Viewpoint: Pharmaceutical Innovation in Europe

Daniel Vasella, MD, chairman and CEO of Novartis AG, warns that changes are needed if Europe is to remain a key site for pharmaceutical innovation. He explains his concerns to Emma Baines, MSc.

Since he took up his role as chief executive at the newly formed Novartis in 1996, Dr Daniel Vasella has been credited with building the company into a market leader. His tactic has been to invest heavily in innovation, spending far more on research and development than other pharmaceutical companies. As a result, Novartis has had more drug approvals in the past 5 years than any other pharmaceutical company.

In the past, much of the basic research needed for pharmaceutical innovation has been carried out in Europe, but Novartis, despite being based in Switzerland, moved its research headquarters to the United States in 2002. And, says Dr Vasella, “Unless changes are introduced to the way research is funded and regulated in Europe, investment in pharmaceutical innovation will continue to leave Europe, at a serious cost to the health and wealth of European nations.”

According to Dr Vasella, the multiple layers of bureaucracy in Europe mean that new products take longer to come to market than in other countries, such as the United States. “This increases the costs of launching new drugs for the pharmaceutical companies,” he explains.

Dr Vasella says, “European regulators have started creating ‘artificial delays’ in how quickly patients get access to new drugs, because of the implementation of cost-benefit studies and through delaying the reimbursement of a new drug by up to 3 years.” These delays, he believes, put obstacles in the way of evaluating efficacy and safety and slow down the final stages of drug development, making it less cost-effective for pharmaceutical companies to develop drugs in Europe than elsewhere.

Another obstacle to pharmaceutical innovation in Europe is that the market here is less attractive than in the United States. Dr Vasella explains, “We don’t have a single European market, either from the point of view of pricing or from the point of view of regulation. In the short term, this probably doesn’t directly affect pharmaceutical innovation overall, because it is balanced out by opportunities in other countries such as the United States, where there is an attractive market situation and rapid access. But European patients pay the price through delayed access to better treatments.”

The European Union is, in theory, a single market, with a free flow of products between countries, but in reality there are differences in pricing between EU countries because prices are set by individual governments. This combination can mean that more money is made by intermediaries from a particular drug than by the pharmaceutical firms themselves.

According to Dr Vasella, this is a serious problem. “If you have a situation where a third party is profiting from parallel importing and is making more money than the company that invented, developed, and marketed the drug, then there is something wrong with the system.”

Another area in which Dr Vasella feels Europe is losing out to the United States and other countries is in the amount of high-quality basic research that it supports. This is also related to how easy it is for researchers working in academia to bring the results of their work to the market. “Academic institutions are a great source of innovation,” says Dr Vasella. “In the United States, the professors and scientists are given more freedom than in Europe, and they have access to funds and venture capital that allow them to create their own start-up companies. This means that top scientists are more likely to be retained in academia.”

“However,” Dr Vasella says, “this pattern is changing. Despite European researchers having access to fewer resources than their US colleagues, there are now as many biotech start-up companies in Europe as in the United States. There seems to be more courage, guts, and optimism in Europe than we saw in the past. If you are going into biotech, you have to be willing to fail, and in Europe this has traditionally been less well tolerated than in the United States.”

But the most serious advantage that US researchers have over their European equivalents, from the point of view of pharmaceutical companies looking for innovation in biomedical research, is the amount of money that the US government puts into basic research through funding to the
Spotlight:
Gino Gerosa, MD

Dr Gino Gerosa is associate professor of Cardiac Surgery, chief of the Cardiac Surgery Department, and director of the School of Specialisation of Cardiac Surgery at the University of Padova Medical School, Padova, Italy. He speaks to Mark Nicholls about his career and special interests.

Dr Gino Gerosa is a member of the Italian Society for Cardiac Surgery, the New Technology Committee of the European Association for Cardio-Thoracic Surgery, and the American Association for Thoracic Surgery. He now operates at the leading edge of cardiac surgery, with specific interests in robotic surgery, transplantation, artificial hearts, minimally invasive surgery, tissue engineering, and regenerative medicine.

But, he also recalls the days when he was learning his skills. “I wondered whether I was physically and mentally equipped to sustain the stresses of specialising in heart surgery and able to perform those operations with acceptable results.”

It was time spent with Donald Ross, DSc, FRCS, at the National Heart Hospital in London, United Kingdom in the 1980s that helped Dr Gerosa focus on a career in cardiac surgery. He regards Dr Ross as an inspiration and a “mentor for excellence.”

Dr Gerosa says, “I always dreamed of becoming a heart surgeon, and I became fascinated with the heart operations I watched while in the 4th year of medical school at the University of Verona, Italy. The year after, I went to London and spent some time as a visiting student with Donald Ross at the National Heart Hospital, and that was the final click.” Dr Gerosa explains, “He was not only a mentor but a man with an incredible stamina, superb surgical skill, an unexhausted scientific curiosity—and an elegant taste to fully enjoy the spirit of life.”

Dr Gerosa mentions Sir Magdi Yacoub, FRS, FRCS, as a man who inspired the idea of the scientist–surgeon. Another influence was Dr Gerosa’s Italian mentor, Dino Casarotto, MD, a professor at the Institute of Cardiac Surgery at the University of Padova, “who taught me the full dedication needed for this profession.”

Dr Gerosa was in residency at Verona University, Italy, from 1983 to 1988, and he worked as a registrar at the Department of Cardiac Surgery at Verona University Hospital from 1989 to 1992. He then moved to the Department of Cardiac Surgery, Padova University Hospital, where he worked until 2000 before taking up his current position.

In recent years, he has developed his specialist interests and was involved in performing the first Italian totally endoscopic robot-enhanced coronary bypass on a beating heart in 2001. He was the first Italian—and one of the first in Europe—to perform totally endoscopic robot-enhanced pulmonary vein isolation for lone atrial fibrillation. “Robotic surgery is solo surgery,” he explains (see Figure). “You have to reinvent your surgical technique and skill because you don’t have an assistant helping you through the procedure. On the other side of the coin, the fine degree of movement offered by the telemanipulated instruments allows you to surgically perform in a way that is impossible
for human hands.” He recalls one occasion in particular. “I still remember the exact moment when I completed the totally endoscopic coronary artery bypass anastomosis. Such joy and satisfaction, and all the team members were clapping.”

But Dr Gerosa admits there have been disappointments. “Unfortunately, the great expectation for cardiac surgeons to be competitive with interventional cardiologists in terms of less invasiveness for myocardial revascularisation has been substantially frustrated by the introduction of drug-eluting stents.” He has clear views on where the future lies in response to what he calls the “less than satisfactory” results of drug-eluting stents, and he advocates a return to a hybrid procedure for treating patients with coronary disease. This would be a left internal mammary artery anastomosis to the left anterior descending coronary artery, combined with stents on the remaining affected vessels, thus getting the best results from both techniques.

Dr Gerosa also expresses great satisfaction as he recalls performing one of the first stem cell transplantations in a patient with ischaemic cardiomyopathy in 2002. “I have vivid memories of those days and of that patient who had so much trust in the ability of such therapy to solve his illness,” he says. “In Padova, we are still working in that field, and we are exploring the ability of stem cells to recreate human valves and to regenerate the failed myocardium. When I think of the success and failure in this field, I feel that we can compare this experience to the first heart transplantation performed in 1967.”

He refers to the expectation, enthusiasm, and hype after the first human heart transplantation that was followed by “rather unsatisfactory” results. This meant that in the 1970s, only centres in Cape Town, South Africa and Stanford, United States continued to perform heart transplants for some years. “At the beginning of the 1980s, the discovery of cyclosporine totally modified the results, improving organ and patient survival, and the scenario changed completely,” he explains. “I believe that with stem cells we are mimicking that experience. We need to clarify some things and find the missing pieces to complete the puzzle. We can then properly use stem cells to solve the problem of the failing heart. We are still in a phase of full research, but there is light at the end of the tunnel.”

Dr Gerosa feels that cardiac surgery is about to enter a new phase. “I believe that we are at the end of cardiac surgery as we have interpreted it in the last two decades. Cardiac surgeons are retraining to perform and optimise minimally invasive cardiac and intravascular procedures. In addition, cardiac surgeons should acquire the knowledge to employ gene-enhanced cell therapy and tissue-engineering techniques.”

Dr Gerosa believes that a shortage of organ donors is driving the need to find additional solutions. “Heart failure is one of the most rapidly evolving fields,” he says, “where cardiac surgeons will be able to perform by combining new surgical techniques, cell therapies, and mechanical devices.”

Yet, alongside all the innovation and technical advancement, Dr Gerosa also believes that cardiac surgeons in Western countries should put more effort into providing cardiac surgery care for patients in developing countries, along the lines of Sir Magdi Yacoub’s Chain of Hope organisation.

Talking about his personal life, Dr Gerosa says he was born in Rovereto, in the mountains in northern Italy. Away from work, he enjoys skiing and golf. He is married to Janine Gerosa, whom he met while training in London, United Kingdom, and he takes great pride in their 3 children Edoardo (age 15), Carlo Andrea (age 12), and Filippo Alberto (age 6). “Fatherhood is a lot more complicated and rewarding than cardiac surgery,” he says with a smile.

He describes his children as his proudest achievement, but he also lists his 1991 article that reviewed the experience of the Ross operation (a procedure where the patient’s normal pulmonary valve is removed and used to replace a diseased aortic valve, and the pulmonary valve is then replaced with a pulmonary homograft) in children. He said it was the first article postulating the ability of the pulmonary autograft to grow after transplantation into the aortic position.

Mark Nicholls is a freelance medical journalist.

References

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History of Cardiology: The Use of Bloodletting

From ancient times to the early 20th century, bloodletting has been seen as the answer to many conditions, including some manifestations of cardiovascular disease. Diana Berry looks back at when it was in vogue and why.

Since the early 20th century, the medical profession has learned to revere, preserve, and sustain that amazing carrier of oxygen and nutrients: the blood. Prolonged extraction of this liquid is no longer considered therapeutic except in cases of primary and secondary polycythaemia, but it has taken many centuries to arrive at this conclusion.

Bloodletting is a medical practice that was employed by many ancient peoples including the Egyptians, the Aztecs, the Mesopotamians, and the Greeks. Hippocrates mentioned the practice, but it was some centuries later that the popularity of the procedure increased with the advocacy of Claudius Galen in the second century AD. Not only was he the first physician to take a patient’s pulse, but he discovered that veins and arteries were filled with blood rather than air as had previously been thought. His belief in bloodletting was based on the necessity of balancing the 4 “humours”—phlegm, black bile, yellow bile, and blood—to achieve health. To achieve this balance, physicians would either bleed the patient to remove an excess of blood, or employ emetics or diuretics to induce vomiting or urination.

By the second millennium, and with the decline of the humoural system, bloodletting was undertaken by barber–surgeons on the recommendation of physicians. The practice was used both prophylactically and therapeutically into the 19th century (see Figure), although its efficacy was widely debated. The lancet was the primary instrument for bloodletting, but other methods included cupping, scarification, and leeching.

Cupping could be either “wet” or “dry.” Originally, animal horns were used, but these were later replaced by sophisticated cupping sets. Dry cupping necessitated the heating of the cup or glass, which was placed over the skin. As it cooled, it created a vacuum, bringing blood to the surface.

In the 1830s, Victor-Theodore Junod, MD, of Paris, France, believed in the therapeutic effect of “producing a fainting fit by drawing the blood from the brain to the foot without letting blood.” Scarcification involved a device consisting of small blades that were used to make several small incisions in wet cupping. This practice was often combined with warm sulphur baths. On a visit to Hungary in 1815, Richard Bright, MD, of Edinburgh, Scotland described seeing “a row of half-naked figures like those in the bath on whom a poor miserable surgeon was practising the operations of cupping and scarification, studiously inflicting as many wounds as possible.”

The application of leeches as a method of bloodletting was particularly popular with the French physician Francois-Joseph Victor Broussais, MD, who believed gastroenteritis to be the “basis of all pathology.” He decided that gastroenteritis could be aborted by the application of as many as 50 leeches. The method became so popular that over 40 million leeches were imported into France in the year 1833.

In their 1838 textbook, Dr Bright and Thomas Addison, MD, wrote that “when we have reason to think that the heart is excited by a plethoric condition, very moderate general or local bleeding may occasionally be employed with advantage.”

The exposure of the weaknesses of bloodletting came about mainly through the work of Pierre Charles Alexandre Louis, MD, of la Charite Hospital, Paris, France. He first criticised the technique in 1828, and he later produced statistical proof that bloodletting was of little value for treating pneumonia and was dubious for other ailments. In 1830, the British physiologist Marshall Hall, MD, FRS, also denounced bloodletting. He outlined the severe symptoms such as syncope, convulsions, coma, and delirium that he believed might be directly traced to that “minute instrument of mighty mischief,” the lancet.

Despite bloodletting’s gradual loss of credibility, it was still advocated as a treatment for cardiac problems as late as the 1920s. In the revised ninth edition of the textbook written by the world-renowned physician, Sir William Osler, MD, bloodletting was recommended for relief of the “embarrassed circulation” in cardiac insufficiency. The text states, “In those cases of dilation, from whatever cause, in mitral or aortic lesions or distention of the right ventricle in emphysema, when signs of venous engorgement are marked and when there is orthopnoea with cyanosis, the abstraction of 20–30 ounces of blood is indicated. This is the occasion in which timely venesection may save the patient’s life. It is particularly helpful in the dilated heart of arteriosclerosis.”

Diana Berry is a medical historian and freelance medical writer.

References