

In Memoriam

A tribute to Attilio Maseri

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A native of Udine in Northeastern Italy, Prof. Attilio Maseri graduated from the University of Padua Medical School in 1960 and immediately moved to Pisa, where he trained in Cardiology (1963) and Nuclear Medicine (1968). During this period, he served Research Fellowships at Columbia University (1965) and Johns Hopkins University (1966) in the USA. In 1967, he became Assistant in Medicine at the University of Pisa and head of the coronary research group of the Institute of Clinical Physiology directed by Prof. Luigi Donato. In 1979, he became Professor of Cardiovascular Medicine at the Royal Postgraduate Medical School of the University of London and Director of Cardiology at Hammersmith Hospital. In 1991, he returned to Italy as Professor of Cardiology at the Catholic University of the Sacred Heart in Rome. From 2001 to 2008, he was a Professor of Cardiology at the Vita-Salute San Raffaele University in Milan.

His initial research interest was the measurement of coronary blood flow with radioisotopes, a technique that he pioneered.¹ In Pisa, he also made the first clinical observations on the mechanisms of angina pectoris at rest, showing that it could be caused by coronary spasm.² He also demonstrated that coronary spasm could be prevented by the administration of calcium antagonists.³ Another fundamental contribution to cardiology was his demonstration that coronary microvascular dysfunction can cause myocardial ischaemia.⁴ Subsequent research in London and Rome provided the first demonstration of the important role of inflammation in acute coronary syndromes.⁵

His early interest in cardiology and in research was intensified when he was a research Fellow at Columbia by his contact with the Nobel Laureate André Cournand. Prof. Maseri loved to recall that he was particularly impressed when as a young research fellow he politely disagreed with Prof. Cournand and provided the reasons. After brief hesitation, Cournand said: 'I am an old fool: obviously your answer is correct'. Maseri learned that if a Nobel Laureate could be challenged by a young trainee, then dogmas can also be challenged! This has been the 'North Star' of Maseri's scientific life. If dogmas can be proved to be wrong, they must be corrected, as had been stated by Carl Popper, one of his favourite philosophers.

The first dogma that he challenged was the notion that myocardial ischaemia cannot occur in the absence of a fixed coronary stenosis.

The starting point in the falsification of this dogma was the simple clinical observation that some patients reported rest angina on some days, while they exhibited excellent effort tolerance on other days. How could a fixed stenosis explain this extremely variable angina threshold?⁶ He then became interested in a paper published by Prinzmetal, an American cardiologist, who suggested that angina could also be caused by an increase of 'coronary tonus'. Maseri was fascinated by this provocative hypothesis and set up a series of studies to test it. First, he demonstrated coronary spasm at angiography.² But this was criticized by important cardiologists noting that it was simply catheter-induced spasm. He then demonstrated that the injection of thallium during rest angina was associated with transient perfusion defects.⁷ But this was criticized as well. Maseri then utilized continuous monitoring of oxygen saturation in coronary sinus blood simultaneous with hemodynamic monitoring. He demonstrated that rest angina was associated with a marked desaturation of coronary venous blood in the absence of an increase of myocardial oxygen

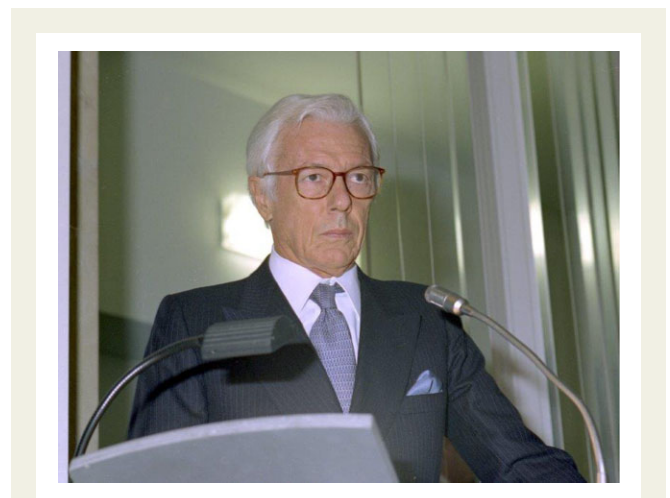


Figure 1 Prof. Maseri during the inaugural lecture at the opening of the academic year at the Catholic University of the Sacred Heart.

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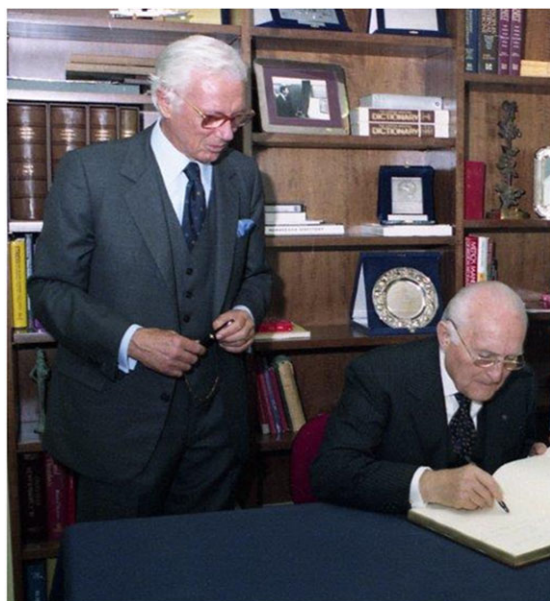


Figure 2 Prof. Maseri with Oscar Luigi Scalfaro, President of the Italian Republic.



Figure 3 Prof. Maseri in Cervinia with Filippo and Roberta Crea: skiing, sailing and tennis were his favorite sports.

requirements.⁸ He had finally proved his working hypothesis: the dogma that myocardial ischaemia could only occur in the presence of a fixed coronary artery stenosis was wrong. Yet, for some more years this strange form of angina was labelled 'Pisa angina' since it apparently could only be found in Pisa. Maseri encountered the same scepticism when he proposed that coronary microvascular dysfunction was another possible cause of ischaemia in the absence of epicardial stenoses.⁴

In science, the test of time is the only credible judge, and we now know that the functional alterations of the coronary circulation are a frequent and clinically relevant cause of angina and myocardial ischaemia. But it took more than thirty years to find recommendations for treating functional alterations of the coronary circulation in the Guidelines of the European Society of Cardiology and in the Universal Definition of myocardial infarction.

In addition to the importance of challenging dogmas, another 'North Star' for Maseri was a cartoon that he projected in his lectures showing a man that looked for something on the floor of a portion of the street not under the spotlight projected by a streetlamp, where many others were already searching. The message is clear: the research (he preferred to call it 'the search') is more difficult and riskier but much more rewarding if pursued in areas which are not crowded. This was the attitude which pushed his curiosity towards the role of inflammatory cells in the pathogenesis of acute coronary syndromes while the interest of the scientific community was stuck on classic coronary risk factors and thrombosis. He published the initial proof that inflammation plays a key role in acute coronary syndromes in 1994 in the *New England Journal of Medicine* showing simply that among patients with an acute coronary syndrome higher circulating levels of C-reactive protein (CRP) were associated with a worse outcome.⁵ This observation opened an entirely new window,^{9,10} although it took 25 years to obtain the proof that the 'inflammatory hypothesis' was correct with the report of the CANTOS trial which demonstrated that canakinumab, a 'pure' anti-inflammatory drug improved the outcome of patients with an acute coronary syndrome and an elevated CRP.

Attilio Maseri has been not only a charismatic and innovative scientist but also a gifted clinician. He genuinely cared about the wellbeing of all his patients. He loved to say: 'Our main goal as doctors is not to prolong the lives of our patients but rather to improve the quality of their lives'. He was very cautious in giving extremely restrictive recommendations on lifestyle; he loved to say: 'It does not make sense to live as a sick person in order to have the privilege of dying in good health'. His attitude towards patients was inspired by what detectives do in spy stories: they look for the culprit to put in jail. He was typically very successful in his quest for the culprit.

Attilio Maseri has also been an outstanding mentor. In Pisa, in London, in Rome and finally in Milan, he created successful and enthusiastic teams of researchers. He strongly believed in teamwork. His curiosity was contagious, his ability in teaching rigorous scientific methodology was outstanding. He loved to say: 'Our major challenge as researchers is to ask ourselves important questions. Not all questions are equally important; it is more difficult to identify important questions than to elaborate complex experimental protocols to prove them'. He was also extremely direct. On one occasion he told a young cardiologist who was a good clinician but without a strong talent for research: 'You are a good goal keeper, why do you want to make goals? In a good team all players are important, not only those who score' (Figures 1–3).

Attilio Maseri has been an inspiration and model for many cardiologists and researchers who were lucky enough to learn from him and then become successful cardiologists all over the world. His leadership in motivating basic research based on clinical observations is recognized internationally. He has been one of the true precursors of translational medicine.

We pay a tribute to this giant of Cardiology, to this gentleman with a generous and noble soul, to this Master who has taught the values of Medicine and Science to a large array of pupils who in turn have amplified his teaching around the world.

Prof. Maseri has received prestigious international prizes including the King Faisal International Prize in Medicine, the Distinguished Scientist Award of the American College of Cardiology, the Gold Medal of the European Society of Cardiology, and the Grand Prix Scientifique de la Fondation Lefoulon-Delalande. Pope John Paul II awarded him the title of Commander of the Knights of the Order of St. Gregory the Great.

I met Attilio Maseri when I was 25 years old. I worked with him initially in Pisa and then in London. I have been his successor as Professor of Cardiology at the Catholic University in Rome. He has been a second father to me and a continuous source of scientific and human inspiration. When I told him that I was named the new Editor-in-Chief of the *European Heart Journal* he simply told me 'Now build a strong team: teamwork is the key to a successful and pleasant life'. I fully agree with you Prof. Maseri: cooperation among human beings makes our planet a better place.—Filippo Crea

During our five decades of friendship my admiration for Attilio Maseri grew exponentially. He was the quintessential 'triple threat' physician-scientist who excelled in each of the three legs of the academic tripod. As a superb cardiologist he recognized important unsolved clinical problems; as a transformational clinical scientist he solved many of them; as a spell-binding teacher he communicated the new information—at the bedside, on the lecture podium, and in print. His enthusiasm for the evolution of cardiology, especially coronary artery disease, was infectious.

As Isaac Newton said: 'I can see so far because I stand on the shoulders of giants'. Attilio Maseri was such a giant, a true visionary who expanded the horizons of cardiology. He will be sorely missed.—Eugene Braunwald

Conflict of interest: none declared.

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Aside of our mutual scientific interests and research interactions, Attilio Maseri, and his wife Francesca, who unfortunately died about twenty years ago, became close friends with my wife and I. We spent valuable time together in many different places in the world.

There is one aspect I would like to emphasize. Aside of the 'triple threat' physician-scientist, as defined by Prof. Braunwald, Attilio had a competitive mind in many other fields. Two personal examples: he always tried to convince me that his Spanish was better than my Italian (probably correct), and more important to him was to be sure that I accepted that his tennis game was superior to mine (probably incorrect).

We lost an outstanding clinical scientist, we lost a man full of curiosity and motivation, and at a more personal level, we lost the friendship of a dear couple, Attilio and Francesca. —Valentin Fuster

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Events and Meetings

The anticoagulation grey zone

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Mark Nicholls reports on an ESC 2021 debate over whether anticoagulation should be given to all patients for stroke prevention in atrial fibrillation.

Two leading experts examined whether anticoagulation should be given to all patients with atrial fibrillation and a CHA₂DS₂-VASc score of 1 in a lively debate at ESC 2021.

The subject, which has polarized opinion, was one of a number of controversial and divisive subjects expertly and enthusiastically tackled during 19 Great Debate sessions at the digital congress.

This debate saw Prof. Gregory Lip and Prof. Alexander Niessner (Figure 1) square up to one another across the virtual debating chamber.

On the key point that 'anticoagulation should be given to all patients with atrial fibrillation and CHA₂DS₂-VASc score of 1', Prof. Lip argued the 'pro' position in favour, while Prof. Niessner discussed the 'con' arguing against the move.