A View From Malta: Albert Fenech, MD

Until 1995, Malta Had No Resident Interventional Cardiology Service, but Times Are Changing

Cardiology is a relatively new speciality in Malta. Dr Albert Fenech, professor and interventional cardiologist at St Luke’s Hospital in Guardamangia, Malta, returned to the island 12 years ago to help the speciality’s development. He talks to Ingrid Torjesen, BSc.

Although the small island of Malta (Figure 1) is a Mediterranean country, coronary heart disease is the main cause of death, and the island’s population has one of the highest incidences of diabetes mellitus in the world. For many years, Malta had the status of a British protectorate, so the population tended to eat foods popular in the United Kingdom rather than follow a typical Mediterranean diet. It joined the European Union in 2004.

Before 1995, Malta did not have a resident interventional cardiology service, and although cardiologists would occasionally visit the island to provide outpatient services, medical professionals had to fly most patients who needed surgery or angioplasty off the island for treatment. Every year, about 300 patients travelled to the United Kingdom for these procedures to be performed.

Then, in 1995, everything changed. Dr Albert Fenech, currently a professor and interventional cardiologist at St Luke’s Hospital, Guardamangia, Malta, and Alex Manchè, MD, currently the senior consultant cardiothoracic surgeon at St Luke’s Hospital, returned to the island from the United Kingdom to set up a cardiology service. The island now offers the full range of cardiology services, from simple procedures right up to a heart transplantation programme.

“The only people we send abroad now, and purely because there isn’t enough of a workload to justify doing it, are patients who need complicated redo cardiac surgery, which has a high mortality,” says Dr Fenech. “Patients who have had previous cardiac surgery or valve replacement who need another thoracotomy, redo cardiac surgery, or a redo bypass are sent to a centre in the United Kingdom that specialises in such complicated procedures.” In 12 years, this has applied to only 3 patients. “Just 3 patients in the past 12 years would have put an unfair demand on the surgeon and an unfair expectation on the patient,” he explains.

Figure 1. Malta and the islands of Comino and Gozo were a former British protectorate. It joined the European Union in 2004.
Malta now has 4 interventional consultant cardiologists and 2 non-invasive specialists. All the doctors come from the island and showed a great interest in cardiology at an early stage of their careers. They received their basic training abroad, and all their interventional training was carried out by Dr Fenech. The two cardiac surgeons received much of their training in the United Kingdom before deciding to settle in Malta and complete their training under Dr Manchè.

“It was not difficult to provide the on-the-job training required because there was a great demand for cardiology services,” says Dr Fenech. “For 4 years, I was the only consultant here, so I did every case and we split it day by day. Each of the new specialists in training had their own day in the cath lab, and that is how we went on with it.” He continues, “Once they had done their general medical training, it was a matter of doing so many cases per year to get accredited locally, and then to do so many per year to remain accredited. Under the system we have here, cardiologists become accredited by virtue of the fact they have so many cases under their belt.”

Malta has 1 main hospital, St Luke’s. Though considered a top-class facility at the time of its construction in 1939, it is now too cramped and was constructed of materials such as marble, which are no longer considered appropriate in a medical care setting. “As the building was not originally designed to house a cardiology and cardiac surgery department, when one was added in 1995 it was cramped because it had to be ‘shoe-horned’ in,” says Dr Fenech.

However the situation will soon improve dramatically. A brand new hospital building, with a purpose-built cardiology department, has been built at a different site. The new Mater Dei Hospital (Figure 2) opened at the end of June, and hospital departments have begun migrating across to the new facility. Dr Fenech says, “Although there is still only going to be the 1 general hospital on the island, it will be a spanking new one on an excellent site, with a much bigger footprint and much better amenities than the old one. It has been built specifically with cardiac surgery and cardiology in mind.”

At present, Malta does not have a cardiology society under the European Society of Cardiology, but Dr Fenech says that the 6 cardiologists and 3 cardiac surgeons are very keen to set one up, even if this means affiliating it with another organisation. He says, “I have been working towards that, and I was told we need about 50 people to make it viable. That includes the cardiac nurses and general physicians who are interested in cardiology. I think we will get enough people, and we are very keen to do that because we do sterling work here. For the size of the population, our rates of intervention compare very well with the rest of Europe.”

As a small country with a close-knit community, Malta has the potential for doctors working there to feel closeted and cut off from their colleagues in the rest of the world. However, Dr Fenech says they have avoided such problems by having all their cardiologists and surgeons attend at least 1 conference per year to ensure they keep in touch with the latest developments and their peer group. Indeed, he actually considers Malta’s small size, of just 100 square miles and a population of only 400,000, an advantage. Its smallness makes it a very friendly place.

“You tend to develop a closer relationship with the patient

### Facts About Malta

- Great Britain acquired possession of Malta in 1814. The island staunchly supported the United Kingdom through both World Wars and remained in the Commonwealth when it became independent in 1964.
- Malta became a republic in 1974.
- Malta’s main commercial activities are freight transshipment, finance, and tourism.
- Malta became a European Union member in May 2004.
- Malta has total land area of 316 km².
- The estimated population for 2007 is 401,880.
- The country comprises Malta and the adjacent islands of Gozo, Comino, and the tiny, uninhabited Filfla.
- Life expectancy at birth for men is 79.1 years; and for women, 81.4 years.
- The gross domestic product per capita is $21,000.

Data from CIA Factbook 2007
that is extended to outside the hospital and that is most rewarding,” Dr Fenech says. “You tend to get recognised more easily, and it is just satisfying to see people going about their daily routines dressed in clothes as opposed to pyjamas, as you saw them in hospital. They often come up to you in the street and want to tell you how they are doing.”

Malta has some beautiful scenery, and another obvious advantage of living and working there that Dr Fenech appreciates is the pleasant climate of hot summers and mild winters, which contrasts markedly with that of the United Kingdom where he worked before. “The bottom line here is that I spent 20 years in the United Kingdom, and I hardly ever saw my patients once they came out of hospital,” Dr Fenech says. “But here, you tend to see the fruits of your work quite often.” He emphasises this point, saying, “The whole purpose of medicine is to allow people to lead a normal life, so I derive much pleasure in getting the feedback and seeing patients having a good time and leading normal lives as a result of my handiwork. That, at the end of the day, is what we are here for.”

Ingrid Torjesen is a freelance medical writer.

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**Spotlight: Giancarlo Agnelli, MD**

**A Man Whose Mission Is to Make Anticoagulation Safe and Reliable**

Giancarlo Agnelli, MD, professor of internal medicine at the University of Perugia, Italy, and director of the division of internal and cardiovascular medicine, has gained recognition for his research on thromboembolism. He tells Emma Baines, PhD, about his search for ways to make anticoagulation treatment safer and more reliable.

Dr Giancarlo Agnelli, professor of internal medicine and director of the division of internal and cardiovascular medicine at the University of Perugia in Umbria, Italy, has been working on treatments for thromboembolism for the past 35 years. To date, his most important research has been the identification of new thrombolytic agents, and the determination of the optimum duration of anticoagulant treatment after a thrombotic event. But he continues to work toward a much larger goal. As he says, “My life’s dream is to find a drug to replace warfarin.”

Dr Agnelli was born in the town of L’Aquila in the Abruzzi region of central Italy in 1950. At age 19, he went to study medicine at the University of Perugia, where he studied under Paolo Larizza, MD, then professor of internal medicine at the university. Dr Agnelli attributes much of his success to the support that he received from Dr Larizza at the time. “I was lucky to have such an outstanding teacher,” he says. “He was a great man and had a positive influence in the department of internal medicine in Perugia for a number of years.” While working for Dr Larizza, he started working in haematology; this led to an interest in the mechanisms underlying coagulation and thrombosis.

After finishing his medical training, Dr Agnelli became an assistant professor in the department of internal medicine at Perugia (Figure 1) at the very young age of 24. Despite offers from universities around the world, he has remained there throughout his career, except for brief sojourns abroad.

In 1981, he went to Canada and spent 3 years working at McMaster University in Hamilton, Ontario, where he became an associated member of the research centre. While there, Dr Agnelli began doing research on thrombosis, under the guidance of Jack Hirsch, CM, MD, FRCP(C), FRACP, FRSC, DSc, professor emeritus in medicine, director of the Henderson Research Center, McMaster University, and chair of the department of medicine at McMaster at the time.

While in Canada, Dr Agnelli worked on an analysis of
heparin, attempting to separate the components that have beneficial antithrombotic effects from those that have negative side effects. The project saw partial success. “We achieved something, but the problem is still there. I cannot claim that we solved this issue,” he says.

Dr Agnelli also worked on the identification of safer thrombolytic agents. He worked with one of the first teams to investigate tissue plasminogen activator—now a widely used treatment for myocardial infarction and pulmonary embolism. They proved that tissue plasminogen activator was less haemorrhagic than traditional thrombolytic agents such as streptokinase. They also revealed boluses, rather than a long infusion, as the best way to use tissue plasminogen activator.1 “It seems obvious now, but if you look back to the early 1980s, you see that people used to use thrombolytic agents for hours and hours.” He recalls, “We were the first to show that they are more effective when used as a bolus.”

Dr Agnelli continued to collaborate with researchers at McMaster after his return to Italy. He carried out a number of clinical trials, including the first clinical trial in Italy on prevention and treatment of thromboembolism. In 2001, he published an important study clarifying, for the first time, how long one should give anticoagulant treatment after a thrombotic event.2

Recently, he has worked on the development of new antithrombotic agents, hoping to find a compound as effective as warfarin, but safer and easier to use. Although warfarin can effectively help prevent strokes in patients with risk factors such as deep vein thrombosis (Figure 2) or atrial fibrillation, it can cause bleeding complications. But, as Dr Agnelli explains, the dosing causes most problems. “The dose can range from 0.5 mg to 15 mg per day, so you need tight blood control. We are looking for something that can be given as a fixed dose. We’re really working hard to replace warfarin, and I believe that it will happen. The only question is when,” he says.

Dr Agnelli took part in work on the direct thrombin inhibitor ximelagatran, which seemed promising, but the drug was withdrawn from clinical research in early 2006 because of concerns about hepatic safety. Dr Agnelli is now working on other thrombin and Xa inhibitor compounds such as dabigatran etexilate and rivaroxaban (BAY 59-7939), which will soon go into phase 3 trials as a fixed-dose treatment for deep vein thrombosis.3

During the next few months, Dr Agnelli will shift some of his attention to focus on a new area of thrombosis research. He wants to explore the relationship between cancer and thrombosis. Up to 15% of cancer patients have a thrombosis at some point in the progression of the disease, and it often proves fatal. Dr Agnelli, therefore, intends to set up a large study looking into the prevention of this complication in cancer patients. “Everybody believes that cancer patients die from cancer,” he says, “but the second main cause of death in cancer patients, after progression of the disease, is thrombosis.” He explains, “In many cases it comes at the very end stage of the disease, when the patient has not long to live anyway, but in some cases it comes nearer the beginning of the disease. This means that some patients are given a lot of treatment, including complicated surgery and expensive chemotherapy, only to die from, say, a pulmonary embolism.”

He adds that some evidence suggests that giving anticoagulation agents such as heparin along with chemotherapy could prolong life and improve outcomes in cancer patients, although the mechanism underlying this effect is not clear. “It’s something that people still consider a bit strange and esoteric, but I think that this field is going to explode in the coming years,” he says.

Dr Agnelli admits that the decision to remain in Italy rather than going to the United States to work has meant giving up a number of research opportunities. “Limited public funding for research and an overabundance of bureaucracy in the Italian system are major stumbling blocks to anyone wanting to carry out any intensive research programme in Italy,” he says. “The bureaucracy can really make your life complicated,” he continues, “and sometimes I ask myself what I could have achieved if I’d worked at one of the large American research centres. But, on the other hand, my career has progressed well here. And I’ve been lucky enough in recent years to have a group working for me that it would be almost impossible to abandon. They’re high-quality people, both in terms of science and also as human beings, and that is a serious compensation.”

When not at work, Dr Agnelli likes to ski, and he enjoys playing other sports. “Like all Italians, I like football,” he says. He has a wife and 3 sons, and eventually he wants to retire to Sardinia. “I have had a really lucky life,” he says.
History of Cardiology: Wilhelm Ebstein, MD

Who Was the Man Who Identified the Rare Congenital Heart Defect Known as Ebstein’s Anomaly?

Wilhelm Ebstein (left) identified the rare congenital cardiac anomaly that now bears his name. His story is well known to consultant cardiothoracic surgeon Igor E. Konstantinov, MD, PhD, of the Sir Charles Gairdner Hospital, Perth, Australia, who has a passionate interest in the history of cardiology and has written reviews and biographies of key figures from the past. He talks about Dr Ebstein’s life and legacy with Mark Nicholls.

Wilhelm Ebstein was the son of a merchant, Louis Ebstein, and his wife Amalie. He was born at Jauer in Silezia, Poland, on November 27, 1836. In 1885, when he was 19, he began his medical studies, initially at the University of Breslau, Poland, but within a few months he moved to the University of Berlin, Germany, to study under a number of influential teachers including Albrecht von Graefe, MD, Ludwig Traube, MD, and in particular Rudolf Virchow, MD. He enthusiastically attended Dr Virchow’s in-depth pathological demonstrations, which were later to influence his own work and findings.

Dr Igor E. Konstantinov and colleagues have written a historical account entitled “Wilhelm Ebstein and Ebstein’s Malformation.” In this article, Dr Konstantinov writes, “It is without doubt that Ebstein’s later accurate description of the cardiac anomaly that bears his name was closely associated with Virchow’s methodology in pathology.”

Dr Ebstein obtained his medical degree from the University of Berlin in July 1859, and in 1861 he was appointed assistant physician at the All Saints Hospital in Breslau (now Wroclaw). By the end of that decade, he had qualified to lecture at the university. Soon after, he served in the Franco-Prussian War. and on his return from the war in 1870, he was appointed medical officer to the state almshouses in Breslau. In 1874, Ebstein went to Göttingen, Germany, as professor of medicine, where he worked for the remainder of his life, dying on October 22, 1912, at the age of 75, of cerebral apoplexy.

During his life, Ebstein was a prolific writer, but of his 272 published articles, only 12 related to cardiovascular disease. He became known at the time primarily for his work on the pathology and treatment of metabolic diseases, including diabetes mellitus, gout, and obesity. But for cardiologists, it is his description of Ebstein’s anomaly that is of the greatest interest.

Dr Konstantinov says, “Ironically, Dr Ebstein’s description of a congenital heart condition with which his name is most readily identified in the current era was almost overlooked at the time.” The description arose after a young labourer was admitted to All Saints Hospital in late June 1864, where the attending physician, after a thorough examination, diagnosed a congenital cardiac defect. The patient, who was 19, died 8 days later. The following day, Dr Ebstein performed a post mortem examination. He recorded his findings in a highly detailed and clear fashion, and in such a way that his description still has relevance today. He particularly noted, “The tricuspid valve was extremely abnormal in appearance.”

Ebstein concludes that the cardiac pathology consists of 3 components. These are a severe malformation of the tricuspid valve, absence of the Thebesian valve of the coronary sinus, and a patent foramen ovale. Dr Ebstein published his case report in 1866, and although subsequent writers referred to the report in the years that followed, it was not until 1927 that it was first described as “Ebstein’s disease.”

References
Today, Ebstein’s anomaly of the tricuspid valve, also referred to as Ebstein’s malformation, is now widely recognised as a congenital heart lesion that involves abnormal attachments of the tricuspid valve leaflets to the annulus of the tricuspid valve and displacement of the valve toward the apex of the right ventricle. With greater malformation and leakage of the tricuspid valve, the right atrium enlarges as it receives a greater blood volume, and the right ventricle also dilates and is displaced downwards (see Figure).

The anomaly occurs in <1% of patients with congenital heart disease, and 50% of those with Ebstein’s anomaly also have an atrial septal defect. About 1 in 4 have episodes of tachycardia that, most commonly, result from an abnormal accessory conduction pathway, the Wolff-Parkinson-White syndrome.

Dr Konstantinov believes that Ebstein’s publication was a landmark in the description of a new entity. “Not only was it an accurate account, but it provided a strong basis for the development of repair techniques for this rare anomaly 100 years later,” he says. “Today this abnormality can be repaired with very good results.” Dr Konstantinov emphasises that the major contributions to our current understanding of surgical repair of Ebstein’s anomaly were made by Gordon Danielson, MD, from the Mayo Clinic, Rochester, Minn, and Alain Carpentier, MD, PhD, from the Hospital Broussais, Paris, France.

Dr Konstantinov concludes, “The major contribution of Dr Wilhelm Ebstein to cardiology was a detailed description and recognition of the key features of a rare congenital cardiac anomaly that now bears his name. Dr Ebstein’s detailed description allowed for development of a proper surgical technique to repair this anomaly but was recognised mainly after his death. But,” he explains, “although this association with the anomaly assured immortality of his name, as often happens in medicine, the description of the anomaly was not his primary interest.”

Mark Nicholls is a freelance medical writer.

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