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NEWSLETTER

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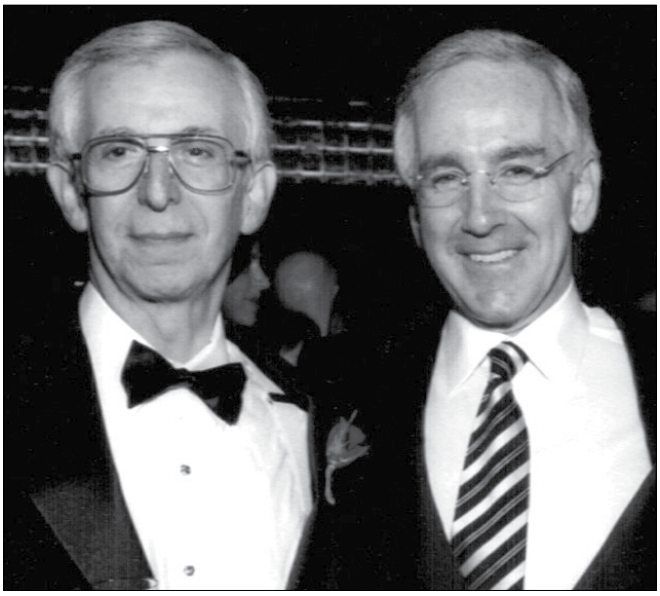
Outliers All



The May 8, 2009, 9th John Jones Surgical Day was a bit of an outlier because the entire day was taken up by a single program, except for a short business meeting and a lovely evening dinner party. Henry Spotnitz and his committee assembled 24 beneficiaries of Eric A. Rose's inspiration and guidance to produce a most enjoyable celebratory tribute to an organized, innovative leader. This was a gathering of outlier individuals who had become virtuosos in their respective fields, as defined by Malcolm Gladwell , by virtue of having completed a minimum of 10,000 hours of practice. Gladwell argues that extraordinary achievement is only moderately dependent on being personally gifted but is a culmination of hard work, and fortuitous circumstances, such as the nurturing company of likeminded individuals and having a great coach. He is right about the constellation of factors but is not so knowledgeable about surgical training's duration: 10,000 hours equate to a mere 2.5 years of 80-hour weeks, and to just 2 years of the virtuosos' likely work-week hours.

This was not a guild meeting of cardiac surgeons, and those who stayed home thinking that it would be, will see the error of their ways when the symposium is published as a supplement to the World Journal of Surgery, hopefully in December. The topics were conceptual and applicable to a broad swath of clinical and investigative medicine. The focus was on innovative therapies and recognizing that really new technology is inherently disruptive and risk ridden. Reaching the potential envisioned by its originators typically requires several iterative improvements and sometimes a leap of faith to cross a chasm of doubt and disappointment. This process is far more comfortable and promising if it is imbued with cross-discipline participation and basic science collaboration. Eric's early incorporation of internist Ann Marie Schmidt's basic science group within his Department continues to be a great example of the productivity that accrues from multidiscipline melding.

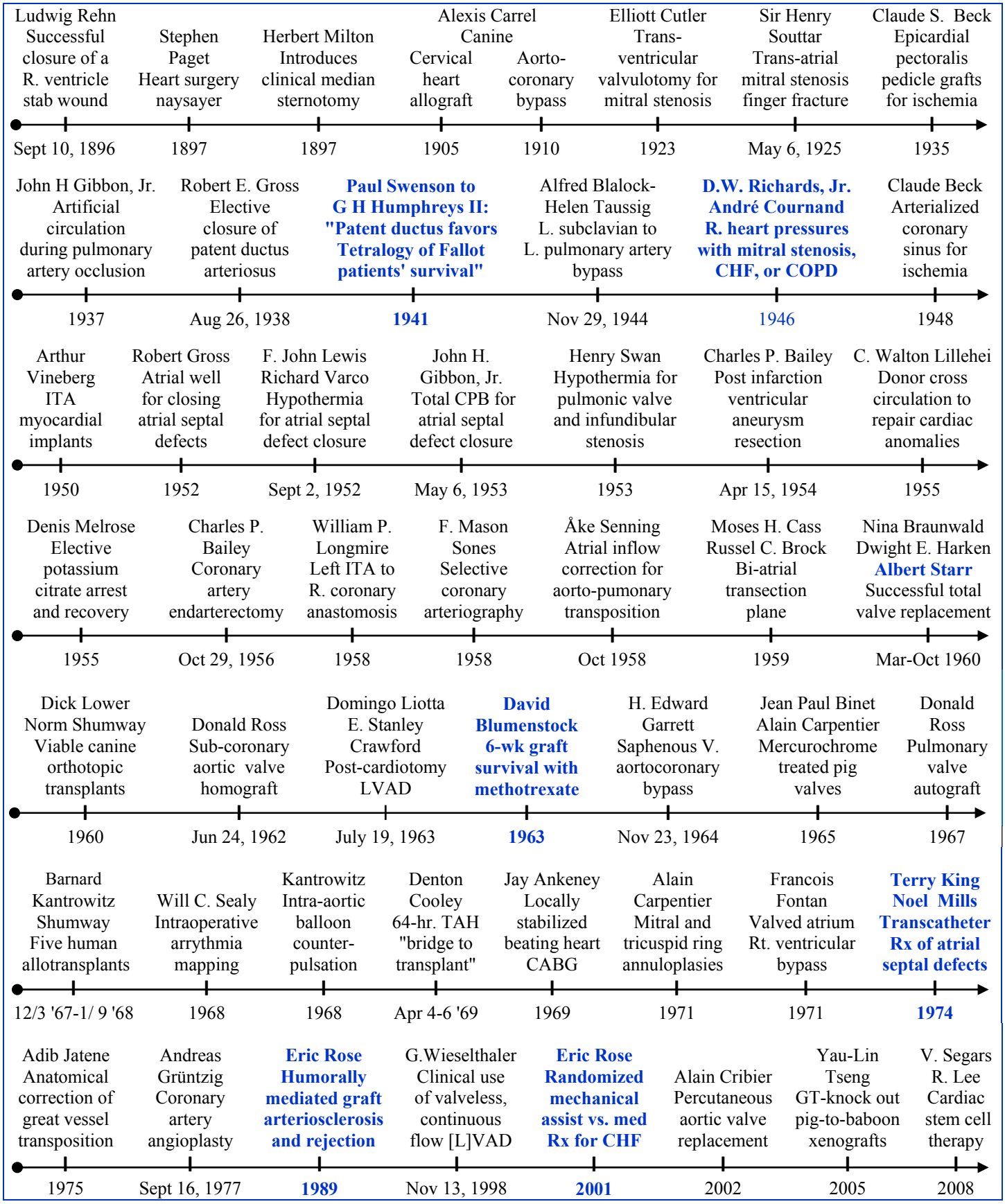
Several speakers explored training in and acceptance of new techniques. The private practice community led the way in training and early adoption of laparoscopic cholecystectomy, which rapidly supplanted the open operation, despite an early unacceptable incidence of bile duct injuries. Mini-thoracotomies arose simultaneously at multiple sites and are now well accepted as viable approaches to the coronaries and interior of the heart; whereas, more than a decade after their introduction, video assisted lobectomies for stage I, non-small-cell lung cancer account for <10% of US lobectomies. Ostensibly, this reluctance reflects fear of uncontrollable bleeding and not doing an adequate cancer operation, neither of which has been a problem in the hands of VATS advocates.

Lesions that are generally refractory to surgical treatment, such as glioblastomas and esophageal and pancreas cancers merit out-of-box thinking. Extended pancreatectomies to encompass vascular encroachment together with neo-adjuvant down staging are being employed in an appropriately small number of centers with somewhat encouraging anecdotal results. This calls into question the wisdom of tying ourselves to the $p < 0.05$ mast, particularly, in poorly served clinical settings. Maybe a 20% probability that an apparent advantage wasn't just a chance event might be worthy of acceptance until more evidence accumulates or something more promising comes along. Similarly, survival and disease free survival, although conveniently dichotomous, are neither patient-centric, nor appropriately individualized outcome measures. Patients' assessment of success and that of their families need more prominence in reported outcome measures. For example, tough drug regimens and big surgery need a home run outcome in children to qualify as a success, not just the couple of comfortable years that might justify similar treatment for a 65-year old.

One speaker said: "People always tend to do things better when they are around Eric," which is what the day was all about. That is a treasured trait, which is hard to describe but often immediately apparent, as in: "He's really cool, Dad" [Nicholas Guillem, at age 8 (now 11), to his father José, after meeting Dr. Rose on Madison Avenue].

Jim Chandler

1. Gladwell M. The 10,000-hour Rule. In Outliers: the Story of Success. New York: Little, Brown and Company; 2008.
2. McKenna RJ Jr, Houck W, Fuller CB. Video-assisted thoracic surgery lobectomy: experience with 1,100 cases. AnnThorac Surg 2006;81:421-5.



Principal events in cardiac surgery's insurgent evolution: **blue type** indicates association with the Columbia University Medical Center and its antecedents in this figure, as well as in the list of references.

Cardiac Surgery's Insurgent Evolution

James G. Chandler and
Stephen E. Novak, Head, Archives and Special Collections, Augustus C. Long Health Sciences Library

Insurgent evolution is an oxymoron, linking insurrection with its near opposite, orderly progression. Yet, both are good descriptors of cardiac surgery's largely 20th century development and the 18th century guerilla warfare that won independence for America.[1] Each was essentially an American-British endeavor, with significant contributions from German and French speaking Europeans. Both were idealistically imbued, hallmarked by successful probes, and cowing push backs that marginalized the insurrectionists. Certain advances came at great cost to unwitting, desperate patients in one campaign and to unwitting, colonial bystanders in the other. Bold moves and perseverance eventually triumphed, paving the way for evidenced-based, sustained achievements that continue to mitigate cardiac disability and advance political discourse throughout the world.

Fin de Siècle Beginnings

Insurgency cannot exist without an establishment. At the turn of the 19th century, medical hierarchies in the British Isles and continental Europe viewed attempts to operate on the heart as frivolous and harmful misadventures. Despite John Jones' participation in the Medical Department of the Continental Army, P&S, having just affiliated with Columbia College in 1891, was now part of New York's medical establishment, as was the Presbyterian Hospital, beginning with its conception by James Lenox in 1868.[2] Although neither institution is on record as saying so, insurrection, in any form, was antithetical to the cultures of both institutions, well into the 20th century.


Ludwig Rehn. (1849-1930)[3]

Ludwig Rehn of Frankfurt, who had previously documented predisposition to urinary bladder tumors among aniline dye workers, recognized that his successful 1896 closure of a right ventricle (RV) knife wound was a seminal event that others would emulate.[3] The establishment, however, looked upon his procedure as an insurgence, and, for a time, even denied that the operation had occurred. English surgeon, Stephen Paget[4] (1855-1926), writing in 1897, in his single-author text book, *Surgery of the Chest,* stated that "Surgery of the heart has probably reached the limits set by nature to all surgery: no new method, and no new discovery, can overcome the natural difficulties that attend a wound of the heart. It is true that heart suture has been vaguely proposed as a possible procedure, and has been done on animals, but I cannot find that it has ever been attempted in practice." Stephen Paget occasionally shows up in the literature with "Sir" before his name, probably from confusion with his famous pathologist father, Sir James Paget, a relationship that added gravitas to his son's opinions. Rehn was not deterred and, by 1907, had accumulated 124 cases of cardiac suture with a 40% recovery rate.

Surgical anatomist John Skandalakis[5] examined a variety of surgical canards including remarks about operating on the heart


Stephen Paget (1855-1926)
Founder, Research Defense Society

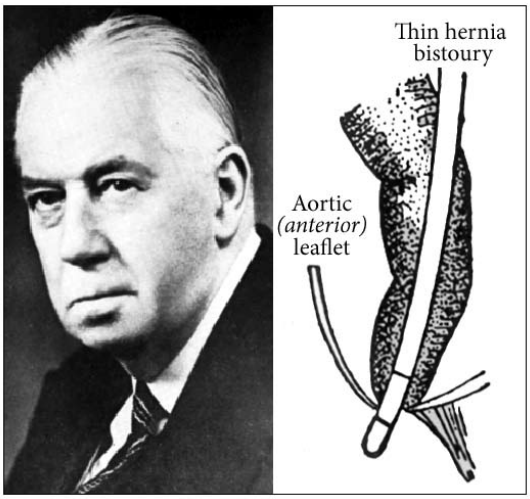
attributed to Theodor Billroth (1829-94), in an informative and entertaining article entitled, *Nihilism: A Benign Denial.* For cardiac surgery, Skandalakis' title was inappropriate: hierarchical denial was often vituperative and would harass cardiac surgery's evolution for half a century. Its tenacity is well illustrated by attitudes towards the treatment of debilitating mitral stenosis. Daniel Samways[6] analyzed post mortem findings in 70 Guy's Hospital mitral stenosis cases in 1896, noting that left atrial hypertrophy, or a combination of hypertrophy and expansion, characterized cases with tight stenosis, suggesting that the atrium had hypertrophied to overcome increased outflow resistance. Samways noted that he was dissenting from William Osler's assertion that dilatation was the dominant feature and a protector from back-up pulmonary hypertension. The following year, fellow Englishman, Herbert Milton,[7] working in Cairo's Kasr El Ani Hospital, described accessing the heart clinically through a median sternotomy, noting that the incision was well tolerated and provided excellent access that "required no great stretch of fancy to imagine the possibility of plastic operations in some… of its valvular lesions." Their rationale and enthusiasm were not contagious. A quarter of a century followed beset with rehashing the benefits of atrial dilatation and doubts that orifice enlargement would be beneficial. Rheumatic "fibrosis" was deemed to preclude the atrial myocardium from propelling additional blood through even the most commodious exit.

Sorties and Push Backs

In 1923, Peter Bent Brigham's Elliott Cutler[8] (1888-1947), encouraged by cardiologist-convert, Samuel Levine, exposed the heart of a 12-year old child with severe mitral stenosis through a median sternotomy. He then introduced a valvulotome through the apex of the left ventricle (LV), designed to capture punched out fragments to avoid embolization, attempting an imagined double commissurotomy. The rationale was that some insufficiency would be better tolerated than tight stenosis. The child's recurrent hemoptysis ceased and she would survive for another 4½ years. Two years later, Henry Sessions Souttar,[9] of London, introduced his finger through the left auricular appendage to use as a blunt dilator to enlarge a moderately stenotic mitral orifice in a severely incapacitated 15-year old girl. He reasoned that an atrial approach would facilitate finding the concave center line of the valve. He was surprised to feel more of an insufficiency jet and less stenosis than expected, constituting another advantage of approaching the valve from above. These findings changed his plan, which had been to introduce a thin hernia bistoury alongside of his finger to add a more concentrated disruptive force. Three months after the operation, the patient declared that she felt perfectly well, but objectively, she was dyspneic with the slightest

exertion. She lived for 7 more years in and out of the hospital with recurrent attacks of rheumatic fever.

Comas et al.'s[10] retrospective on this first ever clinical, mitral-valve finger fracture describes the medical community's disenchantment with her modest improvement, noting that the original referring physician chose not to join Souttar in reporting the case. Yet, the procedure's uniqueness was clearly appreciated, at least locally. The patient's heart, with its deformed mitral valve, remains preserved in the Museum of the Royal London Hospital. Souttar went on to become President of the British Medical Association in 1945 and was knighted in 1949, but he was never referred another mitral stenosis patient. The 1943 edition of Sir Thomas Lewis' (1881-1945) standard text, Diseases of the Heart, epitomized prevailing opinion, with Lewis writing that among the symptoms associated with mitral stenosis, "there are none that can be ascribed properly and usefully to this deformity of the valve…Surgical attempts to relieve cases of MS…by cutting the valve have so far failed to give benefit. I think that



Sir Henry Souttar (1875-1964) and his planned bistoury-assisted mitral valve finger fracture[9,10]

they will continue to fail… because [it] is an erroneous idea, namely, that the valve is the chief source of the trouble." Sir Thomas was "Britain's Einthoven," pioneering in electrocardiography and a recent recipient of the Royal Society's prestigious Copley Medal for his investigations of the mammalian heart.

Bold Moves and a Winning Laboratory

Lewis' dour commentary coincided with the availability of penicillin to the civilian community and was made just 3 years before the Dickinson Richards and colleagues' right heart catheterization studies were beginning to define RV hypertension beyond auscultation, and only 5 years short of a panoply of successes in surgically alleviating mitral stenosis.[11] On January 30, 1948, Horace G. Smithy,[12] of Charleston, South Carolina, successfully resurrected Elliott Cutler's trans-ventricular punch operation in a 21-year old woman with end-stage rheumatic heart disease, who would survive for 10 months. This was followed by triple reprisings of Souttar's trans-atrial approach, beginning with Charles P. Bailey's June 10th finger-guided lateral commissurotomy in a patient who would live for 38 years.[13] Dwight E. Harken[14] followed with a successful finger fracture, in Boston, on June 16th; and Russell C. Brock did the same thing, in London, on September 16th. These successes were surrounded by some agonizing failures. Charles Bailey had had his privileges suspended in at least two Philadelphia hospitals because of on-table deaths. Dwight Harken recalls profound discouragement before his successful 1948 procedure in a recorded 1973 interview conducted by W. Gerald Rainer.[15] Naysayers still decried wanton insurgency in the 1940s, but these men are remembered by most as pioneers, along with their enterprising 1950s colleagues. Smithy succumbed to his own rheumatic aortic stenosis in October 1948, at the age of 34. Bailey and Harken were born in 1910 and both lived until 1993, with Bailey enjoying a second career as a New York attorney, specializing in cases involving physicians accused of malpractice.

Finger fracture or commissurotomy was not the answer for every stenotic mitral valve; in fact, up to 40 % of patients selected on the basis of clinical and radiographic signs were not significantly improved. Richards and his colleagues[16] were now passing their catheters into the pulmonary artery (PA) and studying mitral stenosis patients pre- and post-operatively.[17] Patients with primarily stenotic valves improved if they had pulmonary hypertension at rest, and,


Cardiac surgery pioneers, in 1982. *Standing:* Charles Hufnagel, Viking Björk, Frank Gerbode, Henry Swan, Charles Bailey, Wilfred Bigelow; *Seated:* Denton Cooley, C. Walton Lillehei, Dwight Harken, and Conrad Lam; Notably missing: Robert Gross, William Longmire, and Richard Varco.
Photograph courtesy of W. Gerald Rainer

particularly, if they had also been in and out of congestive heart failure. Their studies also defined patients with mitral stenosis, typically combined with insufficiency, who had hypodynamic hearts, differentiated by exhibiting pulmonary hypertension only with exertion. These were the "Lewis patients," who could now be segregated as being at high risk for not surviving the operation and unlikely to benefit if they did.

Dickinson Richards' Cardiopulmonary Laboratory was a remarkably productive unit of Columbia's Bellevue Medical and Chest Service for thirty years from the time that Paris-born and fellow Nobel Laureate, André Frédéric Cournand (1895-1988) came to Bellevue in 1931 to be a tuberculosis service resident, until their retirement in 1961. They shared the 1956 Prize for Physiology or Medicine with Werner Forssmann, who began it all in 1929, by catheterizing his own right atrium, as recounted by his daughter, Renate Forssmann-Falck.[18]

Dickinson Woodruff Richards, Jr. (1895-1973) graduated from P&S in 1922 to join two previous maternal Lambert generations of New York physicians. An uncle, Adrian V. S. Lambert (1872-1952), was an 1896 P&S graduate, Director of the Madison Avenue Presbyterian Hospital's Surgical Service, and blood donor to his infant daughter, Mary, in Carrel's 1908, life-saving, direct transfusion.[19] In

King Gustaf VI Adolf addressing Laureates Andre Cournand, Werner Forssmann, and Dickinson Richards, Stockholm, 1956

M. Irené Ferrer in 1983

1921, Dr. Lambert founded a thoracic surgery service at Bellevue and went on to be a major philanthropic supporter of the institution's anesthesia training program, as well as of its Cardiopulmonary Laboratory. Cardiologist M. Irené Ferrer (1915-2004) joined the team in 1946, 5 years after graduating from P&S. She added a fresh clinical perspective and the lustre of another prestigious family, this time with a Cuban heritage, which she shared with brothers, Columbia surgeon, José M. Ferrer and, actor-director, Mel Ferrer.

The Ductus Arteriosis Botalli and an Opportunity That Went South

Continued patency of the ductus arteriosis burdens the LV with additional work to maintain an adequate systemic output, stresses the pulmonary arterial system, and serves as a nidus for bacterial endarteritis. Intuitively, its closure should eliminate all three risks, and lead to a longer life expectancy. In Robert E. Gross' prepared mind, four factors argued for attempting surgical closure in the late 1930s: modern endotracheal anesthesia allowed for safe collapse of a portion of the lung for doing the needed dissection. The characteristic rough "machinery" murmur, coupled with a Corrigan, water-hammer, pulse and measureable wide pulse pressure, offered diagnostic assurance. Emile Holman, at Western Reserve, had shown that dramatic reversal of LV decompensation followed excision or ligation of larger peripheral arteriovenous aneurysms. And, finally, animal and human-cadaver dissections suggested that the surgical approach should not be difficult in a child.

Robert E. Gross (1905-1988)[21]

Gross[20] selected a 7-year old girl, with cardiac enlargement and all of the classical findings as his first case. He performed the operation despite William Ladd's opposition, accessing the ductus through a left anterolateral thoracotomy, and ligating it with a single heavy silk ligature, after assuring himself that temporary occlusion had no ill effect. Whereas preoperatively, her daily blood pressures' mean values had been 114/38; postoperatively, her pressures averaged 108/80 over 3 weeks. No further follow up was included in his report, which was in print within 6 months.

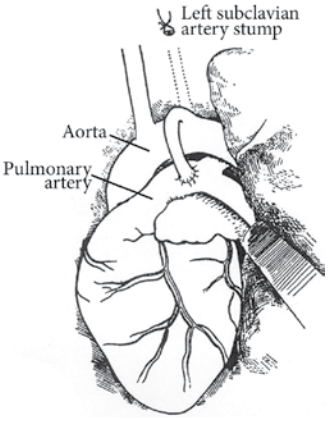
Gross subsequently provided a very meaningful personal follow up in an unpublished 1987 autobiography.[21] "Eleven children were operated upon satisfactorily for ductus closure by ligation. The twelfth was a fourteen-year-old girl also treated by ligation. She was well at the time of hospital discharge. Two weeks after that, there was a party for her at her home. While dancing with friends, she suddenly collapsed on the floor and was instantly dead! … Autopsy examination showed that the ductus ligature had cut through, permitting massive hemorrhage. I never again ligated a ductus. All subsequent patients were handled by careful local dissection placing double clamps on the ductus, then cutting the ductus in half and meticulously closing each end by suturing. This… was used with total satisfaction up through the last ductus operation I performed, which was number 1,610, in March 1972."

Shortly thereafter prostaglandin metabolism alterations were associated with persistent ductus patency in lambs and then humans. Pharmacological inhibition of its synthesis with acetylsalicylic acid, then indomethacin, and, more recently, ibuprofen has been generally successful in achieving closure in newborn infants. Despite its success, debate continues about who should be treated and when, particularly in prematurely born infants in whom delayed spontaneous closure commonly occurs.[22]

Three years before Gross did his first case, George H. Humphreys, II (1903-2001) encountered a persistent patent ductus in a dog. The animal's chest had been opened for an experiment to determine positive pressure ventilation's effects on cardiac output, involving himself, Richmond Moore, and Virginia Apgar. The open ductus would vitiate their experiment, so Dr. Humphreys ligated it and went on with the planned protocol. The ligation was so easily accomplished that Humphreys proposed doing it clinically*. Pediatric Chairman, Rustin McIntosh objected, citing diagnostic uncertainty, variability in its ill effects, and that ductus patency may sometimes be compensating for associated intra-cardiac anomalies.[23]

In September of 1939, after having gone to Boston to observe Dr. Gross ligating a ductus, Humphreys did the first ductus arteriosis ligation in New York, assisted by Dr. Moore, with Virginia Apgar providing the anesthesia. Two years later, Paul Swenson, who by that time had been a Presbyterian Medical Center radiologist for 10 years, asked Dr. Humphreys whether, besides closing a patent ductus, could he surgically create one?[24,25] He explained that he had just come from a young woman's autopsy, whom he had followed with repeated yearly fluoroscopies. Initially, she was not cyanotic, but, over the last several years, she developed progressively deepening cyanosis that became associated with episodes of unconsciousness, the last of which proved fatal. Her autopsy showed an atretic pulmonic valve, infundibular hypertrophy, a high ventricular septal defect with an overriding aorta, and a nearly completely closed ductus. Swenson hypothesized that the ductus had supplied sufficient PA flow to the lungs when she was young, but did not grow with her,

*This section includes information from Kenneth Forde's personal copy of Dr. Humphreys privately published memoirs, "Eight Rabbits, a Century of Memories: 1903-1999, Book I: The First Four, 1903-1951"; pp.176, 225-6.

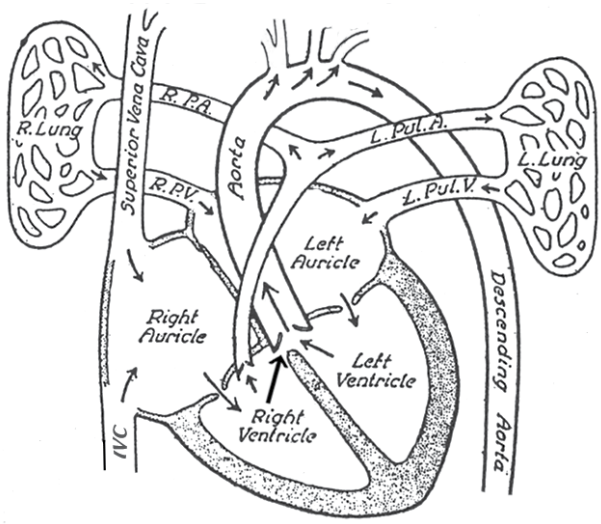


Canine left subclavian to pulmonary artery shunt.[26]

and gradually became inadequate, accounting for her becoming cyanotic and its recent worsening.

Humphreys was aware that Gross' group[26] had published an article, ostensibly to win over skeptical pediatricians, describing the deleterious effects of end-to-side, left subclavian-to-PA anastomoses in dogs. He and Blakemore had studied experimental carotid-jugular fistulas, giving him first-hand knowledge that the closer an arteriovenous fistula was to the heart, the greater was its adverse effect. Humphreys' mind was prepared too, but negatively, so he dismissed Swenson's suggestion, probably without recalling McIntosh's prescient observation.

Alfred Blalock (1899-1964) and Helen Taussig's (1898-1986) report of their eponymous shunt encompassed only three cases and was in print just 3 months after the third patient's operation.[27] Each of the three procedures was different, challenging Blalock's and Vivien Thomas' on-the-spot ingenuities.[28] The first was an end-to-side, left subclavian artery-to-left PA, continuous, non-absorbable-suture anastomosis in a year and a half old child. The subclavian artery was smaller than hoped for, and no thrill could be felt after the anastomosis was completed. The second patient had a right sided aortic arch, which was not fully appreciated, until the left chest cavity was opened. So, the left sided innominate artery was used, dividing it at the origins of the subclavian and common carotid arteries and anastomosing it, end-to-side, with a continuous suture to the left PA. This time, there was a palpable thrill when the clamps were removed. The third patient had normal arch anatomy. Blalock elected to operate through the right chest cavity, to use the innominate artery again, since the second patient had a more dramatic improvement than the first child. Exposure of the right PA was more difficult than exposing the left PA, as would be anticipated, but the anastomosis again yielded an immediate thrill. These patients were 11 and 6 years old.



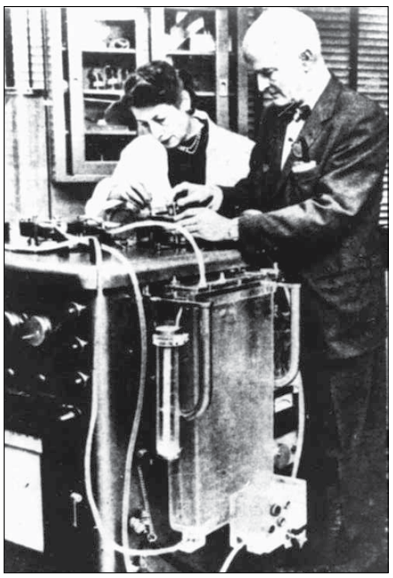
Tetralogy of Fallot's pulmonic stenosis, high ventricular septal defect, and dextraposed aorta favor RV outflow into the aorta.[27]

Both showed widening of their pulse pressures and improved arterial O_2 saturation percentages from the 20s and 30s before operation to the 70s and mid-80s before discharge.

The worldwide impact of their publication was tremendous.[29] This was partially due to the clarity of Taussig's introductory discussion of the importance of the amount of blood going to the lungs as opposed to the presence of a right-to-left shunt, per se, and compensatory polycythemia, as well as the paper's clear illustration of the flow patterns associated with tetralogy of Fallot's anatomy. "Blue-baby" parents, who had previously received only dismal prognoses, flocked to Baltimore, and pediatricians grasped the broader concept that a surgical procedure could have life-altering benefit for many children afflicted with congenital heart disease. The five-year followup data were a little sobering: 67% of the patients were still benefiting from the shunt, but many shunts closed or had insufficient flow (uninterrupted, non-absorbable suturing), and some 36 % had required a second operation.

The Flip Side: Too Much PA Flow

Huge ventricular septal defects cause the two ventricles to function as if they were a single chamber, exposing the lungs to excessive PA flow as the post-partum pulmonary resistance quickly becomes much less than that in the systemic circulation. This induces incremental resistance in the smaller pulmonary vessels, eventually impairing blood-gas exchange. A moderately stenotic pulmonic valve would be a godsend, as its entry-point resistance would act as a pressure dam, directing more flow to the systemic outflow and protecting the smaller pulmonary arteries. Constriction of the PA would accomplish the same thing, but experimental PA bands usually eroded through the vessel wall. William "Harry" Muller Jr.[30] added PA wedge excision to reduce the lumen to about a third of its original size and then encircled the narrowed segment with a broad, polyethylene band. His first patient was a 5-month old infant with a single-ventricle heart operated upon on July 11, 1951. At 6 months, the infant's heart had shrunk and he appeared to be thriving. More experience suggested that the operative mortality was unacceptable if the septal defect was coupled with great vessel anomalies; otherwise PA banding was a durable solution and even allowed some regression of pulmonary arteriolar medial hypertrophy.[31]



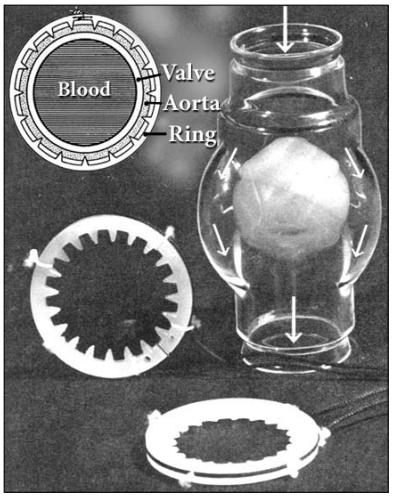
John & Mary Gibbon with a preclinical, fixed-screen-oxygenator H-L machine.[32]

"Waiting for Godot" †

John Heysham Gibbon Jr. (1903-73) married Dr. Edward Churchill's research assistant, Mary ("Maly") Hopkinson in 1930, "which was not only the beginning of a wonderful union but also the start of a lifelong professional collaboration."[32] They returned to Philadelphia for good, in 1935, where John was appointed as a Harrison Surgical Research Fellow at the University of Pennsylvania. Gibbon published his first paper on artificial

†Parisian, Irish expat, and 1969 Nobel Laureate, Samuel Beckett's (1906-1989) best known play premiered at the Théâtre de Babylone on January 5, 1953, just months before Gibbon's successful clinical cardiopulmonary bypass.

circulation in 1937, describing a pump-oxygenator circuit designed to support short-term PA occlusion to remove pulmonary emboli.[33] The oxygenator consisted of a vertical rotating cylinder that received a pumped stream of venous blood near the top of its inner surface. The rotation caused the blood to spread out in a thin layer as it spiraled down in a 95% oxygen atmosphere to be collected in a stationary reservoir at the bottom for infusion into an arterial cannula. Pumping was done by alternately pressurizing and venting enclosures that housed rubber finger-cot extensions between paired, one-way, main-line valves. Compression emptied the cots, which then refilled on venting, producing a pulsatile flow. In more than 60 experiments, he and Maly ultimately succeeded in supporting a few cats through 30 minutes of PA occlusion and having them survive for a few hours afterwards. They struggled with issues of priming volume, balancing inflow with outflow, foaming, air emboli, hemolysis, and thrombosis. Surmounting these obstacles to achieving a safe and efficient heart-lung machine would vex its development for nearly two more decades and cause others to seek alternatives.



Hufnagel descending aorta valve with fixation rings that grip but do not crush aorta (white arrows indicate flow path).[35]

Estragon: He's puffing like a grampus.
Pozzo: The answer is this. [Much that's ejected comes back.]

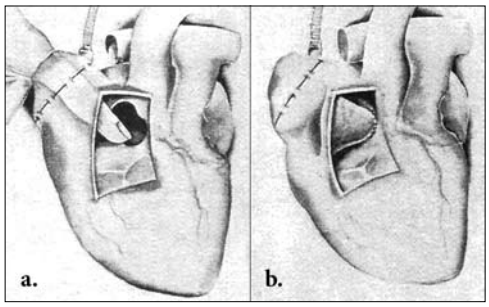
In 1946, Charles A. Hufnagel (1916-89) began designing a descending aorta "check valve" to be inserted just beyond the origin of the left subclavian artery. This proved to be a six-year project, involving 300 animal implants.[34] Most of the energy went into testing and achieving a non-thrombotic blood interface and finding a means of fixing a rigid valve body within the divided ends of the descending thoracic aorta. A single-piece, molded, methyl-methacrylate body ensured a smooth interior that was acceptably thrombo-resistant. A light-weight polyethylene ball precluded backward flow by seating in the proximal end of the valve at the onset of diastole.

Ligature encirclement was a fixation non-starter, as continuous circumferential pressure guaranteed erosion and fatal hemorrhage. Fixation by toothed rings that engaged but did not crush the aortic wall proved to be a partial answer. The compliance mismatch between the rigid valve body and the aorta resulted in erosion in at least one instance and was a source of emboli in another. Wrapping the divided aorta ends with semi-elastic bands to limit their expansion seemed to eliminate both complications.[35] A new silicone-covered, hollow nylon ball made the valve's closing click less perceptible to the patient. Hufnagel operated on his first of 23 patients, beginning in September 1952. All had end stage disease with LV dilatation and diastolic pressures of 40mmHg or less. Six patients died in the hospital, but the 17 survivors were greatly improved. Hufnagel's animal data suggested that the valve in the proximal descending aorta eliminated 75% of regurgitant LV reflux. Gordon Murray[36] (1894-1986), of Toronto, check mated both compliance mismatch and sound perception, in 1955, with a small series of aortic-valve homografts placed slightly lower in the descending aorta. Mid-20th century knowledge of anomalous and disease-distorted anatomy was not going to be satiated by ectopic valves, extra cardiac shunts and banding: it was time to go inside.

Vladimir: Our Saviour. Two thieves. One is supposed to have been saved and the other ... *(he searches for the contrary of saved)* … damned.
Estragon: Saved from what?

The patent foramen ovale, as an uncomplicated septum secundum defect, was the logical target for nascent intracardiac surgery because of the thinner atrial walls and the lower pressures within them. The "from what" was left-to-right shunting leading to pulmonary vascular overload and right sided cardiomegaly, as well as an anatomical proclivity to endocarditis. Left-to-right shunting was typically well tolerated until the second or third decade of life when irreversible pulmonary vascular resistance gave rise to bi-directional shunting and progressive congestive heart failure. Earlier symptomatic failure was known to develop in children with large holes and shunt volumes, but early symptoms were also potential indicators of unrecognized associated anomalies.

Bailey[37] developed an "atrio-septo-pexy" in 1952, which involved introducing his finger through the right auricular appendage to guide suturing the right atrial wall to the rim of the defect.



Cut away views of Bailey's atrio-septo-pexy:
a. bare finger identifing defect; b. completed septopexy, showing residual right atrial chamber.[37]

Each stitch began and ended on the external surface of the invaginated wall. Since he could not see inside, he kept catching his glove, so he removed it and risked his bare finger. The result was an occluded defect with a doughnut shaped passage around it connecting the vena cavae to the tricuspid valve. The technique was innovative but not well suited to the typically eccentrically located patent foramen.

Later in the year, Gross[38] reported on six patent foramen ovale cases, which he approached by suturing a rubber well to the right atrial wall and incising the wall within the enclosed area. Blood rose freely in the well, which was 15-cm deep when properly supported by an assistant. Gross then worked by feel and coordination with another assistant to steady his needle holder once a suture was passed through one rim edge, to allow Gross to grasp the needle with a clamp and bring it into view, for reloading and passage through the opposite rim. He and his team even closed a large hole with a patch using blindly placed, interrupted, mattress sutures. The well technique was tried by others but not seeing was frustrating and error prone, leading to on-table deaths.

Wilfred G. Bigelow[39] (1913-2005), of Toronto, had reported in 1950 that hypothermia could be used to slow metabolism, diminishing the need for oxygen to a small fraction of what was normally required. Anesthetized dogs cooled to a core temperature of 28°C became narcotized by their hypothermia, no longer requiring anesthesia, and soon ceased spontaneous breathing. Cooling to 20°C brought their heart rates down to 15 to 30 beats per minute, which typically lapsed into shock-resistant, ventricular fibrillation. Rapid rewarming, supported by cardiac massage, even at this point, could sometimes reverse the entire process.

F. John Lewis (1916-1993) and Richard L. Varco[40] (1912-2004), of the University of Minnesota, had witnessed an unsuccessful 1951 cardiopulmonary bypass (CPB) supported attempt to close an ostium primum defect.[41] They were impressed with CPB's inherent complexity and its coronary-sinus and Thebesian-vein blood drenched field vs. the simplicity and dry field that could be achieved with hypothermia and combined inflow and outflow occlusion. Cooling, however, was neither simple nor efficient. Patients were anesthetized and then wrapped in channeled rubber blankets filled with cold water. Rewarming was done by immersion in a tank of warm water, which was far quicker than the cooling process. They operated upon 11 atrial septal defects, beginning with a 5-year old child on September 2, 1952 whose uneventful closure of a patent foramen ovale was likely the world's first successful open heart operation. Ventricular fibrillation occurred in four patients, causing abandonment of the intended closure in one and, fortunately, eventual shock conversion to sinus rhythm in all four. Their longest occlusion period was just under 8 minutes.

Henry Swan[42] (1913-96), of Denver, extended Bigelow's observations regarding hypothermic ventricular fibrillation in dogs, finding that it was associated with sudden decreases in *hypercapnea* and potassium. Hyperventilating from the beginning, to ensure continuous hypocapnea, reduced the incidence of fibrillation, and, if it occurred, potassium infusion into the aortic root potentiated its conversion by electric shock. He employed these principles in an initial series of 15 patients, describing closure of intra atrial septal defects, pulmonary valvotomies, and stenotic infundibular myotomies. Ventricular fibrillation occurred in two patients, who were easily defibrillated after potassium infusion. The longest period of total inflow occlusion was 8.5 minutes, suggesting, again, a need to work quickly, and perhaps accounting for Swan's reluctance to close the high ventricular septal defects in his tetralogy of Fallot patients.

Estragon: He should be here.
Vladimir: He didn't say for sure he'd come.

Michael E. DeBakey (1908-2008) visited Gibbon and advised him to replace the finger cots with roller pumps that DeBakey had developed during his Tulane medical student days.[43] Gibbon abandoned the vertical cylinder oxygenator in favor of rotating vertical discs and later changed to a stationary bank of screens, working without interruption until 1941, when he enlisted in the Army Medical Corps. Gibbon returned in 1946 to follow in the footsteps of his Professor-of-Surgery father at Thomas Jefferson University. A former World War II transport pilot, turned Jefferson medical student, arranged a meeting between Gibbon and Thomas J. Watson, Sr., chairman of International Business Machines. From that time on, IBM not only funded Gibbon's work but assigned several of its engineers to his laboratory and ultimately built the model that was to be used on human patients.[44] The culmination of their collective labors was embodied in Gibbon's May 6, 1953 seminal success with his second CPB patient, an 18-year old girl with a large intra atrial septal defect.[45] The heart-lung machine assumed her cardio-respiratory functions for 26 min, allowing for precise closure of the large defect. She was operated upon 15 months after a misdiagnosis-related, on-table death. The long interval between attempts typified Gibbon's careful and contemplative approach.

Unlike the allegorical Godot, Gibbon did show up… at a September 16, 1953, University of Minnesota Cardiovascular symposium. The host institution's Surgical Department was, at the time, one of the most vibrant in the world. Owen Wangensteen had been its Chairman for 26 years and was now only 57-years old. He and Physiology Department Chairman, Maurice Visscher, had forged a relationship that nurtured talent and defended open minded thinking. Gibbon was lecturing to the choir, but not preaching, because his 3rd and 4th patients had died. He would do no more open heart surgery himself but continued an already distinguished academic career as Jefferson's Chairman of Surgery until his retirement in 1967. Dr. Gibbon died during a tennis game on February 5, 1973. He had mailed a manuscript recapping *The Development of the Heart-Lung Apparatus,* 18 days earlier, which, in the manner of Godot, remained unpublished for 5 years.[46]

Vladimir: Try as one may.
Estragon: We should turn resolutely towards Nature.

C. Walton Lillehei (1918-99), on whom Wangensteen had done an extended cervical-mediastinal node dissection for lymphosarcoma, was in the choir. He would soon work with Richard DeWall[47] on a disposable bubble oxygenator, but his current focus was on controlled cross-circulation and the "Azygos Flow Principle."[48] The latter was based on the dog's experimental tolerance of azygos-vein flow as the sole input into the heart for up to 30 minutes, which amounted to only 10% of basal cardiac output. Adding a safety factor for clinical perfusion, this translated to a targeted 25% of resting cardiac output. Controlled cross circulation involved linking an ABO-Rh compatible donor and a patient through aortic and caval catheters in each. The donor's heart and lungs would support the patient while the inflow to his own heart was occluded. Pumps in circuits going to and from the patient maintained a balanced "Azygos perfusion rate," as they were driven by the same motor shaft. When the heart was open, the reduced perfusion rate minimized coronary-sinus and Thebesian-vein flow requiring only intermittent suction to maintain a clear operating field.

By mid 1955, Lillehei[49] was able to report results in 32 patients in a series that began in March of the previous year. Isolated ventricular septal defects accounted for 22 of the procedures. Seven of these patients died during their hospitalization due to respiratory complications or incomplete closure of the defect, and, in only one instance, from heart block. There were two donor complications, an air embolus in one and profound hypotension in the other that required opening the chest for cardiac massage. Both survived. The paper concludes with an addendum: "…since submission of this report, successful direct vision repairs [that do not] require a donor… have been performed… [using] a heterologous lung oxygenator [or] multiple transfusions of arterialized venous blood."

Estragon: Let's pass on now to something else, do you mind?
Vladimir: I was just going to suggest it.

Dennis Melrose[50] (1921-2007), of London, initiated CPB's last half of the 1950s booming maturation by demonstrating that a 1mg/ml concentration of potassium citrate in the coronary arteries would arrest a dog's heart in diastole, lowering its need for oxygen. Washing out with blood would, almost as quickly, restore the heart's rhythmic beating. Potassium citrate infusion could be coupled with cooling to 25°C to further reduce metabolism and extend the safe period of arrest. Washout of a cooled, potassium-arrested heart often resulted in ventricular fibrillation, but the residual potassium virtually assured that it would respond to a single shock. CPB cooling and rewarming required only access to hot and cold running water and incorporation of a heat exchanger in the circuit. Even Henry Swan was happy to see the cumbersome cooling blankets and his original immersion

tank depart, the latter on its way to the Smithsonian Institution.

Mr. Melrose came to San Francisco to work with Frank Gerbode (1907-84) in 1956. Between then and 1959, Gerbode, Melrose, and John Osborn used elective arrest, with and without hypothermia, to repair a variety of lesions and developed a disposable filming oxygenator.[51,52] These same years witnessed K. Alvin Merendino's[53] posteromedial annuloplasties for mitral insufficiency in Seattle, the Cleveland Clinic's F. Mason Sones, Jr.[54] (1918-85) introducing selective coronary arteriography, and Conrad Lam, at Henry Ford Hospital, independently exploring acetylcholine infusion to arrest the heart and then using it in 80 clinical cases. Clarence Crafoord-trained, Åke Senning[55] (1915-2000), of Stockholm, capped these remarkable 3 years with a triple header. In October 1958, he used atrial flaps to reroute a heart's inflow to match up with its transposed great arteries in a 9-year old boy, who thrived for 20 years. [56]Later in the year, he introduced elective ventricular fibrillation to prevent air embolism during refilling of the heart. He completed the triumvirate, in October 1959, by installing the first totally implantable pacemaker.

Senning's operation would be performed for more than 30 years, despite the 1975 introduction of a successful, more direct, arterial switch procedure by Adib Jatene, of São Paulo.[57] Senning moved to Zurich to be Chairman of Surgery in 1961 where he built centers of excellence in both cardiac surgery and renal transplantation. In the 70s, Senning would encourage Andreas Grüntzig and unambiguously endorse his work as the second author of Grüntzig's transformative *Nonoperative Dilatation of Coronary-Artery Stenosis*.[58]

The late 50s were not good years for Columbia Presbyterian's budding cardiac surgery program. Humphreys had gathered a team to begin open heart surgery before he left on sabbatical in 1954.[‡] He would eventually do some himself, but Ralph Deterling, Presbyterian Hospital's closest approximation to an insurgent (excepting surgical oncologist, Danny Martin), was to have the principal responsibility. Aaron Himmelstein,[59] who had just returned from Mt. Sinai, and Baba Bhonslay were to assist him. Cardiologists Alfred Fishman and pediatrician Sydney Blumenthal were to select patients, do the catheterizations, help in their aftercare, and be part of the team. Robert Loeb objected to Fishman working so closely with the surgeons, thinking that they were "… experimenting with crude mechanical methods on the most vital organ in the body...." Fishman was able to mollify Loeb, but the Chairman of Medicine was not going to be supportive. Deterling left to take the Surgical Chair at Tuft's Medical School in July of 1959, and Himmelstein moved up to head the division. His tenure was to be cut off at 5 months by an aggressive glioblastoma that caused his death on December 18th, less than a week after a fruitless craniotomy. Jim Malm had just finished his chest residency at Presbyterian in July and Fred Bowman had done the same at Roosevelt Hospital. They would team up and catch up, but it would take about 6 years.[60, 61]


Aaron Himmelstein (1914-1959)

CPB also had a ways to go, but its future was assured. Direct contact between blood and oxygen was problematic, more so with bubbling. Micro-porous membrane technology solved the problem, first with sheets and then with hollow fiber coils, with oxygen flowing inside and blood flowing around them. This made for compactness, even with four square meters of diffusion surface and an incorporated heat exchanger, diminishing priming volumes to crystalloid alone. These elements became the industry standard in the mid 1980s.[62] CPB's progressive refinements are well detailed in the December 2003, volume 76, *Annals of Thoracic Surgery* 74-page supplement, covering a May 2003 celebration of the 50th Anniversary of Gibbon's success.

Catheter based repair of intracardiac defects were on the horizon, and, not surprisingly, uncomplicated atrial septal secundum defects were once again the number one target. Terry King and Noel Mills,[63] of Tulane University, reported the first five patients to have non-operative closure of a foramen ovale in 1974. They had worked out the procedure in dogs, sizing the defect from the radiographic image of a balloon within it, as echocardiography was not yet available. Closure was done with a detachable, dual umbrella sandwich. In 2003, Mills and King reported a 27-year follow up of these patients and reviewed the work of others.[64] None of their patients had experienced endocarditis, hemolysis, metal fractures, device migration, or impingement on the mitral or tricuspid valves.

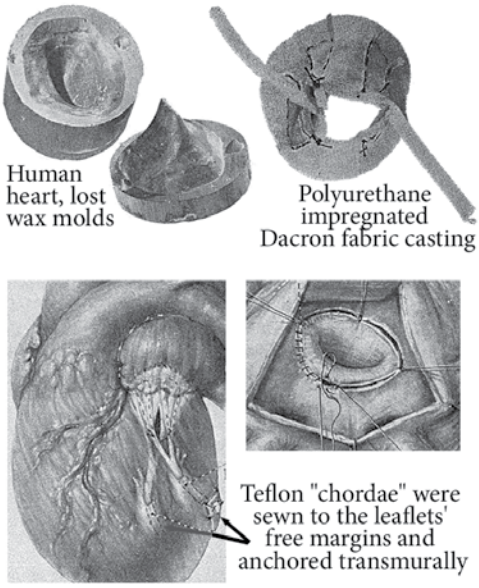
How Long Will My New Heart Valve Last?


Nina Braunwald and A. Glen Morrow in 1960

The 1960 US Presidential election brought a generational change to the Office that was matched by a series of sentinel, orthotopic total valve replacements. Andrew "Glenn" Morrow, Chief of the National Heart Institute's Surgical Clinic, assisted and encouraged Nina Starr Braunwald (1928-92) in modeling normal mitral valves. She used the lost wax process that is common in the jewelry industry, to make plaster molds for casting the mitral annulus and leaflets of canine and, later, human hearts in flexible polyurethane foam reinforced with Dacron fabric. Even when the design and operative procedure were finalized only four dogs had survived from 8 to 40 hours. Multiple deaths were related to technical difficulties imposed by the thin walls and small size of the canine atrium that were not anticipated to be factors in the larger left atrium of patients with severe mitral disease.[65] Two patients with debilitating mitral valve disease were scheduled for total valve replacement on successive days. Technical woes carried over to the first patient: a suture line tear had to be repaired and the Teflon® [polytetrafluoroethylene (PTFE)] "chordae tendineae" were mistakenly crossed within the ventricle, resulting in thrombotic occlusion of the valve on the third postoperative day.

The second patient, a 44-year old woman, was operated upon on March 11th. The curled and immobile mitral leaflets were ex-

[‡]Humphreys GH, II. Eight Rabbits, a Century of Memories: 1903-1999, Book II: The Fifth and Sixth, 1951-1975. Privately published; 1999. pp.382,386-7,416.



Braunwald's 1960 mitral valve.[65]

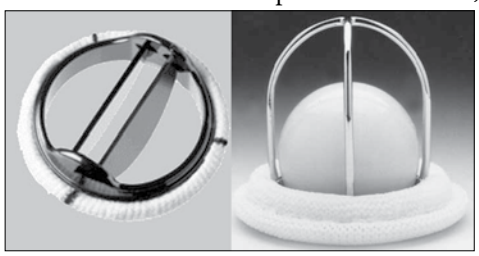
cised along with their chordae. The replacement valve's PTFE chordae were brought out through the ventricle wall near the bases of their respective papillary muscles. When the annulus suture was completed, the atriotomy was closed, leaving a temporary opening in its center for the operator's finger to remain inside. The vena cava tourniquets were then loosened to allow half-normal venous return to enter the heart to adjust the PTFE cord lengths to minimize regurgitation. The patient did well at home for 4 months but died suddenly, presumably of an arrhythmia, as the implanted valve and chordae were found to be thrombus free.[66]

M. Lowell Edwards and Albert Starr approached mitral valve replacement as an engineering construct. They decided to forgo the expansion and contraction of the annulus that facilitated complete opening and closing of the mitral valve and accepted that an occluder of some sort would be in the flow path. Edwards came back with successive prototypes in a matter of weeks, while Starr struggled with repeated deaths from thrombotic occlusion killing the animals just days after what seemed like perfect replacements. Once they settled on a caged-ball design, a few key refinements yielded a vivarium full of clicking dogs.[67] Cardiologist Herbert Griswold urged Starr to move to people. Griswold had a "houseful" of candidates who were otherwise not going to go home. Starr's first patient had a fatal air embolus 10 hours after the operation, but number two, a functional class IV, 52-year old truck dispatcher, sailed through and was alive and well 9 years later.[68] This was the beginning of a series of successful total replacements that soon extended to aortic and tricuspid valves.

Dwight Harken[69] was frustrated by poor results that regularly followed aortic valve "plasties," no matter how innovative, or performed by him or others. He turned to the Davol Company, in nearby Providence, to make a stainless-steel-caged ball valve. He and Harry Soroff developed a pulse duplicator that could vary and record amplitude, rate, peripheral resistance, and time in diastole to optimize their design. This became the prototype of everybody's pulse duplicator. Harken's second implant was successful in September to be followed by a successful Starr-Edwards aortic valve replacement in October, rounding out a remarkable 8 months.[70] Harken's[71] restless mind would propel him towards counter pulsation and other things, while Starr would focus on perfecting prosthetic valve replacement to zero intra-operative mortality. Aortic valve replacements are now done mainly for calcific stenosis in individuals in their seventh and eighth decades who typically recover slowly, or incompletely, from open CPB procedures. Catheter based replacement with a valve-incorporating stent would be particularly attractive in this setting and is being actively pursued.[72]

Winners

Mechanical prosthetic valve proliferation spilled over into the next decade. Engineers sought a less obstructive outflow and fabrication simplicity. Surgeons wanted to explore new surfaces and channeled flow, hoping to abrogate the need for life-long anticoagulation and negotiating a safe zone between hemorrhagic and embolic disasters. There were two spectacular winners, based on their design durability, mimicry, and 25- to 40-year outcomes. The Starr-Edwards valve underwent iterative improvements and model expansion through 1965. Since then, it has had no major changes, is known to function for as many as 40 years, and is still being implanted today[73]. St. Jude Medical is named for the Patron Saint of desperate cases and lost causes, and the company's bi-leaflet, pyrolytic carbon valve has proven worthy of the name. It was first implanted clinically, in October 1977, by Demetre Nicoloff in St. Paul, Minnesota, whose group has reported on 25 years of its use.[74] The valve comes in several models, has many emulators, and, along with them, is the most used contemporary mechanical valve.

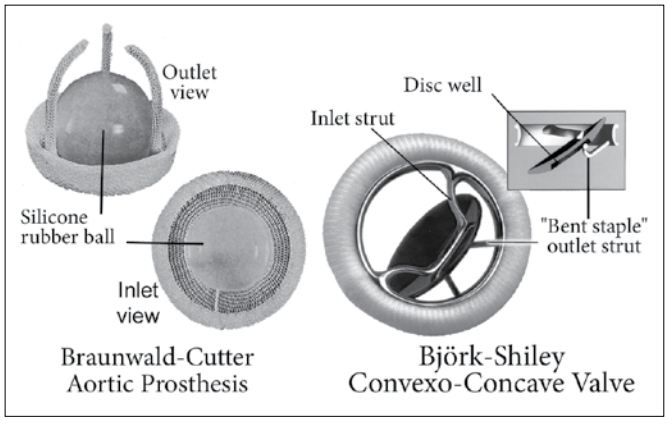


1977 St. Jude bi-leaflet pyrolytic carbon valve

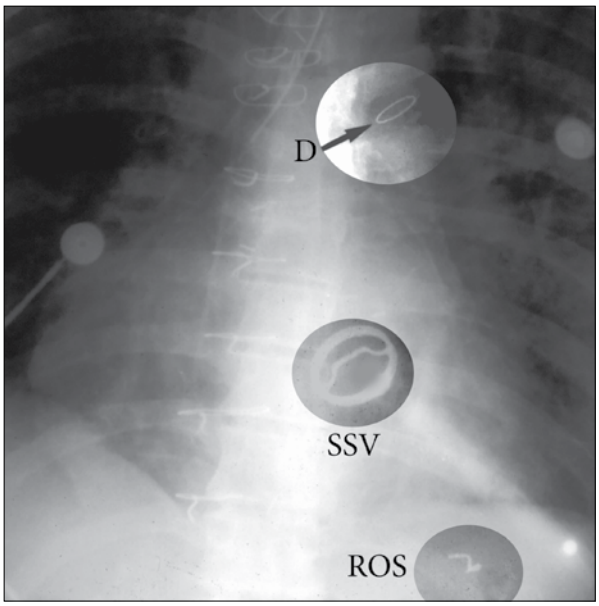
Baxter Starr-Edwards valve, minimally changed since 1965

Well-intentioned Missteps

Viking Björk and Lowell Edwards' protégé, Donald Shiley, introduced a less obstructive tilting disc occluder in 1969.[75] The disc tilted about one horizontal strut and was restrained by another, shaped like a bent staple that engaged a well, molded into the disc. Björk and Shiley tinkered repeatedly with the design over the next 7 years, simplifying the fabrication process and reshaping the disc to discourage areas of slower flow. Nina Braunwald[76] had been thinking for some time that completely enclosing a mechanical valve's frame in permeable cloth would encourage formation of the thrombo-resistant pseudo-intima that she had observed in dogs. Cutter laboratories responded in 1970 with ball valve design that incorporated a cloth covered, modified restraining cage and a softer ball to preserve the covering.



Both valves failed to achieve the goal of avoiding life-long anticoagulation. Braunwald's cloth covered, open cage design and softer ball allowed wear to erode tolerances to the point that some balls escaped.[77] This proved to be time related, necessitating replacement at about 4 years. Björk and Shiley's penultimate tinker caused imbalanced strut loading that could fatigue fracture the "bent staple"



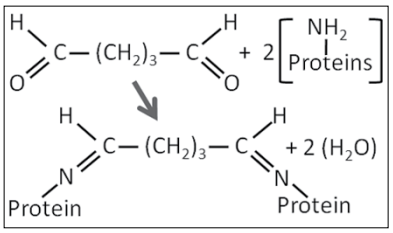
C/C valve strut fracture: Huge left atrium & pulmonary congestion; SSV, single-strut valve; D, disc in aorta; ROS, retrojetted outlet strut in inferior pulmonay vein tributary.

strut, freeing the disc to go with the flow.[78] Abrupt complete incompetence of either valve was fatal in the aortic position and required expeditious CPB supported replacement to save patients with mitral fractures. The Björk-Shiley fractures were not implant-time related and sufficiently rare, that risk stratifications had to be developed to guide decisions regarding prophylactic replacement.[79] Shiley valve implantees still exist, but nearly all are now at low risk.[80]

Nonthrombogenic Valvular Surgery

Two strategies exist to achieve this goal. Their commonality is biologic tissue, homografts and modified heterografts in one instance and native valve repair rather than replacement in the other. Jacques Oudot implanted the first aorto-iliac homograft, which had been preserved at 4°C in saline-diluted human serum in 1950, at Paris' Salpétrière hospital. Twelve years would elapse before Donald Nixon Ross[81] would place a freeze-dried preserved aortic valve homograft in its proper sub-coronary position at Guy's Hospital. The latter half of this interval coincided with incremental disaffection for abdominal aortic homografts based on reports of aneurismal degeneration. Ross would note calcification and a tendency to develop insufficiency in his aortic homografts and conceived what became known as the Ross Procedure. The patient's pulmonic valve is used to replace a diseased aortic valve and an aortic homograft replaces the transferred pulmonic valve, where it will be subject to less stress than it would encounter in the aorta.[82] This was a particularly attractive concept in children as the autograft in the aorta was capable of real growth. Ron Elkins and his colleagues[83] at the University of Oklahoma went a step further, excising the diseased valve along with the aortic root, transferring the patient's PA root as a valve containing cylinder, implanting the coronary ostia into it, and reconstructing the PA with an aortic root homograft. Both variants are used today.[84]

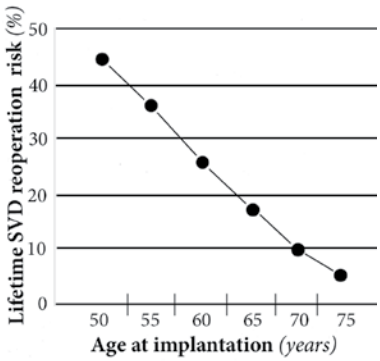
Two interrelated issues had to be surmounted to use a heterologous valve: its structural integrity had to be preserved because it would not be a living tissue, and preservation would be unachievable without mitigating the valve's xenogenic antigenicity. Alain Carpentier[85] explored a variety of tanning and embalming fluids, discovering that forceful washing away of passenger leukocytes and glutaraldehyde tanning addressed both issues. Glutaraldehyde's two CHO groups



Glutaraldehyde protein cross linking

avidly seek free protein N-terminals linking two proteins per molecule, while its central three methyl groups give it flexibility to insinuate itself within a protein's structure. Cross-linking can be extended by polymerizing glutaraldehyde, at the expense of lesser penetration.

The Hancock Company introduced the first commercially available pig valve in 1970, besting Carpentier by a year. Porcine valves are now manufactured by many companies in a variety of conformations, but the Carpentier-Edwards Perimount bovine pericardium valve currently owns that market in the US. The Perimount valve's principal virtue is to have isolated all points of attachment from flexure stress. It is also less vulnerable than most tissue valves to calcific structural deterioration when implanted in middle aged individuals.[86] A slower contractility rate [change in pressure /change in time ($\Delta p/\Delta t$)] has been hypothesized to account for biologic valves' durability in older individuals.[87] Structural valve deterioration and calcification are related to variable expression of proinflammatory mediators and osteogenesis-associated factors.[88] Contractility stress may be a major expression modulator and the link between age and biologic valve durability.



Weibull distribution of Perimount structural valve deterioration (SVD).[85]

Carpentier[89] ignited interest in repairing mitral and tricuspid insufficiency with his introduction of annuloplasty rings in 1971, just as *The French Connection* and "Popeye Doyle" began their cross-Atlantic, decade-long run in movie theaters. He would later classify anatomical types and expand his repair to include resecting apposition-interfering bulges in an invited lecture, entitled, *The French Correction*.[90] Subsequent years saw an eruption of various shaped annuloplasty devices and a rebirth of "Teflon" neo-chordae in 1985, with Tyrone David's[91] use of Gor-Tex™ (ePTFE) sutures to replace damaged chordae. Recently, Perier and his Bad Neustadt[92] colleagues countered Carpentier with *Respect Rather than Resect*, advocating attaching accessory neo-chordae, as needed, to achieve smooth apposition rather than sacrificing leaflet surface area.

In 1996, Carpentier's group performed the first video-assisted, mini-thoracotomy, mitral valve repair, compiling a series of 22 cases over 14 months.[93] It was not long before others added robotic assistance, prompting FDA observational trials enrolling 150 patients between 2000 and 2002 that had typical operating times of 4 to 5 hours.[94] Expense and time notwithstanding, a single center accumulated a 300-patient series of robotic assisted mitral repairs in just 6 years, with 92% having none to moderate regurgitation and 94% freedom from reoperation at 2 years.[95] This fast paced approach to valve repairs has not extended to the aortic valve. Despite Hufnagel, Harken, and Bailey's independent early efforts, cusp-based repair techniques for aortic valve insufficiency have not gained wide acceptance and have only recently been categorized into anatomical types.[96]

Myocardial Revascularization

"In certain cases of angina pectoris, when the mouth of the coronary arteries is calcified, it would be useful to establish a complementary circulation for the lower part of the arteries. I attempted to perform an indirect anastomosis between the descending aorta and the left coronary artery. It was, for many reasons, a difficult operation. On account of the continuous motion of the heart, it was not easy to dissect and to suture the artery."

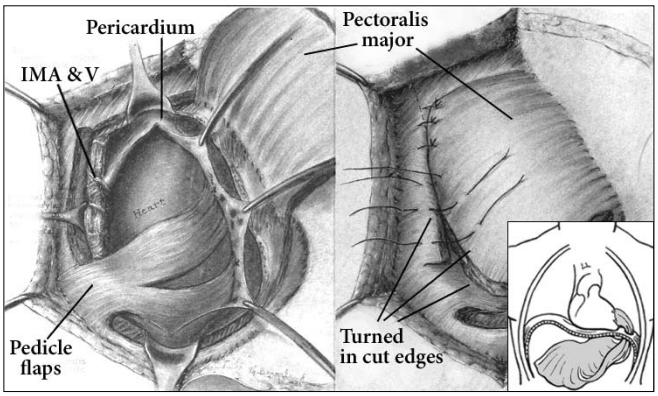
Alexis Carrell, 1910 [97]

Carrel (1873-1944) eventually succeeded, using a carotid artery homograft and soft clamp occlusion across the heart's "pedicle" to do the carotid-to-coronary anastomosis, but the dog did not survive because the anastomosis took too long. Direct anastomosis to a coronary artery was sufficiently daunting to inspire efforts to furnish an adventitious myocardial blood supply. The long-term efficacy of these would be debated, but there was no doubting that they shared the serious handicap of not being immediately beneficial.

Beck I

Claude S. Beck (1894-1971), who had helped Elliott Cutler develop his punch valvulotome, moved in 1924 to Western Reserve University and Lakeside Hospital in Cleveland, where he began a crusade against myocardial ischemia. Observing that divided constrictive pericarditis adhesions bled freely from both sides, Beck theorized that intentional adhesions to the epicardium would develop anastomoses with smaller coronary branches and compensate for a mainline occlusion. He showed that these hook ups did occur in animals, that they protected hearts from later coronary occlusion, and that pre-existing ischemia favored their formation.

Many dogs later, in 1935, Beck[98] divided the left pectoralis major muscle's insertion, and fashioned the muscle into three interlacing flaps in a 48 year old male farmer suffering from angina pectoris. He resected the anterior ends of the 3rd through 5th ribs, and



Beck I and cardio-omentopexy (inset) myocardial revascularization.[98,99]

opened the pericardium, which allowed him to turn the cut ends of the flaps down to the epicardial surface, dragging the internal thoracic (née mammary) bundle along with them. Flap-to-flap sutures maintained the muscle-to-epicardial apposition. Subjectively the patient was greatly improved. This procedure became known as the Beck I Operation. The comparable procedure in dogs significantly reduced the lethality of later coronary artery ligation as long as the intervening interval was at least two weeks. Beck did this operation on 37 patients with an operative mortality rate of 8%, generally with subjective improvement but always lacking objective data.

Cardio-omentopexy

Laurence O'Shaughnessy,[99] of London's Lambeth Hospital, had similar thoughts about adhesions to the epicardium but chose the greater omentum, "the body's adherence specialist," to provide the vascularity. His dog injection studies showed that connections formed between omental vessels and the coronary circulation after just one week. Greyhounds that had ligation of the left anterior descending (LAD) artery and a cardio-omentopexy were eventually able to run with the pack chasing the electronic hare round the full 525-yard course. The omentum was not only inherently adhering; it could also be brought into epicardial apposition with a much less operative trauma. O'Shaughnessy did a series of six clinical cardio-omentopexies in 1936 with four long-term survivors; all were relieved of their incapacitating angina. One of the deaths was from uremia 3 months after the operation, providing O'Shaughnessy with an opportunity to do a human specimen injection study. Dilute India ink made its way through the omental vessels and eventually appeared in the chambers of the heart. O'Shaughnessy was killed while caring for the wounded the day before the British evacuation from Dunkirk in May 1940.

Beck II

In 1945, Beck turned his attention to arterializing the coronary sinus, which normally functions to convey venous effluent from the ventricles into the right atrium.[100] It is a valveless conduit except for a single one-cusp valve at its termination. Since most dogs survived coronary sinus ligation, he postulated that Thebesian veins could take care of the myocardial venous effluent, leaving an arterialized sinus free to reverse-perfuse the myocardium with oxygenated blood. This was to become the Beck II operation, but arterializing the sinus proved to be tricky. The sinus was very fragile and aortic flow through a brachial artery autograft overwhelmed the sinus in the one patient operated upon in 1945, who died the following day. The task of finding ways around these problems fell largely upon National Heart Institute Special Fellow, Ferdinand F. McAllister,[101] who would examine the relevant variables in successive series of canine aorta-to-coronary sinus vein grafts.

He began by showing that arterial flow had to be severely restricted by a small-orifice aorta-graft anastomosis. Beck had proposed ligation of the sinus, as a first step to "toughen it up" for suturing, and, also, as a secondary procedure, to eliminate the central arterial-venous fistula. McAllister demonstrated that complete ligation was harmful in both settings. An arterialized sinus needed a pressure "bleed-off" into the right atrium or the pressure in the veins and capillaries would approach that in the aorta, leading to stagnation, intra-myocardial hemorrhage, and aorta-sinus graft thrombosis. The arteriovenous fistula was well tolerated, providing there was flow limitation at the graft's origin, and better yet, if coupled with narrowing of the coronary sinus opening. Under these conditions, dogs would be more likely to survive a 3-week delayed LAD artery ligation than those who had had a Beck I. Despite Mac's careful work, translating and assessing the efficacy of this balancing act in the clinic was problematic.

Beck would report 145 Beck I and II's over a 9-year period with a 7.5% operative mortality for the Beck I and 26% for the Beck II. The latter was staged, partially ligating the sinus first and vein grafting to it as a second, separate procedure. Some patients even required a third operation to close down a raging arteriovenous fistula. When queried, 80% of Beck II patients reported less, or no, angina without a specified activity level.[102]

Vineberg's Operation

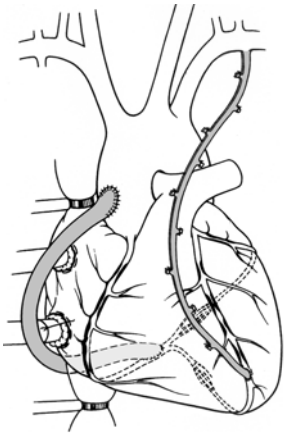
In 1946, Arthur M. Vineberg[103] (1903-88), of McGill University, published his first paper describing tunneling the internal thoracic artery (ITA) through the substance of the LV wall and fixing its ligated end at the apical end of the tunnel. A single-dog, ITA-injection study, 4 months after the procedure, showed complete ITA patency, apical-to-base flow through ramifications of the left coronary artery, and eventual spillover into the aortic root. Vineberg would pursue the procedure in dogs, showing that bleeding from the open side branches within the tunnel was initially carried away by myocardial sinusoids. Two weeks after implantation the side branches began to sprout arterioles that would eventually connect with similar sprouts from coronary branch vessels. This intermingling required an ischemic myocardial environment and was favored by careful handling of the ITA. Vineberg[104] deferred operating on his first patient until 1950 and would report having done only 57 cases over 8 years. His operative mortality in patients who had angina at rest was 59% (10/17) vs. 5% (2/40) in those with angina limited to exertion. Two-thirds of the survivors had no or only occasional anginal pain. This cautious advancement did not discourage a chorus of naysayers, who doubted the persistence of ITA patency and disparaged the efficacy of tiny vessel hookups. Sones soon confirmed Vineberg's injection studies with selective coronary angiography, marginalizing, but not silencing, the naysayers. Donald B. Effler (1915-2004) and his colleagues at the Cleveland Clinic would report 1,100 ITA implants in 1968, with 92% persistent patency, and demonstrable coronary communications in 54%.[105] In all, more than 10,000 Vineberg operations were performed between 1958 and 1975.[106] The results were notably variable, yet the procedure went on to overlap H. Edward Garret's[107]1964 successful saphenous-vein, aortocoronary bypass for 11 years.

Direct Coronary Artery Revascularization – "Success Has Many Fathers"[§]

Charles Bailey,[108] still in Philadelphia, performed the first coronary artery endarterectomy on October 29, 1956. Blalock-trained, William P. Longmire (1913-2003) leveraged UCLA colleague Jack Cannon's[109] expertise with superficial femoral artery endarterectomies, reporting a series of five patients in 1958.[110] The procedures, in both instances, were done without CPB or preoperative angiography. Longmire selected patients with severe angina, without ECG evidence of infarction, on the premise that they would have a proximally located occlusion of at least one of the three major coronary trunks with collateral supported distal patency. Beth Israel pathologist, Monroe Schlesinger had shown this to be true in beautifully injected coronary artery specimens, in a 40-page article, published in 1938.[111] Longmire planned to make a longitudinal arteriotomy at the distal extent of a palpable occlusion, reasoning that he and Cannon could take the time needed for careful disobliteration, as the distal collateral circulation would be unaffected.

In 1962, David C. Sabiston, Jr.[112] (1924-2009) did the first great saphenous vein aortocoronary graft on a 41-year old man, who had previously had a right coronary endarterectomy, relieving his now recurrent angina for a year. The graft was anastomosed, end-to-end, to the transected right coronary distal to its occlusion. Postoperatively, the patient had a fatal stroke, and the anastomosis was found to be occluded, ceding precedence to Garret's aforementioned later success.

In the same year, Effler[113] and his Argentine protégé, René Favaloro (1923-2000) became the first to use CPB to treat a post-os-



Left ITA to LAD and vein graft to right coronary artery

tial coronary lesion, employing hypothermic circulatory arrest, to do an open endarterectomy and vein-patch closure on the left main artery. Their chain-smoking colleague, Mason Sones' high-volume coronary arteriographic screening provided an abundance of carefully defined cases that was, at the time, unique to the Clinic, and would soon jump start them on both vein and ITA bypasses.

John E. Connolly's[114] 1978 Presidential Address to the Samson Thoracic Surgical Society on *The History of Coronary Artery Surgery* offers a detailed, first-hand presentation of the overall subject, including his own 1962 transaortic treatment of a right coronary ostial occlusion.[115] Connolly, in common with others, credits Vasilii I. Kolessov,[116] of Leningrad as doing the first clinical ITA-coronary artery bypass. Kolessov reported on six patients in 1967, apparently operated upon in 1966, with one death and mitigation or alleviation of angina in the survivors, adding that his series had now expanded to 12. He used neither CPB nor coronary angiography, harkening back to the 1958 premises of Longmire and Cannon regarding where lesions ended and the safety of working on an already occluded artery. Westaby and Bosher's Landmarks in Cardiac Surgery quotes William Longmire, in 1958, as admitting to having "… also performed a couple of the earliest internal mammary to coronary anastomoses. We were forced into it when the coronary artery we were endarterectomissing [sic] disintegrated"[117]

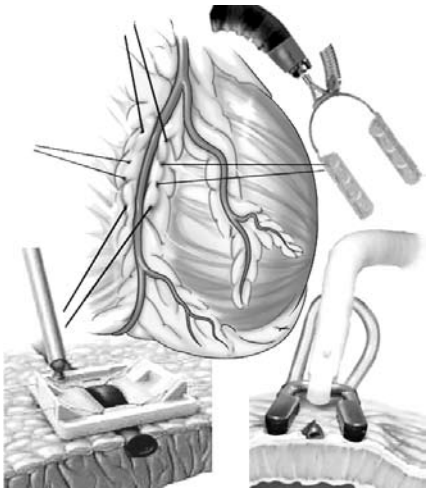
ITA bypasses were technically challenging and slow to catch on. In 1968, George Green[118] used Julius Jacobson's 16x operating "diploscope" and 9-0 nylon suture to do left ITA-LAD bypasses on 31 patients with severe, multiple-vessel disease - two thirds had documented infarcts and half were in mild to moderate failure. CPB and normothermic, electrically-induced fibrillation kept the field reasonably still. Occlusion times averaged 30 minutes for the ITA-LAD anastomoses. Vein grafts to right coronary branches were also done in half of the patients, using the microscope when the implantation sites were 2.0 mm or less in diameter. Two patients had postoperative ECG evidence of fresh infarctions. The others were relieved of their angina and most of their failure symptoms.

ITA bypasses proved to have superior patency compared to vein grafts, but their true impact, when other variables are taken into account, is on patient longevity.[119] Their survival advantage over vein grafts fits nicely into the catheterization era.[120] Siphoning moderate and single-vessel disease into the cath lab makes it even more imperative to use the best graft in patients with the worst disease. Lytle and his colleagues at the Cleveland Clinic have evidence that two ITA-to-coronary artery bypasses offer a survival advantage over having only one.[121]

Off Pump and What Next?

Out east, and a little farther from Lake Erie, Case Western Reserve's Jay Ankeney[122] began doing coronary artery bypasses without CPB, in 1969, stabilizing the implant site with four traction sutures. By 1985 he had operated on 733 patients with an operative mortality of 2.2%. Saphenous vein was used for 622 LAD and right

[§]"Success has many fathers, but failure is an orphan" John F. Kennedy, with reference to the Bay of Pigs fiasco.


Off pump CABG stabilization devices

coronary grafts. In 1973, he switched to left ITA-LAD bypasses and did 461 of these for a total of 1,123 grafts over 16-years. A 23-year follow-up study of his LAD bypasses showed saphenous vein grafts to be open in 60% of 40 patients and ITA grafts to be patent in 90% of 107 patients.[123] Ankeney made a movie of his technique in 1972, but did not publish his work, until prompted by the appearance of the "Octopus" and other stabilization devices, which sparked a broader interest in working without CPB.[124]

Ankeny unwittingly provided the root procedure for an acronymic lexicon that is not altogether consistent. His operation becomes an OPCAB, implying operating through a sternotomy, in addition to pump eschewal. MIDCAB (Minimally Invasive Direct) usually means doing the same thing through a small anterior thoracotomy but can be an "on-pump" procedure with femoro-femoral bypass and elective arrest. TECAB (Total Endoscopic) is a multi-port, video-assisted, thoracoscopic procedure. In its full-bloom format, it incorporates robotic assistance, femoro-femoral CPB, catheter-based, supra-valvular, balloon occlusion, and cardioplegia.[125] MECC [CAB] (Minimal Extra Corporeal Circulation) refers to a kinder and gentler, small prime, pump-oxygenator, trialed against both conventional CPB supported open CAB, as well as OPCAB.[126] The short-term outcomes in these trials have been acceptable but not significantly better than those achieved in Cleveland, with and without CPB.

"Circuit Breaking" Surgery

Supraventricular Tachycardia

In 1968, Will Sealy and his Duke colleagues encountered a 32 year old man with severe drug-resistant Wolff-Parkinson-White Syndrome that had become his predominant rhythm, driving his heart into chronic failure. Typically, the syndrome consists of brief episodes of supraventricular tachycardia, due to an aberrant atrio-ventricular muscle bridge that transiently acts as a parallel bypass around the atrioventricular node gate-keeper. They used open epicardial mapping to show that his aberrant muscle was reverse conducting back to the atrium to complete a re-entry circuit and perpetuate his tachycardia. A full thickness 5-cm incision, along the base of the right ventricle, adjacent to the atrium, immediately normalized the ECG, resulting in a "Shot heard 'round the world"** case report and a new era in the treatment of severe arrhythmias.[127]

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, affecting approximately 2.5 million people in the US. AF can be paroxysmal, persistent, or permanent, with the latter two having more complex pathophysiology. It is not an innocuous rhythm disturbance. It abolishes the "atrial kick," diminishing cardiac output in already compromised hearts and gives rise to embolic strokes, as well as to complications from their warfarin prophylaxis. AF is present in nearly 50% of patients undergoing mitral valve repair or replacement and is an independent risk factor for postoperative mortality and morbidity. The AF is unlikely to disappear without specific treatment unless it is of very recent onset. The most reliable way to abolish AF and atrial flutter is the Maze III procedure. As the name implies, it is a third iteration of interruptive full-thickness atrial incisions and running suture closures concocted by James L. Cox and his associates at Washington University in St. Louis.[128] The left atrial incisions encircle the pulmonary veins and then extend as two linear spokes, one going to the mitral valve annulus and the other to the base of the auricular appendage, which is resected. The right atrial complex consists of a linear incision from the orifice of the superior vena cava to that of the inferior vena cava and a "T" from that incision to the tricuspid valve's annulus, and from there to the excision line for the right auricular appendage.

Excision of the left auricular appendage is a particularly important part of the procedure, which needs to be a flush closure with no residual nook. When properly done, it is a bastion against strokes. Since its 1995 introduction, the Washington University Maze III experience has resulted in 90+% freedom from AF or flutter. The tedium of incising and closing discouraged broad acceptance, so now there is a Maze IV that substitutes bi-polar radiofrequency ablation for the incisions and has provided 80 to 90% freedom from AF or flutter at 12 months.[129] A recent review of endocardial catheter ablation reports results, ranging from 50% single-session "success" with established AF, to as high as 85% in treating paroxysmal AF.[130]

Veli Topkara and his colleagues at Columbia[131] have explored microwaves, laser, and radiofrequency, to make lesion sets, varying from pulmonary vein isolation alone to the full Maze III, and doing some epicardial ablating in other patients. Overall, their arrhythmia-free rates at 12 months were about 75%. Off-pump, epicardial surgical ablation is an attractive approach, particularly for patients with AF unassociated with structural cardiac disease.

Ventricular Tachycardia

Charles P. Bailey performed the first reported successful excision of a post-infarction aneurysm in 1954 with no means of salvaging the patient should marginal muscle have escaped his Satinsky clamp.[132] He justified the risk by the potential to improve ventricular function and avoid embolization or sudden death, noting that rupture was a rare event. There is no mention of aneurysm-associated paroxysmal ventricular tachycardia (VT) and fibrillation as the cause of sudden death, which had been recognized by (then not "Sir") Thomas Lewis in 1909.

The advent of CPB offered an expanded opportunity to eradicate ischemia-associated VT by coronary revascularization and aneurysm excision if one were present. A decade of experience showed that revascularization and resection of grossly injured myocardium, alone or in combination, had just a slightly better than 50% chance of abolishing VT.[133] Hope reappeared in 1978 when intraoperative provocative mapping suggested that selective subendocardial resection or a girdling trench would eliminate all reentrant circuits and prevent recurrent VT.[134] Despite improved and computerized probes, open, mapping-directed, subendocardial resection still leaves about 20% of patients vulnerable to induced VT and at risk for spontaneous VT and sudden death.

Ventriculotomy for treating VT in the absence of an aneurysm is at a double disadvantage because cardioplegia masks some pro-

**Emerson, RW. Concord Hymn. 1837; describing the impact of the April 19, 1775 battle at Old North Bridge in Concord, MA.

vocative sites and the heart disease of patients with drug resistant VT keeps the operative mortality near 10%. Image-guided, catheter-based mapping and ablation is a less hazardous and more flexible format. It is adaptable to sub-xiphoid epicardial ablating, can utilize all energy modalities, and is acceptably repeatable. Implantable cardiac defibrillators have proven effective, so much so, that they have become a budget issue. If frequently triggered, they compromise a reasonable life style. So, treating drug resistant VT today should begin with diagnostic imaging and catheter based ablation and, then, balancing the latter with the appropriateness of implanting an automated defibrillator.[135]

Chronic Heart Failure (CHF): Making the Best of What You Have

CHF is a progressive myocardiopathy, characterized by LV dilatation and poor contractility that can be temporized with polypharmacy and electrophysiological intervention. Twenty-first century optimal medical therapy (OMT) includes antiarrhythmics, anticoagulants, cardiac-specific beta blockers, and after load reduction, typically using a combination of diuretics, calcium channel blockers, and angiotensin converting enzyme (ACE) inhibitors. CHF is 67% ischemia based and often complicated by conduction abnormalities, potentially malignant arrhythmias, and dilatation-related mitral insufficiency. Left bundle branch block affects about 25% of CHF patients, delaying the onset of LV contraction. This results in septal shifting towards the relaxing RV, transiently displacing a fraction of LV volume that should have been ejected into the aorta and simultaneously impeding RV filling. Biventricular-pacing resynchronizes the onset of systole and, in conjunction with implantation of an automatic defibrillator, has been shown to decrease 3-year mortality and cardiac related hospitalization rates compared to OMT alone.[136]

Stem Cell Cardiomyocyte Replenishment

Experimental and, more recently, clinical trial data indicate that infusion of autologous bone marrow progenitor cells into an infarct-related artery will augment functional recovery. Successfully reperfused acute myocardial infarction patients had progenitor cells harvested from their bone marrow and were then randomized to have their marrow progenitor cells or placebo media infused into the reopened infarct artery. Both groups received OMT, and all but three of the 204 patients were available for 1-year follow up. The combined endpoint of death, myocardial infarction, or necessity for further revascularization was significantly reduced in the bone marrow derived progenitor cell infusion group.[137] Bone marrow infusion was also associated with significant improvement in EFs and end-diastolic volumes in patients with baseline sub-median EF values, which appears to be compromised by having been an after-the-fact stratification.[138]

Cardiomyoplasty and Passive Restraint Devices

Surgical interest in treating CHF began with Juan C. Chachques and colleagues'[139] 1985 introduction of "Dynamic Cardiomyoplasty." This involved severing the origins and insertion of the left latissimus dorsi muscle, preserving its thoracodorsal vessels and innervation, and implanting it with pacing leads. The muscle and its attached leads were then introduced into the chest through the bed of the resected second rib. The heart was exposed through a sternotomy, and the pericardium opened to implant a set of epicardial sensing electrodes. The latissimus was then wrapped around both ventricles and sutured to itself to form a somatic muscle vest about the heart to be paced by amplified signals emanating from the epicardial electrodes.

Chachques acquired a personal series of 212 patients, including 26 who went on to transplantation, which was not seriously compromised by their having had the myoplasty. At least 2000 cases have been done throughout the world, with variable and always uncontrolled results. The reported dimensional data suggest that the muscle wrap restricts dilatation and negative remodeling. EFs were only minimally improved from a mean 20% at base line to 23% at 6 to 12 months.[140] Advocates of the procedure see it as appropriate for New York Heart Association (NYHA) Class III ("rarely out of the house") and not Class IV ("Bed, Bath, and [Not] Beyond") patients, as they believe that a minimum of 3 months of muscle pacing are required before the myoplasty is fully effective.

Two companies are conducting clinical trials on simpler, passive, elastic ventricular restraints. One is a proprietary-knit, polyester mesh cap that is introduced through a sternotomy and fitted over the ventricles like legless panty hose. The trial had two strata with all patients receiving OMT. The first stratum compared adding or not adding the restraint to OMT in 393 patients. The second assessed its use in tandem with mitral valve repair or replacement vs. repair or replacement alone in 107 patients.[141] The enrollees' NYHA Classes ranged from II (slight limitations) to IV. The passive restraint was associated with smaller mean LV end diastolic and end systolic volumes in both strata that were sustained over 3 years. EFs, however, were not significantly different with and without the device in either stratum. The other device is an elastic Nitenol mesh that can be placed through a video-assisted, mini-thoracotomy. It has been used on 51 Class II or III patients with EFs of 35% or less in an uncontrolled observational study.[142] End diastolic and systolic LV volumes were smaller and exercise tolerance improved at 6 months with no mention of EF or any hemodynamic data

Surgical Ventricular Restoration (SVR)

Despite successful early reperfusion, approximately 20% of myocardial infarctions result in progressive LV dilatation and conversion of its normal elliptical shape into a sphere as an integral part of the evolution of CHF. SVR is directed at reducing ventricular volume in a cold cardioplegia arrested heart to a normative 60mL/m2 and restoring its three dimensional elliptical profile with the expectation of improved contractility and hemodynamics. SVR was performed on more than a thousand patients at 12 centers throughout the world between 1998 and 2003 in a prospective, uncontrolled observational study.[143] Concomitant CABs were performed on 95% of the enrollees and mitral valve repair or replacement in almost 25%. Scarred areas were excluded by patch or direct closure and dimensional reshaping was done using an elliptical mannequin. The mean EF increased from 30% preoperatively to 39% before discharge. Mitral valve repair or replacement patients started with lower values and were discharged with EFs similar to those of patients not needing a mitral valve procedure. Overall 5-year survival was 68% with 78% freedom from CHF-related readmissions and the majority converting from NYHA Class III or IV to Class I or II. A recent study by one of the principal investigators in the large study showed that these good results could be obtained in globally dilated ventricles, as well as in those exhibiting a more localized aneurysm profile.[144]

Transplantation

Allotransplantation

Heart Transplantation has a history beginning with Carrel and Guthrie[145] in 1905 and a far older presence in romantic and religious fables, exemplified by the story of Pien Ch'iao. Ch'iao was a

Pien Ch'iao at work in Fourth century BC China.[145]

renowned 4th century BC practitioner of Taoist, Chinese medicine, which attributed all ills to stagnated internal yin and yang forces.[146] His legendary treatment of two sick soldiers began with diagnostic examinations, which revealed that one had a strong spirit but a weak will and the other was weak in spirit with a strong will. To correct these imbalances, he anesthetized them with powerful medicines that made them unconscious for three days, allowing him to cut into their chests and exchange their hearts. When they awakened both were markedly improved.

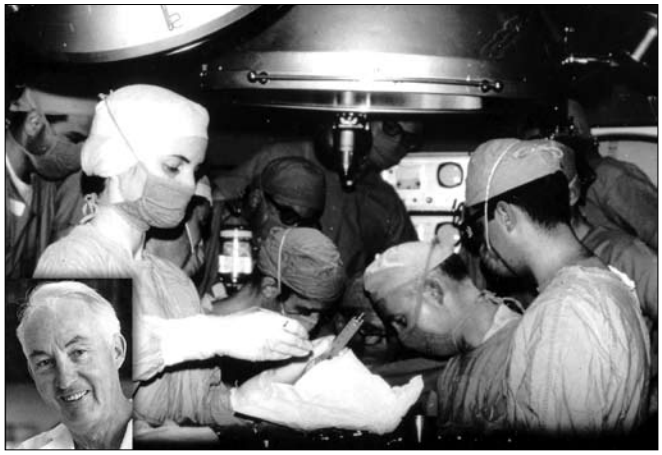
In 1933, Frank Mann and his colleagues[147] at the Mayo Foundation's Division of Experimental Surgery and Pathology resurrected Carrell and Guthrie's heterotopic canine heart transplants into the neck. The pulmonary and systemic veins were ligated as part of the harvest procedure, leaving only the aorta and PA to be anastomosed, respectively, to the cranial end of the host's transected carotid and to the proximal end of the transected jugular vein. Only the right side of the heart performed any work, and it was minimal. Host arterial blood perfused the coronary arteries, which drained into the right atrium and then out through the PA, into the central jugular vein. The hearts continued to beat for a mean of four days with the longest functioning for 8 days. This was enough time for the investigators to note that the denervated, heterotopic heart's pulse rate increased when the host exercised and that it was more sensitive to intravenous thyroxin than the host's heart. Histologic sections of hearts that had ceased beating showed an infiltration of both monocytes and polymorphonuclear cells that was essentially identical to what Mann and his coworkers had observed in renal allografts.

Vladimir Demikhov began transplanting canine hearts in the Physiology Department of the M. V. Lomonosov, Moscow State University, in 1940, putting them in the groin. In 1946, he decided that he had enough experience to work out a means of placing them in the thorax. His method involved inserting the donor heart by "piggy backing" it on to the host heart, since he had no other means of supporting the host during the process of making the donor heart connections. After months of on-table deaths, he succeeded in completing an operation on October 12, 1946 that left a puppy's heart and the native adult heart beating in the host animal's chest with survival of both for 5 days. This first canine intra-thoracic heart transplant was unknown outside of Eastern Europe until the publication of an English language translation in 1962.[148] It preceded Gibbon's successful CPB by 6½ years and clearly antedated Lower and Shumway's 1960 Surgical Forum report of 6- to 21-day survivals of five orthotopic canine transplants. Demikhov would be visited by both Adrian Kantrowitz and Christiaan Barnard in the mid 1960s.

Norman Shumway (1923-2006) came to Stanford in 1957, directly from his training at the University of Minnesota. His skills reflected those of Lillehei and Varco and were especially easy to appreciate when packaged with Shumway's humility and respect for the thoughts of others. Norm Shumway, Richard Lower (1929-2008), and veterinarian, Ray Stoffer, along with a string of residents, beginning with Ed Stinson, pursued the technical and physiologic variables of thoracic heterotopic and orthotopic heart allografts in the early 1960s, using out-bred animals and no immunosuppression.[149] Keith Reemtsma (1925-2000), in New Orleans, followed a different course, staying with the cervical cardiac transplants and focusing on how to mitigate rejection. In 1962, he reported that the purine antagonist, methotrexate, prolonged survival of non-working heart allografts out to 26 days.[150] David Blumenstock and his colleagues[151] at the Mary Imogene Bassett Hospital extended Reemtsma's observation to orthotopic allotransplants in 50 unrelated, mongrel dogs. Only 8 of their animals survived for longer than a day, but 5 of the 8 survived for 17 to 42 days.

Shumway's group perfected total excision of the heart and its isotopic replacement preserving the heart by immersion in cold saline as they did with allografts and using the same bi-atrial implantation technique. This model provided an opportunity to assess the denervated heart out beyond two years. The re-implanted hearts functioned well and showed no tendency towards chronic degeneration. Sympathetic and parasympathetic innervation of the heart typically reappeared after two years.[152] As of 1964, enough was known from animal work and inferred from clinical renal allografts to consider transplanting a human donor heart into a recipient with end-stage CHF.

The 37 days from December 3, 1967 to January 9, 1968 witnessed three surgeons transplanting five human hearts.[153] Three recipients died within hours, and the two survivors lived for 18 and 15 days, dying of pneumonia in the first instance and of multiple complications in the second. The recipients were among the sickest of patients, ranging in age from 18 days to 57 years, with Adrian Kantrowitz being the surgeon responsible for both the youngest and



Norman Shumway(inset & at patient's left) performing first successful adult US heart transplant with Edward Stinson, January 7, 1968
Lane Medical Archives, Stanford University Medical Center

Barnard, DeBakey, and Kantrowitz CBS-Face the Nation 1967

the oldest. Immunosuppression was extrapolated from dog kidney data and probably was more aggressive than it needed to be, contributing to the two late deaths. Christiaan Barnard's "First Ever" captured most of the attention of the press, with the other two surgical teams wishing that he had garnered it all.

Richard Lower had been recruited to the Medical College of Virginia by David Hume in 1965 to extend Hume's respected renal transplant program to include hearts.[154] Lower performed his first human heart transplant in May 1968, obtaining the heart from a black man with an unsurvivable head injury. The recipient lived for only a few days. The donor's family, who could not be located when the donor was about to die, instituted a multi-million-dollar, Tucker vs. Lower suit, and the Commonwealth of Virginia charged him with murder. The press brought race into play, based on Barnard's first donor also being black, and both recipients being Caucasians. Defining death, based on brain rather than heart function, started state-by-state in 1970. Lower was exonerated in 1972, but brain death would not be uniformly accepted until the early 1980s.

By the end of October 1968, 65 allotransplants had been performed, and just 32 were alive, causing most groups to pause, or quit. These were generally good decisions because it was not necessary for multiple surgeons and, particularly, for an expanded number of patients, to go through the near-term travails. Shumway's group was one of few in the world that pressed on. In 1973, they introduced endocardial biopsy to detect rejection before ECG amplitude reduction and monitor the effectiveness of its treatment. They were early users of cyclosporine for cardiac grafts, beginning in 1980, and OKT3 (mouse anti-human CD3 monoclonal antibody) in 1987. Shumway and Bruce Reitz performed the first successful human heart-lung transplant in 1981.[155] Shumway remained observant and respectful of the work of others, even abandoning his time-honored Cass-Brock,[156] Lower[157] bi-atrial implantation for Sievers' less tricuspid-annulus distorting, bi-caval technique in 1992.[158]

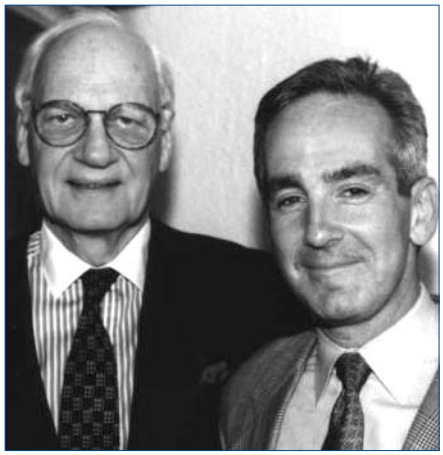
Keith Reemtsma returned to Columbia, as chairman, in 1971 and stimulated interest in cardiac xenografts and rat transplant models but did not encourage clinical heart allografting until 1977[159]. The program would do less than 20 grafts a year for the 6 years before cyclosporine became available. By year 10, Columbia surgeons were doing more than 50 transplants per year and by year 20 they had implanted 937 cardiac allografts, including 23 that were heart-lung transplants, with an overall 1-year survival of 80% and 60% for 5 years.[160] These results were not substantially different from those reported in Stanford's 30-year experience with 954 transplants in 885 patients.[161]

Donor allocation has cardiac-specific limitations that are aggravated by an ever broadening demand-supply disparity. A maximum cold ischemia time of 4 to 5 hours has so far precluded human lymphocyte antigen (HLA) matching, even though it is known that mismatching affects short-term survival in dogs and is associated, clinically, with both fatal rejection and accelerated graft atherosclerosis.[162, 163] There is some promise that preservation with normothermic whole blood perfusion might extend the safe time and allow HLA matching to be included in allocation.

Current matching is based on urgency, height and weight differences, and ABO compatibility (not identity), which is sometimes abrogated in infants, as their antibody titers against A or B are usually low. The introduction of tacrolimus as an alternate to cyclosporine in 1994 and mycophenlate mofetil as another purine synthesis inhibitor should further extend survival. Having a choice within the various classes of drugs has allowed patient-specific tailoring, but chronic immunosuppression is still associated with proclivity to infections and lympho-proliferative and cutaneous malignancies. Malignancies and allograft vasculopathy are the leading causes of death in long-term survivors. [164]

Xenotransplantation

Eric Rose assumed Columbia's Chair of Surgery in 1994, ensuring that Reemtsma's interest in xenografts as a future means of meeting organ replacement demand would remain on the front burner for another 14 years.[165] The potential for cardiac xenografting currently lags well behind implantable mechanical assist devices for both temporary bridging to allotransplantation and for life-long "destination" use. Should the balance shift, Dr. Rose will still be on the winning side, as he has a foot firmly planted in both camps.


Keith Reemtsma and Eric Rose

Only four instances of baboon- or chimpanzee-to-human cardiac xenografting have been reported: two adult recipients died within hours without the stigma of hyperacute rejection. James Hardy's (1918-2003) January 23, 1964 chimpanzee graft was the first clinical, Christian-era, heart transplant.[166] It supported an adult patient for 4 days and showed the infiltrates that Mann and his colleagues had observed in 1933, implying it had undergone cell-mediated rejection. The 4th graft was from an ABO incompatible baboon, which marginally supported an infant recipient for 21 days. It was found not to have a lymphocyte infiltrate and may have undergone humeral rejection.

Hyperacute rejection requires pre-formed antibodies to a donor antigen as well and their sufficient collocation to trigger complement binding. This suggests that dilution, antibody absorption, blocking its synthesis, and antigen deletion as candidate strategies for preventing it. The major target of natural IgM and IgG primate antibodies to pig tissue is the terminal carbohydrate epitope, Galactose α(1,3)Galalactose (Galα1,3Gal).[167] Galα1,3Gal is formed by α1,3galactosyl transferase linking the two galactose molecules together. Galα1,3Gal is highly expressed in pig endothelial cells and, hence, readily available for collocation and complement binding. Colonies of genetically engineered α1,3galactosyl transferase gene-knockout (GalT-KO) pigs have existed since 2003. GalT-KO pig hearts do not undergo hyperacute rejection by baboons but are still vulnerable to acute humeral rejection. Heterotopic, non-working cardiac grafts from these pigs, combined with administration of a Gal analog to soak up antiGal antibodies, have survived in baboons for up to 6 months. When they failed, it was from microangiopathic ischemia without features of acute humeral rejection, suggesting a move towards development of GalT-KO pigs that are also transgenic for primate anti-thrombotic genes.

Mechanical Circulatory Support

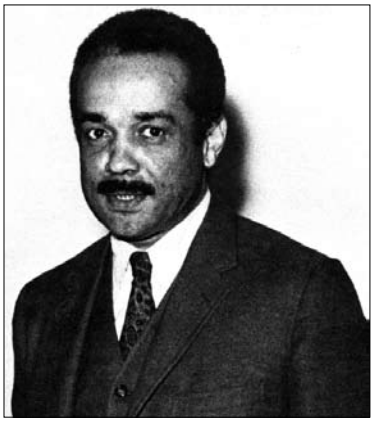
Mechanical circulatory support is prototypical Americana, combining Yankee ingenuity, Confederate know how, and injection of a talented Dutch immigrant. It encompasses intermittent intra-aortic balloon inflation for short-term support, devices designed to mimic the actions of the heart's ventricles, and pulseless spinners. Dwight Harken was among the first to think about treating a failing or faltering LV by timing withdrawal and reinjection of arterial blood to coincide, respectively, with the onsets of systole and dias-

tole. Withdrawal decreased after load, lessening stroke work, and maybe even increasing the EF, and the reinjection increased diastolic pressure to enhance coronary perfusion. Adrian Kantrowitz[168] designed an intra-aortic balloon to accomplish the same thing with a less bulky controller and a thinner insertion profile that has been the most used circulatory assist device for nearly 40 years.

The pedigree of ventricular assist devices and total artificial hearts is difficult to follow because of many parallel activities, but Willem Johan Kolff[169] (1911-2009), who had worked on developing a successful dialysis machine in Nazi occupied Holland, Bertram Kusserow, Domingo Liotta, and William Pierce appear to be the real pioneers. Kusserow developed several lever-activated, implantable pumps, beginning in 1958 at Yale, then at the University of Vermont. His most innovative model was reported in 1960.[170] It was powered by an external rotating magnet worn in a vest affixed to the dog's chest that allowed the pump to be completely isolated within the body.

Kolff came to the US, in 1950, to go to the Cleveland Clinic, specifically, to develop a total artificial heart (TAH). Over the next decade, he produced several prototypes that were implanted in dogs.[171] Keith Reemtsma lured him away in 1967 to head the University of Utah's Institute for Bioengineering. Argentine Dominigo Liotta began working on a TAH in 1958, in Lyon, France and then continued his work at the University of Cordoba, in Argentina, where he was joined by his brother Salvador in doing hundreds of TAH animal experiments. That came to a halt in 1961, when DeBakey recruited Domingo to Houston. DeBakey directed him to forego the more problematic TAH and develop a left ventricular assist device (LVAD).

Within a year, Liotta had a working, coaxial-tube LVAD. The inner tube had a thin walled flexible segment with unidirectional valves at both ends and extensions beyond them for sewing. The outer tube had thicker walls, with sealed ends, bonded to the inner tube around its valve sites, and fitted with a side arm for the admission of air to repetitively compress the valve bracketed inner segment. Blood was taken from the left atrium and delivered to the ascending aorta. In 1962, Liotta[172] was able to report LVAD pump runs up to 44 hours in 47 dogs. Future Jacobson Innovation Award winner, William S. Pierce,[173] then at the University of Pennsylvania, reported his early TAH experience at the same meeting. His pump runs were noticeably shorter, since the dogs' chests remained open. He remarked upon the difficulty in balancing flow in the two sides of the heart. Both men would later turn to calves; Pierce would go to Pennsylvania State University, at Hershey and eventually develop an electrically driven, pulsatile TAH. Liotta[174] implanted his LVAD in a patient who could not be weaned from bypass in 1963 and would work covertly on a TAH with Denton Cooley at the Texas Heart Institute, while maintaining his "day job" with DeBakey at Baylor.[175]


Jack Norman in his pre-Cooley Harvard faculty days.[177]

Adrian Kantrowitz (1918-2008) and his engineering scientist brother Arthur (1913-2008) designed their own LAVD, which Adrian implanted in two patients early in 1966, one of whom survived for 12 days. Liotta added a velour "pseudo-endocardium" to make his LVAD more thromboresistant, and DeBakey implanted it in a patient who could not be weaned from bypass in August 1966. This was a stunning success: her heart recovered to be self sustaining over 10 days, the LVAD was removed, and she was discharged after another week of observation.

Cooley persuaded an engineer, who was working in a combined Baylor-Rice program, to do some off hour work on a power console for Liotta. The TAH that resulted comprised two air-driven reciprocating pumps made of Dacron-impregnated silastic and activated by dual external power units. Liotta began testing it in calves in January 1969. In March, Cooley implanted the Baylor indirectly funded TAH as a bridge to allografting, while DeBakey was attending a National Institutes of Health artificial heart meeting, creating a rift that persisted until 2007. John C. Norman, Jr. joined Cooley in 1972 and developed the first abdominal LVAD.[176] Jack Norman and Cooley used this device until 1978. Norman was the founding editor the Texas Heart Institute Journal and later chaired the Department of Surgery at Marshall University, in West Virginia.[177]

The Jarvik 7 Heart

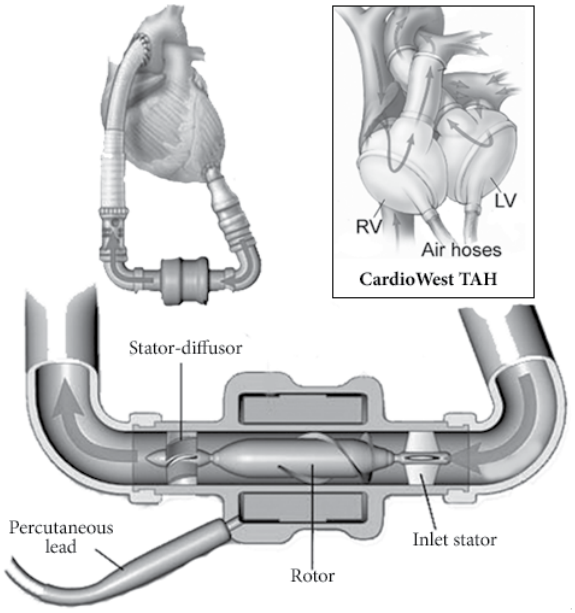
Physician and bioengineer, Robert Jarvik, joined Kolff's group in 1970. Kolff was working on both pneumatically and electrically driven TAHs, and Jarvik tipped the balance towards the former. Twelve years, $160 million in Federal funding, many long-surviving calves, and six design iterations later, William Devries implanted the "Jarvik 7" in a patient with no intention of replacing it in December 1982.[178] The Jarvik 7 had two double walled polycarbonate ventricles that were fitted with inflow and outflow Björk-Shiley tilting disc valves. Implanting it mimicked putting in an allograft but took more than twice the time. Post operatively, there were many complications, including strut fracture of the "mitral" Björk-Shiley valve on day 13, which was heralded by massive pulmonary edema, necessitating its immediate replacement. The patient died on the 112th postoperative day. Devries moved to Louisville's Humana Hospital and did three more Jarvik 7 destination implants that were less complicated, with one patient surviving for 2 years. The lifestyle had to be foreboding and the cost was enormous, leading both the profession and the public to view life-long TAH dependence as gruesome and amoral.

Cardiac Transplantation: Any Role Left? [179]

Martin Cadeiras and his colleagues could have included *The Audacity of Hope*[††] as a subtitle for their 2007 article, but a sea change had clearly transpired in the quarter century preceding its publication. First, DeBakey was right about an LVAD being less problematic than a TAH.[180] LVAD use, as a bridge to allotransplantation, has shown that more than 90% of patients have sufficient RV function to benefit from LV augmentation alone.[181] This might have been predicted, from François Fontan's[182] success with his 1971 RV bypasses and that of their follow-on, valveless, cavopulmonary conduits in patients with good [or well supported] single ventricle function.[183]

Jarvik was wrong in favoring a pneumatic drive: it requires a bulkier console and a thicker transmural connection that has a tendency to lurch, inviting infection along its tract.[184] Jarvik's widely used LVAD, which supported a patient for more than 7 years,[§] en-

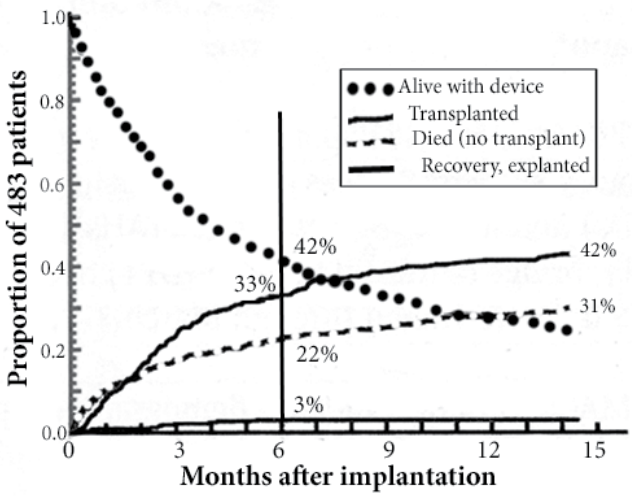
[††] Obama BH. The Audacity of Hope: Thoughts on Reclaiming the American Dream. New York: Random House; 2006.
§ British clinical psychologist, Peter Houghton shared his personal perspective: Houghton P. Living with the Jarvik 2000: a five-plus year experience. Artif Organs 2006;30:322-3. Mr. Houghton died on Nov 25, 2007



Electrically driven HeartMate II® LVAD[188] and CardioWest™ [Jarvik] TAH (insert) with dual air hose conections.

dorses this concept.[185] Yet, his TAH design, which is a refinement of the device implanted in 1982, remains pneumatically driven.[186] Electric pumps can produce pulsatile flow with push plates and even wireless energy transmission, but LV augmentation does not need to be pulsed, allowing for simpler designs with a wear-free magnetically suspended rotor as their only moving part.[187, 188, 189] Longer periods of non-pulsatile LVAD bridging simply require awareness that higher doses of pressors will be needed to support transitioning to pulsed flow when the allograft is installed.[190] A substantial portion of this sea roiling knowledge is based on pivotal studies, initiated by physicians and surgeons who are, or were, associated with the Columbia University Medical Center.[191]

Eric Rose and his colleagues'[192] *Long-term use of a left ventricular assist device for end-stage heart failure* was the bellwether for clinical trials of LVAD destination use. The study randomized more than 100 NYHA Class IV patients, who were ineligible for allografting, to receive a left ventricular assist device and OMT or OMT alone. Use of the device offered a significant two-fold survival



INTERMACS interim data adapted from abstract for December 2008, Southern Surgical Association presentation[180]

advantage at 1 year and better quality of life that were partially offset by nearly three times more morbidity and mortality over 2 years, largely attributable to infections and mechanical failures. When all patients had passed the 2-year mark, the significant two-fold survival advantage extended out to two years.[193]

Annetine Gelijns' group[194] endorsed the NIH sponsored Interagency Registry of Mechanically Assisted Circulatory Support (INTERMACS) devices in 2006, which is now underway.[195] The registry attempts to include all FDA approved LVAD and TAH uses for bridging to transplantation or heart recovery and as destination therapy. As of March 31, 2008, 94 sites have prospectively enrolled 483 patients. Bridging to transplantation was the predominant treatment strategy, accounting for 80% of enrollees. Support-free recovery was anticipated for 5%, and 15% were designated as permanent implants. The 6-month outcomes are shown in the figure for all enrollees, with proportionally more transplants and deaths without transplantation occurring in patients who had progressed beyond 6 months. As anticipated, central nervous system events and cardiovascular, or respiratory, failure were associated with the majority of the deaths.

The most welcome and cost effective outcome of prolonged LVAD support is for the native heart to undergo positive remodeling and recover sufficient competence to sustain an independent reasonable life style. Birks and her Imperial College, Royal Brompton, and Harefield National Health Service Trust colleagues already have a foot in this door.[196] They have reported that LVAD support for a mean of 320 days allowed 11 of 15 carefully selected patients with non-ischemic cardiomyopathy to recover sufficient myocardial function to have their LVADs removed. Their subsequent freedom from recurrent heart failure was 100% at 1 year and 89% at 4 years with near normal quality of life assessments. Remodeling was assisted by reducing after load with ACE inhibitors, beta-blockers and spironolactone, until diastolic volume reached a stable minimum. Then a β2 receptor agonist was introduced to promote modest myocyte hypertrophy in conjunction with a selective β1 receptor blocker to keep heart rates less than 100 beats per minute.

Endothelial and cardiomyocyte progenitor cell therapy could extend LVAD protected remodeling to patients with ischemic cardiomyopathy.[197] In some instances, the process might need to be jumpstarted by preliminary mitral annulus tightening, scar excision, or ellipsoidal reshaping. Ongoing studies of the intracellular signaling that modulates both the development of dilated myocardiopathy and its reversibility are approaching a level that should lead to therapeutic interventions.[198] Growing new vessels, repopulating myocytes along with cells that foster electrical coupling, and manipulating intracellular events to promote contractility and diminish apoptosis might flip current INTERMACS outcome ratios towards a dramatic increase in successful bridging to sustainable recovery.[199]

References: Blue indicates CUMC and its antecedents

Fin de Siècle Beginnings

1. Harken AH. The phenotype of the cardiothoracic surgeon. John H. Gibbon, Jr. Lecture. J Am Coll Surg 2009; 209:(in press).

2. Chandler JG, Novak SE, Forde KA. Big (Brick and mortar) names on campus. John Jones Surgical Society News Letter 2007;10:6-7.

3. Dietrich H, Dietrich B. Ludwig Rehn (1849-1930) – pioneering findings on the aetiology of bladder tumors. World J Urol 2001;19:151-3.

4. Paget S. Surgery of the Chest: Chapt X, Wounds of the Heart. New York: E.B. Treat; 1897. p.121.

5 . Skandalakis JE, Mirilas P. Nihilism: a benign denial. World J Surg 2003;27:748-52.

6. Samways DW. The left auricle in mitral stenosis: hypertrophy and dilatation Br Med J 1896;2:1567-68.

7. Milton H. Mediastinal surgery. Lancet 1897;149:872-5.
Sorties and Push Backs

8. Cutler EC, Levine SA. Cardiotomy and valvulotomy for mitral stenosis. Experimental observations and clinical notes concerning an operated case with recovery. Boston Med Surg J 1923;188:1023-7.

9. Souttar HS. The surgical treatment of mitral stenosis. The Br Med J 1925;2:603-6.

10. Comas GM, Widmann WD, Hardy MA. The legacy of Sir Henry Souttar: pioneer of the first mitral valvulotomy. Curr Surg 2006;63:476-81.

11. Bloomfield, RA, Lauson HD, Cournand, A, Breed, ES. Richards, DW JR. Recording of right heart pressures in normal subjects and in patients with chronic pulmonary disease and various types of cardio-circulatory disease. J Clin Invest 1946;25:639-64.

12. Smithy HG, Boone JA, Stallworth JM. Surgical treatment of constrictive valvular disease of the heart. Surg Gynecol Obstet 1950;90:175-92.

13. Bailey, C. P. The surgical treatment of mitral stenosis (mitral commissurotomy). Dis Chest 1949;15:377-97.

14. Harken DE, Ellis LB, Ware PF, Norman LR. The surgical treatment of mitral stenosis; valvuloplasty. N Engl J Med 1948;239:801-9.

15. Rainer WG. Pioneer interviews: Dwight Emary Harken, April 12, 1973. http://www.ctsnet.org/sections/residents/pioneerinterviews/article-1.html

16. Ferrer MI, Harvey RM, Cathcart RT, Cournand A, Richards, DW. Hemodynamic studies in rheumatic heart disease. Circulation 1952; 6: 688-710.

17. Ferrer MI, Harvey RM, Wylie RH, Himmelstein A, Lambert A, Kuschner M, et al. Circulatory effects of mitral commissurotomy with particular reference to selection of patients for surgery. Circulation 1955;12:7-29.

18. Forssmann-Falck R. Werner Forssmann: a pioneer of cardiology. Am J Cardiol 1997; 79:651-60.

19. Chandler JG, Novak SE. The pre-renaissance evolution of vascular surgery. John Jones Surgical Society News Letter 2008;11:8.

20. Gross RE, Hubbard JP. Surgical ligation of a patent ductus arteriosis; report of first successful case. J Am Med Assoc 1939;112:729-31.

21. Moore FD, Folkman J. Robert Edward Gross. http://www.nap.edu/reading-room.php?book=biomems&page=rgross.html

22. Clyman RI, Chorne N. Patent ductus arteriosus: evidence for and against treatment. J Pediatr 2007;150:216-9.

23. Shumacker HB Jr. The Evolution of Cardiac Surgery. Bloomington: Indiana University Press; 1984 p.43-4.

24. Ibid; p.67.

25. Wigh R. Paul C. Swenson (1901-1962) Radiology 1963;80:688-9.

26. Eppinger EC, Burwell CS, Gross RE. The effects of the patent ductus arteriosus on the circulation. J Clin Invest 1941;20:127-43.

27. Blalock A, Taussig HB. The surgical treatment of malformations of the heart in which there is pulmonary stenosis or pulmonary atresia. J Am Med Assoc 1945;128:189-202.

28. Thomas VT. Partners of the Heart: Vivien Thomas and His Work with Alfred Blalock: An Autobiography. Philadelphia: University of Pennsylvania Press; 1998.

29. McNamara DG. The Blalock-Taussig operation and subsequent progress in surgical treatment of cardiovascular diseases. JAMA 1984;251:2139-41.

30. Muller WH Jr, Dammann, JR Jr. Treatment of certain congenital malformations of the heart by the creation of pulmonic stenosis to reduce pulmonary hypertension and excessive pulmonary blood flow: a preliminary report. Surg Gynecol Obstet 1952;95:213-9.

31. Goldblatt A, Bernhard WF, Nadas AS, Gross RE. Pulmonary artery banding: indications and results in infants and children. Circulation 1965;32:172-84.

"Waiting for Godot"

32. Pastuszko P, Edie RN. John H. Gibbon, Jr., the inventor of the first successful heart-lung machine. J Card Surg 2004;19:65-73.

33. Gibbon JH Jr. Artificial maintenance of the circulation during experimental occlusion of the pulmonary artery. Arch Surg 1937;34:1105-31.

34. Hufnagel CA, Harvey WP, Rabil PJ, McDermott TF. Surgical correction of aortic insufficiency. Surgery 1954;35:673-83.

35. Hufnagel CA, Villegas PD, Nahas H. Experiences with new types of aortic valvular prostheses. Ann Surg 1958;147:636-44.

36. Murray G. Aortic valve transplants. Angiology 1960;11:99-102.

37. Bailey CP, Downing DF, Geckeler GD, Likoff W, Goldberg H, Scott JC, et al. Congenital interatrial communications: clinical and surgical considerations with a description of a new surgical technic: atrio-septo-pexy. Ann Intern Med 1952;37:888-920.

38. Gross RE, Pomeranz AA, Watkins E Jr, Goldsmith EI. Surgical closure of defects of the interauricular septum by use of an atrial well. N Engl J Med 1952;247:455-60.

39. Bigelow WG, Lindsay WK, Greenwood WF. Hypothermia; its possible role in cardiac surgery: an investigation of factors governing survival in dogs at low body temperatures. Ann Surg 1950;132:849-66.

40. Lewis FJ, Varco RL, Taufic M. Repair of atrial septal defects in man under direct vision with the aid of hypothermia. Surgery 1954;36:538-56.

41. Dennis C, Spreng DS Jr, Nelson GE, Karlson KE, Nelson RM, Thomas JV, et al. Development of a pump-oxygenator to replace the heart and lungs; an apparatus applicable to human patients, and application to one case. Ann Surg 1951;134:709-21.

42. Swan H. Zeavin I, Blount SG Jr, Virtue RW. Surgery by direct vision in the open heart during hypothermia. J Am Med Assoc 1953;153:1081-5.

43. DeBakey ME. John Gibbon and the heart-lung machine: a personal encounter and his import for cardiovascular surgery. Ann Thorac Surg 2003;76:S2188-94.

44. Miller BJ, Gibbon JH Jr, Gibbon MH. Recent advances in the development of a mechanical heart and lung apparatus. Ann Surg 1951;134:694-708.

45. Gibbon JH Jr. Application of a mechanical heart and lung apparatus to cardiac surgery. Minn Med 1954;37:171-85.

46. Gibbon JH Jr. The development of the heart-lung apparatus. Am J Surg 1978;135:608-19.

47. DeWall RA, Warden HE , Gott VL, Read RC, Varco RL, Lillehei CW. Total body perfusion for open cardiotomy utilizing the bubble oxygenator; physiologic responses in man. J Thorac Surg 1956;32:591-603.

48. Cohen M, Lillehei CW. A quantitative study of the "Azygos Factor" during vena caval occlusion in the dog. Surg Gynecol Obstet 1954;98:225-32.

49. Lillehei CW, Cohen M, Warden HE, Varco RL. The direct-vision intracardiac correction of congenital anomalies by controlled cross circulation; results in thirty-two patients with ventricular septal defects, tetralogy of Fallot, and atrioventricularis communis defects. Surgery 1955;38:11-29.

50. Melrose DG, Dreyer B, Bentall HH, Baker JBE. Elective cardiac arrest. Lancet 1955;2:21-2.

51. Gerbode F, Melrose D. The use of potassium arrest in open cardiac surgery. Am J Surg 1958;96:221-7.

52. Osborn JJ, Gerbode F, Perkins H, Braimbridge M, Melrose D, Kahn P. A disposable filming pump-oxygenator; experimental and clinical use in 70 patients. J Thorac Surg 1959;37:472-81.

53. Merendino KA, Bruce RA. One Hundred and Seventeen Surgically Treated Cases of Valvular Rheumatic Heart Disease with Preliminary Report of Two Cases of Mitral Regurgitation Treated Under Direct Vision with the Aid of a Pump-Oxygenator. J Am Med Assoc 1957;164:749-55.

54. Sones FM Jr, Shirey EK. Cine coronary arteriography. Mod Concepts Cardiovasc Dis 1962;31:735-8.

55. Senning Å. Surgical correction of transposition of the great vessels. Surgery 1959;45:966-980.

56. Rainer WG. Pioneer interviews: Åke Senning, November 14, 1979. http://www.ctsnet.org/sections/residents/pioneerinterviews/article-9.html

57. Hörer J, Schreiber C, Cleuziou J, Vogt M, Prodan Z, Busch R, et al. Improvement in long-term survival after hospital discharge but not in freedom from reoperation after the change from atrial to arterial switch for transposition of the great arteries. J Thorac Cardiovasc Surg 2009;137:347-54.

58. Grüntzig AR, Senning Å, Siegenthaler WE. Nonoperative dilatation of coronary-artery stenosis. N Engl Med 1979;301:61-8.

59. Himmelstein A, Jameson AG, Fishman AP, Humphreys GH 2nd. Closed transventricular valvulotomy for pulmonic stenosis; description of a new valvulotome and results based on pressures during operation. Surgery 1957;42:121-31.

60. Weintraub HD, Sullivan SF, Malm JR, Bowman FO Jr, Papper EM. Lung function and blood-gas exchange, before and after cardiac surgery. J Appl Physiol 1965;20:483-7.

61. Malm JR, Blumenthal S, Bowman FO Jr, Ellis K, Jameson AG, Jesse MJ, Yeoh CB. Factors that modify hemodynamic results in total correction of tetralogy of Fallot. J Thorac Cardiovasc Surg 1966;52:502-13.

62. Leonard RJ. The transition from the bubble oxygenator to the microporous membrane oxygenator. Perfusion 2003;18:179-83.

63. King TD, Mills NL. Non-operative closure of atrial septal defects. Surgery 1974;75:383-8.

64. Mills NL, King TD. Late follow-up of nonoperative closure of secundum atrial septal defects using the King-Mills double-umbrella device. Am J Cardiol 2003;92:353-5.

How Long Will My New Heart Valve Last?

65. Braunwald NS, Cooper T., Morrow AG. Complete replacement of the mitral valve: successful clinical application of a flexible polyurethane prosthesis. J Thorac Cardiovasc Surg 1960;40:1-11.

66. Braunwald NS. It will work: the first successful mitral valve replacement. Ann Thorac Surg 1989;48(3 Suppl):S1-3.

67. Starr A. The artificial heart valve. Nature Medicine 2007;13:1160-4.

68. Starr A, Edwards ML. Mitral replacement: clinical experience with a ball-valve prosthesis. Ann Surg 1961;154:726-40.

69. Harken DE, Soroff HS, Taylor WJ, Lefemine AA, Gupta SK, Lunzer S. Partial and complete prostheses in aortic insufficiency. J Thorac Cardiovasc Surg 1960;40:744-62.

70. Starr A, Edwards ML, McCord. CW, Griswold HE. Aortic replacement: experience with a semirigid ball-valve prosthesis. Circulation 1963;27:779-83.

71. Clauss RH, Birtwell WC, Albertal G, Lunzer S, Taylor WJ, Fosberg AM, Harken DE. Assisted circulation I. The arterial counterpulsator. J Thorac Cardiovasc Surg 1961;41:447-58

72. Webb JG, Pasupati S, Humphries K, Thompson C, Altwegg L, Moss R, et al. Percutaneous transarterial aortic valve replacement in selected high-risk patients with aortic stenosis. Circulation 2007;116:755-63.

73. Gao G, Wu Y, Grunkemeier GL, Furnary AP, Starr A. Forty-year survival with the Starr-Edwards heart valve prosthesis. J Heart Valve Dis 2004;13:91-6.

74. Emery RW, Krogh CC, Arom KV, Emery AM, Benyo-Albrecht K, Joyce LD, Nicoloff DM. The St. Jude Medical cardiac valve prosthesis: a 25-year experience with single valve replacement. Ann Thorac Surg 2005;79:776-82.

75. Björk VO. A new tilting disc valve prosthesis. Scand J Thorac Cardiovasc Surg 1969;3:1-10.

76. Braunwald NS, Tatooles C, Turina M, Detmer D. New developments in the design of fabric-covered prosthetic heart valves. J Thorac Cardiovasc Surg 1971;62:673-81.

77. Blackstone EH, Kirklin JW, Pluth JR. The performance of the Braunwald-Cutter aortic prosthetic valve. Ann Thorac Surg 1977;23:302-18.

78. Lindblom D, Björk VO, Semb BK. Mechanical failure of the Björk-Shiley valve. Incidence, clinical presentation, and management. J Thorac Cardiovasc Surg 1986;92:894-907

79. Chandler JG, Hirsch JL, O'Neill WW, Oesterle SN, Miller DC, Kennedy JA, Faichney A. Radiographic detection of single strut leg separations as a putative basis for prophylactic explantation of Björk-Shiley convexo-concave heart valves. World J Surg 1996;20:953-9.

80. Blot WJ, Ibrahim MA, Ivey TD, Acheson DE, Brookmeyer R, Weyman A, et al. Twenty-five-year experience with the Björk-Shiley convexoconcave heart valve: a continuing clinical concern. Circulation 2005;111:2850-7.

81. Ross DN. Homograft replacement of the aortic valve. Lancet 1962;2:487.

82. Ross DN. Replacement of aortic and mitral valves with a pulmonary autograft. Lancet 1967;2:956-8.

83. Stelzer P, Jones DJ, Elkins RC. Aortic root replacement with pulmonary autograft.Circulation 1989;80:III209-13.

84. Takkenberg JJ, Klieverik LM, Schoof PH, van Suylen RJ, van Herwerden LA, Zondervan PE, et al. The Ross procedure: a systematic review and meta-analysis. Circulation 2009;119:222-8.

85. Carpentier A. The surprising rise of nonthrombogenic valvular surgery. Nature Medicine 2007;13:1165-8.

86. Puvimanasinghe JP, Takkenberg JJ, Eijkemans MJ, Steyerberg EW, van Herwerden LA, Grunkemeier GL, et al. Prognosis after aortic valve replacement with the Carpentier-Edwards pericardial valve: use of microsimulation. Ann Thorac Surg 2005;80:825-31.

87. Craver JM, Jones EL, McKeown P, Bone DK, Hatcher CR Jr, Kandrach M. Porcine cardiac xenograft valves: analysis of survival, valve failure, and explantation. Ann Thorac Surg 1982;34:16-21.

88. Meng X, Ao L, Song Y, Babu A, Yang X, Wang M, et al. Expression of functional Toll-like receptors 2 and 4 in human aortic valve interstitial cells: potential roles in aortic valve inflammation and stenosis. Am J Physiol Cell Physiol 2008;294:C29-35.

89. Carpentier A, Deloche A, Dauptain J, Soyer R, Blondeau P, Piwnica A, et al. A new reconstructive operation for correction of mitral and tricuspid insufficiency. J Thorac Cardiovasc Surg 1971;61:1-13.

90. Carpentier A. Cardiac valve surgery--the "French correction". J Thorac Cardiovasc Surg 1983;86:323-37.

91. David TE, Bos J, Rakowski H. Mitral valve repair by replacement of chordae tendineae with polytetrafluoroethylene sutures. J Thorac Cardiovasc Surg 1991;101:495-501.

92. Perier P, Hohenberger W, Lakew F, Batz G, Urbanski P, Zacher M, Diegeler A. Toward a new paradigm for the reconstruction of posterior leaflet prolapse: midterm results of the "respect rather than resect" approach. Ann Thorac Surg 2008;86:718-25.

93. Loulmet DF, Carpentier A, Cho PW, Berrebi A, d'Attellis N, Austin CB, et al. Less invasive techniques for mitral valve surgery. J Thorac Cardiovasc Surg 1998 ;115:772-9.

94. Nifong LW, Chitwood WR, Pappas PS, Smith CR, Argenziano M, Starnes VA, Shah PM. Robotic mitral valve surgery: a United States multicenter trial. J Thorac Cardiovasc Surg 2005;129:1395-404.

95. Chitwood WR Jr, Rodriguez E, Chu MW, Hassan A, Ferguson TB, Vos PW, Nifong LW. Robotic mitral valve repairs in 300 patients: a single-center experience. J Thorac Cardiovasc Surg 2008;136:436-41.

96. Boodhwani M, de Kerchove L, Glineur D, Poncelet A, Rubay J, Astarci P, et al. Repair-oriented classification of aortic insufficiency: Impact on surgical techniques and clinical outcomes. J Thorac Cardiovasc Surg 2009;137:286-94.

Myocardial Revascularization

97. Carrel A. On the Experimental Surgery of the Thoracic Aorta and Heart. Ann Surg 1910;52:83-95(p93).

98. Beck CS. The development of a new blood supply to the heart by operation. Ann Surg 1935;102:801-13.

99. O'Shaughnessy L. Surgical treatment of cardiac ischæmia. Lancet 1937;229:185-94.

100. Beck CS, Stanton E, Batiuchok W, Leiter E. Revascularization of heart by graft of systemic artery into coronary sinus. J Am Med Assoc 1948;137:436-42.

101. McAllister FF, LeighningeR D, Beck CS. Revascularization of the heart by vein graft from aorta to coronary sinus. Ann Surg 1951;133:153-65.

102. Beck CS, Leighninger DS. Operations for coronary artery disease. Ann Surg 1955;141:24-37.

103. Vineberg AM. Development of an anastomosis between the coronary vessels and a transplanted internal mammary artery. Can Med Assoc J 1946;55:117-9.

104. Vineberg A. Coronary vascular Anastomoses by internal mammary artery implantation. Can Med Assoc J 1958;78:871-9

105. Fergusson DJ, Shirey EK, Sheldon WC, Effler DB, Sones FM Jr. Left internal mammary artery implant--postoperative assessment. Circulation 1968;37(4 Suppl):II24-6.

106. Katrapati P, George JC. Vineberg operation: a review of the birth and impact of this surgical technique. Ann Thorac Surg 2008;86:1713-6.

107. Garrett HE, Dennis EW, DeBakey ME. Aortocoronary bypass with saphenous vein graft. Seven-year follow-up. JAMA 1973;223:792-4.

108. Bailey CP, May A, Lemmon WM. Survival after coronary endarterectomy in man. J Am Med Assoc 1957;164:641-6.

109. Cannon JA, Barker WF, Kawakami IG. Femoral popliteal endarterectomy in the treatment of obliterative atherosclerotic disease. Surgery 1958;43:76-93.RGICAL

110. Longmire WP Jr, Cannon JA, Kattus AA. Direct-vision coronary endarterectomy for angina pectoris. N Engl J Med 1958;259:993-9.

111. Schlesinger MJ. An injection plus dissection study of coronary artery occlusions and anastomoses. Am Heart J 1938;15:528-68.

112. Sabiston DC Jr. The William F. Rienhoff, Jr. lecture. The coronary circulation. Johns Hopkins Med J 1974;134:314-29.

113. Effler DB, Groves LK, Sones FM Jr, Shirey EK. Endarterectomy in the treatment of coronary artery disease. J Thorac Cardiovasc Surg 1964;47:98-108.

114. Connolly JE. The history of coronary artery surgery. J Thorac Cardiovasc Surg 1978;76:733-44.

115. Connolly JE, Eldridge FL, Calvin JW, Stemmer EA. Proximal coronary-artery obstruction; its etiology and treatment by transaortic endarterectomy. N Engl J Med 1964;271:213-9.

116. Kolessov VI. Mammary artery-coronary artery anastomosis as method of treatment for angina pectoris. J Thorac Cardiovasc Surg 1967;54:535-44.

117. Westaby S, Bosher C. Landmarks In Cardiac Surgery. Oxford: Isis Medical Media Ltd; 1997. p.195.

118. Green GE, Stertzer SH, Gordon RB, Tice DA. Anastomosis of the internal mammary artery to the distal left anterior coronary artery Circulation 1970;41(5 Suppl):II79-85.

119. Jones JW, OchsnerJL, Mills NL, Hughes L. The internal mammary bypass graft: a superior second coronary artery. J Thorac Cardiovasc Surg 1978;75:625-31.

120. Cameron A, Davis KB, Green G, Schaff HV. Coronary bypass surgery with internal-thoracic-artery grafts--effects on survival over a 15-year period. N Engl J Med 1996;334:216-9.

121. Lytle BW, Blackstone EH, Sabik JF, Houghtaling P, Loop FD, Cosgrove DM. The effect of bilateral internal thoracic artery grafting on survival during 20 postoperative years. Ann Thorac Surg 2004;78:2005-12-4.

122. Ankeney JL. Off-pump bypass surgery: the early experience, 1969-1985. Tex Heart Inst J 2004;31:210-3.

123. Ankeney JL, Goldstein DJ. Off-pump bypass of the left anterior descending coronary artery: 23- to 34-year follow-up. J Thorac Cardiovasc Surg 2007;133:1499-1503.

124. Borst C, Jansen EW, Tulleken CA, Grundeman PF, Mansvelt Beck HJ, van Dongen JW, et al. Coronary artery bypass grafting without cardiopulmonary bypass and without interruption of native coronary flow using a novel anastomosis site restraining device ("Octopus"). J Am Coll Cardiol 1996;27:1356-64.

125. Argenziano M, Katz M, Bonatti J, Srivastava S, Murphy D, Poirier R, Loulmet D, et al. Results of the prospective multicenter trial of robotically assisted totally endoscopic coronary artery bypass grafting. Ann Thorac Surg 2006;81:1666-74.

126. Puehler T, Haneya A, Philipp A, Wiebe K, Keyser A, Rupprecht L, et al. Minimal extracorporeal circulation: an alternative for on-pump and off-pump coronary revascularization. Ann Thorac Surg 2009;87:766-72.

Circuit Breaking Surgery

127. Cobb FR, Blumenschein SD, Sealy WC, Boineau JP, Wagner GS, Wallace AG. Successful surgical interruption of of the bundle of Kent in a patient with Wolff-Parkinson-White syndrome. Circulation 1968;38:1018-29.

128. Cox JL, Jaquiss RD, Schuessler RB, Boineau JP. Modification of the maze procedure for atrial flutter and atrial fibrillation. II. Surgical technique of the maze III procedure. J Thorac Cardiovasc Surg 1995;110:485-95.

129. Melby SJ, Zierer A, Bailey MS, Cox JL, Lawton JS, Munfakh N, et al. A new era in the surgical treatment of atrial fibrillation: the impact of ablation technology and lesion set on procedural efficacy. Ann Surg 2006;244:583-92.

130. Callahan TD 4th, Di Biase L, Horton R, Sanchez J, Gallinghouse JG, Natale A. Catheter ablation of atrial fibrillation. Cardiol Clin 2009;27:163-78.

131. Topkara VK, Williams MR, Cheema FH, Vigilance DW, Garrido MJ, Russo MJ, et al. Surgical ablation of atrial fibrillation: the Columbia Presbyterian experience. J Card Surg 2006;21:441-8.

132. Likoff W, Bailey CP. Ventriculoplasty: excision of myocardial aneurysm; report of a successful case. J Am Med Assoc 1955;158:915-20.

133. Cox JL. Patient selection criteria and results of surgery for refractory ischemic ventricular tachycardia. Circulation 1989;79(Suppl I):I162-77.

134. Josephson ME, Harken AH, Horowitz LN. Endocardial excision: a new surgical technique for the treatment of recurrent ventricular tachycardia. Circulation 1979;60:1430-9.

135. Herzog E, Aziz EF, Kukin M, Steinberg JS, Mittal S. Novel pathway for sudden cardiac death prevention. Crit Pathw Cardiol 2009;8:1-6.

Chronic Heart Failure: Making the Best of What You Have

136. Anand IS, Carson P, Galle E, Song R, Boehmer J, Ghali JK, et al. Cardiac resynchronization therapy reduces the risk of hospitalizations in patients with advanced heart failure: results from the Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure (COMPANION) trial. Circulation 2009;119:969-77.

137. Schächinger V, Erbs S, Elsässer A, Haberbosch W, Hambrecht R, Hölschermann H, et al for the REPAIR-AMI Investigators. Improved clinical outcome after intracoronary administration of bone-marrow-derived progenitor cells in acute myocardial infarction: final 1-year results of the REPAIR-AMI trial. Eur Heart J 2006;27:2775-83.

138. Dill T, Schächinger V, Rolf A, Möllmann S, Thiele H, Tillmanns H, et al. Intracoronary administration of bone marrow-derived progenitor cells improves left ventricular function in patients at risk for adverse remodeling after acute ST-segment elevation myocardial infarction: results of the Reinfusion of Enriched Progenitor cells And Infarct Remodeling in Acute Myocardial Infarction study (REPAIR-AMI) cardiac magnetic resonance imaging substudy. Am Heart J 2009;157:541-7.

139. Chachques JC, Jegaden OJ, Bors V, Mesana T, Latremouille C, Grandjean PA, et al. Heart transplantation following cardiomyoplasty: a biological bridge. Eur J Cardiothorac Surg 2008;33:685-90.

140. Furnary AP, Chachques JC, Moreira LF, Grunkemeier GL, Swanson JS, Stolf N, et al. Long-term outcome, survival analysis, and risk stratification of dynamic cardiomyoplasty. J Thorac Cardiovasc Surg 1996;112:1640-9.

141. Starling RC, Jessup M, Oh JK, Sabbah HN, Acker MA, Mann DL, Kubo SH. Sustained benefits of the CorCap Cardiac Support Device on left ventricular remodeling: three year follow-up results from the Acorn clinical trial. Ann Thorac Surg 2007;84:1236-42.

142. Klodell CT Jr, Aranda JM Jr, McGiffin DC, Rayburn BK, Sun B, Abraham WT, et al. Worldwide surgical experience with the Paracor HeartNet cardiac restraint device. J Thorac Cardiovasc Surg 2008;135:188-95.

143. Athanasuleas CL, Buckberg GD, Stanley AW, Siler W, Dor V, Di Donato M, et al for the RESTORE group. Surgical ventricular restoration in the treatment of congestive heart failure due to post-infarction ventricular dilation. J Am Coll Cardiol 2004;44:1439-45.

144. Di Donato M, Castelvecchio S, Kukulski T, Bussadori C, Giacomazzi F, Frigiola A, Menicanti L. Surgical ventricular restoration: left ventricular shape influence on cardiac function, clinical status, and survival. Ann Thorac Surg 2009;87:455-61.

Transplantation

145. Kahan BD. Pien Ch'iao. The legendary exchange of hearts, traditional Chinese medicine, and the modern era of cyclosporine. Transplant Proc 1988;20(2 Suppl 2):2-12.

146. Carrel A, Guthrie CC. The transplantation of veins and organs. Am Med 1905;10:1101-2.

147. Mann F C, Priestley JT, Markowitz J, Yater WM. Transplantation of the intact mammalian heart Arch. Surg 1933; 26:219-24.

148. Demikhov VP. Experimental Transplantation of Vital Organs, New York, Consultants Bureau, 1962.

149. Lower RR, Stofer RC, Shumway NE. Homovital transplantation of the heart. J Thorac Cardiovasc Surg 1961;41:196-204.

150. Reemtsma K, Williamson WE Jr, Iglesias F, Pena E, Sayegh SF, Creech O Jr. Studies in homologous canine heart transplantation: prolongation of survival with a folic acid antagonist. Surgery 1962 Jul;52:127-33.

151. Blumenstock DA, Hechtman HB, Collins JA, Jaretzki A 3rd, Hosbein JD, Zingg W, Powers JH. Prolonged survival of orthotopic homotransplants of the heart in animals treated with methotrexate. J Thorac Cardiovasc Surg 1963;46:616-25.

152. Dong E Jr, Hurley EJ, Lower RR, Shumway NE. Performance of the heart two years after autotransplantation. Surgery 1964;56:270-4.

153. Haller JD, Cerruti MM. Heart transplantion in man: compilation of cases. January 1, 1964 to October 23, 1968. Am J Cardiol 1968;22:840-3.

154. Pincock S. Richard Rowland Lower. Lancet 2008;372:712.

155. Caves PK, Stinson EB, Billingham ME, Shumway NE. Serial transvenous biopsy of the transplanted human heart. Improved management of acute rejection episodes. Lancet 1974;1:821-6.

156. Cass MH, Brock R. Heart excision and replacement. Guys Hosp Rep 1959;108:285-90.

157. Lower RR, Shumway NE. Studies on orthotopic homotransplantation of the canine heart. Surg Forum 1960;11:18-9.

158. Schnoor M, Schäfer T, Lühmann D, Sievers HH. Bicaval versus standard technique in orthotopic heart transplantation: a systematic review and meta-analysis. J Thorac Cardiovasc Surg 2007;134:1322-31.

159. Freeman JS, Chamberlain E, Reemtsma K, Steinmuller D. Rat heart allograft survival with donor pretreatment. Circulation 1971;43(Suppl):I120-3.

160. Michler RE, Chen JM, Itescu S, Mancini DM, Oz MC, Smith CR, Rose EA. Two decades of cardiac transplantation at the Columbia-Presbyterian Medical Center: 1977-1997. Clin Transpl 1996:153-65.

161. Robbins RC, Barlow CW, Oyer PE, Hunt SA, Miller JL, Reitz BA, et al. Thirty years of cardiac transplantation at Stanford university. J Thorac Cardiovasc Surg 1999;117:939-51.

162. Rapaport RT, Boyd AD, Spencer FC, Lower RR, Dausset J, Cannon FD, Ferrebee JW. Histocompatibility studies in a closely bred colony of dogs. II. Influence of the DL-A system of canine histocompatibility upon the survival of cardiac allografts. J Exp Med 1971;133:260-74.

163. Rose EA, Smith CR, Petrosssian GA, Barr ML, Reemtsma K. Humoral immune responses after cardiac transplantation: correlation with fatal rejection and graft thrombosis. Surgery 1989;106:203-7.

164. Hunt SA, Haddad F. The changing face of heart transplantation. J Am Coll Cardiol 2008;52:587-98.

165. Rose EA, Pepino P, Fuzesi L, Sanchez JA. Cardiac xenotransplantation. Prog Cardiovasc Dis 1990;33:105-17.

166. Hardy JD, Kurrus FD, Chavez CM, Neely WA, Eraslan S, Turner MD, Fabian LW, Labecki TD. Heart transplantation in man. developmental studies and report of a case. JAMA 1964;188:1132-40.

167. Ekser B, Rigotti P, Gridelli B, Cooper DK. Xenotransplantation of solid organs in the pig-to-primate model. Transpl Immunol 2008; Oct 26, 2008 (E-pub ahead of print).

Mechanical Circulatory Support

168. Kantrowitz A, Tjonneland S, Krakauer J, Butner AN, Phillips SJ, Yahr WZ, et al. Clinical experience with cardiac assistance by means of intraaortic phase-shift balloon pumping. Trans Am Soc Artif Intern Organs 1968;14:344-8.

169. Kolff WJ. The artificial kidney; past, present, and future. Circulation 1957;15:285-94.

170. Kusserow BK. The use of a magnetic field to remotely power an implantable blood pump. Preliminary report.Trans Am Soc Artif Intern Organs 1960 Apr 10-11;6:292-8.

171. Houston CS, Akutsu T, Kolff WJ. Pendulum type of artificial heart within the chest: preliminary report. Am Heart J 1960;59:723-30.

172. Liotta D, Crawford ES, Cooley DA, DeBakey ME, De Urquia M, Feldman L. Prolonged partial left ventricular bypass by means of an intrathoracic pump implanted in the left chest. Trans Am Soc Artif Intern Organs 1962;8:90-9.

173. Pierce WS, Burney RG, Boyer MH, Driscoll RW, Kirby CK. Problems encountered in experiments during the development of our artificial intrathoracic heart. Trans Am Soc Artif Intern Organs 1962;8:118-24.

174. Liotta D, Hall CW, Henly WS, Cooley DA, Crawford ES, Debakey ME. Prolonged assisted circulation during and after cardiac or aortic surgery. Prolonged partial left ventricular bypass by means of intracorporeal circulation. Am J Cardiol 1963;12:399-405.

175. Westaby S, Bosher C. Landmarks In Cardiac Surgery. Oxford: Isis Medical Media Ltd; 1997. pp.282-5.

176. Norman JC, Duncan JM, Frazier OH, Hallman GL, Ott DA, Reul GJ, et al. Intracorporeal (abdominal) left ventricular assist devices or partial artificial hearts: A five-year clinical experience. Arch Surg 1981;116:1441-5.

177. Organ BC. John C. Norman, M.D., F.A.C.S. In: A Century of Black Surgeons: The U.S.A. Experience. Organ CH, Jr., Kosiba MM. eds. Norman: Transcript Press; 1987. p.733-71.

178. DeVries WC, Anderson JL, Joyce LD, Anderson FL, Hammond EH, Jarvik RK, Kolff WJ. Clinical use of the total artificial heart. N Engl J Med 1984;310:273-8.

179. Cadeiras M, von Bayern MP, Deng MC. Cardiac transplantation: any role left? Heart Fail Clin 2007;3:321-47.

180. Wieselthaler GM, Schima H, Hiesmayr M, Pacher R, Laufer G, Noon GP, et al. First clinical experience with the DeBakey VAD continuous-axial-flow pump for bridge to transplantation. Circulation 2000;101:356-9.

181. Morgan JA, John R, Lee BJ, Oz MC, Naka Y. Is severe right ventricular failure in left ventricular assist device recipients a risk factor for unsuccessful bridging to transplant and post-transplant mortality? Ann Thorac Surg 2004;77:859-63.

182. Fontan F, Baudet E. Surgical repair of tricuspid atresia. Thorax 1971;26:240-8.

183. Hirsch JC, Goldberg C, Bove EL, Salehian S, Lee T, Ohye RG, Devaney EJ. Fontan operation in the current era: a 15-year single institution experience. Ann Surg 2008;248:402-10.

184. Sun BC, Catanese KA, Spanier TB, Flannery MR, Gardocki MT, Marcus LS, et al. 100 long-term implantable left ventricular assist devices: the Columbia Presbyterian interim experience. Ann Thorac Surg 1999;68:688-94.

185. Siegenthaler MP, Frazier OH, Beyersdorf F, Martin J, Laks H, Elefteriades J,et al. Mechanical reliability of the Jarvik 2000 Heart. Ann Thorac Surg 2006;81:1752-9.

186 . Roussel JC, Sénage T, Baron O, Périgaud C, Habash O, Rigal JC, et al. CardioWest (Jarvik) total artificial heart: a single-center experience with 42 patients. Ann Thorac Surg 2009;87:124-130.

187. Hoenicke EM, Strange RG Jr, Weiss WJ, Snyder AJ, Rawhouser MA, Rosenberg G, et al. Modifications in surgical implantation of the Penn State electric total artificial heart. Ann Thorac Surg 2001;71(Suppl):S150-5.

188. Miller LW, Pagani FD, Russell SD, John R, Boyle AJ, Aaronson KD, et al for HeartMate II Clinical Investigators. Use of a continuous-flow device in patients awaiting heart transplantation. N Engl J Med 2007;357:885-96.

189. Garcia S, Kandar F, Boyle A, Colvin-Adams M, Lliao K, Joyce L, et al. Effects of pulsatile and continuous-flow left ventricular assist devices on left ventricular unloading. J Heart Lung Transplant 2008;27:261-7.

190. Stewart AS, Russo MJ, Martens TP, Naseem TM, Deng MC, Wang R, et al. Longer duration of continuous-flow ventricular assist device support predicts greater hemodynamic compromise after return of pulsatility. J Thorac Cardiovasc Surg 2008;136:524-5.

191. Morgan JA, John R, Rao V, Weinberg AD, Lee BJ, Mazzeo PA, Flannery MR, Chen JM, Oz MC, Naka Y. Bridging to transplant with the HeartMate left ventricular assist device: The Columbia Presbyterian 12-year experience. J Thorac Cardiovasc Surg 2004;127:1309-16.

192. Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, et al for the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) Study Group. Long-term mechanical left ventricular assistance for end-stage heart failure. N Engl J Med 2001;345:1435-43.

193. Park SJ, Tector A, Piccioni W, Raines E, Gelijns A, Moskowitz A, et al. Left ventricular assist devices as destination therapy: a new look at survival. J Thorac Cardiovasc Surg 2005;129:9-17.

194. Parides MK, Moskowitz AJ, Ascheim DD, Rose EA, Gelijns AC. Progress versus precision: challenges in clinical trial design for left ventricular assist devices. Ann Thorac Surg 2006;82:1140-6.

195. Holman W, Teutenberg J, Naftel D, Milano CA, Pae W, Acker M, et al. Interagency registry for mechanically assisted circulatory support (INTERMACS): interval analysis of registry data. J Am Col Surg 2009;208:755-62.

196. Birks EJ, Tansley PD, Hardy J, George RS, Bowles CT, Burke M, et al. Left ventricular assist device and drug therapy for the reversal of heart failure. N Engl J Med 2006;355:1873-84

197. Segers VFM, Lee RT. Stem-cell therapy for cardiac disease. Nature 2008;451:937-42.

198. Felkin LE, Lara-Pezzi E, George R, Yacoub MH, Birks EJ, Barton PJ. Expression of extracellular matrix genes during myocardial recovery from heart failure after left ventricular assist device support. J Heart Lung Transplant 2009;28:117-22.

199. Laflamme MA, Zbinden S, Epstein SE, Murry CE. Cell-based therapy for myocardial ischemia and infarction: Pathophysiological mechanisms. Annu Rev Pathol Mech Dis 2007;2:307-39.

John Jones Surgical Society Day

Donald West King

The business meeting was brief and ushered in by lunch, as it was last year. President Kenneth Forde and Treasurer John Schullinger both noted the continual generous support that Craig Smith gives to our Society. Ken Steinglass, Jeff Cohen, and Jose Guillem were appointed as new members to the Society's nominating committee.

Dick Edie, speaking for the membership committee reminded those present that the new bylaws no longer restrict Honorary Membership to surgeons. Our first Honorary member of the JJSS is Dr. Donald West King. He has had many leadership roles in medicine, including the Chairmanship of the P&S Dept of Pathology. He is a long-term friend of the Department of Surgery and has been very supportive of departmental programs during Dr Rose's tenure, especially the nurturing of junior faculty.

Festschrift in honor of Eric A. Rose, Chairman of the Department of Surgery, 1994-2008

Eric Rose

Jeffrey Gander, George Comas, Alexander Iribarne

Raja Flores and Michael Argenziano

Paul and Helaine Kurlansky

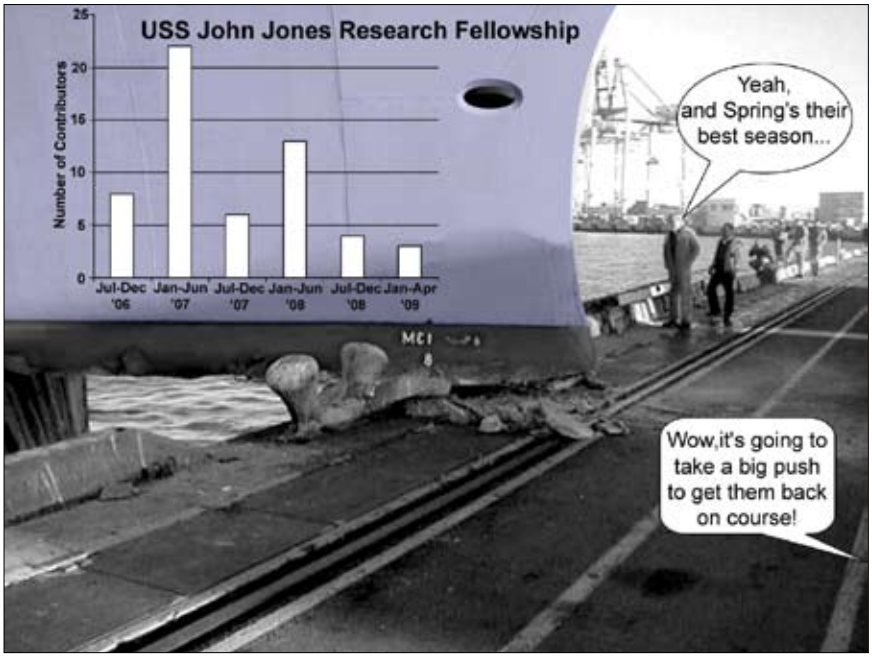
Joanne Starr

Ann Marie Schmidt and Jessica Kandel

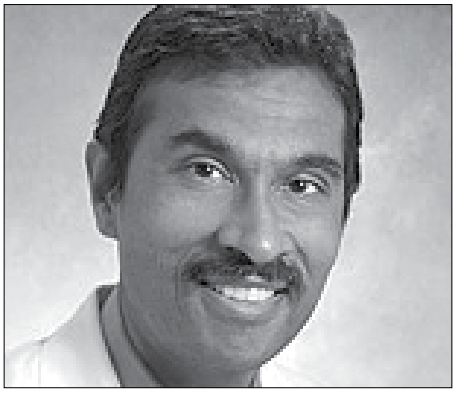
Cindi Chandler and Steve Novak

Dennis Fowler

Andre Campbell and Spencer Amory



The 2008-09 drop off in contributions is dismaying but not demoralizing. It's a steel hull crushing a wooden and concrete dock and steel wins. There is already $120,000 on board - join a winning team and get the ship on to its next port. The John Jones Research Fellowship is an important bulwark for our Society's independence in the face of a well promoted, all encompassing, Society of the Alumni NewYork-Presbyterian/Columbia.



Valluvan Jeevanandam

Thomas Colacchio

Mehmet Oz

Louis Del Guercio, J. B. Price and Foster Conklin

Reception and Dinner at the NYAC

Dick Edie and Professor Aart Brutel de la Riviere from Amsterdam, The Netherlands

Standing: Alan Benvenisty, Steve Ruby, Michael Hirsh, Herb Mendel and Thomas Colacchio;
Seated: Teri Benvenisty, Gail Ruby and Llene Mendel

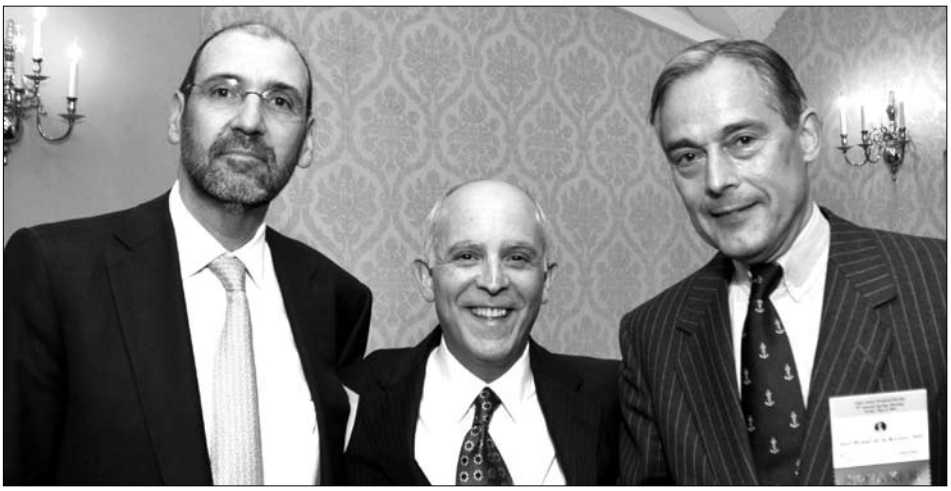
Harriet and Arthur Aufses, Jr.

Eric Rose and Ellise Delphin

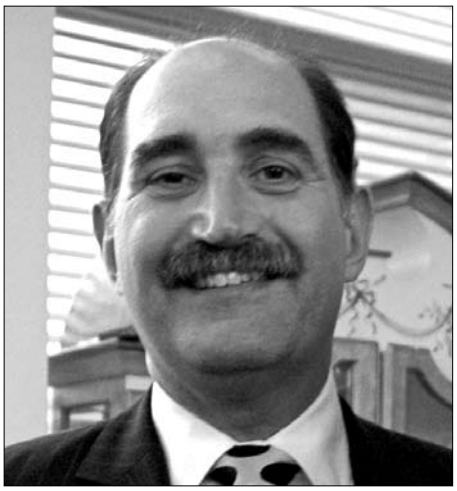
Kay and Ken Forde

Henry and Sharon Spotnitz

Standing: Desmond Jordan, Niloo Edwards, Paolo Pepino and Laszio Fuzesi;
Seated: Mary Bass, Riccardo Pepino, Silvana Pignalosa and Matteo Pepino



Alan Benvenisty, Bill Spotnitz and Professor Aart de la Riviere



Lloyd Ratner

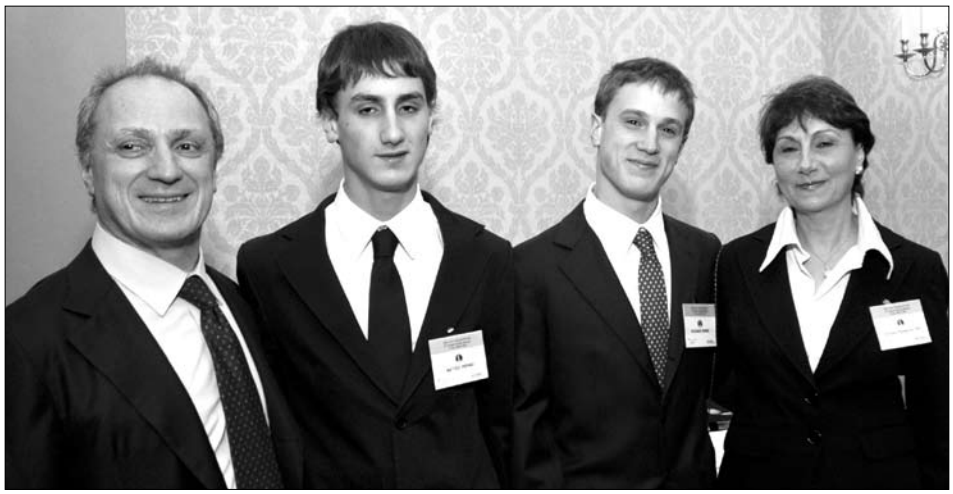
Carol Conklin and Nancy Schullinger

Jose Guillem and Kay Forde

Jim Chandler and Ken Forde

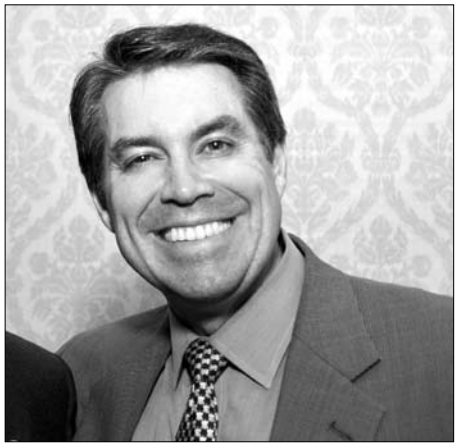
John Schullinger, Peggy and Sherman Bull

Eric Rose responding to the Festschrift



Professor Paolo Pepino with family Matteo, Riccardo and Silvana Pignalosa from Naples, Italy

Mark Hardy, Harold Barker, Ruth Hardy and Kit Barker



Robert Grant

Peggy Bull and Kay Forde

Standing: John Chabot, Andre Campbell, Samuel Weinstein and Jose Guillem;
Seated: Spencer Amory, Joanne Starr, Karen Horvath and Anne Larkin

The John Jones Surgical Society 2009 Reception

95th Annual Clinical Congress
of the American College of Surgeons

Fairmont Chicago Hotel

Tuesday, October 13th
6pm – 8pm

John Jones Surgical Society
177 Fort Washington Avenue, MHB 7SK
New York, NY 10032
Telephone: 212-305-2735
Fax: 212-305-3236
webpage: **www.columbiasurgery.org/alumni/index.html**

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Administrator: *Trisha J. Hargaden*
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