FRANK GERBODE, M.D.

WHO DONE IT?

Given before Chit Chat Club, San Francisco
10 January 1983

On July 20, 1969, Neil Armstrong set foot on the moon. The first man in history to do so. His feat followed by seven years, John Glenn's first orbit of the earth. From that time on, we have come to take for granted to a great degree, feats we would not have dreamed of a mere fifty or even twenty-five years ago. And because of the rapid growth of technology, the scientific advance of modern society, and the overwhelming exchange of information by means of modern media, television, satellites and computers, we often forget and more often do not know or remember the innovators; the men and women whose ideas created these advances.

We can date the more recent advance in space exploration from the launching of Sputnick in the early 1950's. It underscored the marriage of science and creativity. And it is this application of creativity to our modern life that I want to talk about. Who are the innovators, the creators? Is the creation of art different from the creation of science? According to the philosoper Eliseo Vivas:

> "Societies cannot be easily and radically changed by the human will according to plan; rather it is the creativity

with which members of a society are endowed that accounts for the internal dynamics of a society."

Art has always been considered interchangeable with creativity. The acts of painting, writing, and designing architecture are customarily called creativity. But science has become synonymous with invention; science is an ongoing phenomenon and because of its continuum often the original thinker, or creator, remains anonymous, sometimes by design, but most often by the passage of time and the incremental additions to the original creation that further research and innovation often conceal.

Using Neil Armstrong's metaphor of "a giant step for mankind" we realize that man has always been taking steps on the path of creativity. Some of these are giant, but often they are merely small footsteps to greater things and sometimes they are even performed on tiptoe so we are not aware of the imprint of their importance until many years later. Among those who have walked such a path in science, we can mention Ptolemy, Newton, Poincare, Einstein, Darwin and Savin.

It is proper here to ask, "What is science?" The dictionary says it is the body of knowledge by means of which man accounts for all he observes in his world and other worlds that he understands. Some examples are the use of fire, the control of water, the manufacture of clothing and artifacts, the harnessing of nature's

resources --- just follow it from the Stone Age to the Nuclear Age and the path is worn with a chronicle of man's progress.

Lewis Mumford attributes the profound changes in the space-time framework of the civilized world to five key inventions upon which a whole new order of machines were built --- he dates these between 12th and 16th century calling their output "a new kind of megamachine". These five inventions are the watermill, the windmill, the magnifying glass, the printing press and the mechanical clock. For the first time, Mumford said, these inventions allowed us to see both the cosmos and the organic environment in depth. "And in all of the above, we may not be able to actually pinpoint one creator."

To discuss each and all of these would take more time than we have here, but their mention invites me to do two things: One to talk a bit about creativity and another to discuss with you some of the things I know best in the fields of creativity and invention; the art and the science of cardiac medicine and surgery.

Creativity has had many explanations and definitions. Albert Koestler, the philosopher and writer, investigated the subject for years. He states that creativity is bisociation. Bisociation is the synthesis of two opposite ideas into something new.

The result of the synthesis may create shock or humor. And interestingly his study and explanation begins with humor. It is a good example, for in an ordinary joke two totally opposite ideas are presented. Laughter results only if the first and second ideas are successfully opposed.

Example: "I hear you buried your wife last night."
"Had to. Dead, you know."

We can laugh and we do, because we react to the fusion of the straight first line and the unexpected reply in the second. Koestler further states that "all patterns of creativity are tri-valent: they can enter the service of humor, creativity or art. But whatever, according to another study of creativity by a new scientist Calvin Taylor, "The crux of the entire scientific research undertaking is the scientist."

How does one characterize a scientist? Well, some say the scientist is blessed with intelligence. A prevailing view is that the creative person is a curious one, not an "organization man:. He or she creates a kind of conflict. Hans Selye wrote, "Now in my own defense I must state that scholastic standing is not a good guide to a student's ability to do research. Paul Ehrlich got through his final examinations in medicine only because his

professors had the good sense to give recognition to his special talents, and Einstein flunked the entrance examination at the Polytechnical School. Charles Nicolle, the great French bacteriologist, said that inventive genius cannot store knowledge and that inventiveness may actually be killed by teaching fixed ideas and by too much erudition. Still, being a bad student certainly does not augur well for future success in science and when I first announced my intention to go in for basic research as a career everybody was greatly perturbed."

Men such as Selye make things happen.

I feel very fortunate, as we all should, having lived through the last fifty years and witnessed the great advances made in technology throughout the world. We've seen a transition from primitive airplanes to jet propulsion; the development of the whole space program in this country and in Russia. Not the least of the great advances has been the computer industry, which has transformed everything in business and science to a different level. We still do not understand the full dimension of what the computer can do for us. Certainly it would be very difficult to live without it in the future. Not the least of these great advances we have seen have come in medicine, where the entire profession has undergone an evolution never experienced before ~~in~~ this century. It has been said that there have been more advances in the last fifty

years than in all of history. Having participated in the development of cardiac surgery from the most primitive beginnings to cardiac and artificial heart transplantation has been a very privileged position to have been in.

When we started with our first experiments in open heart surgery early in 1950, there was no plastic industry to support the field. Electronics was primitive. But probably the most important event was the realization that the medical profession had to call upon a great many disciplines and industry to help them develop this field. We made the decision in 1955 to employ an engineer to help us full-time with the development of the paraphenalia necessary to do cardiac surgery. We secured a fellowship in the American Heart Association for him --- the first non-medical person to obtain such recognition and support. It took a bit of doing to convince them that a non-medical person should be supported by the American Heart Association. Now it is an accepted fact that Ph.D.'s and others are recognized collaborators, working with us side by side. Many Ph.D.'s, electronic experts, computer scientists and a host of paramedical personnel add a great deal to patient care. It has been a fascinating experience to see how quickly educated non-medical people can acquire the knowledge and skills to make a contribution in medicine.

It has always been discouraging to me to ask medical students, interns and residents the names of those responsible for a given type of procedure, instrument or advance. They simply are not interested in history, or why it was done. I believe the present mode is, "Show me how to do it, so I can do it as soon as possible." However, it is interesting to recall historically how and why things have or have not taken place. For example, a famous surgeon by the name of Stephen Paget in England stated in 1896 that "Surgery of the heart has probably reached the limits set by nature to all surgery."

The first successful operation on the heart was performed in Germany by Ludwig Rehn, in this same year. It consisted of a suture repair of a stab wound of the heart. Just before this event the very famous German surgeon, Bilroth, commented "Any surgeon who would attempt an operation on the heart should lose the respect of his colleagues."

Very few good things come from war, but one major contribution came from Dwight Harkin, who removed foreign bodies from the heart and great vessels very successfully in 134 operations, done in England in a base hospital. These procedures were all performed without the help of a heart-lung machine. Vascular repair and replacement came out of World War II and the Korean conflict.

An electrifying contribution was made by Robert Gross in Boston, who in 1938 ligated successfully a patent ductus arteriosis. This had been tried unsuccessfully previous to his achievement. Shortly thereafter he successfully performed a resection of ~~the~~ a coartation of the aorta. This is a congenital narrowing of the aorta. At the same time the procedure was performed in Stockholm, by Clarence Crafoord, a giant in Swedish thoracic surgery.

These procedures were done with more ease because of the advances in anaesthesia, which permitted the use of the intratracheal tube to facilitate artificial respiration and to prevent the collapse of the lung when the chest was opened.

Just before the war ended, Dr. Helen Taussig of Johns Hopkins persuaded Alfred Blalock, who was then professor of surgery, to anastomose a subclavian artery to the pulmonary artery in a blue child. This is the so-called Blalock procedure, which ~~electrified~~ excited thoracic surgeons through our the world. It was the first time that anything definitive was done for cyanotic children. At that time there were thousands of children with congenital heart disease who needed treatment, and the experience gained in performing this palliative operation, and a similar one designed by Potts in Chicago, kept thoracic surgeons busy for a number of years. It gave them a great deal of experience in studying these patients and opened the door to angiocardiography and cardiac catheterization.

Among the first to perform cardiac angiography were the Spanish, but this country went forward with great energy early in 1940. The first machines to produce serial studies of dye passing through the heart and therefore outlining the abnormalities, were crude, but large companies saw the advantage of developing this type of gear and therefore soon there were machines being offered by General Electric, Siemens and others.

Cardiac catheterization is credited to the efforts of a young surgical intern, Werner Forssman, who introduced a catheter into the right atrium via a peripheral arm vein. He did these experiments on himself. Here is an outstanding example of the incremental steps of science. Forssman was not the first to use catheterization. In 1912, ten years earlier, experiments by Drs. Unger, Loeb and Bleichroeder passed a ureteral catheter into the arm veins up to the axilla on four human subjects. However, Forssman's work in 1922 was more precise and in 1956 he, along with Cournand and Richards, was awarded the Nobel Prize in Medicine. According to Dr. Robert Litwak's study of the history of cardiac surgery, "the committee either was not aware of, or chose to ignore, the earlier contribution of Bleichroeder. Bleichroeder's work was carried out under even greater difficulties than Forssman's and the courage with which it was undertaken cannot be regarded as less conspicuous."

What happened between 1945 and 1955 in this field of cardiac surgery, and in fact thoracic surgery in general, came from the fact that there was a great body of young men who had mostly volunteered in the armed forces and had spent two to four years in the war. When they came back there was very little practice for them. Their jobs had been taken by those who hadn't gone away. Many of them turned to the experimental laboratory, fortunately, to satisfy their interest and to make contributions in experimental surgery.

Some of the English surgeons deprecated the young surgeons who worked hard in the experimental laboratories on animals to perfect the techniques which later transformed the whole field. They were called, "dog surgeons", by some narrow-minded English surgeons. However, there were other English surgeons who believed that experimental surgery would lead the way, and these eventually emerged as the leaders in England, as well as in this country.

Another great factor at this time was the decision of the National Institutes of Health to pour millions of dollars into research in these fields. We must give credit to Congress and the Presidents for having the vision to supply these funds for the development of young, energetic surgeons and physicians.

Another factor which enters this whole picture is the reward for doing experimental surgery, or for having made a contribution. We can often question why people do things. Why, for example, the conquering of Everest was such a remarkable achievement for a man. Why did he do it? He said, "Because it was there." But actually he probably wanted to do it because he knew that if he did, he would, in fact, become immortal. The same is true of the first person who sailed around the world alone, a remarkable feat.

We can say the same of Sir Francis Drake, who sailed around the world, as we have seen in one of our Chit Chat talks, who conquered many seaports on the west coast of America and finally came back to England having completed the circumnavigation with enough loot to pay off all of the Queen's debts and to build the Navy that eventually conquered the Spanish Armada (with the help of a big storm.)

Young physicians and surgeons who went back into academic medicine after the war were really inspired by the advances which had taken place in the few years before they returned. They could see the future quite clearly and had to figure out how to make the best of it. They also knew that if they made a major contribution they would be advanced on the academic ladder, and many of them were, having later become full professors because of

their contributions in clinical and experimental investigations. There is nothing that aids a young academic surgeon more than a solid contribution to the field.

Programs were set up in Societies so that young people could present original work. For example, the Fundamental Forum of the American College of Surgeons was established by Dr. Owen Wangensteen of the University of Minnesota to give the "young Turks" a forum in which they could present original research work and have it published. This has persisted to this day and other Societies have incorporated it in their meetings so that young people can present the findings of their research.

Shortly before, in 1938, a young resident by the name of Dr. John Gibbon had a patient at Massachusetts General Hospital with a massive pulmonary embolism. This young lady gradually died because their wasn't anything at that time that could be done for her. In watching her terminal illness, Dr. Gibbon thought that if he had a heart lung machine to take over the lungs and circulation temporarily he might have removed the thrombus from her lung and saved her life. He was given some space and the funding to start work on a heart lung machine, and his wife, Maley, joined him. Together they worked in the laboratory for several years. They produced a number of models which, however, were not good enough

to use clinically. Finally, after the war, the research was helped by the IBM corporation, who in the end spent about $250,000 and developed quite a good heart lung machine. It was used for the first successful open heart operation by Dr. Gibbon in Philadelphia in 1953. The Mayo Clinic realized at once that this was the way to go, and therefore they got one of Dr. Gibbon's machines and started Dr. John Kirklin, a young staff member, to develop the field of correction of patients with congenital defects. They used the machine successfully for a number of years before another type was developed which was simpler and perhaps less traumatic. It was created in the animal laboratory by another young resident in Minnesota, by the name of Dewall. He conceived of the very simple artificial lung, called the bubble oxygenator. This then, made it quite easy to oxygenate the blood and this device, with many improvements, is now being used widely throughout the world. It is slightly traumatic and not ideal, but it is very useful and inexpensive. Since then other devices have come on the market because industry discovered that it is financially desirable to produce instruments that can be used in open heart surgery. The competition at the present time is intense in this field.

Another type of oxygenator is a so-called membrane oxygenator, which is more like the human lung. We have been working on this

experimentally for about twenty years, and currently are in the final stages of testing one, with the help of a large company involved with medical engineering.

What is it that makes a man conceive of an idea and then gradually work it out and end up with a discovery or a great advance? Concepts are imaginative visions of reality, the authenticity of these must be tested against the truth of reality.

Alexis Carel, early in this century, developed techniques for vascular suture, believing that one could sew arteries together and have them function. This was entirely a new concept, although it had been tried to some extent initially in France. He used this technique to do some of the first transplants of organs from one part of the body to the other, using vascular suture to keep them alive. Thus he anticipated vascular surgery by about forty years or more, and for it obtained a Nobel Prize. Now such techniques are done routinely by residents in every corner of the world. He defined the act of conceptualization as being a function of intuition, which he defined as "the seemingly instinctive impulse of the scientist toward a discovery."

Similarly, the circulation of the blood was discovered by William Harvey, who believed that the blood was pumped in a circular manner. He finally proved it by a few simple tests, and became immortal in his own right.

In recent years there has been a great effort to get away from invasive techniques of injecting dyes and other materials into the body to make a diagnosis. Furthermore, we're reducing x-ray diagnosis, whenever possible. This has led to the development of devices which depend upon sound waves passing through the body, which then outline organs of different densities. With this device one can make a diagnosis of a tumor in soft tissue with reasonable accuracy. However, the latest adventure in this field is nuclear magnetic resonance (so-called NMR).

The basic work which has made this possible is about ~~twenty~~ Thirty-five years old, and was established by Felix Bloch and Edward Purcell, physicists, who, for their work, received the Nobel Prize in 1952.

NMR provides images of the distribution of protons in various parts of the body. The body is immersed in a non-uniform magnetic field which results in tagging different parts of the body by the varying field strengths. The nuclei in the different parts of the field respond with a recognizably different NMR frequency. Through manipulation of the magnetic field radiofrequency signals are detected which can be used to create images by techniques similar to those in x-ray emission computerized tomography. One of the attractive features of NMR imaging is the negligible health hazard. One of the most promising aspects of this technique is its ability to measure blood flow deep within the body and do

so non-invasively as well as imaging the presence or absence of aberrant physiology which can indicate disease processes.

The clinical application for NMR has only come into being in the last few years, largely as the result of the adaptation of these basic findings of Bloch and Purcell. With NMR it will be possible to make diagnoses in soft tissue in the brain and in various other organs without any invasion and without any irradiation. It is truly a remarkable device and will revolutionize diagnostic ability. Unfortunately it costs more than $3 million; in addition to this cost, personnel and housing structures will add a goodly sum to it.

There is always a question when something new and very expensive comes along as to whether this should be put into the stream of medical care, because it inevitably increases the costs. However, this sort of argument has been heard many times in the past fifty years. I can remember discussions we had with key personnel about the value of cardiac catheterization and why it should be incorporated into the program. It took some doing to get it paid for, for example. Very often it is possible to incorporate some sort of research program into the use of a device, and thus obtain research funding for part of the cost, at least.

We cannot talk about advances in medicine without discussing cardiac transplantation. Some of the early work in experimental transplantation in dogs was done in our old surgical laboratory in the old Stanford Medical School at Clay and Webster Streets Dr. Shumway and Dr. Lower were among the first to work in this field, and they added the use of hypothermia or low temperatures to make it possible to transplant a heart from one dog to another. These experiments were viewed with skepticism because the immune rejection phenomenon was still not conquered and it was felt that although it was technically possible to do this procedure that the host would reject the organ within a few weeks. This was certainly true in the beginning before drugs were incorporated into the program to alter the immune rejection phenomenon. The work continued in Dr. Shumway's laboratory at Stanford and we did some work as well in the new laboratories we started in San Francisco. Dr. Lower, who had been with Dr. Shumway, moved to the University of Virginia. He was performing an experimental transplant in a dog while Christian Bernard was in his clinic as a visitor. Actually Bernard had come to the clinic to learn about the techniques of kidney transplantation. He watched Dr. Lower do the experimental cardiac transplantation in the animal. He said, at that time, "I tink I'm going to try this." So when he got back to South Africa, he did try it.

He first developed his technique in animals, but, as you all know, he was the first to successfully transplant a human heart. His work since then has mainly been emphasizing using a transplanted heart as an adjunct heart, more or less like a supercharger in the circulatory system. In any event, the fact that a South African doctor had done the first cardiac transplant hit this country like a severe blow. NIH and those in charge of allocation of funds for research were shocked that we hadn't done this first in this country. Very quickly, therefore, money was pumped into various units to catch up, you might say, and Dr. Shumway launched his program with more blessing from the National Institutes of Health and very soon surpassed the others in numbers and in good results. Since then with the additional support of drugs, such as Cyclosporin and Prednisone, success has been greater than it was initially. Of course we shall have to wait to see whether the drugs themselves produce undesirable side effects. There are a number of surgeons who plunged into the field blindly, without much scientific background, but with technical excellence, and their patients all died.

Heart transplantation now is done in half a dozen centers in the United States, with reasonable success. Of course, it will never reach the number of people who really need a new heart, even in the younger age group.

Then, with regard to the mechanical heart, research in this country has been going forward at a fairly intense pace, since the first human heart was transplanted. And altogether we have spent over $8 million in Federally supported research programs in at least five centers in this country. One of the centers that has done the most experimental work is the Utah group who have recently performed the first human mechanical heart transplantation. There have been lots of reverberations and some people have said that this should not have been done at this stage --- the art being what it is at this time. And perhaps we should have waited until a pump was devised that could be put inside the body, rather than have an external pump requiring tubes to a rather large console. Look upon it as a great achievement and quite exciting and perfectly proper.

One has to credit the recipient, Dr. Barney Clark, the dentist, who was quite brave to offer his body for this purpose. He realized that he had nowhere to go otherwise, and he's too old for a human cardiac transplantation, according to our present guidelines.

One has to remember that if you spend ten to fifteen years working in a field and develop something that is reasonably close to being feasible, there is a great desire to try it. This is inevitable.

The eventual outcome of this experimental human procedure remains to be seen, but for him it is probably not a very promising event. We are certainly far from the possibility of offering this as an alternative to human heart transplantation and as a mode of treatment.

So in closing, we must remember that as we sit here, somewhere someone is creating an idea, experimenting with it, putting it to the test. We may never know his or her name, or we may know it immediately. Whatever, we can remember the words of Wendell Phillips, who said, in 1838, "In every matter that relates to invention, to use, or beauty or form, we are borrowers."