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DIALOGUES

HEMODYNAMICS: from *De Motu Cordis* to intracoronary stents

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The study of the cardiovascular system dates back to the anatomic descriptions and speculations of Antiquity. Little progress was made during the Middle Ages and early Renaissance, until the birth of hemodynamics with William Harvey's groundbreaking discovery of the circulation in 1628, based on experimentation and, to some extent, shrewd hypothesis, as without the microscope he had no proof of the existence of the capillary system. The mercury manometer was invented in 1828 by Jean-Louis Poiseuille. The pioneering work of 19th-century physiologists such as Karl Ludwig, Otto Frank, and Ernest Starling was followed by that of 20th-century clinicians like Helen Taussig, Alfred Blalock, Maude Abbott, and André Cournand. More recent milestones include the advent of investigational catheterization, culminating in percutaneous catheter-based methods for the treatment of certain forms of heart disease.

Keywords: hemodynamics; physiology; Frank-Starling law; catheterization; angioplasty; angiography; balloon catheter; stent; molecular intervetnion

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The tree of hemodynamic knowledge and practice begins with a single trunk whose roots reach 2500 years into the speculations of Antiquity. Anatomical observations account for the compact core of inner rings. Physiological knowledge as such did not really exist, except as a largely speculative superstructure, and this was to remain the case for the first 2000 years, during which growth was slow and the trunk spindly. Intellectual relationships between successive enquirers were often tenuous until the late Renaissance inaugurated the era of empirical and transmissible science.

Figure 1. *Harvey demonstrating the palpitations of the fetal heart of a deer to Charles I, in support of his theory of the circulation of the blood. Engraving by Henri Lemon, 1851, after an oil painting by Robert Hannah, 1848.*

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THE DAWN OF CARDIAC PHYSIOLOGY: FROM HARVEY TO HALES

Along the way, some retrospectively promising shoots were either neglected because they were meaningless given the resources of the time (for example, the conclusion thought to have been reached by Erasistratos in Alexandria that arteries are connected to veins by capillaries), or were murderously pruned by representatives of reigning orthodoxies (as was the case of Michael Servetus, whose contention that blood mixed with air and changed color in the lungs[1] was fated to leave no trace on succeeding medical generations, given that both writings and their author were burned at the stake in 1553 by Calvin's followers in Geneva because of his rejection of the Trinity and the divinity of Jesus).

Only a few decades after Servetus, the exclusively scientific preoccupations of William Harvey (1578-1657), nourished under Hieronymus Fabricius (1537-1619) in Padua, revived the flagging trunk. Harvey's masterpiece, published in 1628, *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus,*[2] signaled the end of the Renaissance and the beginning of the modern era *(Figure 1).* It was short—72 pages—

because to the point. Not only did it eschew theology, but it marked the cusp between the anatomy of the dissection tables of Padua and scientific physiology.

The experimental methods by which Harvey reached his conclusions were to form the basis for all future work in physiology. Cold-blooded animals (small fish, frogs, and snakes) with their much slower heart rate, in particular shrimps with their transparent shells, afforded a direct window onto the heart's action. By combining these observations with the postmortem dissection of humans, Harvey reached the following conclusions:

- The atria contract together, followed by simultaneous contraction of the ventricles, rather than the four chambers contracting independently. The heart expels blood with each contraction and receives blood with each relaxation, the latter thanks in part to the venous valves, which as Harvey explained, allowed the blood to flow easily one way through them, toward the heart, but blocked the passage in the opposite direction.
- Contraction of the heart coincides with expansion of the arteries, which are then filled by positive pressure transmitted from the heart, as opposed to the previous belief that arteries expanded like bellows to draw in blood by negative pressure.
- Andreas Vesalius (1514-1564) was correct in maintaining, against the then established doctrine of Galen (130-200 AD), that "by Hercules!" there are no septal pores between the ventricles; similarly, Realdus Columbus (1516-1559) was correct in stating that all blood from the right ventricle passes through the lungs to the left ventricle.
- Because the volume of blood forced out of the heart in an hour far exceeds its volume in the whole animal, it is inconceivable that it can be absorbed by the body from ingested food and continually replaced by blood manufactured in the liver from chyle. Blood must be therefore in constant circulation.
- Simple experiment shows that there must be connections invisible to the naked eye between arteries and veins. If a tight ligature is applied to the arm, the distal veins appear normal. But if the ligature is loosened just enough to allow arterial blood into the arm, while continuing to bar the return of venous blood, the veins become distended, showing that blood flows from the arteries to the veins, via connections yet to be demonstrated.

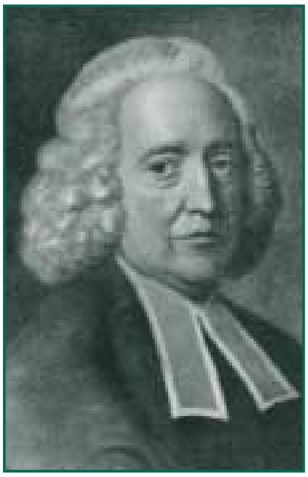

Figure 2. *Stephen Hales. Portrait by Thomas Hudson.*

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These conclusions provided a solid framework for future contributions to cardiovascular physiology. From Harvey onwards growth was exponential, with the trunk of physiology supporting a profusion of new branches. The advent of microscopy enabled Marcello Malpighi (1628-1694) and Anton van Leeuwenhoek (1632-1723) to confirm Harvey's account by describing the flow of blood through capillaries. Working on an altogether larger scale, with horses destined for the slaughterhouse, Stephen Hales (1677-1761, *Figure 2*)[4] performed the first measurements of arterial and venous pressures, calculated stroke volume and cardiac output, and estimated the velocity imparted to the aortic column of blood in systole. The metric-minded Hales was also a clergyman. He thus embodied the distinction between religion and science. The tree was growing in an irrevocably different environment, the thin nutrient of semireligious speculation having been replaced by a rich mulch of experimentation.

THE PIONEERS OF MODERN CARDIAC PHYSIOLOGY

Jean-Louis Marie Poiseuille (1799-1869) invented the mercury manometer in 1828, and later derived his law that flow varies as the fourth power of the radius. But perhaps the supreme example of the new wave of academic physiologists was Karl Ludwig (1816-1895), whose kymograph ("wave-writer" *Figure 3*)[4] was to be used for recording physiological data for the next 100 years. He built the Physiological Institute in Leipzig on a grand scale to his own design, with interconnecting wings devoted to histology and anatomy, physiological chemistry, and the physical study of physiological problems. In reaction against the diehard believers in natural philosophy and vitalism who still plagued academia, his physiological science was uncompromisingly quantitative, analytical, and physicochemical. Physiology underpinned medicine, since "every case of illness is a physiological experiment ...and each physiological experiment is an artificially produced illness."[5] Ludwig's infantry was the animals who provided a wealth of new infor-

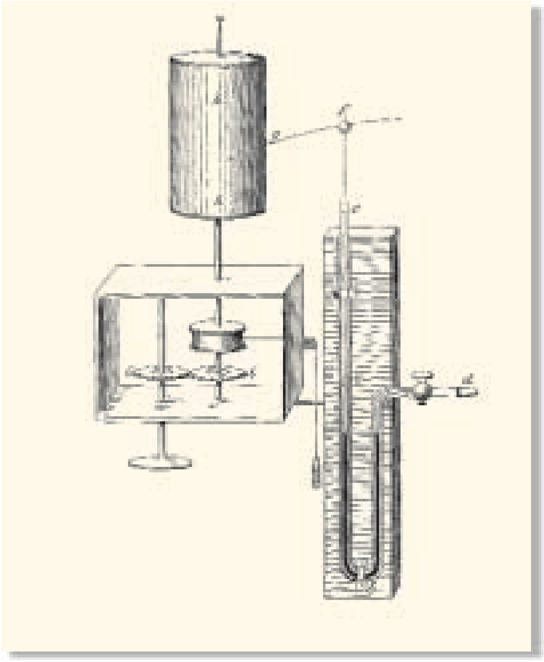

Figure 3. *Ludwig's kymograph, described and published in 1847.*

***Reproduced from reference 4:** Fishman AP, Richards DW, eds. Circulation of the Blood: Men and Ideas. New York, NY; Oxford University Press; 1964. Copyright © 1964, Oxford University Press.*

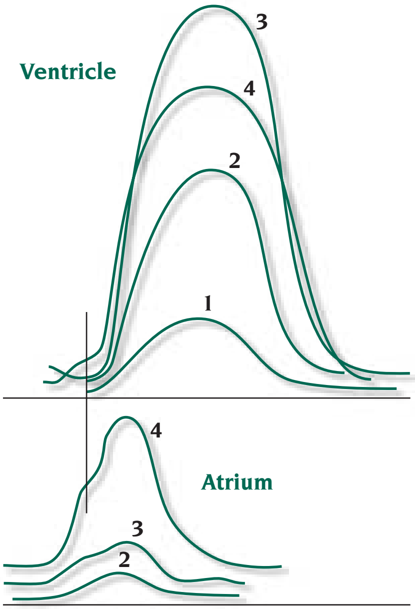

Figure 4. *Pressure curves developed during systolic contraction, and subsequent relaxation, in Frank's frog heart preparation.*

***Reproduced from reference 4:** Fishman AP, Richards DW, eds. Circulation of the Blood: Men and Ideas. New York, NY; Oxford University Press; 1964. Copyright © 1964, Oxford University Press.*

mation on cardiovascular and respiratory physiology. His generals were his assistants and pupils, who carried the campaign far and wide, to Britain, America, and Russia.

Other physiologists with an equal devotion to measurement succeeded in deriving laws. In Germany, Otto Frank (1865-1944) drew on Ludwig's work with the isolated frog heart to derive a law concerning the dependence of the shape of the isometric or pressure curve on the initial tension. The peaks of the isometric pressure curve rise with increasing initial tension (filling), then decline beyond a certain degree of filling *(Figure 4)*.[4] In England, some 15 years later, Ernest Starling (1866-1927) used an isolated dog heart-lung preparation, and concluded, in what came to be known as the Frank-Starling law, that "the law of the heart is therefore the same as that of skeletal muscle, namely, that the mechanical energy set free on passage from the resting to the contracted state depends on… the length of the muscle fiber."[6] In practical terms, if end-diastolic fiber length increases due to increased filling, the heart contracts more strongly to eject the increased volume. The heart compensates for both increased pressure and volume work by dilatation within physiological limits, but can become decompensated by overdilatation.

Starling's thesis, which put together much that had already been appreciated by several late 19th century physiologists in addition to Frank, found intuitive acceptance among his contemporary clinicians, familiar with the enlarged weak hearts that improved in performance when venous pressure was lowered by venesection or tourniquets.[7] It also provided the framework for the more detailed studies conducted by succeeding generations, led notably by Carl Wiggers (1883-1963) at Western Reserve University, Cleveland, Ohio, and Arthur Guyton (1919-2003) at the University of Mississippi. Author of the cardiac cycle graphic since familiar to medical students the world over—the "Wiggers diagram" displaying the interrelationships between electrocardiogram, chamber and aorta pressures, ventricular volume, heart sounds, aortic flow rate, and the venous pulse over a single cardiac cycle *(Figure 5, next page)*—Wiggers was directly inspired by his predecessors. In particular, he spent time in Otto Frank's laboratory in Munich (Wiggers was the son of German immigrants), and subsequently visited Starling's laboratory in London. Echoing Ludwig's "Die Methode ist alles," Wiggers' habit was to "assess scientific reports as much by an investigator's technical habits as by the actual data and deductions."[8] He personally derived most of the variables in his diagram. He was also the first to produce a precise record of the relatively small pressure changes in the pulmonary circulation with respiration. It was a modification of the Wiggers transducer that was subsequently adapted to an intracardiac catheter to measure right heart pressures in unanesthetized humans.

Guyton too had a natural affinity with a range of electronic devices from childhood, and was fond of building analog computers. His particular interest, cultivated over several college summers, was in the mathematical analysis of electronic circuits. He brought this approach to the analysis of physiologic mechanisms, whether renal, respiratory, or circulatory. One of his classic papers begins with a reference to Starling (the curve relating cardiac output to mean right atrial pressure), proceeds to a mathematical analysis of a simplified closed circuit circulatory system and its experimental verification in 47 dogs, and concludes with a formula for venous return as a determinant of cardiac output.[9] This approach was to reach its most remarkable expression in the "Guyton diagram," his 1972 computer model of the cardiovascular system. Resembling a modern circuit board, it was the first to integrate the multiple factors influencing the peripheral circulation, heart, endocrine systems, autonomic nervous system, kidneys, and body fluids.[10] The distance traveled since Starling, who had performed much of his work on the isolated heart despite an all-encompassing knowledge of physiology, had become considerable.

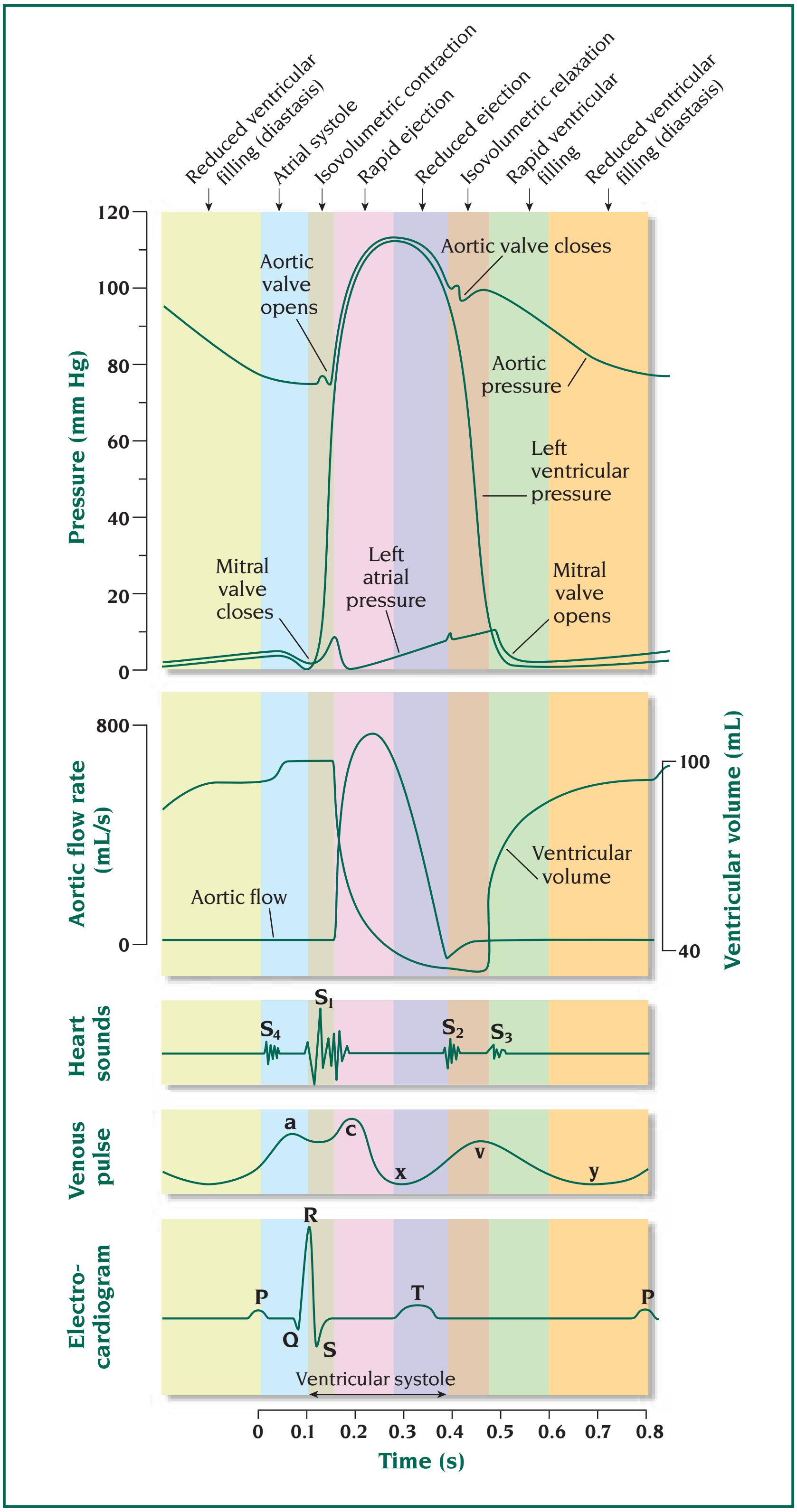

Figure 5. *Wiggers' diagram.*

Dorland's Illustrated Medical Dictionary. *30th ed. Philadelphia, Pa: W. B. Saunders; 2003. Copyright © 2003, W. B. Saunders / Elsevier Sciences.*

THE FIRST CLINICAL APPLICATIONS

Hemodynamic studies such as those conducted by Wiggers and Guyton were blurring the boundaries between physiology and clinical medicine. Wiggers' "every disease is an experiment that nature performs" echoed Ludwig's "every case of illness is a physiological experiment". Helen Taussig (1898-1986) encountered many such experiments in her practice as cardiologist to the children's clinic at Johns Hopkins *(Figure 6)*. Informed by the hemodynamics of the normal and valve-diseased heart, and by the remarkable compendium of the pathology of congenital disease produced by Maude Abbott (1869-1940) in Canada,[11] Taussig was able to propose surgical remedies for otherwise intractable childhood disease, and assist from the head of the table at the initial implementation by Alfred Blalock (1899-1964) of her palliative shunt solution to Fallot's tetralogy.

From the end of World War II onwards, clinical applications of the accumulated anatomic and physiologic knowledge grew in many directions. However, perhaps the single most important branch, and the one that was to support the greatest profusion of applications in subsequent years, first emerged in 1929 in Eberswald near Berlin, when a surgical intern only one year out of medical school, Werner Forssmann (1904-1979) was looking for a rapid and safe method of getting drugs directly into the cardiac chambers rather than injecting them blindly through the chest wall. After initial experiments in cadavers, and against his chief's instructions, Forssman introduced a thin radiopaque urological catheter into his own left antecubital vein, and advanced it into his right atrium guided by a fluoroscopic image projected onto a mirror. He then climbed a flight of stairs to the x-ray department where the catheter's position was documented. In reporting his experiment, he suggested that the method might be useful in physiological studies,[12] and he went on to show, again on himself, that the right heart could be visualized radiographically by injecting iodinated contrast materials through a catheter into the right atrium.

***Figure 6.** Helen Taussig (1898-1986). Copyright © 2006, Johns Hopkins Medical Institutions, All rights reserved.*

Unfortunately, in terms of our tree, the growth of this hugely promising new branch was stunted for over a decade in the absence of immediate practical applications. The requisite transducer technology for measuring flow, pressure, and volume had yet to catch up. Forssmann lost his job and, ironically, all hope of a career in cardiology, becoming a urologist instead.

Beginning in 1941, André Cournand (1895-1988), a French-born physician and physiologist who came to the United States in 1931, carried out extensive studies with Dickinson Richards (1895-1973) at the Columbia University division of Bellevue Hospital using Forssmann's catheterization technique. They established that the catheter could be left in place for long periods without harm, and that the tip could be advanced through the right ventricle into the pulmonary artery, the preferred site for sampling mixed venous blood (the right ventricle acting as mixer). The world's first diagnostic cardiac catheterization laboratory was opened at Johns Hopkins hospital in 1945. Aided by the presence of Taussig and Blalock, catheterization rapidly established itself as a reliable gold standard technique of disease and preoperative assessment. A couple of years later, Lewis Dexter (1910-1995) and colleagues at the Peter Bent Brigham Hospital reported indirect measurement of mean left atrial pressure using a catheter "wedged" in the distal pulmonary artery,[13] thus describing a variable that remains fundamental in cardiac intensive care to this day. The pioneers of cardiac catheterization, Cournand, Richards, and Forssmann, received the Nobel prize in 1956.

Yet this was only the start. In his Nobel lecture, Cournand described Forssmann's catheter as "the key in the lock".[14] It was to remain, in rapidly evolving forms, the mainstay instrument of hemodynamic investigation and, increasingly, therapeutic intervention. In the left ventricle, catheterization was combined with imaging to realize a project outlined by Otto Frank in 1895[15]: it provided the data points that enabled pressure to be continuously plotted against volume through the complete cardiac cycle, thus generating the pressure-volume loop graphic of ventricular function. On the normal loop, all four phases of the cardiac cycle (isovolumic contraction, ejection, isovolumic relaxation, and filling) are clearly separate. The area of the loop measures the net external stroke work, ie, the useful work done by the myocardium on the circulation. The correlation between clinical condition—valvular disease, heart failure, cardiomyopathy—and loop size and shape was so clinically relevant that pressure-volume loops became integral to the assessment, management and teaching of cardiac disease *(Figure 7)*.[16,17]

Less successful, through no fault of the catheter, was the attempt to characterize left ventricular performance in terms of "contractility" based on a high-fidelity pressure recording at a single moment in time and under a single set of loading conditions. Defined as the variable force of ventricular contraction, independent of changes in heart rate, preload, or afterload, contractility became a hemodynamic Holy Grail, pursued as a potentially easy and rapid marker. Eventually, after a decade of effort and the sacrifice of forests of pulp, "contractility" was abandoned, as even in the best of cardiological hands it lacked the scientific underpinnings required to discriminate between normal and abnormal myocardium.[18]

OPENING THE DISEASED ARTERY: THE ADVENT OF ANGIOPLASTY

In other hands, the catheter was a magic wand, sprouting specialties at a touch. In 1958, Mason Sones (1919-1985), a pediatric cardiologist at the Cleveland Clinic, was performing an aortogram in a patient with aortic valve disease when he realized that the catheter had accidentally entered the right coronary artery. Before it could be removed, 30 cc of contrast dye had been released. Expecting the heart to fibrillate, Sones prepared himself to open the chest. In fact the heart went into asystole, and restarted when he asked the patient to cough—on the third cough. If the heart could survive 30 cc of dye into a coronary artery, reasoned Sones, it would readily tolerate the much smaller amounts sufficient to visualize the coronary vasculature: "I knew that night that we finally had a tool that would define the anatomic nature of coronary artery disease."[19] The visualization technique unleashed the diagnostic potential of coronary angiography. After being perfected by using a flexitip catheter with both end and side holes that selectively opacified the coronary arteries when introduced from the brachial artery, angiography quickly became the standard assessment procedure before any coronary intervention. Given the excitement generated by coronary angiography, it took special vision—and some serendipity—to realize, within just a few years, that diagnostics far from exhausted the potential of the endovascular catheter. Charles Dotter (1929-1985) was only 32 when he became professor and chairman of radiology at the University of Oregon medical school in Portland, Oregon. Two years later, in 1963, as he was passing a percutaneously introduced catheter retrogradely through the right iliac artery to perform an abdominal aortogram in a patient with renal artery stenosis, he realized that he had accidentally recanalized an occlusion. As with Mason Sones, accident found a mind fully prepared, in this case for the revolutionary concept of interventional radiology. Dotter immediately mapped the decades ahead, fast-forwarding to improvements such as balloons and stents. Meanwhile, with his trainee, Melvin Judkins (1922-1985), he undertook the first intentional percutaneous transluminal angioplasty in January 1964 on an elderly woman with a nonhealing ulcer and gangrenous toes referred for amputation. Minutes after he dilated her stenosed superficial femoral artery, her foot was warm and hyperemic, and the patient, already 82, was to live a further three years "walking on her own two feet."

Dotter produced a prophetic video the same year starring himself as a once-claudicating patient skipping out of sight down a hospital corridor.[20] His message to the skeptics

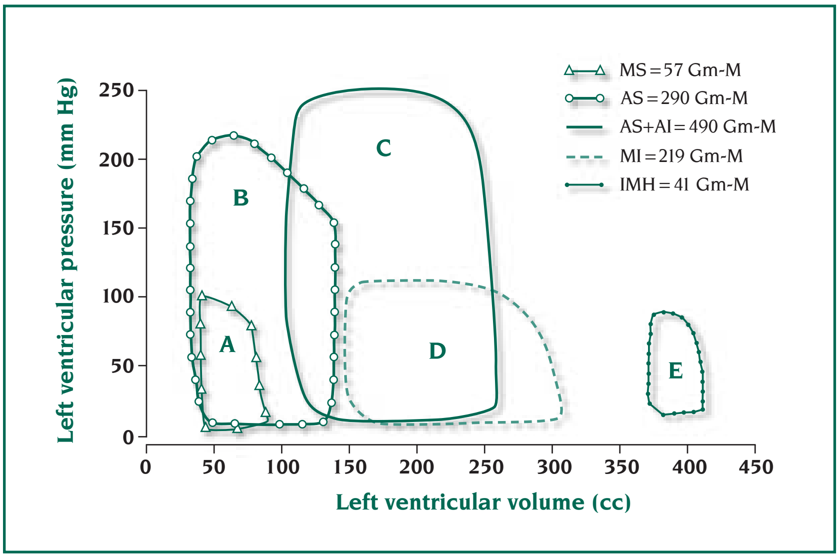

Figure 7. *Left ventricular pressure-volume curves in various conditions. A: Mitral stenosis. B: Aortic stenosis. C: Aortic stenosis and aortic regurgitation. D: Mitral regurgitation. E: Primary cardiomyopathy.*

Reproduced from reference 17: *Dodge HT, Sandler H, Baxley WA, Hawley RR. Usefulness and limitations of radiographic methods for determining left ventricular volume.* Am J Cardiol. *1966;18:10-24. Copyright © 1966, Elsevier.*

was that angioplasty was vessel-friendly: reaming, drilling, plowing and blasting—each illustrated by an industrial close-up—were not involved. However, the technique did have a drawback. Stenoses were dilated with a bougie, so that operators were limited by the diameter of the cut-down artery. Several attempts to design a small-entry balloon catheter were made, including by Judkins (in itself the idea was not new: it had been attempted over 100 years previously for the urethra). But early balloon catheter designs failed either because of poor patient outcome or because the soft elastic of the balloon "dog-boned" (ie, spread laterally) to either side of the stenosis rather than expanding against the stenosis in a forceful radial direction.

Andreas Gruentzig (1939-1985, *Figure 8*),[21] a West German, came to Zurich in 1969 to pursue his interest in dilating arteries through a small aperture. He produced a series of prototype Dotter catheters fitted with balloons, searching for a viable material and design. Containing the expansion of the balloon was a particular problem, given the latex-like materials in common use. The breakthrough came when he crossed the road from the university hospital to the Federal Institute of Technology, and met with Heinrich Hopff, a professor emeritus of organic chemistry with a background in the polymer industry, who suggested he used polyvinylchloride instead. The prototypes with this much sturdier material were handmade by Walter Schlumpff, the husband of Gruentzig's operating room assistant. In 1974, Gruentzig reported that he had successfully dilated peripheral arteries in 15 patients. By 1977, again with Schlumpff's assistance, he was ready to launch a coronary version of his double-lumen balloon catheter.

The first patient was a 38-year-old man with proximal stenosis of the left anterior descending artery. Angioplasty was performed with an emergency bypass team in readiness. It was unnecessary. The patient remained symptom-free for the next 23 years, by which time the site of the original dilatation was still patent.[22] Other efforts at balloon angioplasty started almost immediately, first in New York and San Francisco, and then all over as interventional cardiologists and radiologists attended Gruentzig's courses in Zurich. In 1980 Gruentzig moved to Emory University and was able to report zero inpatient mortality in the first 1000 cases performed by himself or his associates. Safety and efficacy were continuously increased by improvements in catheter design and the introduction of digital radiography. The advance of the technique was so widespread that it soon became autonomous, being barely halted by the premature death of Gruentzig himself with his wife and dogs, one Sunday evening, as he piloted his plane back from a weekend retreat.

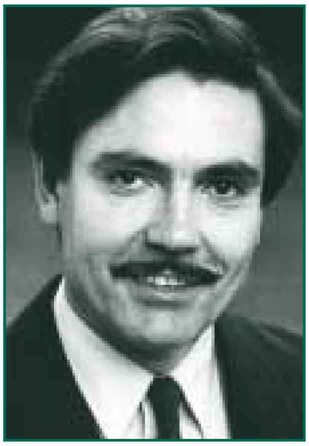

Figure 8. *Andreas Gruentzig (1939-1985).*

Reproduced from reference 21: *Geddes LA, Geddes LE, Boo M, et al. The Catheter Introducers. Chicago, Ill; Mobium Press; 1993(chap 7):71-77. Copyright ©, 1993, Mobium Press.*

KEEPING THE DISEASED ARTERY OPEN: THE STENT

Dotter was a pilot too, a mountaineer, and more. He and Gruentzig were not theoreticians so much as consummate and committed technicians. Dotter invented his own interventional tools, often using unconventional materials: guitar strings, Volkswagen speedometer cables, and the like. He made some of his own catheters, extruding the Teflon tips with a blowtorch, in the same way that Gruentzig fashioned his prototypes in his kitchen with Schlumpff. Dotter was the wider-ranging and more provocative. “The stethoscope and electrocardiograph,” he wrote in a 1962 issue of Electrical Engineering, “are instrumental equivalents of the ear trumpet and smoked drum recorder.” His favorite logo—which he sketched himself, since that was another of his talents—showed a domestic pipe crossed with a wrench. He could see no higher calling than to be a vascular plumber. He was a catheter evangelist, pained by the pain of cardiac surgery. He was known to have conducted Grand Rounds standing next to an oscilloscope; after 20 minutes, he would roll up his sleeve and reveal that he had had a catheter in his heart from the start. He would then plug himself into the oscilloscope and continue Grand Rounds, moving the catheter between heart chambers.

On the Monday after his death, Gruentzig had been due to meet with Richard Schatz, the future designer of the Palmaz-Schatz stent. Complications of angioplasty included reocclusion and collapse of the dilated segment. Dotter and Judkins had speculated in 1964 that a temporary endovascular silastic splint might maintain an adequate lumen after creating a pathway across a previously occluded vessel, including coronary arteries. They coined the term "stent" for vascular implants in their description of endarterial placement of tubular coiled wire grafts in the femoral and popliteal arteries of healthy dogs, but did not develop the idea further. The first applications came in Europe. Five months after Gruentzig's death, Jacques Puel implanted the first coronary stent in a patient in Toulouse, France.

The early days of coronary stenting were not easy. Long-term success was far from predictable. Initial follow-up studies with a self-expanding stent (Wallstent), for example, showed a 24% occlusion rate and a daunting 7.6% 1-year mortality. However, following an array of technical improvements and the introduction of improved antiplatelet therapy in place of anticoagulation, stenting can be said to have come of age in 1996, with the results of the Intracoronary Stenting and Antithrombotic Regimen (ISAR) trial.[23] Primary angioplasty with the stent-armed balloon became the default first-line coronary intervention, including in the emergency situation. Difficulties remain, however, including restenosis and stent thrombosis, the latter all the more serious as it often results in sudden death with little or no prior warning. The recent success of devices eluting antiproliferative drugs in preventing restenosis points the way forward, and is putting an end to alternative approaches such as brachytherapy. Results to date suggest that percutaneous interventions using these devices will provide long-term results as good as with coronary artery bypass grafting, at far less invasive cost.[24]

TOWARD THE ERA OF MOLECULAR INTERVENTION

Proponents of numerous other interventions—and their patients—have been less fortunate. Ablative approaches, such as directional atherectomy, laser revascularization, and rotational ablation using a high-speed diamond coated burr, appeared as promising as stenting in principle, but produced indifferent outcomes and higher rates of periprocedural infarction and major adverse cardiac events. Thrombolysis remains a valid alternative option in the emergency situation, especially when performed prehospital. In general, outside the emergency situation, treatment of coronary disease by percutaneous intervention appears to be moving inexorably away from the plumbing solutions introduced by Dotter and Gruentzig toward approaches grounded in molecular pharmacology and genetic modification, with each step becoming more expensive. Thus catheters are being used during angioplasty for gene transfer—vascular endothelial growth factor (VEGF) or fibroblast growth factor, either as DNA or protein—with the aim of encouraging angiogenesis, in an approach that is still too new for definitive assessment.

BALLOONS AND VALVES

Balloon dilatation has also been used in the treatment of valvular stenosis (whether congenital or acquired). Percutaneous balloon mitral valvuloplasty is now the treatment of choice for young patients with pliable, non-calcified rheumatic mitral stenosis and no left atrial thrombus, outperforming closed surgical commissurotomy, and producing both short and long-term results comparable to open surgical commissurotomy. Balloon dilatation of aortic stenosis in adults proved to be a failure in the majority, but paved the way for a valve composed of three bovine pericardial leaflets mounted within a balloon expandable stent. This valve can be implanted percutaneously, and early results look promising.[25,26]

CONCLUSION

A visitor to the stunted sapling of hemodynamic knowledge in 1600 would be dumbfounded by the strength, height, and breadth of today's tree, dotted with the vigorous growth of leaves afforded by the new specialties. The progression has been natural, from a small core of anatomy through a massive construct of physiology to a crown of therapeutics upheld by the most powerful of bioengineering branches. In recent decades the pace of progress has been stupefying. Millions the world over are benefiting from procedures that were inconceivable only 50 years ago. Could the same rate of growth could continue for a further 50 years? This doesn't seem unlikely if the current blossoming of genomics and proteomics is any indication!

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REFERENCES

1. Servetus M.

Christianismi Restitutio. (Vienne, 1553): English translation of Book V (physiology) athttp: //www.miguelservet.org/servetus/works.htm. Accessed January 3, 2006.

2. Harvey W.

Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus. English translation at http://www.bartleby.com/38/3/1000.html. Accessed January 3, 2006.

3. Shuster A, Shipley AE.

Britain's Heritage of Science. London, UK: Constable & Co, Ltd; 1917.

4. Fishman AP, Richards DW, eds.

Circulation of the Blood: Men and Ideas. New York, NY; Oxford University Press; 1964.

5. Lombard WP.

The life and work of Karl Ludwig.

Science. 1916;44:363.

6. Starling EH.

The Linacre Lecture on the Law of the Heart, delivered at St John's College, Cambridge, 1915. London, UK: Longmans, Green & Co, 1918.

7. Webb-Peploe MM, Shepherd JT.

Veins and their control.

N Engl J Med. 1968;278:317-322.

8. Wiggers CJ.

Physiology from 1900 to 1920: incidents, accidents, and advances.

Annu Rev Physiol. 1951;13:1-21.

9. Guyton AC, Lindsey AW, Kaufmann BN.

Effect of mean circulatory filling pressure and other peripheral circulatory factors on cardiac output.

Am J Physiol. 1955;180:463-468.

10. Guyton AC, Coleman TG, Granger HJ.

Circulation: overall regulation.

Annu Rev Physiol. 1972;34:13-44.

11. Abbott M.

Atlas of Congenital Heart Disease. New York, USA: American Heart Association; 1936 (reprinted 1954).

12. Forssmann W.

Die Sondierung des rechten Herzens [Catheterization of the right heart].

Klin Wochenschr. 1929;8:2085-2090.

13. Dexter L, Haynes FW, Burwell CS, Eppinger EC, Sagerson RP, Evans JM.

Studies of congenital heart disease. II. The pressure and oxygen content of blood in the right auricle, right ventricle and pulmonary artery in control patients, with observations on the oxygen saturation and source of pulmonary capillary blood.

J Clin Invest. 1947;26:554-560.

14. Cournand AF.

Control of the pulmonary circulation in man with some remarks on methodology.

Nobel Lecture, December 11, 1956. http://nobelprize.org/medicine/ laureates/1956/cournand-lecture.pdf. Accessed January 3, 2006.

15. Frank O.

Zur Dynamik des Herzmuskels [Dynamics of heart muscle].

Z Biol. 1895;32:370-447.

16. Sagawa K, Maughan L, Suga H, Sunagawa K.

Cardiac Contraction and the Pressure-Volume Relationship. New York, NY; Oxford University Press, 1988.

17. Dodge HT, Sandler H, Baxley WA, Hawley RR.

Usefulness and limitations of radiographic methods for determining left ventricular volume.

Am J Cardiol. 1966;18:10-24.

18. Harris P.

Contractility revealed.

J Mol Cell Cardiol. 1972;4:179-184.

19. http://www.ptca.org/archive/bios/sones.html. Accessed January 3, 2006.

20. http://www.ptca.org/videos.html. Accessed January 3, 2006.

21. Geddes LA, Geddes LE, Boo M, et al.

The Catheter Introducers. Chicago, Ill; Mobium Press; 1993(chap 7, Andreas Gruentzig):71-77.

22. King SB, Meier B.

Interventional treatment of coronary heart disease and peripheral vascular disease.

Circulation. 2000;102(suppl 4):81-86.

23. Schomig A, Neumann FJ, Kastrati A, et al.

A randomized comparison of antiplatelet and anticoagulant therapy after the placement of coronary artery stents.

N Engl J Med. 1996;334:1084-1089.

24. Serruys PW, Ong ATL, Morice MC, et al. on behalf of the ARTS Investigators.

Arterial Revascularisation Therapies Study Part II—Sirolimus-eluting stents for the treatment of patients with multivessel de novo coronary artery lesions.

EuroInterv. 2005;2:147-156.

25. Reyes VP, Raju BS, Wynne J, et al.

Percutaneous balloon valvuloplasty compared with open surgical commissurotomy for mitral stenosis.

N Engl J Med. 1994;331:961-967.

26. Cribier A, Eltchaninoff H, Tron C, et al.

Early experience with percutaneous transcatheter implantation of heart valve prosthesis for the treatment of end-stage inoperable patients with calcific aortic stenosis.

J Am Coll Cardiol. 2004;43:698-703.