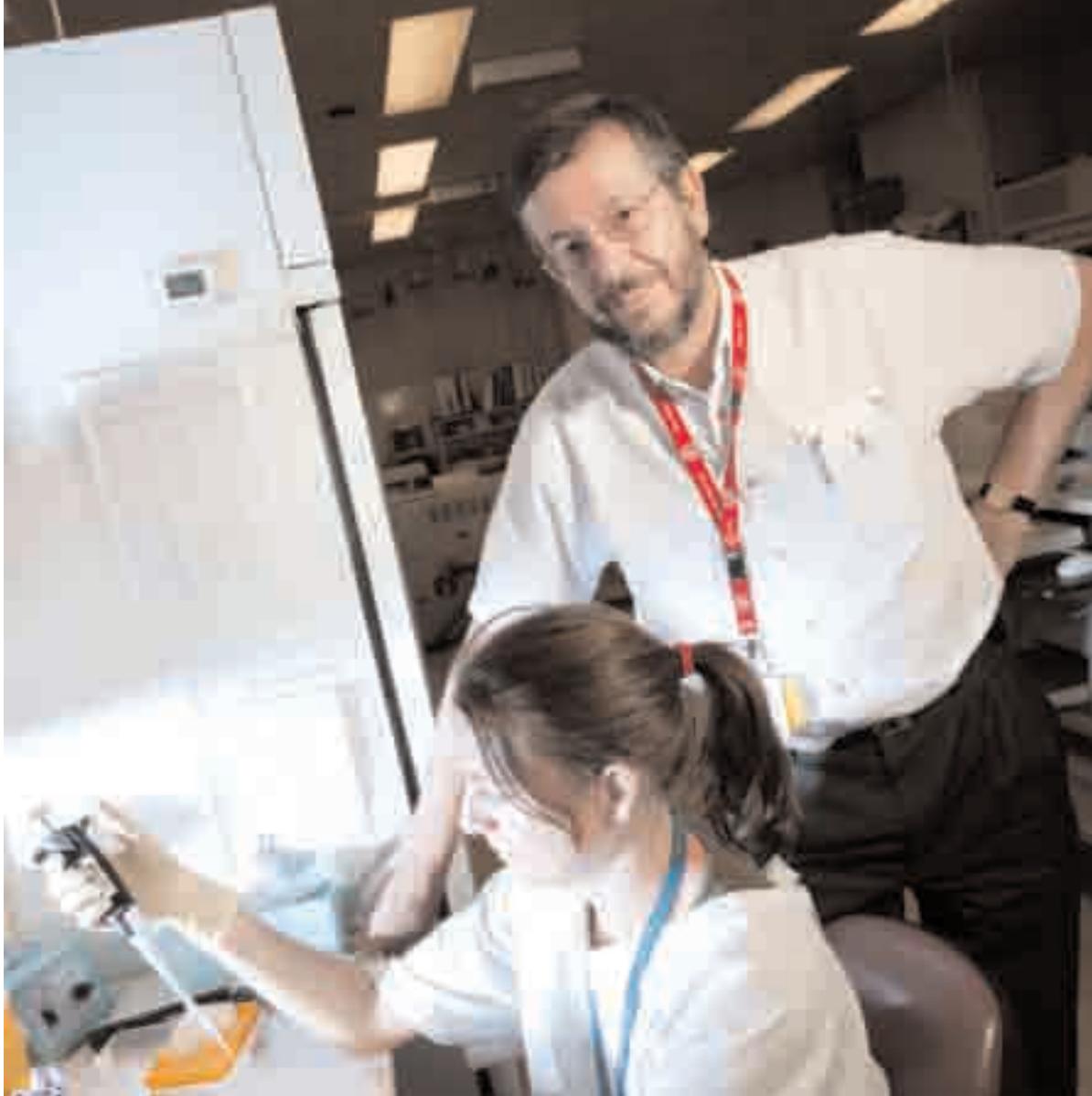
comes from less serious causes. Dr Charles Appleton of Queensland Medical Laboratory says about a third of patients with acute myocardial infarction (AMI) present with an atypical picture and almost half may not initially show a diagnostic electrocardiograph (ECG). Conversely, half of patients with typical symptoms do not have AMI. Despite all this ambiguity, doctors still need to make urgent decisions about reopening blocked coronary arteries (revascularization).

How do doctors decide? They review your history, check your physical signs, take an ECG and do blood tests. Why blood tests?

When heart muscle cells die, they release various proteins, such as aspartate aminotransferase (AST), lactate dehydrogenase (LD), creatine kinase (CK, CK-MB) and troponins, but troponins have the best sensitivity and specificity for heart damage. They have become the preferred test in Australia. Of course no test is infallible; the doctor's experience and judgment still outweigh any test result.

Not all troponins come from heart muscle, but this article deals only with those that do (cardiac troponins). Immunological assays distinguish them from troponins from other tissues. Since normal patients have no detectable troponins in their blood, even minor increases above the normal reference interval (often described as the 99th percentile of normals), indicate damage to the heart muscle. Many pathologists and clinicians see cardiac troponins as a huge advance. They want all patients with chest discomfort consistent with ACS (Acute Coronary Syndrome) to have at least one troponin assay. ACS is caused by inadequate myocardial oxygen supply and includes UA (Unstable Angina) and AMI (Acute Myocardial Infarction or Heart Attack).

Cardiologist Associate Professor David Brieger of Sydney's Concord Repatriation Hospital says: "Cardiac troponins help us in various ways: to confirm or exclude an Acute Coronary Syndrome (Unstable Angina or Myocardial Infarction). When a



Associate Professor Hans Schneider of Melbourne is Director of Pathology at Alfred Pathology Service and also practices in general medicine and endocrinology

patient does have troponin in the blood, its level helps us to assess the patient's risk of reinfarction or death. This in turn enables us to pull out the stops for those at highest risk. They need coronary angiography within 48 hours; some will have a stent at the same time. Others will need open bypass surgery during the same admission."

An editorial in the *British Medical Journal* summed up: "The assessment of patients with chest pain is a difficult skill, informed by clinical judgment. Troponins can help in diagnosis, risk estimation and as a guide to treatment."

Troponins have led to 20-30 per cent more people than before being diagnosed with myocardial infarction: people who would have been missed before.

Imagine it's Saturday in a country town like Mount Gambier. Bill Jones, aged 50, is umpiring the local football match. His GP is treating his blood pressure but Bill hasn't managed to stop smoking. About noon he comes off the field, complaining of pain behind his breastbone. His mates

drive him to the local hospital where his GP gives him Anginine which relieves his pain by about 2 pm. His first ECG is normal, as is his cardiac troponin. Could it not be his heart at all? Could Bill could have angina (pain from a shortage of blood to the heart, but not as severe as a full-blown heart attack)? The GP starts him on aspirin and observes him closely.

About 8 pm, Bill has a repeat ECG and blood troponin. The former still looks normal, but the latter is now raised. This is serious. His GP rings Dr Philip Tideman, the on-call cardiologist at Flinders Medical Centre in Adelaide, and faxes Bill's ECGs to him. Philip directs the Integrated Cardiac Assessment Regional Network that now covers 56 hospitals throughout South Australia. Cardiologists rostered 24 hours seven days respond within ten minutes to such calls.

Dr Tideman and Bill's GP at Mt Gambier have worked together before. They agree that, despite the still normal ECG, the raised second troponin level means Bill has probably had a heart attack

from a clot in one of his coronary arteries. He is now at high risk. The GP continues the aspirin, but adds other drugs (the anticoagulant Clexane, Aggrastat and a beta blocker). He organises the Royal Flying Doctor Service to airlift Bill to the Flinders Centre, where Dr Tideman is waiting. Bill settles in well. Dr Tideman takes him to the Cardiac Catheter Laboratory and does an angiogram (an X-ray of the coronary arteries outlined by a dye). As expected, Bill has a 90 per cent blockage of one of his heart arteries. While Bill is still on the catheter table and fully conscious, Dr Tideman uses X-ray control to insert a stent (strut) to open up that artery.

Only days after he got his chest pain, Bill goes back home to Mt Gambier! How different from the bad old days when a heart attack meant you lay, terrified, stock still in hospital for weeks on end. Finally when you went home, doctors warned you dramatically to be careful, whatever that meant.

Not so long ago, we used to say that about one third of us would die from ischaemic heart disease, one third from cancer, and the rest from all other causes combined. Though cardiovascular disease is still common, our chances of returning to a normal productive life are now much better than they were 20 or even 10 years ago.

It was the raised repeat troponin level that led to Bill's early diagnosis and so to his successful prompt transfer and treatment. Dr Tideman is one of the many doctors who sees troponins as a valuable tool.

The ideal blood marker would be:

- 100 per cent sensitive to myocardial damage (no false negatives)
- 100 per cent specific for the myocardium (no false positives)
- Virtually absent in normal circulation
- Easy to assay
- Stable in storage
- Its level would also rise quickly after a serious event and stay high for some time

To a great extent the cardiac troponins T and I meet these criteria. Hence they have become a key marker of Acute Coronary Syndrome. But the myocardial damage detected by troponins does not always reflect ischaemic coronary artery disease. Other causes: strenuous exercise, heart failure, stroke, pulmonary embolus, pericarditis, myocarditis, episodes of hypertension or arrhythmia, trauma to the heart (including cardiac massage or heart surgery), kidney failure and sepsis.

Associate Professor Peter Hickman, Chemical Pathologist at Canberra Hospital, says junior hospital doctors fear myocardial infarction and hence are often alarmed when one of their patients has high cardiac troponin readings, even if it is due to one of these other causes. But this alarm may be a good thing since raised troponins from any cause are still a

warning of increased clinical risk. A high reading in the absence of clinical evidence of ischaemia should lead to a search for other causes of myocardial damage. As one journal said: "Positive troponin values are independent predictors of poor outcomes in the short and... long term."

Associate Professor Hans Schneider of Melbourne wears various hats. He is Director of Pathology at Alfred Pathology Service and practices in general medicine and endocrinology. He endorses the growing use of cardiac troponins: "They have very few false positive results. Troponins are now clearly a key marker of myocardial damage. They have almost completely displaced CK and CK-MB assays at the Alfred."

The new definition of AMI dating from the year 2000 is largely based on the criterion of raised cardiac troponin reading. So we are now detecting AMI in people we would have missed (or called angina) before. This change of definition

has led to an apparent rise of 20-30 per cent in recent figures for AMI.

Troponins T and I are the commonly assayed cardiac troponins. Some laboratories choose to assay one, some assay the other. Dr Graham Jones, Staff Specialist in Chemical Pathology at St Vincents Hospital in Sydney, says the practical advantage of Troponin T assays is that there is only one method and one type of reagent; hence Troponin T results from various laboratories, even in different countries, are directly comparable.

However Troponin I readings from various laboratories are harder to compare. Since an international Working Party agreed on standards for troponin I assays, the readings are coming closer together. For the moment, Graham advises clinicians to check the system and cutoffs in their own laboratory.

Queensland Medical Laboratory has sent a typical (anonymous) report of a

MARKERS OF CARDIAC DAMAGE

| | |
|-------------------|------------------------------------|
| Date | 18/03/05 |
| Time | 10:30 |
| Lab No | 6768814 |
| Troponin T | +++ 0.27 ng/mL (0.00-0.10)* |
| Total CK | +++ 560 U/L (0-140)* |

6768814 The TnT indicates that recent myocardial infarction (6 hours to 7 days) is likely.

Dr Philip Tideman,
cardiologist at Flinders
Medical Centre in
Adelaide



patient with figures suggesting a recent AMI.

After myocardial damage, troponins take 4-6 hours to rise, peaking at 12-24 hours. So values on admission can mislead. If a test is negative at first, it is advisable to repeat it 6-12 hours later. Moreover, since levels stay up for up to 14 days, troponins are of little help to diagnose reinfarction.

Most laboratories can issue results within one hour of getting the sample. In fact, the biggest delay is in getting the sample to the lab through city traffic or from the country. Many or most troponin assays take place in busy, large labs on large analyzers using standardised methods (with meticulous calibration, appropriate reagents and quality control to produce numerical results).

But as we have seen, time is often of the essence. Not all hospitals, rooms or surgeries have quick access to such a lab.

Troponins are helping us to diagnose ACS and hence offer customised early definitive treatment.

Current research may bring us even better markers (to reduce the need to wait for 6 - 12 hours for a second troponin where the first reading is normal). Possible early markers include myoglobin, Ischaemia Modified Albumin and Fatty Acid Binding Protein.

Not so long ago, we used to say that about one third of us would die from ischaemic heart disease, one third from cancer, and the rest from all other causes combined. Though cardiovascular disease is still common, our chances of returning to a normal productive life are now much better than they were 20 or even 10 years ago.

All in all, our future looks brighter. 🔥

GPs NOTE: This article is available for patients at <http://pathway.rcpa.edu.au>

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