

Barber Poles, Battlefields, and Wounds That Will Not Heal

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Having grown up playing baseball in a small town in Maryland, I was always reminded of the four baseball Hall of Famers who lived there: Babe Ruth, whom you might have heard of; Jimmy Fox; Lefty Grove; Al Kaline; and, a future Hall of Famer, Cal Ripkin Jr., who just broke the record for consecutive games played. I, too, dreamed of some day playing in the Major Leagues. I didn't make it in baseball, but I certainly have played in the big leagues of academic surgery with the likes of Jay Ballantyne and Dick Jesse. For this, I am extremely privileged and grateful.

I have chosen "Barber Poles, Battlefields, and Wounds that Won't Heal" as the title of my Presidential Address. This reflects a personal flavor and, perhaps, requires a brief explanation. I have tried to weave three determining threads of my life into the fabric of this presentation. The first thread was my decision to become a surgeon—"the barber pole." The second was my opportunity to go to Vietnam with the US Marine Corps—"the battlefield." The third was my choice to go to M.D. Anderson and dedicate my career to the care of the patient with head and neck cancer—"the wounds that won't heal." In this address, my message concerns issues of image, challenge, conflict, crisis, and a disease called cancer.

THE BARBER POLES—SYMBOLS OF TURF AND IMAGE

All nonsurgeons love to point out that the first surgeons were really only barbers and not much has changed since.¹ Actually, the genome of surgery is entwined with that of medicine and yet it has a distinguished image all its own. After 1540, barbers were organized into a guild along with the surgeons. Interestingly, however, the surgeons were forbidden from shaving anyone. Today, surgery is preeminently the profession of the dynamic person to whom the sovereign test of thought lies in performance.² This history of the barber-surgeons since the early 14th century is largely a pageant of great personalities. Great achievements, yes, but more so, unique characters. Under the Romans, surgery prospered and was sustained by the Pax Romana. Not until the hordes from Germany overran the cradle of civilization did surgery decline. During the following 1,000 years, it

became a despised and neglected practice. Much of this has been blamed on the church, which prohibited the practice "Ecclesia abhorret a sanguine," which means the church abhors the "shedding of blood." As civilization regained its hold upon the people, surgery revived. The most notable and significant exception during this era was in the arena of the battlefield. Surgery prospered with the bloody strife of men, medicine did not.² The barber's identification with war produced the characteristic colors wrapped around a pole: red for blood and white for bandages. Battlefield surgery was brutal, but so were the radical procedures performed by surgeons in the early 1900s to treat cancer.

Hippocrates said "war is the only proper school of the surgeon." In the 4th and 5th centuries B.C. Hippocrates laid the foundations for surgery based on principles of direct observation. The scripts of Hippocrates and his pupils were included in 72 books and labeled under the title *Corpus Hippocraticum*. Practical hints within the corpus suggested: "the surgeon must keep his nails neither projecting beyond the fingertips nor very short and all operations must be practiced with each hand so that both hands can attain ability, grace, speed, elegance, and readiness." As you may or may not know, the *Corpus* also contained a section entitled *The Aphorisms*. An interesting *Aphorism* described: "diseases not cured by drugs are cured by surgery, diseases not cured by surgery are cured by fire, diseases not cured by fire should be considered incurable." This could be the earliest evidence of the relative value of surgery, chemotherapy, and radiation. As we read on, *The Aphorisms* further advised that "surgery is not every man's act" and suggested "surgery has to be performed carefully without force and aggressiveness." In 1585, this was embellished to describe a surgeon as one with the eye of a hawk, the heart of a lion, and the hands of a woman. *The Aphorisms* also addressed the aspects of unnecessary surgery when it recorded "it is a shame not to accomplish what you are looking for from surgery."³

Throughout the ages, surgeons have always been able to refine their skills and develop innovative ways to care for the wounds inflicted by all sorts of instruments of destruction: swords, halberds, pikes, arrows, lances, muskets, boiling tar, mustard gas, flame throwers, napalm, AK47s, and punji sticks. It is no accident that one of the world's most illustrious surgeons, Ambrose Paré, who took surgery out of the age of superstition into the age of common sense and accurate observation,⁴ was Napoleon's surgeon. John Hunter was the renowned British Naval surgeon with Admiral Nelson, and William Thacher was the surgeon with General Washington at Valley Forge and who attended the wounded Lafayette at the Battle of the Brandywine. The first great war surgeon, however, was Paul of Aegina, who practiced during the Byzantine Empire, centuries before Ambrose Paré. He lived with the soldiers and sailors, treated

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their injuries, and, most important, recorded it all in the *Seven Books of Medicine*. The battlefield was and still is the great academy of the surgeon. As oncologists today, we have our own barber poles— those symbols of our profession, our specialty, and our society, which give us our image.

The caduceus, the symbol of the US Army Medical Corps, is the winged staff of Mercury, the messenger of the Gods, entwined with two snakes. The official symbol of the medical profession and the AMA is the wooden staff of Aesculapius, the God of healing, father of Greek Medicine, with only one snake wrapped around it. I am not sure of the significance of the one or two snakes, but the snakes, in general, were symbols of wisdom. The statue of Aesculapius is also depicted on the American College of Surgeon's seal.

The logo for the American Cancer Society reflects the two serpents, but the staff is replaced with a sword. This gives a more military feel and, again, the analogy with war is appropriate. "Wisdom with violence, kill the cancer."

The American Radium Society's symbol is Odens' two ravens: Hugin, representing thought and reflection, and Munin, representing memory and remembrance. These two ravens spend their day flying through the expanse of the universe returning each evening to perch on Odens' shoulders and whisper in his ears the events and progress observed. This image expresses the Society's emphasis on knowledge, wisdom, and learning as it relates to thought, reflection, memory, and remembrance. Obviously, a concept which has no connotations of turf, but rather a truly multispecialty mentality.

Our own Society's symbol features the crab and the surgeon's knife. The crab is the fourth astrologic sign of the zodiac, called Cancer. The word for crab is *carbinos* in Greek and, in French, *cancerie*. We often refer to our symbolic enemy as the crab. The crab is a superb scavenger and, perhaps, a fitting symbol for cancer because the malignant cell is so capable of using whatever is in its environment as a support system. Rudyard Kipling has a poetic description of our esteemed crustacean: "Cancer the crab lies so still that you might think he is asleep if you did not see the ceaseless play and winnowing motion of the feathery branches around his mouth."⁵ This is so like the cancer cell remaining dormant waiting for some change in the host's immunity. However, is this what the emblem of our Society should be? Certainly, not just the scalpel and the crab. Images are important. We are a multidisciplinary society focused on cancer. We need something to reflect this. Regardless of our name or emblem, our Society's image should be represented by three "I's" — inviting, involvement, and inspiring.

Inviting

We must extend a warm invitation to those who desire to communicate, educate, and push back the frontiers of knowledge. Our Society must always give the impression of being user-friendly, embrace all disciplines, and eliminate divisive feelings and attitudes.

Involvement

If we are to have a meaningful society we must be involved in all aspects of cancer patient care, prevention, diagnosis, treatment, rehabilitation, education, research, and com-

munity service. By the very nature of our membership we have the expertise in all of these areas. Our annual meeting must reflect the latest in medical knowledge and provide a forum for our members to present their prized work. We must seize every opportunity to disseminate this information and expertise to our peers, to governmental agencies, and to society in general. We must get involved individually to influence and guide our communities as to the proper priorities in healthcare and cost-containment. Remember how you felt when you first joined? We must welcome our new members as well as our perspective members and show them how much we value their decision to join us. We must give them every opportunity to showcase their talents and to get involved. The work of the Society is through its committees. Each new member should be immediately placed on a committee and strongly encouraged to present a paper during the Annual Meeting within 2 years after joining. Involvement means buying into the society, and I do not mean just paying your dues. Nothing beats having responsibility and, along with it, accountability.

Inspiring

If we are to realize these goals and give substance to these activities our Society must be respected. We must elevate our rhetoric so as to capture the ethical high ground and stimulate our imagination and ingenuity. We must put aside all our petty quarrels and turf battles. We must turn down the noise of descent and turn up the music of cooperation. We must inspire our young members and future members to commit to a career of challenge, dare to be great, be role models, and inspire through our personal contacts in our daily lives. It is inspiring to be part of a society with a proud tradition, confident in its ability to represent the best and to address the important issues in cancer care, now and in the future. In a society where perception means everything we must be perceived as inviting, involved, and, above all, inspiring.

Now I turn to the second part of my address:

BATTLEFIELDS

My personal battlefield was in Vietnam. I know my participation in the Vietnam War changed my life and I am sure that there are many battlefields today that will change the lives of all of you, physicians and patients alike. Webster's definition of a battlefield is "an area of conflict, a combat arena, struggle places where decisions are made in a state of armed conflict." Today, as in the past, we have many analogies or symbols of battlefields. The war on poverty, the war on drugs, and, now, the war on cancer. The battlefields are in the streets of our cities, the classrooms of our schools, and the laboratories of our research institutions. As oncologists, our cancer battlefields depict images of burning, slashing, and vaporizing. Picture, if you will, the operating room with its determined skillful surgeon fighting to encircle an invasive malignancy; circulating chemotherapeutic agents dueling with mutating cancer cells; DNA strands snapping as cancer cells are bombarded by photons and electrons, and the explosions of deep-seated cancer cells as they are penetrated by targeted particles of the atom. Certainly all military images with battlefield connotations.

In order to extend this theme, allow me to use four unique battlefields that illustrate challenges, conflicts, or crises, if

you will, facing our profession. The Chinese, in their language, express crisis as a two-part character. The first stands for danger and the second, opportunity. Each of these battlefields depicts danger but also a chance to seize the opportunity.

The first battlefield is Pickett's Charge. It took place at Gettysburg, Pennsylvania, on July 3, 1864. Major General George Pickett led a division of confederate soldiers across a treeless, open wheatfield, up a slight grade in face of a withering field of fire from the union soldiers dug in along Cemetery Ridge. Those of you who have been to this battlefield can appreciate the courage of these soldiers as they charged across this inconsequential piece of real estate. Three thousand soldiers lost their lives. This became the high water mark of the confederacy. Perhaps, this is somewhat analogous to the turf war that has waged in recent times between general surgeons and otolaryngologists as to who is best suited to care for the head and neck cancer patient. I believe, as Pickett's charge was the last gallant effort by the confederacy, the edict from the American Board of Surgery to the program directors in general surgery requiring their residents to have hands-on training in head and neck surgery is the last gasp of fantasy from the leadership in general surgery. It was a valiant but futile effort to maintain its position and involvement in the treatment of head and neck cancer. To show you the way things have changed, approximately 38 years ago, in 1958, the Training Committee of the Society of Head and Neck Surgeons chaired by Dr. Art James sent out a questionnaire to the chiefs of surgical services in 213 hospitals with 4-year approved general surgical residencies.⁶ Seventy of these institutions also had approved ENT residencies as well. One hundred and seventy-six of these chiefs replied that there was little or no head and neck surgery training for ENT residents. In fact, if you desire to do head and neck surgery, you must be a board certified general surgeon. In 1987, 9 years ago and 29 years after Dr. James' questionnaire, the Long Range Planning Committee of the Society of Head and Neck Surgeons sent out a questionnaire to its membership which, at the time, consisted of approximately 20% otolaryngologists and 50% general surgeons. One question asked was "how many members did major head and neck operations in the last year?" The response was correlated with their specialty background. I suspect that, if today, a similar survey was made in hospitals with 4-year approved general surgery residencies there would be very little or no head and neck cancer surgery training for general surgery residents; a 180 degree turn around from 1958. Can the American Board of Surgery reverse this trend? Not if their strategy reflects the famous charge of General George Pickett. In my opinion, this battle is over, so let's bury the animosities, recognize the need for excellence, and devote our energies to the training of qualified young people who are dedicated to the care of the patient with head and neck cancer and who will develop innovative effective treatment strategies for the future.

In 1876, the battle at The Little Big Horn, as everyone knows, pitted a very glamorous, but arrogant Colonel George Armstrong Custer against a large, well-motivated Sioux war party led by Sitting Bull and Crazy Horse. He and his men were surrounded and although they made a courageous stand, no one survived. Today, we stand on the

HMO managed care battlefield where we are surrounded by men dressed in Madison Avenue pinstripes and armed with managed care contracts rather than dressed in war bonnets and armed with bows and arrows. The obvious issue is over the right of a patient to choose his or her own physician. In reality, however, this is a battle for control—control of physicians by bureaucrats, politicians, and big business. We now have words like down-sizing, right-sizing, and re-engineering. We are being monitored by self-serving bureaucrats in insurance companies, by case managers within our own institutions each demanding adherence to practice guidelines that often restrict our ability to tailor our treatment to the individual patient. This can potentially compromise the quality of our patient care. I suspect it will not be long before capitation will have us all with our necks in the guillotine. Unless we can become extremely cost-efficient, we will cease to be able to pay for our own expenses much less carve out a livelihood from our profession or support resident teaching and translational research. There is a natural bias in any capitated system to withhold treatment for personal gain just as there is a bias in a fee-for-service system to provide excessive care for personal gain. The determining factor in both systems is the patient's trusted advocate, the physician, and his or her moral behavior. Because of our own greed, we find ourselves in this battle for survival. Unfortunately, too many of us put our style of living as more important than perpetuating the respect and goodwill of our patients, which we inherited from the dedicated sacrifices of our physician ancestors. If we act like a trade or business rather than a profession, we shouldn't complain about words used to describe us such as healthcare providers and our patients as clients. Simon H. Rifkind, a lawyer, expressed his views about how a profession loses its professionalism.

First, the place of self-interest. The profession excludes it, a trade emphasizes it. Second, the relative weight assigned to obligations and rights. The profession assigns great weight to its obligations. A trade assigns such weight to its rights. Third, a profession encompasses the obligation to share information with fellow professionals. Trades treat private knowledge as a business secret. Fourth, a profession must be practiced in the spirit of public service. A trade has no such commitment.⁷

Our answer to this attack is to continue to emphasize quality. We, as physicians, are the only advocates our patients have to maintain the high standard of medical care this country has enjoyed through the dedicated efforts of men and women with integrity. Character is the currency of credibility. If we are to prevail we must provide credible leadership. To sum up the situation, I quote from a Roman Centurion in 66 A.D.: "We trained hard, but it seemed that every time we were beginning to form up into teams, we were reorganized. I was to learn later in life that we tend to meet any new situation by reorganizing and a wonderful method it can be for creating the illusion of progress while producing confusion, inefficiency and demoralization."^{7a}

On the third battlefield, two of the most prestigious professions have positioned themselves in direct confrontation over the issue of tort reform. In many ways it reminds me of the two proud armies meeting on the battlefield at Waterloo, dressed in all their glorious military regalia. This was no chance meeting. This was a strategic encounter with

both sides well-fortified on a battlefield that was not level. Geography played an important part in the outcome, with the two parties maneuvering for the high ground. The English ultimately occupied the slopes and the French were in the valleys. Napoleon's strategy, however, was valid and allowed for some of his early successes. His failure at Waterloo and ultimately his surrender and subsequent abdication were due to a succession of mistakes by his lieutenants, unusually poor staff work, and an uncharacteristic lack of coordination among the infantry, artillery, and cavalry units. This confrontation has been listed as one of the decisive battles of the Western World. How today's titanic struggle with the legal profession will end, no one can be sure. But let us be careful we do not, like Napoleon, jeopardize our cause because of flaws within our own ranks, greed, lack of discipline, and moral and ethical turpitude. The playing field is not level because all the judges and most of the members of legislatures are lawyers. The insurance companies control the gatekeepers, determine who is insurable, what the premium will be, whose bills will be paid, and how much will be paid. If that isn't control of the battlefield, I don't know what is. We do know from history that, although Wellington won the battle, it was not nearly as personally satisfying and gratifying to him afterwards. I am not sure either group will be declared the winner in this battle but we must always keep the welfare of our patients foremost.

The walrus in Lewis Carroll's *Alice in Wonderland* speaks as if he is visualizing the uninitiated physician facing the opposing lawyer on the witness stand. "The time has come," the lawyer is saying, "to speak of many things: of duty, of dereliction, of negligence, and of obscure pains." This may have been the same thought in the minds of the "Cuirassiers" of the French cavalry as they met the Scottish Highlanders arranged in the classic defensive formation—the British square. I am sure the pains weren't obscure, but were very real, just like our own pains when we are served a malpractice suit. The problem is a basic conflict in philosophy. Lawyers approach truth through the adversary system while physicians require the objective scientific method.⁸ I am not sure these two philosophical approaches can ever be reconciled.

The last example is a molecular battlefield. Recently, we celebrated the 50th anniversary of the landing on Normandy, code name "Overlord." The whole purpose of this epic human endeavor was to establish a beachhead on the continent of Europe. This was without precedence in the annals of warfare. Its success, however, was probably as much a result of fortuitous events and circumstances as it was to premeditated and calculated decisions. Whether or not the men of the US 29th Infantry Division could have established, maintained, and extended the landing at Omaha Beach depended a lot on totally unplanned actions and reactions by both sides, developments related to the Germans as well as the Americans. Properly prepared and trained soldiers, however, were able to take advantage of these opportunities. Similarly, each cancer cell must establish its own beachhead as it tries to invade the normal tissues. The fiercest battlefield, this molecular struggle, is waged in the cellular trenches. Here the host, or the soil, is struggling to recognize the mutated guests, or seeds, which have become an invading rogue army using every type of

deception to establish a beachhead. There are no prisoners taken on this battlefield. The warriors include the checkpoint gene, the suppressor gene, the T-cell, and the antibodies. There are resistance, intensification, and regulators. As you may have noticed, all of these terms have battlefield implications. With our ability to manipulate genes it will not be too long before we can either pacify the seed or transform the soil into a minefield.

This brings me to the last part of my address:

WOUNDS THAT WON'T HEAL

What are the characteristics of wounds and wound healing? How are they similar to cancer growth and invasion?

Apollo and a nymph created Asclepius. Apollo chose the centaur Crion whom he trained in the art of healing wounds to raise and educate Asclepius. Asclepius excelled as a physician and was a legendary figure in Homer's *Iliad*. He cured a Spartan girl who suffered from dropsy by severing her head, holding her upside down to drain the fluid, and then successfully returned her head to her neck. Wouldn't we all love to practice head and neck surgery this way? In the *Iliad*, 147 types of wounds were categorized by location. They were also classified as to the type of weapon used to produce it. The mortality rate from these wounds was high: 78%. Homer's description of wounds and their care was so detailed as he was considered to be a military surgeon and followed the Hellenic army during the Trojan campaign.³

The historical chronicle of the wound and its care is intimately interwoven with the barbers and the battlefield. The ancient Egyptians described a cautery used in wounds that would not heal—literally translated as "firestick." This was similar to our term used for the bovie—"the flame stick." Sushruta in 600 A.D. described the divisions of the surgical art into eight categories, of which suturing wounds was one. Heliodorus, a Greek during the First and Second centuries of the Roman Empire, is supposed to have been the first surgeon to describe a technique of tying blood vessels. This was a significant event in dealing with traumatic wounds. Dealing with wounds came in many packages. The Africans used sharp bones to close wounds, but one of the most unique methods is the use of ants by tribes in the Amazon. Large, live soldier ants are set into the open wound. They promptly sink their jaws into one side of the wound and their rear claws grip the other side. At this point the ant is beheaded. As it dies, the shriveling of its body draws the edges of the wound together. Even in death, it will not release its grip.² Perhaps this is the oldest description of Steri-strips.

John Bell of Edinburgh, Scotland was one of the most skillful operating surgeons of the 18th century. His most enduring contribution to surgery, *Discussions on the Nature and Cure of Wounds*, was published in 1795. The theme of the paper: the advantage of securing first intention in healing rather than waiting for it to close by nature. By the way, he was the first to tie off the carotid artery in the neck successfully as part of the care of a neck wound.

In making an analogy between battlefield wounds and cancer wounds, can we understand the similarity between the mechanism by which tissues heal and cancers invade?⁹ Perhaps the activity of mitotic inhibitors or stimulators may extend beyond their role in initiating repair. They may be involved in a fundamental way in neoplasia. Cells have a

genetically programmed life cycle and up to a certain point in the aging process they have the ability to revert to a less differentiated state with mitotic potential if proliferation is stimulated. Proliferating epithelial cells produce a collagenase and they can also induce mesenchymal cells to elaborate a similar substance. Could neoplastic cells also acquire this ability and could this account for the invasive properties of malignant cells? As it is with all cells, multiplication, function, and death are interrelated and can be the result of injury from any cause. Initially, the cells migrate to bridge the gap caused by loss of tissue, mitosis occurs to replace lost cells and, finally, the cells age to the stage where they can replace function. One stimulus (injury) causes both locomotion and mitosis. Within 12 to 24 hours cells are actively synthesizing DNA. Within 24 to 36 hours active mitosis is occurring.¹⁰ Within the wound there is a loss of the normal mitotic inhibitor. There is an activation of the mitotic genes. The younger aging cells are able to revert to mitosis but not the older aging cells. In fact, this process is actually accelerated. With the aging genes inactivated and with the loss of the epidermal activity inhibitor, the older cells respond by apoptosis. This provides a critically important safety factor in any wound healing. The accelerated rate of aging of the nonmitotic cells greatly increases the rate of cell loss and thus effectively prevents the high mitotic activity induced by the tissue injury or wound from leading to the appearance of a tumor-like growth. Perhaps cancer is a wound that does not stop healing.

It appears that tissue cells have two sets of genes—one controlling mitosis and the other controlling aging. They may be activated alternatively but never simultaneously. Cell death is not due to wear and tear but to a genetically programmed suicide at a specified time. What separates the various tissue types is the rate that these genetically controlled events occur. The cell function kicks in at some stage in the aging process. Thus, all functioning cells are dying cells. An exception is nerve cells, which lost their mitotic property after birth and, thus, are all functioning and, thus, are all in a phase of dying. Some of us can attest to this fact better than others.

Recently, there have been delineated several aspects of wound healing that parallel tumor growth. Key aspects of a program normally involved in wound healing has been detected in tumors and tumor-derived cell lines and appears to be activated in cancer.¹¹ This program includes an adaptation of glycolytic metabolism, secretion of proteinases, and activation of endonucleases.¹² Normally, this process is appropriate for facilitating debridement during the healing of a wound; however, it could be subverted to provide cell

invasiveness characteristic of malignancy. Wound-healing-like activity within tumors progresses normally through the hemorrhagic and inflammatory stages but fails at the mesenchymal ingrowth phase. Thus, no significant collagen deposition is detected. Fluid from tumors markedly prohibit fibroblasts proliferation and collagen synthesis.¹³ Thus, cancer is indeed like a wound that will not heal. Perhaps with recognizing this analogy between cancer and the reparative process we can develop strategies to defeat the cancer cells' relentless invasion.

In closing, I have completed the circle from barber poles, to battlefields, to the care of wounds, and from the healing of wounds to cancer. I have touched on our Society, the training of the new generation, conflicts, images, crises, and challenges to our profession. I have tried to suggest a correlation between wound healing and cancer.

Although this address may have no profound message, I have had fun writing it and I have particularly enjoyed sharing it with you. It is a distinct honor and privilege to occupy this podium as your President and I will forever hold this event in a special place among my memories. Thank you.

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