

# Centennial Changes in Surgical Care and Research

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## HISTORICAL PERSPECTIVES

One hundred years ago, the 21st meeting of the American Surgical Association (ASA) began with R. F. Wier stating in his Presidential Address, “I shall turn aside from the well trodden goal of ornate speech and oratorical display and tread for a few minutes the narrow path of scientific investigation.” His address, entitled “Perforating Ulcer of the Duodenum,” essentially was based on 60 cases published by others in the 5 years preceding the meeting, and noted that the outcome of the reported cases was related to the time of operation. All 25 patients in whom closure was carried out 30 or more hours after perforation died, but 8 of the 12 patients in whom closure was performed less than 30 hours after perforation survived. The 33% mortality in those patients was contrasted favorably with the 60% mortality reported by a European surgeon. Wier noted that in 51 of the collected cases, the diagnosis was “right or approximately so” in 25%. His only patient with a perforated duodenal ulcer presented 4 days after perforation and died quickly after surgical closure.<sup>1(pp238–9)</sup>

At that 1900 meeting, by design of the Program Committee (then called the Committee on Annual Meetings), the Presidential Address, the next 10 papers, and a general discussion formed a de facto symposium on gastric surgery that provides us with a close-up view of American surgery at that time. W. L. Rodman noted that treatment of gastric ulcer by either gastroenterostomy or excision of the ulcer was attended by a 15% mortality and that the first episode of hemorrhage should be treated with “masterly inactivity” and “free use of normal salt solution.”<sup>1(p239)</sup> William J. Mayo’s paper on “Malignant Diseases of the Stomach and Pylorus,” is said to be the first paper in our Transactions referring to X-ray of the gastrointestinal tract. Both the X-ray and gas-

trodiaphanoscopy (a technique of transillumination of the stomach akin to the candling of eggs) had been proposed as means of localizing gastric tumors, but Mayo expressed skepticism about both modalities.<sup>1(p241)</sup> B. F. Curtis attributed gastric atony to rapid eating. Gastroplication and gastrorrhaphy were reported to give good results, but the outcome depended on careful selection of cases. Curtis noted that the condition appeared to be systemic, usually requiring not only gastrorrhaphy but also right nephrorrhaphy, hepatorrhaphy, and even removal of a T-shaped segment of the abdominal wall (the Depage-Hannecart procedure) to reduce the volume of the abdominal cavity and thereby improve support of the abdominal viscera. He noted that in women, suspension of the genital organs was also required.<sup>1(pp241–2)</sup> Even so, such extensive “suspension procedures” were associated with what today would be called poor outcomes.

Two papers presented gastric surgery in a more favorable light. John M. T. Finney emphasized that the treatment of acute gastric ulcer perforation was entirely surgical and stated that operation should be performed promptly to remove the cause of shock, rather than postponed until the patient recovered from shock.<sup>1(p240)</sup> Frederick Kammerer reviewed benign obstruction of the pylorus and described his use of Murphy’s button to perform a posterior gastroenterostomy, which he claimed to be totally successful in avoiding postoperative gastric obstruction.<sup>1(p240)</sup>

Two other papers published in 1900 in Volume 32 of the *Annals of Surgery* provide additional insight into the state of American surgery at that time. A. V. Moschowitz, in a review of 97 cases of tetanus, recorded a 42% mortality,<sup>2</sup> and C. L. Gibson, in his report of 1,000 operations for acute intestinal obstruction and gangrenous hernia, reported similarly high mortalities: 67% in patients with umbilical and ventral hernias and 50% in 30 patients undergoing resection of gangrenous bowel with formation of an “artificial anus.”<sup>3</sup>

During the past century, operations for the treatment of peptic ulcer have undergone continued modification and refinement, but have been performed far less often since the microbial etiology of many peptic ulcers was identified and treatment with antimicrobial agents and acid secretory suppressants was instituted. Similarly, the surgical treatment of gastric cancer has been refined and integrated into programs

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of multimodal therapy to improve survival. The use of Murphy buttons to reestablish gastrointestinal continuity was superseded by handsewn anastomoses, which have in turn given way to mechanically placed staples—the modern analog of the Murphy button. Tetanus immunization has essentially eliminated tetanus as a surgical complication, and improved perioperative management, made possible by greater understanding of pathophysiology, current diagnostic technologies, modern anesthetic techniques, and antibiotics, has significantly reduced mortality associated with “gangrenous hernia.”

The changes in the surgical treatment of those diseases have been paralleled by improvements in the care of injured patients. Many of the changes in trauma and burn care have resulted from surgical experience gained in armed conflicts in which members of this Association have participated and provided important professional leadership.

The last annual meeting of the 19th century, which occurred within months of the end of the Spanish-American War, included a symposium on “military surgery.” Dr. Nicholas Senn and Dr. G. R. Fowler, both of whom had served in Cuba, delivered papers in which they described the use of the first-aid package in the treatment of gunshot wounds and discussed the organization and limitations of military field hospitals, respectively.<sup>4</sup> Dr. C. B. Nancrede, a future ASA President, who had served with the 5th Army Corps and had treated more than 1400 wounded patients, noted that small-arms fire did not “produce such destruction of bone as often to demand amputation if sepsis can be secured; hence, removal of the limbs for extensive fracturing of the long bones was almost unknown.” He considered “antiseptic occlusion” and fixation to be the best treatment for bone and joint wounds. In response to critics who had said that there had been inadequate fixation of extremity wounds, Nancrede replied, “Certainly some of us know quite as well as our critics what ought to be done, but we only did what we could and did not attempt the impossible as those who kept out of the way of bullets and hard work thought we should have done.” He also considered “antiseptic occlusion” to be the best treatment for thoracic, abdominal, and articular wounds. He stated that “. . . all perforating ball wounds of the abdomen operated upon, I am informed, perished, while a number I saw recovered without intervention, antiseptic occlusion being relied upon. The Spanish surgeons reported similar results after undoubted intestinal perforation.”<sup>1(p225)</sup> On the basis of his earlier civilian experience, reinforced by his experience in the field, he concluded that if operation could not be carried out before peritonitis occurred, surgical intervention actually decreased the patient’s chance for survival of a penetrating abdominal wound that involved hollow viscera.

As part of that symposium, a Dr. Ferrebee is credited with saying that more men had been lost in a recent street fight in Cincinnati than in the Puerto Rican campaign, in which only 49 men had been killed and wounded. Later in the discussion, Ferrebee stated, “The nursing force during our late war

was extremely defective in very many respects. . . .” He noted that the majority of nurses were male and were “of very little value.” He considered there to be no reason why women nurses should not staff division and brigade hospitals.<sup>1(pp225–6)</sup>

Other speakers decried the disappearance of hospital organization that had been developed during the Civil War, and attributed that to lack of support by the Congress prior to the conflict. It was noted that line officers paid little attention to the advice of medical officers in regard to patient care, military hygiene, and even sanitation. The Association passed a resolution expressing its opinion that instruction in hygiene and camp sanitation should be provided at the military academy at West Point. Copies of the resolution were sent to the President, the Secretary of War, both houses of Congress, and the Superintendent of the military academy.<sup>1(p226)</sup> The response to that resolution and others that were sent to the Army and other governmental bodies in the first half of the 20th century can be broadly interpreted as “don’t call us, we’ll call you.”

No papers were given on burn care, still largely eclectic, at that meeting. Even so, there were intimations of modern burn care in the first decade of the 20th century. Dr. Haldor Sneve, a surgeon in St. Paul, Minnesota, identified four major determinants of outcome in burn patients. He recommended the administration of salt solutions by ingestion, infusion, clysis, and even enemas to prevent shock. He described the use of cutaneous xenografts from dogs, rabbits, guinea pigs, and chickens, and favored the latter, presumably because the holes produced by plucking the feathers would allow drainage of suppurative material. Sneve also identified toxemia, which we would recognize today as burn wound infection, and commented on metabolic exhaustion as a consequence of wasting in patients who were successfully resuscitated.<sup>5</sup> Sneve was 30 years ahead of his time and his recommendations went unheeded and largely unrecognized.

The first significant armed conflict of the 20th century in which the United States was involved was World War I (1914–1918). In his 1916 Presidential Address, “Preparedness,” Robert G. LeConte advocated an increase in the number of physicians in the armed forces and proposed universal military training.<sup>6</sup> Eleven papers about wartime surgery were presented at the 1916 meeting. A. M. Fauntleroy, a U.S. Navy surgeon, advanced the concept that wounds encountered in warfare were totally different from wounds encountered in civilian practice,<sup>7</sup> a concept which I feel has shackled military surgery ever since and fostered acceptance of less-than-optimal outcomes. Dr. Fauntleroy stated that infection in some form was always found in war wounds and discussed the central role of enteric organisms in primary wound infections, noting that laboratory studies had identified the soldier’s clothing as the proximate source of the primary wound infection, with the original source of the infecting organisms being the soil where the injury occurred. He also reviewed the controversy of antiseptic

solutions versus hypertonic salt solution for wound dressings and irrigation, and stated "...the Dakin fluid is the antiseptic of choice among the great majority. . . ."

The usefulness of the first-aid packet carried by each soldier, highly praised in 1899, was considered severely limited in the treatment of wounds produced by fragments of shells and antipersonnel weapons. Dr. Fauntleroy contrasted his observations in military hospitals in France with the experience in the Boer War, in which treatment with "opium, starvation, and rest in the Fowler position" was associated with better survival of patients with penetrating abdominal injuries than was operation. He noted that in the present war, when the patient could "receive prompt attention the results from operative treatment had been most encouraging in improving the statistics as compared with the expectant line of treatment." Dr. Fauntleroy noted that other surgeons believed that operation would achieve greater survival than expectant treatment in patients with shrapnel, shell, and bomb wounds, and felt that the good results obtained in patients with intestinal resection for multiple wounds of the intestines supported the concept of early surgical intervention. The effectiveness of antitetanic serum in virtually eliminating tetanus in the wounded was noted, and Alexis Carrel was credited with identifying the importance of rapid transportation and promoting the use of motor ambulances to effect early treatment of the wounded.

J. M. Flint discussed the localization and extraction of projectiles and shell fragments in combat casualties.<sup>8</sup> The radiologic techniques he described included operations directly under the fluoroscopic screen, which were little used because of the difficulty in maintaining asepsis; the use of the ring compass; the use of the Irvin Profoundometer; the Sutton localizer; and the vibratory magnet of Bergonié. Dr. Flint claimed that "astonishing accuracy" permitted removal of all fragments that "it seemed desirable to extract." He reported that 80% of the procedures were done with local anesthesia.

At the 1917 meeting, C. L. Gibson, who had visited Carrel in his hospital in Compiègne and the Allies' Franco-British Hospital at Annel, described the use of continuous irrigation with Dakin's solution for the treatment of soft tissue wounds.<sup>9</sup> E. W. Archibald and W. S. McLean stated that shock was the consequence of a plasma deficit<sup>10</sup> and not due to pain, as some still proposed, and noted that they gave a "great deal of salt solution" and preferred to give it intravenously rather than depositing it under the breast, from which site they thought it was absorbed too slowly. To compensate for the "transitory" effect of salt solutions, they also gave a colloid solution consisting of 25 g of gelatin in 1 L of saline. They had used blood transfusions in three cases and considered them to have no more permanent effect than gelatin or salt solutions. They found injections of pituitrin to exert no beneficial effect in patients with severe shock. Anticipating by 70 years the current interest in hypertonic salt for trauma resuscitation, they speculated that

"hypertonic salt solution at twice decinormal strength would be of some promise."

At the 1918 meeting, Dr. A. Primrose noted that whole blood had been transfused successfully for the first time in war.<sup>11</sup> He reported 10 patients to whom he had given blood transfusions. One patient, who had experienced hemolysis, illustrated the importance of preliminary tests of donor-recipient compatibility. Even so, Primrose noted that the occurrence of hemolysis was sufficiently rare that tests of compatibility could be omitted when the need for blood was urgent. Interestingly, Dr. Primrose perpetuated the distinction between hemorrhage and shock and agreed with others who felt that blood transfusion was valueless in shock. He qualified that opinion, noting that if the shock was accompanied by hemorrhage, transfusion could be life-saving. He further noted that "the Americans on the western front have ingeniously succeeded in keeping blood drawn from the donor in cold storage for 48 hours or more in anticipation of an emergency." This appears to be the first mention of a military blood bank in the surgical literature.

Also at the 1918 meeting, D. F. Jones discussed the role of the evacuation hospital in the care of the wounded.<sup>12</sup> He noted that casualties arrived at the base hospital an average of 3 days after being wounded. In such patients, the success of wound treatment was dependent on early radical excision of devitalized tissues, not the type of antiseptic used. Dr. Jones noted that the casualty clearing stations, established to provide early care to the seriously wounded who would require further care at the base hospital, had actually done much harm because inexperienced surgeons at those facilities performed incomplete operations which predisposed patients to infection and delayed transfer to the base hospital. Dr. Jones advocated staffing the evacuation hospitals and mobile units with experienced surgeons transferred there from the base hospitals—that is, the provision of definitive care at the earliest possible time.

At the Association's business meeting in 1918, the Assistant Secretary, F. T. Stewart, read a letter from Gen. J. M. T. Finney (another future ASA President), then the Chief Surgical Consultant for the American Expeditionary Force,<sup>1(p546)</sup> who emphasized the importance of surgical expertise, noting that he had what he termed an "all star cast" directing specialty care in the Army: Maj. Joel E. Goldthwait (orthopedics), Maj. Hugh H. Young (genitourinary diseases), Maj. Thomas Case (in radiology), Maj. Harvey W. Cushing (neurosurgery), Maj. Vilray Blair (maxillofacial surgery), Maj. James F. McKernon (nose and throat), and Maj. George W. Crile (research). Gen. Finney noted that they had organized an experimental surgical department, directed by Maj. Walter B. Cannon and connected with the central laboratory.

In his Presidential Address, "The Influence of War Surgery Upon Civil Practice,"<sup>13</sup> at the 1919 meeting, L. F. Pilcher noted that during World War I, 35,000 physicians had joined the military and 14,000 were sent overseas. (In his 1920 Presidential Address, G. E. Brewer recorded that

107 ASA Fellows held commissions in the United States' and allied armies.<sup>14</sup> Pilcher noted that the surgical experience during the war had resulted in many modifications and adaptations of surgical technique, as well as the introduction of new antiseptic agents. He recorded that more than 93% of all casualties who lived to come under surgical care recovered from their wounds and that between 70% and 80% of all casualties returned to duty within 2 months.

Antoine Depage, an honorary fellow of the Association, a colonel in the Belgian Army, and Director of the Belgian Red Cross, reviewed his experience in the treatment of war wounds using Carrel's antiseptic technique,<sup>15</sup> and concluded with a single paragraph on abdominal wounds, stating "Such general accord has been established that all surgeons think that early intervention should be resorted to." He credited the placement of treatment facilities within 2 to 3 km of the front with reducing mortality from abdominal wounds from 65% to 45%. Also at that 1919 meeting, George W. Crile discussed the importance of surgical judgment and meticulous technique in the successful treatment of patients with war wounds,<sup>16</sup> and concluded that "...the one agent of successful surgery, whether war surgery or civil surgery, is the good surgeon."

The theme of early care at specialized treatment centers by experienced surgeons reverberated throughout the 1918 and 1919 meetings. Later in 1919, a special report by Elliott Cutler (also a future ASA President), "War Surgery Under Frontline Conditions," summarized the work performed by Casual Surgical Team No. 506, working in two hospitals in France.<sup>17</sup> The team recorded 576 cases during a 51-day period in the summer of 1918. Dr. Cutler, in discussing what he called chest-diaphragm-abdomen cases, noted that the need for surgery depended on the size and kind of missile involved and stated that small shell fragments and bullets reaching the liver through a lung and diaphragm may not require operation. He stressed the importance of adequate debridement of all wounds and of transporting "head cases" to a site where specialists could carry out the necessary surgery.

At the business meeting that year, a resolution was approved to petition the Surgeon General of the Army to make all clinical records of his office available for study by the medical profession.<sup>1(p554)</sup> The Surgeon General's response is not recorded and it is uncertain how many of the medical profession studied those records.

Burn care changed little throughout World War I. In 1919, Dr. A. M. Fauntleroy described the extant techniques of burn care in a report of 32 patients with severe extensive burns sustained in a shipboard coal dust explosion.<sup>18</sup> Immediate care consisted of applying aqueous picric acid dressings in which the patients were transported to a hospital. At the hospital, morphine sulfate was given as needed for pain control, and severe cases received continuous proctoclysis of normal salt solution to which sodium bicarbonate had been added. The initial dressings were then removed and a fresh wet picric acid dressing was applied. Nine of his

patients died within 48 hours and another died with bronchopneumonia in the third week. After resuscitation, patients were given water and large quantities of nutritional liquids every 2 hours by mouth including "two or three egg-nogs to which whiskey was added during the night." In the fourth and fifth week, to combat what was termed "exhaustion," a tonic of phosphorous, strychnine, and quinine was administered.

The burn wounds were treated with boric acid ointment; areas of eschar floating on "choked up pus" were either debrided or left untouched, depending on the surgeon's preference. When the "crusts" were finally removed, application of a thin layer of boric acid ointment was associated with "a quick bridging over of the raw surface with new skin and complete healing with no scar formation in a few days time." Surprisingly, Fauntleroy concluded "that the less encouraging the burn surface appears during the initial dressings, as far as to macroscopic appearance, irregularity of surface due to... dead skin, etc., the better will be the ultimate result." Areas of deeply infected tissue were treated with many agents, including open air, exposure to electric light, boric acid ointment, liquid petrolatum, paraffin, wet dressings, and continuous irrigation. Continuous irrigation with hypertonic salt solution, Dakin's solution, normal salt solution, and a modified Dakin's solution were reported to be equally effective. Dr. Fauntleroy wrote that his techniques of wound care were responsible for reepithelization of large areas of skin and "the non-necessity for application of skin grafts."

During the interval between the end of World War I and the entry of the United States in World War II (1918–1941), the problem of shock was studied by Walter B. Cannon, C. J. Wiggers, and other physiologists, as well as Arthur Blalock, Dallas B. Phemister, and other surgeons.<sup>19</sup> At the beginning of World War I, many physiologists and surgeons considered shock to be the result of stimulation of the "depressor nerve" and failure of the vasomotor center.<sup>19(p9)</sup> In studies conducted during the war, Walter B. Cannon focused attention on changes in the peripheral vasculature.<sup>20</sup> His studies and those of Keith<sup>21</sup> and Robertson and Bock<sup>22</sup> illustrated the importance of plasma loss, hemoconcentration as a manifestation of plasma leak due to capillary damage, and a disproportion of vascular volume and blood volume. Later studies by Cannon focused on local "toxemia"-induced capillary changes in the area of injury attributed to "histamine-like substances."<sup>23</sup> Blalock and Phemister and their associates developed techniques to partition fluid loss, showed that fluid loss into the area of injury was much greater than previously estimated, and concluded that such losses could reduce venous return and cardiac output enough to cause circulatory failure.<sup>24</sup> Similarly, our understanding of the pathophysiology of "anhydremia" in burn injury had been advanced by the identification of blister fluid as a filtrate of plasma by Underhill in the course of his studies of patients from the Rialto Theater fire in New Haven in 1921.<sup>25</sup> Consequently, the use of saline infusions

and blood transfusions became common in the treatment of injured patients in World War II, but the volume of fluid required was still unappreciated, as indicated by the high occurrence rate of renal failure in patients with severe mechanical and thermal injuries (18.6% in 427 unselected autopsied battle casualties dying in Army hospitals in Italy in World War II).<sup>26</sup>

Sulfonamides and other antimicrobials were synthesized and developed between the two world wars, and penicillin, discovered in 1928, finally became available in the early years of World War II.<sup>27</sup> These agents strikingly decreased wound infections and other infections in combat casualties in World War II.

At the 1943 meeting, Dr. A. O. Whipple described “Basic Principles in the Treatment of Thermal Burns”<sup>28</sup> and emphasized the importance of “well organized burn teams” for the successful management of fluid and electrolyte imbalance, wound care, and early wound closure. He noted that topical sulfonamides had not fulfilled their early promise, but that was simply because the wrong sulfonamides had been used.

In 1944, then-Col. Edward D. Churchill (another future ASA President), the Surgical Consultant to the North African and Mediterranean Theater of Operations, submitted a paper in absentia that described the care of casualties at that time.<sup>29</sup> He emphasized the use of whole blood as a part of resuscitation to optimize the patient’s response to surgery, the specific use of antibiotics as an adjunct to meticulous surgery, and the importance of minimizing the time lag between initial surgery and early reconstructive procedures to ensure continuity of care. The latter concept extended the role of the “field trauma center” into the rehabilitation phase.

In his 1949 Presidential Address, Fred W. Rankin, who had served in the U.S. Army in both world wars, reviewed his experience as a General and Director of the Surgery Division of the U.S. Army in World War II.<sup>30</sup> Dr. Rankin cited four factors as being most important in the reduction of mortality and morbidity rates for battle injuries in World War II: the availability of excellently trained young surgeons who could perform surgery in combat areas; improved methods of resuscitation, including the ready availability of blood and blood plasma; the availability of antibiotics and chemotherapeutic agents used “only as adjuncts to surgery”; and improved means of transportation, including aircraft, for movement of convalescent patients over long distances, even to the continental United States. As a result of those improvements in care, the percentage of combat casualties dying of wounds was reduced to 3.3% from the World War I level of 8.1%. The mortality rates of patients with life-threatening wounds of the head, chest, and abdomen were reduced to approximately one third of the rates in World War I.

The fluid resuscitation of burn patients was also improved during World War II. Early in that conflict, a formula (one of, if not the first) to predict fluid needs on the basis of

extent of burn was promulgated by the National Research Council to standardize the fluid resuscitation of burned soldiers. The formula was based on plasma volume changes identified by Dr. Henry Harkins in a canine model of burn injury.<sup>31(p1013)</sup> During the first year of the war, Cope and Moore at the Massachusetts General Hospital<sup>31(p1013)</sup> and Lund, Davidson, and Levenson at the Boston City Hospital<sup>32</sup> studied patients burned in the 1942 Coconut Grove fire, defined the magnitude of fluid and electrolyte shifts during the resuscitation period, and identified inhalation injury as an important comorbid factor. On the basis of that experience, Cope and Moore formulated the Burn Budget Formula, which is still used today.<sup>31</sup> The Brooke Formula, developed by C. P. Artz and his staff at the Army Burn Center, which emphasized the crystalloid component of fluid resuscitation, simplified the logistics of burn patient resuscitation for the military.<sup>33</sup> By the end of the Korean conflict, prompt adequate fluid resuscitation had essentially eliminated renal failure as a consequence of burn injury.

The surgical care of the mechanical trauma patient also further improved during the Korean conflict (1950–1953). The transport of combat casualties to the initial treatment facility was further accelerated by the use of helicopters in that conflict. The repair and even replacement of injured vessels, initiated by Frank Spencer, John H. Davis, and Carl Hughes, all of this Association, became commonplace.<sup>34,35,36</sup>

During the Vietnam conflict (1965–1973), further improvement in combat casualty care resulted from improved perioperative management based on increased understanding of the pathophysiologic response to injury, the availability of broad-spectrum antibiotics and topical antimicrobial burn wound agents, improved radiology capability at forward hospitals, improved anesthetic management, and the availability of an adequate number of board-eligible and -certified surgeons and other medical specialists. Helicopter transport of casualties from the site of injury to a definitive treatment facility increased the number of admissions with life- and limb-threatening injuries, who would not have reached the hospital in prior conflicts. The surgical capabilities of the surgeons at those hospitals achieved unprecedented survival for such patients, and improved survival and decreased morbidity for all combat casualties. Only 582 (2.5%) of 23,396 wounded casualties admitted to Army hospitals from October 1, 1965, to June 30, 1967, died (Table 1).<sup>37(p240–1)</sup> The benefit of early care given by surgical specialists in specialized treatment facilities, i.e., military trauma centers, was again clearly evident, as had been noted by Rankin almost 20 years earlier.

The improvements in care that have increased the survival of trauma and burn patients in the past century can, I believe, be credited to the planned concentration of categorical patients at specific treatment facilities, the care provided by certificated, experienced surgeons, and the implementation of research programs in which clinical and laboratory investigative capabilities were effectively integrated and focused on the injured patient (Table 2).

**Table 1. MORTALITY OF WOUNDED PATIENTS IN MILITARY CONFLICTS: 1898–1975**

|                                             | Mortality % |
|---------------------------------------------|-------------|
| Spanish-American War*                       |             |
| Abdominal wounds                            | 65          |
| World War I*                                |             |
| Abdominal wounds                            | 45          |
| All wounds                                  | 8.1         |
| World War II†                               |             |
| Abdominal wounds                            | 15          |
| All wounds                                  | 3.3         |
| Korean Conflict‡                            |             |
| Abdominal wounds                            | 8.85        |
| Vietnam Conflict‡                           |             |
| All wounded admitted to U.S. Army hospitals | 2.5         |

\* Data from Depage.<sup>15</sup>† Data from Rankin.<sup>30</sup>‡ Data from Whalen et al.<sup>37</sup>

## INTEGRATED BIOMEDICAL RESEARCH IN THE U.S. ARMY

The U.S. Army's primacy in the conduct of integrated clinical and laboratory research began on June 16, 1822, when William Beaumont undertook the care of Alexis St. Martin, who had sustained a penetrating upper abdominal

wound.<sup>38(pp158–81)</sup> A gastrocutaneous fistula formed through which Beaumont was able to observe the gastric mucosa. Beginning in 1825, he conducted a total of 238 experiments in which he observed and described the response of St. Martin's gastric mucosa to a variety of stimuli and took samples of the gastric juice for analysis. Beaumont enlisted the aid of Robley Dunglison, Professor of Medicine at the University of Virginia, who confirmed that the gastric juice contained muriatic acid. Hoping to identify other components of gastric juice, Beaumont contacted Benjamin Silliman, Professor and Chairman of Chemistry and Natural History at Yale University. Silliman provided little data, but encouraged Beaumont to send a sample of gastric juice to Prof. Jons Jacob Berzelius, the renowned Swedish chemist, who in 1834 informed Beaumont that he had been unable to analyze the gastric juice. That reply and St. Martin's flight brought to a close Beaumont's multidisciplinary, multiinstitutional, international research project, which had expanded knowledge of the general physiology of digestion and identified the acid content of gastric juice.

Dr. R. M. Zollinger was fond of pointing out that soon after arriving at the fort on Mackinac Island, Beaumont wrote to and received permission from his friend Joseph Lovell, the Surgeon General, to conduct a private practice and thus became the first military physician known to "moonlight." If Beaumont had not had permission to conduct a private practice he would in all likelihood not have been allowed to care for St. Martin.<sup>38(p179)</sup>

**Table 2. COMBAT CASUALTY CARE INNOVATIONS IN 20TH CENTURY CONFLICTS**

| World War I                                                               | World War II                                                 | Korean Conflict                                                                     | Vietnam Conflict                                          | Operation Desert Shield/Storm                                             |
|---------------------------------------------------------------------------|--------------------------------------------------------------|-------------------------------------------------------------------------------------|-----------------------------------------------------------|---------------------------------------------------------------------------|
| Common use of intravenous fluids for resuscitation                        | General availability of whole blood and plasma               | Fluid resuscitation adequate to prevent renal failure                               | Use of mechanical ventilators in theater of operations    | Attachment of burn teams to evacuation hospitals in theater of operations |
| Whole blood transfusions introduced                                       | Formula-based estimation of burn patient resuscitation needs | Use of hemodialysis in theater of operations                                        | Improved radiology capability                             |                                                                           |
| Antitetanic serum                                                         | Use of antibiotics                                           | Primary repair and vascular grafts for injured vessels                              | Monitoring of organ function in theater of operations     |                                                                           |
| Prompt debridement of soft tissue wounds with Dakin's solution irrigation | Use of fixed-wing aircraft for patient transport             | Selective use of helicopters for patient transport                                  | Blood gas measurements at evacuation hospitals            |                                                                           |
| Prompt operation for penetrating abdominal wounds                         | Availability of well-trained young surgeons                  | Surgery performed by Board-certified or board-eligible surgeons at mobile hospitals | Use of topical antimicrobial chemotherapy for burn wounds |                                                                           |
| Radiologic localization of foreign bodies                                 |                                                              |                                                                                     | Common use of helicopters for patient transport           |                                                                           |
| Use of motor ambulances for patient transport                             |                                                              |                                                                                     | Surgical specialist care provided only by specialists     |                                                                           |
| Planned use of surgical specialists                                       |                                                              |                                                                                     |                                                           |                                                                           |

The Army's support for integrated research has continued since that time. Walter Reed's studies of yellow fever had a clinical component in Cuba and a laboratory component at the then-new Army Medical School, which had been established by Surgeon General G. M. Sternberg.<sup>39(pp55-8)</sup> Reed also studied the typhoid epidemics that affected military operations in Cuba and recruits in military camps in the United States, even after the war ended.<sup>39(p87-8)</sup>

In World War I, Gen. Finney established an experimental surgical department in connection with his hospital's central laboratory, directed by then-Maj. Walter Cannon, a much-respected physiologist who apparently worked with George W. Crile, who was Finney's Director of Research.<sup>40</sup> Cannon conducted laboratory studies in a small number of injured soldiers studied by others that corroborated the clinical findings indicating that the severity of shock was related to the magnitude of blood volume deficit.<sup>19</sup> The results of those "integrated" studies were published in the Special Report Series of the Medical Research Committee of Great Britain.<sup>20-23</sup>

The Board for the Study of the Severely Wounded continued the tradition of integrated research in World War II. This multidisciplinary Board, organized by Edward Churchill, was appointed in September 1944 and focused on specific problems identified in the course of caring for combat casualties.<sup>40</sup> The Board evaluated the effect of injury on hepatic and renal function, refined the diagnosis of acute renal failure (then called lower nephron nephrosis), and evaluated various treatment measures. In a premonition of future interest, a 10% solution of hypertonic saline was used in the treatment of one patient with renal failure but no effect on urinary output was observed.<sup>40(p187)</sup> Alkali infusions were found to be largely ineffective in preventing renal failure and, if given in quantity sufficient to induce alkalosis, appeared to cause further damage of injured renal tubules. The Board studied the crush syndrome in battle casualties and cautioned against excessive fluid administration in patients with renal failure. Lastly, they made extensive observations on the general pathology and pathophysiology of traumatic shock, in which they cataloged temporal changes in various organs.<sup>40</sup> Dr. Churchill proudly noted that precise measurements had quantified the physiologic response to injury.

During the Korean conflict, the Army Medical Service Graduate School Surgical Research Team in Korea further documented the pathophysiologic response to blood loss and injury.<sup>41</sup> Fluid resuscitation volumes were adjusted upward on the basis of those studies and a striking reduction in the incidence of acute renal failure in the severely wounded was observed, which has persisted in subsequent conflicts and in civilian practice (Table 3).<sup>42-44</sup> A renal failure treatment unit with hemodialysis capability was established in the theater of operations. The investigators at that unit identified a subset of patients with high output renal failure, which confirmed that postinjury renal failure could be of variable severity and that renal impairment after

**Table 3. RENAL FAILURE IN COMBAT CASUALTIES AND CIVILIAN TRAUMA PATIENTS**

|                          | Incidence of Renal Failure                                   |
|--------------------------|--------------------------------------------------------------|
| World War II*            | 18.6%                                                        |
| Korean Conflict†         |                                                              |
| Prior to 1952            | 36% of autopsied casualties                                  |
| 1952-1953                | 0.5% of casualties                                           |
| Vietnam Conflict‡        | 1/1319 casualties overall, 1/423 severely injured casualties |
| Civilian Trauma Centers§ |                                                              |
| 5-year review, 1991      | 0.098% of 72,757 admissions                                  |

Data from \* Mallory<sup>26</sup>; † Teschan et al.<sup>42</sup>; ‡ Whelton and Donadio<sup>43</sup>; and § Morris et al.<sup>44</sup>

injury was more common than previously believed.<sup>42</sup> Studies at that unit led to the concept of prophylactic hemodialysis to prevent occurrence of the systemic complications of uremia.<sup>45</sup>

The Vietnam war was the last conflict in which integrated research was conducted in the theater of operations. The Trauma Study Section of the U.S. Army Medical Research Team in Vietnam, to which I was assigned in 1968, collected data on the bacteriology of war wounds, conducted studies of the hemodynamic and pulmonary responses to wounding,<sup>46,47</sup> assessed the affect of injury on circulating levels of liver enzymes, and measured the changes in the volume and composition of gastric secretions that occurred after injury.

In 1943, the U.S. Army Surgical Research Unit (now the U.S. Army Institute of Surgical Research) was established and charged with determining the role of antibiotics in the treatment of war wounds.<sup>48</sup> The Unit confirmed the effectiveness of penicillin as an adjunct to surgical debridement in the control of wound infection which supported widespread antibiotic use throughout the remainder of World War II.<sup>30</sup> The thousands of burn injuries generated by the nuclear detonations at Hiroshima and Nagasaki redefined the mission of the Institute to focus on treatment, teaching, and research as related to burn injury and trauma. In its new mission, the Institute was monitored and reviewed by the Surgeon General's Advisory Committee on Metabolism in Trauma, chaired successively by F. D. Moore, W. A. Altemeier and J. A. Schilling. Such oversight validated the relevance, credibility, and quality of the Institute's research activities.

The successful resuscitation of patients with massive burns using formulae developed during the 1940s and 1950s emphasized the problems of burn wound management. The treatment of burn wounds had changed little since the descriptions of Fauntleroy in 1919<sup>18</sup> and Whipple in 1943.<sup>28</sup> The use of the exposure technique, reintroduced by A. B. Wallace in 1947, seemed only to delay but not prevent burn wound suppuration.<sup>49</sup> In the early 1960s, correlative clinical



**Figure 1.** The multiple indurated and slightly raised areas of dark discoloration, and the edematous, erythematous margins of unburned skin of the burns on this leg are pathognomonic of invasive burn wound infection caused by *Pseudomonas aeruginosa*. A full-thickness biopsy taken from the right side of the leg at the lower margin of the figure (arrow) was used to confirm the diagnosis. This infection is commonly fatal and was the cause of death in 60% of burn patients who died at burn centers in the 1950s and early 1960s.

laboratory studies, directed by John Moncrief and A. D. Mason, at the Institute of Surgical Research revealed that invasive burn wound sepsis was the cause of death in 60% of the burn patients who died at that burn center<sup>50</sup> (Fig. 1). Development of a reproducible, clinically relevant model of invasive burn wound sepsis permitted rapid evaluation of topical antimicrobial therapy, which, when found effective, was transported to the clinic.<sup>51</sup> The use of topical antimicrobial chemotherapy in combination with early burn wound excision has produced a ten-fold reduction in invasive burn wound sepsis as a cause of death in burn patients who die at burn centers<sup>52</sup> (Fig. 2).

As is usually true in biomedical research, the solution of one problem typically reveals other previously unknown problems. Improvements in burn wound care accentuated the importance of smoke inhalation injury as a comorbid factor in burn patients. Once again, clinical studies and the development of an animal model identified useful tech-



**Figure 2.** Twice-daily application of mafenide acetate (Sulfamylon, Bertek Pharmaceuticals, Sugar Lake, TX) burn cream, as shown here, to the burn wounds of this 79-year-old man who sustained a 40% total body surface area flame burn, limits the proliferation of bacteria on and in the burn wound. The use of topical chemotherapy combined with prompt excision of the burned tissue has reduced the incidence of fatal invasive burn wound sepsis by a factor of 10 and revolutionized burn wound care.

niques for diagnosing inhalation injury and demonstrated the effectiveness of high-frequency ventilation in reducing the morbidity and mortality associated with smoke inhalation.<sup>53</sup> Other integrated programs of clinical and laboratory research have been applied to eliminate life-threatening bleeding and perforation due to Curling's ulcers.<sup>54</sup> Studies quantifying and describing postinjury hypermetabolism, which have led to the development of metabolic support regimens that can minimize the previously common erosion of lean body mass and accelerate convalescence after burn injury, have been beneficial to all surgical patients, not just burn patients.<sup>55,56</sup>

These advances in the care of burn patients illustrate the advantages of the reiterative clinic-to-laboratory-to-clinic research cycle that characterizes effectively integrated clinical and laboratory research (Table 4). Specific conditions must be met to conduct such a research program. First, there must be a dependable density of patients of interest to permit completion of studies within realistic time limits, a requirement readily met in a busy intensive care unit, as

**Table 4. ADVANCES IN BURN PATIENT MANAGEMENT: 1940–2000**

| Therapeutic Innovation                                                                                                                                                                                                                                                                                                                                                                           | Clinical Effect                                                                                                                                                                                                                                                                                                                                   |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Prompt formula-based infusion of adequate resuscitation fluid<br>Use of topical antimicrobial burn wound chemotherapy and early burn wound excision and closure<br>Use of fiberoptic bronchoscopy and prophylactic use of high frequency interrupted flow positive pressure ventilation<br>Prophylactic use of antacid agents<br>Provision of adequate nutrition and effective metabolic support | Elimination of early postburn acute renal failure<br>Control of burn wound bacterial density and decreased incidence of invasive burn wound sepsis<br>Accurate diagnosis and reduced mortality of inhalation injury<br><br>"Elimination" of stress ulcer bleeding and perforation<br>Preservation of lean body mass and accelerated convalescence |

indexed by the success of the research programs at both military and civilian burn and trauma centers. The number and type of dedicated clinical study areas needed are dictated by the disease of interest and investigator expertise; for example, the controlled environment metabolic study room at the U.S. Army Institute of Surgical Research (commonly known as the U.S. Army Burn Center) made it possible to characterize and dissect the metabolic response to burn injury.

An experienced multidisciplinary clinical staff is also needed to identify clinical problems of significance as appropriate research topics. That requirement was met at the Army Burn Center by a steady supply of board-eligible and -certified surgeons and other specialists, i.e., drafted doctors who were euphemistically termed "obligated volunteers." Particularly helpful were the personal referrals of promising young investigators by surgical chairmen. There must also be a cadre of technologically capable laboratory scientists who can apply state-of-the-art assays and develop clinically relevant animal models. An enlightened assignment policy on the part of the U.S. Army Medical Corps maintained a relatively stable multidisciplinary burn center staff with a basic complement of surgeons, anesthesiologists, pathologists, and nephrologists, and a variable mix of pulmonologists, cardiologists, endocrinologists, and hematologists, plus nurses, physical and occupational therapists, and dietitians. The laboratory scientists included veterinarians, physiologists, biochemists, microbiologists, and biostatisticians. There should be sufficient stability and flexibility of clinical and laboratory staff to permit the rapid formation of research teams with the capabilities required to address newly identified research questions in an opportunistic fashion.

In the aggregate, the members of an integrated research team constitute a critical scientific mass that will prevent research stagnation and redundant efforts, accelerate clinical application of laboratory findings and identification of new research questions, expedite identification of the limitations and side effects of new treatments, enhance internal quality control, and increase the efficiency and economy of resource utilization and the capture of unexpected benefits of the research performed.<sup>57</sup> An indigenous program of clinical and laboratory research defines a center of excellence. Many treatment facilities can and do provide excel-

lent care, but to function as a center of excellence, clinical expertise must be joined with research activities to generate information that will form the basis for further improvements in care.

In emulation of burn and trauma centers of excellence, many institutions have established multidisciplinary research centers and teams to optimize research effectiveness, facilitate scientific mentoring, and develop integrated research programs.<sup>58</sup> Multidisciplinary projects organized by such teams and focused on specific diseases have received National Institutes of Health funding.<sup>59</sup> Those grants have been found to provide the necessary infrastructure for collaborative, correlative clinical research.

## FUNDING FOR MEDICAL RESEARCH

Changes and advances in clinical care have been accompanied by changes in the funding of medical research. During the 20th century, the predominant source of funding for biomedical research changed from private foundations to public purse, and back to private sources and industry in the 1990s. In the later half of the 19th century, medical research in the United States was largely funded by industrialists such as John D. Rockefeller and Andrew Carnegie. Although they were accused of using medical research to launder their business profits, Carnegie, at least, felt strongly about high-quality education and sponsored the Flexner Report, which was published in 1910 and subsequently purified medical education in the United States.<sup>60</sup>

The National Institutes of Health (NIH), which began life in 1866 as the Federal Bacteriological Laboratory at the Marine Hospital on Staten Island and assumed its present name and location in 1930, gradually replaced philanthropic foundations as the principal source of funding for biomedical research.<sup>60</sup> Even though there has been a long-term progressive increase in support of laboratory-based research and a corresponding decrease in support for clinical research, the NIH has a record of support for integrated research programs, as exemplified by NIH-funded Clinical Research Centers and program project grants focused on specific diseases such as trauma and burns.<sup>48</sup> Other governmental agencies that provide funding for biomedical research include the National Science Foundation, the National Aeronautics and Space Administration, the Veterans

**Table 5. NIH FUNDING OF INJURY-RELATED RESEARCH**

| Year | Total NIH Budget*† | NIH Injury Research*‡ | Percentage of Total Budget |
|------|--------------------|-----------------------|----------------------------|
| 1992 | 10,000             | 119.0                 | 1.2                        |
| 1993 | 10,300             | 126.0                 | 1.2                        |
| 1994 | 10,650             | 160.5                 | 1.5                        |
| 1995 | 11,300             | 146.9                 | 1.3                        |
| 1996 | 11,900             | 150.6                 | 1.3                        |
| 1997 | 12,750             | 155.0                 | 1.2                        |
| 1998 | 13,648             | 161.1                 | 1.2                        |
| 1999 | 15,612             | 158.8                 | 1.0                        |
| 2000 | 17,950             | 176.2                 | 0.98                       |
| 2001 | 20,643§            | 182.4§                | 0.88                       |

NIH, National Institutes of Health.

\* In \$ million.

† Data from FASEB Newsletter.<sup>66</sup>

‡ Data from J. Barklow, NIH Office of Communications (personal communication).

§ Projected.

Administration, and the Departments of Agriculture, Energy, and Defense.

Nongovernmental organizations and foundations provided important funding of trauma-related research throughout the 20th century. The Shriners Hospitals for Children provides generous funding, over \$20 million annually, for integrated research at their four burn centers and 17 orthopedic hospitals (N. C. McCollough, Medical Director, Shriners Hospitals for Children, personal communication, Feb. 28, 2000). At least since 1993, industry has displaced all others as in providing the highest dollar amounts for biomedical research. In 1998, grant-making foundations contributed about \$265 million to medical research, compared to government support of about \$15 billion and industry support of about \$18 billion.<sup>46</sup> This change has created a new set of problems related to data ownership and security, secrecy agreements, conflicts of interest, and publication delay or outright censorship, to name just a few.<sup>62</sup> Even though the former director of the NIH predicted that biomedical research had entered a “steady state,”<sup>63</sup> the U.S. Congress approved a 15% increase in the NIH budget for 1999 and again for 2000. Those increases and the projected increase of 5.3% for fiscal year 2001 for a total budget of almost \$20 billion may reestablish the NIH as the major source for funding for biomedical research and alleviate some of those problems.<sup>64</sup>

Even with the recent large increases in the NIH budget, however, funding for research on injury, which in the United States is the disease responsible for the greatest number of years of productive life lost,<sup>65</sup> remains fixed at approximately 1% of the total budget (Table 5) (J. Burklow, National Institutes of Health, Office of Communications, personal communication, Mar. 20, 2000).<sup>66</sup> That level of expenditure for injury research has been classified as “underfunding” in relation to the “burden of disease.”<sup>67</sup> The

U.S. Army Biomedical Research budget, which has exceeded \$200 million for over a decade, is dwarfed by that of NIH, but in accordance with a primary focus on the care of combat casualties, the fraction of funds dedicated to mechanical trauma and burns is several-fold greater (Table 6) (Maj. Gen. J. S. Parker, Medical Corps Commander, U.S. Army Medical Research and Materiel Command, personal communication, Mar. 2, 2000). Eight to twelve percent of that budget has supported trauma-related research in general, and 2% to 4% has been expended annually for burn-related research (C. W. Goodwin and D. Zolock, U.S. Army Institute of Surgical Research, personal communication, Mar. 24, 2000). One could make the case that those percentages represent underfunding in relation to the importance of combat casualty care to the military.

Not only have the sources of research money changed but the recipients of that money also have changed. A special Career Opportunities Subcommittee of the Federation of American Societies for Experimental Biology has recently reviewed the current status of physician-scientists in the United States.<sup>68</sup> That committee identified an ever-increasing number of physicians who list patient care as their major professional activity and a decrease in those reporting research as their primary activity. Since 1982, the fraction of NIH-funded physician-scientists has decreased as the increase in NIH grants to PhD faculty has exceeded the increase in NIH grants to physician-scientists. Similarly, many more PhDs and many fewer MDs are active members of initial review groups for the NIH Center for Scientific Review or review panels of specific Institutes. The number of PhDs receiving NIH research awards over the last 30 years has expanded markedly, with a much slower increase in the number of funded MDs. In the past 30 years, the number of first-time MD applicants for NIH grants has remained relatively constant (average 825/year). An encour-

**Table 6. SELECTED SOURCES OF FUNDING FOR INJURY RESEARCH\***

| Year | U.S. Army Biomedical Research† |                                                |                                       | Shriners Hospitals‡ |                                 |
|------|--------------------------------|------------------------------------------------|---------------------------------------|---------------------|---------------------------------|
|      | Total                          | Combat Casualty<br>Care Amount<br>(% of Total) | Burn Injury<br>Amount<br>(% of Total) | Total               | Burns<br>Amount<br>(% of Total) |
| 1980 | 91.5                           | 7.5 (8.2%)                                     | 2.161 (2.4%)                          | 3.59                | 1.84 (51%)                      |
| 1990 | 254.1                          | 30.2 (11.9%)                                   | 6.018 (2.4%)                          | 18.48               | 8.3 (43%)                       |
| 2000 | 204.88                         | 21.2 (10.4%)                                   | 7.846 (3.8%)                          | 23.5                | 11.6 (49%)                      |

\* In \$ million.

† Data from J. S. Parker, U.S. Army Medical Research and Material Command, and C. W. Goodwin and D. Zolock, U.S. Army Institute of Surgical Research (personal communications).

‡ Data from N. C. McCollough, Medical Director, Shriners Hospitals for Children (personal communication).

aging note is the fact that first applications from MD/PhDs have doubled since 1984. Even so, PhDs currently receive approximately 70% of the research grants, with MDs and MD/PhDs receiving the remaining 30% (Table 7).

The predominance of PhDs as principal investigators has contributed to the disproportion in support received by departments of medicine and surgery. In fiscal year 1993, medical school Departments of Medicine received \$1,218.1 million from NIH, and Departments of Surgery \$174.1 million or only one seventh as much. Departments of Medicine received 615 awards from the NIH but Departments of Surgery received only 123 or one fifth as many. Since the rates of success were identical (23%),<sup>69</sup> that disparity may reflect the greater intensity of the clinical care obligations of surgeon-scientists, which limits their time available for grant writing, as well as research time per se.

These changes in the distribution of research funds are attributed to curricular emphasis on primary care in medical school, the indebtedness of the medical school graduate (an average of \$75,000.00 for 50% of graduates), the time required to prepare for a research career, clinical department emphasis on income generation, and a decrease in NIH

funding.<sup>68</sup> In fiscal years 1993 and 1994, the funding of first-time, unsolicited competing R01 applications was 11.7% and 12.3%, respectively; funding rates were as low as 9.2% and 7.9% at specific institutes. The R29 awards had funding rates of 23.1% and 19% in those 2 years.<sup>70</sup> Of particular concern is the fact that during the period 1986–1995, two of three renewal applications were not funded.<sup>68,70</sup> The declining involvement of MDs in research accelerates in the transition period from residency to scientific independence. MD recipients of both F32 fellowship awards and T32 training grants decreased 43% and 26%, respectively, between 1985 and 1997.

The FASEB Subcommittee on Career Opportunities has made recommendations to redress the identified “unbalanced” distribution of research support.<sup>68</sup> The first recommendation is to change the premedical and medical school curricula to demonstrate that research results form the basis of medical practice and ensure continual improvement in care. Another recommendation was a national program to forgive the indebtedness incurred during medical school of those who undertake research training and pursue a research career, although an interest-free delay in repayment might

**Table 7. RECENT TRENDS IN NIH RESEARCH FUNDING\***

|                                        | PhD   | MD plus<br>MD/PhD | PhD/MD<br>Ratio |
|----------------------------------------|-------|-------------------|-----------------|
| NIH grants, 1982–1997                  | +105% | +26%              | ↑               |
| NIH Review Panel membership, 1980–1995 |       |                   |                 |
| Center for Scientific Review           | +12%  | –13%              | ↑               |
| Institute-specific                     | +16%  | –17%              | ↑               |
| NIH Research Project grants            |       |                   |                 |
| First-time applicants                  |       |                   |                 |
| Average number/year, 1978–1998         | 2400  | 826               |                 |
| Receipt of funding, 1986–1995          | 22%   | 21%               |                 |
| Previously funded applicants           |       |                   |                 |
| Success rate 1986–1995                 | 33%   | 34%               |                 |
| Overall receipt of grants              | 70%   | 30%               |                 |

\* Data from Zemlo et al.<sup>68</sup>

be a more appropriate concession. The Subcommittee also recommended that NIH and other foundations expand the support available for the training and mentoring of physician-scientists. Lastly, the Subcommittee felt that the academic milieu should be made research-friendly to support physician-scientists throughout their entire careers. The members of the American Surgical Association have a long history of supporting the involvement of medical students in the research process, and have been effective role models as surgeons who are actively involved in the research process.

In an attempt to alleviate the previously noted imbalance between PhD investigators and MD plus MD/PhD investigators, the NIH has recently provided additional support for clinically oriented integrated research in the form of K08 Mentored Clinical Scientist Development Awards and K23 Mentored Patient-Oriented Research Scientist Development Awards (Scott Somers, National Institutes of Health Office of Communications, personal communication, Nov. 14, 1999).<sup>68</sup> The number of applications for K08 awards has increased and the applicants' success rate has been 50%. The K23 awards also appear to be popular, although they are considered by some to be compromised by the commonly imposed salary cap of \$75,000, which makes meeting financial obligations difficult for a debt-laden postgraduate physician.<sup>68</sup> To relieve that potential limitation, Dr. John Mannick has developed an innovative program whereby the vascular societies augment the salary support of specific K08 awards to vascular surgeons (J. A. Mannick, Professor of Surgery, Harvard Medical School, personal communication, Mar. 20, 2000). The NIH initiatives have also included large-scale collaborative project awards, the "GLUE" and "mini-GLUE" grants capped at \$5 million and \$300,000 per year, respectively, for up to 5 years.<sup>71</sup>

In further response to the perceived imbalance between laboratory and clinical or patient-oriented research (POR), the NIH appointed the Clinical Research Study Group, chaired by G. H. Williams, to analyze the review of POR grant applications by the NIH Division of Research Grants. On the basis of the recommendations of that study group, the Center for Scientific Review (CSR) has established new panels and reconfigured study sections.<sup>72</sup> New NIH review procedures have also been instituted that are intended to protect clinical research proposals from unfair competition in the peer review panels that are now dominated by basic scientists.<sup>73</sup>

## FUTURE OPPORTUNITIES

To fill the existing void in research support for the surgeon-scientist and provide "seed money" for promising young surgical investigators, the ASA and other surgical associations have established research fellowship programs. In 1982 the American Surgical Association validated its commitment to the support of the surgeon-scientist by establishing the Research Fellowship Awards that are made annually by the ASA Foundation. The American College of

Surgeons has also awarded fellowships since 1987 to assist entry-level academic surgeons in establishing an independent research program. The College currently awards up to eight faculty fellowships annually with a stipend of \$40,000 per year for 2 years, and up to nine 2-year research scholarships for surgical residents with a stipend of \$30,000 per year.<sup>74</sup> The College also awards the George H. A. Clowes, Jr., MD, FACS, Memorial Research Career Development Award, which consists of a grant of \$40,000 per year for 5 years. In 1998 and 1999, there were only 46 and 34 applicants respectively for the 15 faculty fellowship awards made in those years (K. S. Guice, Director of Fellowship Department, American College of Surgeons, Chicago, IL, personal communication, Feb. 16, 2000).

The American Association for the Surgery of Trauma also supports trauma research by granting up to three fellowship awards of \$35,000 per year for 2 years. In each of the last 3 years, that organization has made three fellowship awards, but received only 13, 9, and 6 applications in 1997, 1998, and 1999, respectively (H. G. Cryer, Secretary-Treasurer, American Association for the Surgery of Trauma, personal communication, Feb. 25, 2000). The Surgical Infection Society has recently increased the stipend of their Junior Faculty Research Fellowship to \$40,000 per year and anticipates an increased number of applicants.<sup>74</sup> The Society for Surgery of the Alimentary Tract also funds a career development award, which currently provides a grant of \$80,000 for 2 years of research support to a young faculty member.<sup>74</sup>

The ASA Foundation has awarded 13 fellowships since 1982. The fellowship consists of a grant of \$25,000 in the first year and \$30,000 in the second, to which \$5,000 for equipment and supplies can be added each year if requested by the sponsoring department. The record of the 10 recipients who have completed their fellowship as of this year is nothing short of spectacular. I contacted each of those 10 individuals to determine how the fellowship was used, how it affected their career, and their thoughts about how the fellowship could be improved; these data are detailed in Table 8. The beneficiaries of our Foundation's fellowships have established an outstanding record of scientific productivity and are certain to contribute to the surgical advances of the next century. All recipients said that the fellowship had a significant positive effect on their research career, and consider it to have been invaluable by allowing them to focus on their research project. Many cited the fellowship as providing external validation of the merit of their research and generating a "halo effect" both locally and nationally. Several stated that receipt of the fellowship freed them from additional unwanted administrative chores and facilitated more rapid maturation of their research program. The recipients cited as a particular benefit their attendance at the annual meeting of the Association at which time they had the opportunity to report to the Association, establish contacts with members having similar research interests, and

**Table 8. SURVEY OF RECIPIENTS OF ASA FOUNDATION FELLOWSHIPS**

|                                          |      |
|------------------------------------------|------|
| Number completing fellowship             | 10   |
| Year after residency fellowship received |      |
| First                                    | 5    |
| Second                                   | 3    |
| Third                                    | 2    |
| Use of award money                       |      |
| Postdoctoral fellow or technician salary | 5    |
| Equipment and/or supplies                | 8    |
| "Fenced" time                            | 4    |
| Increased productivity with award        | 10   |
| Publications resulting from award        |      |
| Specific papers                          | 2-7  |
| Related papers                           | 6-12 |
| Subsequent competitive funding           |      |
| National Institutes of Health            |      |
| R01                                      | 8    |
| K08                                      | 1    |
| R29                                      | 1    |
| Canadian Medical Research Council        | 1    |
| Foundation grants                        | 7    |
| Directing active research laboratory     | 10   |
| Accelerated promotion                    | 5    |

interact with the membership at large. Three recipients have become active members of the Association.

With such benefits, one would think that the ASA would be overcome by research fellowship applications, but this is not the case. In 1998, the Foundation received only seven applications and awarded just one fellowship, a nadir which was at least partially corrected in 1999 when we received 26 applications and were able to make the two most recent awards. The negative factors that appear to limit the long-term research careers of surgeons in general also may be acting to limit interest in research fellowships. Medical education indebtedness and the emphasis on generation of income from patient care may reduce the attractiveness of research fellowships on the part of both entry-level faculty and the department chairman. It comes as no surprise that all of the previous fellowship recipients feel that a larger stipend would improve the ASA Research Fellowship.

The 1998-1999 report of the Association of American Medical Colleges on medical school faculty salaries indicates that the mean annual compensation of full-time assistant professors of surgery at private medical schools who receive a single fixed salary component is slightly more than \$203,000.<sup>75</sup> For a research fellowship to provide the Fellow with "fenced" research time of 1 day per week and be salary-neutral for the sponsoring department, a stipend of \$40,000 per year is required. In recognition of that fact, and to provide stipends comparable to those of other professional organizations, I am pleased to announce that the ASA Foundation has increased the stipend of the ASA Foundation Fellowship to \$40,000 per year, which we hope will securely "fence" appropriate research time for recipients whose work will advance surgery in the 21st century.

**Table 9. EXTENT OF BURN ASSOCIATED WITH 50% MORTALITY (LA<sub>50</sub>) U.S. ARMY INSTITUTE OF SURGICAL RESEARCH**

| Age Group                | 1945-1957 | 1987-1991 |
|--------------------------|-----------|-----------|
| Pediatric (0-14 yrs.)    | 51%       | 72%*      |
| Young adult (15-40 yrs.) | 43%       | 82%†      |
|                          |           | 73%‡      |
| Older adult (>49 yrs.)   | 23%       | 46%§      |

\* 5 years.

† 21 years.

‡ 40 years.

§ 60 years.

The American Surgical Association and its members played an important role in the delivery and improvement of surgical care during war and peace throughout the 20th century. The changes in surgical care illustrate the importance of military and civilian centers of excellence focused on categorical diseases and the importance of research Fellows, both the drafted doctor de facto type at the Army Burn Center and this Association's research Fellows, in advancing surgical science.

Without documentation, this review would be simply anecdotal, but the improvement in burn care that has resulted from integrated clinical and laboratory research carried out over the past 50 years can be documented in specific and discrete fashion (Table 9). Comparing the current mortality of burn patients as related to age and burn size with that of burn patients treated in the earlier period (1945-1957) confirms the significant reduction in mortality and also identifies those patients who would have died had they been burned just 50 years ago but survive today because of the improved care they receive.<sup>76</sup> Additionally, the application of the knowledge and treatment techniques that have improved burn patient care to other injured patients has extended the benefits of burn research to a much greater universe of patients and improved their outcomes over the past century. Many have called the past century the "Century of the Surgeon," and the spectacular advances and revolutionary changes in surgical care that have occurred in the past 100 years certainly justify that title. However, if two centuries comprise an era, we may in this millennial year be, not at the end of the "Century of the Surgeon," but at the midpoint of the "Era of the Surgeon."

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