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

### Principal events in cardiac surgery's insurgent evolution:

**Ludwig Rehn**
- Successful closure of a R. ventricle stab wound
- Sept 10, 1896

**Stephen Paget**
- Heart surgery naysayer
- 1897

**Herbert Milton**
- Introduces clinical median sternotomy
- 1897

**Alexis Carrel**
- Canine Cervical heart allograft
- 1905

**Elliott Cutler**
- Aorto-coronary bypass
- 1910

**Sir Henry Claude S. Beck**
- Trans-ventricular valvulotomy for mitral stenosis
- 1923

**D.W. Richards, Jr.**
- Trans-atrial mitral stenosis finger fracture
- May 6, 1925

**Claude Beck**
- Epicardial pedicle grafts for ischemia
- 1935

**John H Gibbon, Jr.**
- Artificial circulation during pulmonary artery occlusion
- 1937

**Paul Swensson to G H Humphreys II**
- "Patient ductus favors Tetralogy of Fallot patients' survival"
- Aug 26, 1938

**John H. Gibbon, Jr.**
- Total CPB for atrial septal defect closure
- May 6, 1953

**Henry Swan**
- Hypothermia for pulmonic valve and infundibular stenosis
- Apr 15, 1954

**Nina Braunwald**
- C. Walton Lillehei
- Donor cross circulation to repair cardiac anomalies
- Mar-Oct 1960

**Norm Shumway**
- Viable canine orthotopic transplants
- Oct 29, 1966

**Alain Cribier**
- Transcatheter Rx of atrial septal defects
- July 19, 1993

**Eric Rose**
- Humorally mediated graft arteriosclerosis and rejection
- Dec 3 '67-1/ 9 '68

---

**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.
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. Each was essentially an American-British endeavor, with significant contributions from German and French speaking Europeans. Both were ideationally 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. 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 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. The establishment, however, looked upon his procedure as an insurance, and, for a time, even denied that the operation had occurred. English surgeon, Stephen Paget, (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 “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 examined a variety of surgical canards including remarks about operating on the heart

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 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, 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 (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, 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 bousty 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
privileges suspended in at least two Philadelphia hospitals because surrounded by some agonizing failures. Charles Bailey had had the same thing, in London, on September 16th. These successes were for a 10-month period. This was followed by triple reprisings of Souttar’s fruit fracture, in Boston, on June 16th; and Russell C. Brock did the same thing, in London, on September 16th. These successes were accompanied 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. Naysayers still decried wanton insensitivity 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 were now passing their catheters into the pulmonary artery (PA) and studying mitral stenosis patients pre- and post-operatively. Patients with primarily stenotic valves improved if they had pulmonary hypertension at rest, and, 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.

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. On January 30, 1948, Horace G. Smithy, 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. Dwight E. Harken 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. Naysayers still decried wanton insensitivity 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 were now passing their catheters into the pulmonary artery (PA) and studying mitral stenosis patients pre- and post-operatively. Patients with primarily stenotic valves improved if they had pulmonary hypertension at rest, and, 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.

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. On January 30, 1948, Horace G. Smithy, 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. Dwight E. Harken 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. Naysayers still decried wanton insensitivity 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 were now passing their catheters into the pulmonary artery (PA) and studying mitral stenosis patients pre- and post-operatively. Patients with primarily stenotic valves improved if they had pulmonary hypertension at rest, and, 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.

John Jones Surgical Society Volume 12, Number 1 Spring 2009

Gross 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. “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.

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. "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.

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. “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.

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. "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.

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

Humphreys was aware that Gross’ group 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. Each of the three procedures was different, challenging Blalock’s and Vivien Thomas’ on-the-spot ingenuities. 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.

Both showed widening of their pulse pressures and improved arterial O₂ 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. 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. 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.

“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.” 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...
circulation in 1937, describing a pump-oxygenator circuit designed to support short-term PA occlusion to remove pulmonary emboli. 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).

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. Most of the energy went into testing and achieving a non-thrombogenic 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. A new silicone-covered, hollow nylon ball made the valve’s closing click less perceptible to the patient. Hufnagel operated on his first of 2 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 Murray6 (1894-1986), of Toronto, checked 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.

Bailey7 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. 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, Gross8 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. Bigelow9 (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.
The culmination of their collective labors was embodied in Gibbon’s May 6, 195 seminal success with his second CPB patient, an 18-year old girl with a large intra atrial septal defect. She was operated upon 15 months after a misdiagnosis-reversal. She was 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 high ventricular septal defects in his tetralogy of Fallot patients.

**Estragon:** Let’s pass on now to something else, do you mind?

**Vladimir:** I was just going to suggest it.

Dennis Melrose (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 success. In each 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:** Try as one may.

**Vladimir:** 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. 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 1945 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. 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. 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 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.
Aaron Himmelstein (1914-1959)

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.\(^{31,32}\) These same years witnessed K. Alvin Merendino\(^ {33} \) postero medial annuloplasties for mitral insufficiency in Seattle, the Cleveland Clinic’s F. Mason Sones, Jr.\(^ {34} \) (1918-85) introducing selective coronary arteriography, and Conrad Lam, at Henry Ford Hospital, independently exploring acetycholine infusion to arrest the heart and then using it in 80 clinical cases. Clarence Crafoord-trained, Åke Senning\(^ {35} \) (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.\(^ {36}\) 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.\(^ {37}\) 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.\(^ {38}\)

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.\(^ {4}\) 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,\(^ {48}\) 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.\(^ {60,61}\)

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 septum defect repairs 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?

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 curved and immobile mitral leaflets were ex-


John Jones Surgical Society Volume 12, Number 1 Spring 2009
coronary stent would be particularly attractive in this setting and eighth decades who typically recover slowly, or incompletely, from done mainly for calcific stenosis in individuals in their seventh and to zero intra-operative mortality. Aortic valve replacements are now Starr would focus on perfecting prosthetic valve replacement October, rounding out a remarkable 8 months.

Harken’s second implant was successful in September to be their design. This became the prototype of everybody’s pulse duplic
amplitude, rate, peripheral resistance, and time in diastole to optimize Soroff developed a pulse duplicator that could vary and record am
formed by him or others. He turned to the Davol Company, in nearby Providence, to make a stainless-steel-caged ball valve. He and Harry
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 Harken69 was frustrated by poor results that regularly followed aortic valve “plastics,” 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 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, mim- icry, 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 today73. 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.

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 Braunwald76 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 im-balanced strut loading that could fatigue fracture the “bent staple”
strut, freeing the disc to go with the flow.** Strut failure was a major issue in the aortic position and required expedient CPB support 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.** Shiley valve implantees still exist, but nearly all are now at low risk.**

**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’ Salpêtrière hospital. Twelve years would elapse before Donald Nixon Ross 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. This was a particularly attractive concept in children as the autograft in the aorta was capable of real growth. Ron Elkins and his colleagues 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.

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 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 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 Carpenter-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. A slower contractility rate [change in pressure /change in time (Δp/Δt)] has been hypothesized to account for biologic valves’ durability in older individuals. Structural valve deterioration and calcification are related to variable expression of proinflammatory mediators and osteogenesis-associated factors. Contractility stress may be a major expression modulator and the link between age and biologic valve durability.

Carpentier 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 Connection*. Subsequent years saw an eruption of various shaped annuloplasty devices and a rebirth of “Teflon” neo-chordae in 1985, with Tyrone David’s use of Gor-Tex® (ePTFE) sutures to replace damaged chordae. Recently, Perier and his Bad Neustadt 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, completing a series of 22 cases over 14 months. 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. 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. 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.
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

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 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 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.

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. 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 M. McAllister, 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 arterialized 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.
Vineberg’s Operation
In 1946, Arthur M. Vineberg (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 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%. In all, more than 10,000 Vineberg operations were performed between 1958 and 1975. The results were notably variable, yet the procedure went on to overlap H. Edward Garret’s 1964 successful saphenous-vein, aortocoronary bypass for 11 years.

Direct Coronary Artery Revascularization – “Success Has Many Fathers”
Charles Bailey, 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 expertise with superficial femoral artery endarterectomy, reporting a series of five patients in 1958. 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 trunklets 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. 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. (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 and his Argentine protégé, René Falveloro (1923-2000) became the first to use CPB to treat a post-os-
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 bypass showed saphenous vein grafts to be open in 60% of 40 patients and ITA grafts to be patent in 90% of 107 patients. 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.

Ankeney 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. 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. 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 atrioventricular 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.

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.

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 tool 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. 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.

Veli Topkara and his colleagues at Columbia 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. 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. 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. 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.

**Chronic Heart Failure (CHF):**

**Making the Best of What You Have**

CHF is a progressive myocardialopathy, characterized by LV dilatation and poor contractility that can be temporized with polymedication 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.

**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 re-opened 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. 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.

**Cardiomyoplasty and Passive Restraint Devices**

Surgical interest in treating CHF began with Juan C. Chachques and colleagues in 1985 introduction of “Dynamic Cardiomyoplasty.” This involved severing the origins and insertion of the 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. 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. The enrollee’s 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. 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 2005 in a prospective, uncontrolled observational study. 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.

**Transplantation**

*Allotransplantation*

Heart Transplantation has a history beginning with Carrel and Guthrie in 1905 and a far older presence in romantic and religious fables, exemplified by the story of Pien Ch’iao. Ch’iao was a...
renowned 4th century BC practitioner of Taoist, Chinese medicine, which attributed all ills to stagnated internal yin and yang forces. 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 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. 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 (1929-2006) 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 Stinso, pursued the technical and physiologic vari-
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. 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. Shumway remained observant and respectful of the work of others, even abandoning his time-honored Cass-Brock, bi-atrial implantation for Sievers’ less tricuspid annulus distorting, bi-caval technique in 1992.

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. 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.

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. 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 mycophenolate 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.

**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. 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.

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. 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, Galα1,3Galα1,4 lactose α(1,3)Galα1,4 lactose (Galα1,Gal).

Keith Reemtsma and Eric Rose

**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 reinsertion of arterial blood to coincide, respectively, with the onsets of systole and diastole.
trole. Withdrawal decreased after load, lessening stroke work, and maybe even increasing the EF, and the reinfusion increased diastolic pressure to enhance coronary perfusion. Adrian Kantrowitz\textsuperscript{268} 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\textsuperscript{369} (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.\textsuperscript{270} 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.\textsuperscript{171} Keith Reentsma lured him away in 1967 to head the University of Utah’s Institute for Biomedical Engineering. Argentine Domingo 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\textsuperscript{72} was able to report LVAD pump runs up to 44 hours in 47 dogs. Future Jacobson Innovation Award winner, William S. Pierce,\textsuperscript{172} 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\textsuperscript{24} 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.\textsuperscript{175}

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 of his own 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.\textsuperscript{176} Jack Norman and Cooley used this device until 1978. Norman was the founding editor of the Texas Heart Institute Journal and later chaired the Department of Surgery at Marshall University, in West Virginia.\textsuperscript{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.\textsuperscript{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?\textsuperscript{179}

Martin Cadeiras and his colleagues could have included The Audacity of Hope\textsuperscript{24} 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.\textsuperscript{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.\textsuperscript{181} This might have been predicted, from François Fontan’s\textsuperscript{182} success with his 1971 RV bypasses and that of their follow-on, valveless, cavopulmonary conduits in patients with good [or well supported] single venous function.\textsuperscript{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.\textsuperscript{184} Jarvik’s widely used LVAD, which supported a patient for more than 7 years,\textsuperscript{24}...
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 LV AD 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 colleagues192 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 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’ group194 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 cardiomyopathy 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

[Graph showing survival rates for LVAD patients]
References: Blue indicates CUMC and its antecedents

Fin de Siècle Beginnings

24. Ibid; p.67.
30. Muller WH Jr, Dammann, JR Jr. Treatment of certain congenital malforma-

"Waiting for Godot"

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 ventilricular septal defects, tetralogy of Fallot, and atioventricu-


**Circuit Breaking Surgery**


**Chronic Heart Failure: Making the Best of What You Have**


151. Blumenstock DA, Hechtman HB, Collins JA, Jaretzki A, Hosbein JD, Zingg RGICAL...
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
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.
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
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

Editor: James G. Chandler
Administrator: Trisha J. Hargaden
Design: Richard V. Miller-CUMC IT

John Jones Surgical Society Volume 12, Number 1 Spring 2009