MEDICAL PRACTICE

Spring Books

The spirit of San Michele lives on

ELLIOT PHILIPP

Axel Martin Frederik Munthe was born on 31 October 1857 in Oskarshamn Kalmar, in Sweden, and died in 1949 aged 92 in Stockholm. He had close connections with the Swedish royal family, and some have even suggested that he might have been an illegitimate child of a member of that family. He was a physician who became a psychiatrist after studying neurology in Uppsala, Sweden, as well as in Montpellier and Paris. In Paris he studied under the great Jean Martin Charcot. In 1908 he was made physician to the Swedish royal family.

His claim to fame, however, rests on his autobiography, which, as with so many autobiographies, is a mixture of fact and imagination. Some say there was more imagination than fact; others say that even if it was not always true at least it was well told. It was, indeed, astoundingly well told, and *The Story of San Michele*, which appeared in 1929 and was named after the place where he made his home in Anacapri, was probably the most successful medical autobiography ever written. Surprisingly, though, it does not mention either his wife or children, though he had sons who must have been young when he wrote the book and who are still alive today. That must be unique—for a man to appear so warm and apparently to give so much of himself in an autobiography and yet conceal so much about his personal life. But those who read the book cherish it, not least because it shows what a wonderful empathy he had with his patients.

Munthe was an immensely colourful doctor who qualified in medicine at a younger age than anyone before him, and practised in many countries. His outstanding qualities were courage, sensitivity, culture, medical excellence, and an ability to mix with all kinds of men and women at all levels of society, from royalty to the dying in the slums of Naples. His courage was shown on many occasions: early in life when he publicly quarrelled with his master, the great Charcot, at the Sal Pètrièrre in Paris and later when he worked day and night in the Naples slums helping cholera victims. He dared to think originally and scientifically, and although he did many experiments on animals, the kindness he displayed to them, particularly to the primates and dogs, was remarkable.

Axel Martin Frederik Munthe. Reproduced with permission from *The Story of San Michele*. Axel Munthe. London: John Murray, 1936.

The Axel Munthe prize: spawned by inspiration

Bring to Capri, where Munthe lived and wrote, the beautiful and intelligent Princess Desiree from Sweden to present the "awards." Bring to Capri the glamorous Italian actress Claudia Cardinale and her husband to do the same, and bring too some 50 of the world's

greatest scientists in reproductive physiology—of whom six were to be judged and the remainder to be judges—and you have the ingredients of what turned out to be the most civilised contest imaginable. The six were to be honoured with an Axel Munthe award for scientific achievement, but only one of them was to receive an added prize of \$25 000 for being first among the first. The meeting was held in the last three days of September 1985.

The dynamo who thought out the competition was Vincenzo Abate, a gynaecologist of sensitivity and skill who was the first doctor in Italy to set up a successful centre for in vitro fertilisation. Abate had the idea that a scientist who specialised in reproductive medicine should receive a prize every third year and that this prize should take its place alongside the Nobel prize for medicine. The prize would be restricted to those working on research topics related to reproduction. A small group of experts were selected to form the scientific committee and a larger group to make up the advisory committee. Each member of the latter was invited to recommend a scientist for consideration for the Axel Munthe award.

Twenty names were put forward, from which a shortlist of six was selected by the scientific committee, all of whom received papers detailing the achievements of each nominee. A decision was made to award each of the six shortlisted candidates a small statuette, a lithograph, a cheque, and a complimentary return journey for themselves and their spouse together with accommodation for the three days in Anacapri when the formal presentation and announcement of the overall winner would be made. The winner was also to receive a prize of \$25 000 to be used at his own discretion, but if possible to further scientific research on reproduction.

So who were the chosen six and what had they done? The first thing that is obvious to anyone working in reproductive medicine is that they had all "fed" on one another and mutually stimulated one another's thought processes. Medicine in the modern world is driven by such interchange. Another thing that was noticeable was that none of them were the sort of men or women who slouched about. Their one characteristic, as a journalist observed, was that though all were charming and all special in their own ways, all had a similar inner tension. And each, when presenting their case, said that the most important characteristic for scientific research was perseverance.

The meeting was skilfully arranged, and Professor Luigi Mastroanni set the scene when he announced that "The Axel Munthe award is unique and important because it provides emphasis and visibility for an area of research which has the greatest possible potential to have an impact on the world about us and on individuals—those living and those yet to be born. It is especially important, then, that the emphasis is on both humanitarian and scientific achievement. The scientists gathered in Anacapri researched not only so that those disadvantaged by the curse of infertility should have children but also that those disadvantaged by the curse of too many children should have means of restricting their families." "Quality not quantity of life is our aim," claimed another scientist. Each shortlisted candidate was then introduced by a fellow specialist and made a short presentation.

The shortlist

PROFESSOR MIN CHUEH CHANG

Professor Chang, who was born in Taiyuan, China, in 1908, came to the podium diffidently, with the slight stoop of a man who has looked down a microscope all his life. He is really the father of research into reproductive physiology, particularly those aspects of spermatozoal physiology and the factors that affect their production and fertilising capacity, as well as the site of fertilisation. He was the first to realise the mechanism by which eggs are fertilised, by discovering the phenomenon of capacitation by which process sperm are changed in the female reproductive tract so that they may penetrate the eggs. Chang was the first to achieve fertilisation of a mammalian egg in vitro, and some of Professor Robert Edwards and Mr Patrick Steptoe's work (both of whom were members of the scientific committee and were present at the award ceremony) has been based on this.

Chang, in common with the other candidates on the shortlist, spoke not only of what he had done in the laboratory and with patients, but of his philosophy. For him life and work were inseparable. His origins from a poor district of China, where there was terrible overpopulation, had inspired his work on oral contraception, and this had gone hand in hand with his work on fertilisation. In his view it was necessary for a scientist to be the right man in the right place at the right time. His place had been not only in Cambridge University, England, where he received his PhD in 1941 and his ScD in 1969, but also in the department of animal husbandry in the University of Edinburgh. His greatest achievement, however, was to be the principal scientist with the Worcester Foundation and at Boston University in the United States.

PROFESSOR PIERO DONINI

The second man nominated (in alphabetical order) was Professor Donini, an Italian, born in 1910, whose research into human chorionic gonadotrophins preceded and led to the development of the use of human menopausal gonadotrophins as ovarian stimulants. It was Donini, in 1948, who first extracted hormones from the urine of menopausal women and showed that they were like the hormones produced by human pituitary glands. In 1949 he predicted their potential for the treatment of women and men who had gonadal infertility. Singlehanded he developed a technique to extract gonadotrophins, first from the chorion and then from the urine. His philosophy was to try and try again, but he emphasised that he had had the good fortune to work with fellow scientists who had helped him immensely. His creed was, therefore, not only perseverance but cooperation and collaboration.

PROFESSOR PAUL FRANCHIMONT

Candidate number three was Professor Franchimont, born in Liège and professor of medicine and dean of the faculty of medicine there, who was nominated for his research on reproductive hormones. He came to the podium walking with sticks because of a cruel illness that had made this necessary, yet his gentle, purposeful way was clear. He discovered inhibin, a gonadal hormone believed to regulate the secretion of gonadotrophins and specifically follicle stimulating hormone. His research has included working out the chemistry of the hormones, and many of those who were present at the ceremony thought that his approach was perhaps the most exciting because he was persisting with promising methods that had not yet achieved full potential. He thus showed courage of two orders: against physical infirmity and against taking the easy way by researching into topics that had more obvious promise than his, which was down an unexplored path.

A short break

Having been feasted, stimulated, and made to think by those three men and the three who proposed them, those present at the ceremony were then treated—and treated is the right word—to a projection of a film made by Lennart Nilsson. This showed the miracle of human sperm formation, ovum formation and maturation, fertilisation, and oocyte development in the uterus. This was no ordinary showing of a film that had already been projected on our television screens in England. This was a demonstration by the master himself, the master of photographic art and the master of inventiveness in microphotography. He explained some of the techniques of his film making, but the applause showed that even men and women who had worked in reproductive medicine for decades were moved by the sheer beauty as much as by the technical excellence of this wonderful film, and by Nilsson's enthusiasm as he explained the difficulties he had had to overcome and how he had done it.

On the second day the three remaining candidates presented their work.

On with the shortlist

PROFESSOR ELWOOD JENSEN

Professor Jensen is an American whose looks belie his age and who has the body, stance, and movement of a fine athlete and mountaineer. After a brilliant career as a research worker he became the medical director of the Ludwig Institute for Cancer Research in Zurich. Later, as an organic chemist and surgeon, he became professor for biological sciences in Chicago. He postulated the two step hypothesis of steroid hormone action and has led in the "molecular biology of steroid hormone action." He was able to show those present at the meeting how his work had led him and his team to identify and elucidate the role of oestrogen receptors, particularly in cases of breast cancer. Serendipity had led hormone research to a rational handling of cancer, and his philosophy included being alert for the unexpected and irrelevant observation and having adequate controls for all experimental work.

PROFESSOR ERNST KNOBIL

Professor Knobil, born in Berlin, Germany, in 1926, graduated in the United States in 1948 and is now professor of medical sciences and neuroendocrinology in Houston, Texas. He explained how he had been worried and ashamed when he tried to explain the menstrual cycle with its 28 day calendar to medical students. He did not know how it was triggered; there were too many gaps in the traditional explanation; he had failed to obtain understandable results when he tried to estimate daily concentrations of luteinising hormone and follicle stimulating hormone. It was only when in desperation he turned to estimating these hormones every 20 minutes that he found out that there was a pulsatile release of hormones. He then looked for the site of the pulse generator and discovered the importance of this generator by making a lesion in the arcuate nucleus of monkeys and making an artificial hypothalamus. He thus discovered that the brain supplied an hourly clock which in its turn regulated the ovaries' 28 day clock. His work was the basis for the treatment of hypothalamic amenorrhoea.

Professor Knobil is still looking for the pulse generator, but others have taken up his work and many women have become pregnant as a result of hormone releasing factors that were discovered by Andrew Schally (a member of the scientific committee), who has been awarded a Nobel prize. Schally discovered, and Knobil made it a practical proposition to use, luteinising hormone releasing hormone.

DR SHELDON SEGAL

Dr Segal is director of the Population Council and a great research worker on contraceptive methods. He perhaps has demonstrated his humanitarianism more obviously than the other candidates, for he has gone out to India and other Third World countries and started huge birth control and sterilisation clinics. He may be one of the greatest leaders in the scientific application of contraceptive measures, and it is his work that has led to the development of the new implantable contraceptives that may be placed under the skin of the

forearm in small, specially designed plastic tubes to give effective contraception with minimal side effects for up to five years. He was the man who stimulated not only research but the practical application of his results.

Professor Sheldon Segal, director, Population Division, The Rockefeller Foundation, New York.

Decision time

On the third day of the meeting scientific and advisory committees met in the chapel of Axel Munthe's home in San Michele. There the discussions centred not so much on the individuals but on the purpose, the future, and the administration of the Axel Munthe awards. Lobbying and persuading was strictly forbidden. We had merely to vote. The method of voting was for discussion. We were told that we would not be informed of the result until we had all left the island so that there could be no last minute changes, and so it was that although we had sat in conclave a little like the cardinals electing a Pope there was no smoke, white or black, for four weeks after the meeting, until three members of the committee had counted the votes. All we were told was that if there was a tie, or something approaching it, some of us would be called back again. None of us were.

We left Anacapri satiated with intelligent science and good friendship and also with a better understanding of the brotherhood of men and women who strive for the improvement of the quality of human life. Above all, we were all grateful not only to Vincenzo Abate and the team that had organised this gathering so well but also to the generosity of the international constructional engineer, Steven Newburg, and to Cesare Brescia, as well as the pharmaceutical companies, banks, and others who had provided the necessary money to allow Vincenzo Abate to fulfil his dream in the spirit of Axel Munthe. . . and the winner? Professor Sheldon Segal, to whom I extend my warmest congratulations.