Reflections on Medical Education in the 1940's and the Conquest of Diseases

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I. World War II

At the inception of the U.S. entry into WW II, most medical schools organized and contributed a General Hospital. These General Hospitals were tertiary-care units that provided complex care to the wounded and seriously ill. The staffs of these hospitals were volunteer faculty from each medical school. They were comprised of the best and brightest faculty both senior and junior physicians. Nurses and other health professionals joined and served with their unit.

I will use the University of Pennsylvania as my example. It was the 20th Army General Hospital and it was stationed in India to care for the Indochina and Burma casualties. The Hospital Commander was Brigadier General Isadore Ravdin, an ambitious general surgeon. The Chief of Medicine was Francis C. Wood who pioneered the precordial chest leads of the EKG. The General Hospital Administrator was John Mitchell, a pediatrician. I will discuss each of these men later.

II. Medical Schools

I must digress to briefly discuss the traditional medical school of the late 19th and early 20th century. I again will use Penn as an example. In Philadelphia, there were wealthy and accomplished families who took a great interest in the medical schools. At Penn, the predominant families were the Peppers. Medical schools had few resources for faculty support, so many academic physicians who contributed greatly to teaching of medical students and residents were men of wealth, either inherited or by marriage. In the late 19th century, William Pepper was the Chair of Medicine at Penn. He was instrumental in luring William Osler to Penn. His family was a major financial supporter of the medical school. Before and during WWII, a son, O.H. Perry Pepper was Chairman of Medicine at Penn. The junior faculty used to remark that if you wanted to be chair of medicine at Penn, "you had to come out of or get into a Pepper pelvis." The dominance of several prominent families in

other medical schools was common, for example the Cabots and Bowditchs at Harvard. Medical schools had the reputation of accepting more first-year students then they could accommodate in the second-year. Hence in the classic welcoming address to first-year classes, the dean would say, "Look at the person on your right, look at the person on your left—one of you won't be here next year."

III. Emergence of Modern Medical Schools

At the conclusion of WWII when the staff of the Army General Hospital returned from the war, there were differences in the attitudes of these younger physicians who had been to war and the more senior and older faculty who had maintained the medical school and its affiliated hospitals. The Chiefs of Service in the Army gradually assumed the leadership of the medical schools. John Mitchell, the Administrator of the 20th General Hospital, became dean. Pepper was prepared to step down and Francis Wood, the Army Chief of Medicine, assumed the Chair of Medicine. Isadore Ravdin the Commandant and Chief of Surgery was a shrewd politician and soon became the medical school's Chief of Surgery.

These young Turks knew that many older WWII veterans would be applying to medical school and a change in the school's culture was necessary. I entered the University Of Pennsylvania School of Medicine in 1948 and approximately half my class of 98 were veterans and our class ages were older than the fourth-year students. The GI Bill paid a maximum of $500.00 for tuition. When I gave my voucher to the Bursar, she gave me enough change to buy a Medical Dictionary. The tuition at Penn today is $48,876 per year.

When the dean, Dr. Mitchell welcomed our class he was very reassuring. He told us we had been carefully selected and if we worked hard he was confident we all would graduate. Attire for classes was suits and ties. In the labs, we removed our jackets and wore lab coats. Men's suits were scarce

after the war and most of us had just one or two. One could determine who were anatomy partners by the distinctive odor of our cadavers emanating from our clothing.

IV. The Curriculum

A. The First Year

The format for basic science courses was at 8:00 am, a lecture by the professor. Then we adjourned to the laboratory which was instructive and also a social event. During the first semester, gross anatomy occupied every morning six days a week and was an exhaustive dissection with great attention to minor structures and rote memorization. I am not sure that I knew which side of the body the liver occupied although I knew every ligament, muscle and other structures in great detail. The afternoon was devoted to histology and neuroanatomy that were more interesting.

The second semester was wonderful; we had biochemistry in the morning. The morning lectures by the professors were fascinating, showing that metabolism occurred in sequential steps. We then went to the laboratory and carried out basic and simple experiments. At 11:00 am, we met in small groups of 8 to 10 with our instructor. The instructors were physicians who had finished their residency, primarily internal medicine. They were preparing for careers in academic medicine and had come to basic science departments to acquire research skills. In the late 1940's and early 1950's there was little basic research in Clinical Departments. My biochemistry instructor was Roscoe Brady, a young internist who later spent his career at the NIH studying infusion of enzymes in children with genetic enzyme deficiencies. Brady, like all the instructors, would elaborate on the important clinical aspects of the morning lecture and how the concepts applied to disease. It was an instantaneous and dramatic clinical correlation.

Physiology was the coolest course with a professorial lecture at 1:00 pm and then a laboratory that exemplified the principles and drove home the important points. For example, the circulatory system: we first studied a schema of the circulation constructed of glass tubes of various sizes simulating the arteries, hypodermic needles for the capillaries and rubber tubes or drains for the veins. The heart was a bottle of water on a pulley that could be elevated to simulate hypertension or the system could be bled. We recorded pressures, flows and other measurements to determine the mechanics of the system. The really neat part was the next afternoon we had an anesthetized dog, where we could carry out the same maneuvers and determine how the neuroendocrine systems modified the response. Most of our experiments were similar; a mechanical schema followed by similar experiments on anesthetized animals. My physiology instructor who met with us in small groups was Truman Schnabel who later established the first cardiac cathertization laboratory at the Hospital of the University of Pennsylvania.

This plan of instruction was, I believe, successful because it made the student responsible for acquiring many of the details of each subject. We had to read extensively and consume a textbook and organize the material since all exams were essays including the National Boards. It was important to master the principals of each subject and to understand the details.

B. The Second Year

Pathology was similar to our current curriculum with emphasis on interpretation of pathological slides and examination of diseased organs. However, one morning a week we did experimental pathology in small groups. For example, we took mammary cancer cells from mice and compared the distribution of metastasis when cells were treated with sialidase that removes sialic acid from their surface to untreated cells when these cell suspensions were injected into syngenic mice. The organs involved by metastasis were altered by removing sialic acid.

A second-year course related to Pathology was Clinical Laboratory Methods where we learned how to do all of the laboratory studies we would do on our patients as clinical clerks and as interns and residents. We did the complete CBC, urine studies and special tests on body fluids. We learned how to use a Beckman Spectrophotometer for more detailed analysis. In my opinion, one of the major detriments to medical education today was the law requiring laboratory certification in 1985 (CLICA) which forced the closure of student-resident laboratories on each medical ward.

Pharmacology was again centered in the laboratory after the morning lecture and was probably the most interesting and challenging course. We carried out experiments on anesthetized animals that our faculty had recently published. My instructor was James Echenhoff, who with Robert Dripps and Julius Comroe, went over to HUP and began one of the first Divisions of Anesthesia. At the same time, Beecher at Mass General was also starting a residency and these were the first Departments or Divisions of Anesthesia.

Microbiology consisted of lectures in immunology and a laboratory focused on the culturing and identification of bacteria and fungi preparing us for our clinical responsibilities on the wards. The lectures were primarily on humeral immunity as cellular immunity was in its infancy. The discovery of cellular immunity was defined by Merrill Chase and Karl Landsteiner. Landsteiner had discovered the blood groups in 1900 and was awarded the Nobel Prize in 1930. In his acceptance address he said, "I don't deserve a Nobel Prize for discovering the blood groups, I deserve it for the discovery of cellular immunity". He was right.

V. Influence of The National Institute of Health

I would like to take a few minutes and tell you about the NIH which has had such a significant impact on the building of academic medical centers[1] . The

NIH traces its roots back to 1887 when a one room laboratory was founded called, "the Laboratory of Hygiene" and the first director was Joseph Kenyoun. He had been a physician in the Marine Hospital Service. He was the sole staff for this lab; he had a microscope and microbiologic supplies. It turns out that the Hygiene Laboratory was really a diagnostic laboratory for infectious disease because cholera was very prevalent in the merchant seaman. The Marine Hospital Service was founded to provide medical care to the merchant seaman. This also explains why public health officers now wear Navy uniforms. You can trace their beginnings back to the Merchant Marines. In 1891, the Hygiene Laboratory was moved to Washington DC. Later, two divisions called the division of bacteriology and pathology were added. In 1902, there were three additional components, chemistry, pharmacology and zoology. These new programs were funded so that the Public Health Service could afford scientists (PhD's) to direct them. A number of notable advances were made by the laboratory. It helped define the pure food and drug act of 1906 and was instrumental in helping regulate antitoxin vaccines. In 1912, the Hygiene Lab was authorized to conduct research in non-contagious diseases. Dr. Joseph Goldberger undertook a study of an epidemic that was occurring in the southern U.S. It was Pellagra with symptoms of hypersensitivity to sunlight, diarrhea and mental cognitive dysfunctions. Dr. Goldberger discovered that Pellagra was due to a lack of niacin or Vitamin B3. This was a major accomplishment.

In 1930, The Hygiene Laboratory was renamed, The National Institute of Health (singular). Congress, for the first time, established fellowships for scientists to come to the NIH to be trained. However, the Great Depression occurred in the 1930's and there was very limited funding. In 1938, citizens of this country were alarmed because of the incidence of cancer. The National Cancer Institute was established and the NCI funding was, for the first time, designated so that it could be awarded to non-federal employees and scientists. This opened up, for the first time, an opportunity for Universities to apply to the NIH for funding of their faculty. In 1944, the

Public Health Service Act defined the shape of medical research in the U.S. The NCI's budget at that time was four million dollars.

Dr. James Shannon shaped the NIH and academic medicine. James Shannon was a graduate of NYU Medical School. He worked with Homer Smith who was a prominent nephrologists and he received a Ph. D. in physiology. He was on the faculty at NYU for fifteen years. Shannon was offered an opportunity to establish a laboratory in the basement of Goldwater Hospital located on Welfare Island (now Roosevelt Island) in the middle of the East River. He attracted a group of young physicians who were quite exceptional to join him and undertake research on renal diseases.

WWII broke out and the Army was desperate to find anti-malaria drugs because quinine was so toxic. Shannon and his group of young physicians were asked to help in this endeavor. They worked on Atabrine and established the dosage of this drug. Later they worked with the pharmaceutical industry. Shannon's group defined chloroquine that becomes the standard anti-malaria drug for the next decade.

Congress, at the end of the war, authorized that the NIH consisted of the National Cancer Institute (NCI) and the old Hygiene Laboratory was renamed The Bacteriology Institute. Congress also authorized an Institute for Experimental Biology, an Institute of Physiology, and an Institute of Neurosciences. Shannon recognized that these institutes should not be named for disciplines in medicine, but should be named for diseases to protect their funding. As he said, "nobody ever died of physiology". The institutes were renamed the Heart and Lung Institute, the Arthritis and Metabolic Disease Institute and later Diabetes was added. The Mental Health and Infectious Disease and Allergy Institutes have been added since then. These institutes were also authorized to continue funding non-federal research. University research began to flourish at this point. The event that added the most money to the distributions of the NIH was Sputnik. That rocket was launched by Russia and immediately thereafter NIH's budget

grew considerably. We used to say "you could take a pen, drop it on a piece of paper, fold it and send it to the NIH and you got money".

VI. Clinical Years

Many medical schools including Harvard taught outpatient medicine and all of the subspecialty clinics in the third year. Penn, on the other hand, had all of the inpatient services, Medicine, Surgery, OB Gyn and Pediatrics in the third year. There were few lectures but every week there was assigned reading in Cecil and Loeb's Textbook of Medicine and in Christopher's Textbook of Surgery. Two evenings each week we met with a young faculty member in small groups to discuss the weeks reading assignment. If you quote me I will deny it, but I was thankful for the Merck Manual and MacGregor Surgical Synopsis. Nevertheless, we covered the broad fields of medicine and surgery which supplemented our study of our own patients. Our fourth year had no electives and we rotated through the major ambulatory and subspecialty clinics.

The Department of Surgery was the dominant department at the Hospital of the University of Pennsylvania primarily because of Isadore Ravdin's eminence and the famous surgeons he was able to develop or recruit.

The Chair of the Department of Medicine was Francis C. Wood; he was a gentleman in every sense as "he never inflicted pain". If it was necessary to reprimand a resident or young faculty it was carried out in a constructive mode. He had an iron fist encased in a velvet glove. Everyone was treated with respect and genuine kindness. His rounds three afternoons a week with the third-year students were carried out at the bedside and he examined the patients illustrating fine points of the physical exam. He often selected the most prosaic patient rather than a fascinoma to examine and discuss. His insights and ability to elicit areas of the history that we had overlooked made these patients fascinating. At my 50th class reunion, we had a questionnaire

and one item was, "your most memorable experience"- Fran Wood's rounds were by far the most frequently noted. He was a role model for a generation of physicians.

VII. Conquest of Diseases

I would now like to turn to my internship and residency by presenting three diseases which were our great challenges in the early 1950's.

A. Poliomyelitis

Polio has been endemic since antiquity. Hieroglyphics depicted ancient Egyptians with atrophic extremities. Poliomyelitis was a common and challenging infectious disease in the 1940's and early 1950's[2]. Epidemic polio was unknown in the U.S. before the 20th century. It rapidly became one of the most dreaded childhood diseases and also affected young adults. In the spring and summers of the 1930's through 1950's there was a panic among U.S. parents that closed swimming pools and shut down summer camps[3]. The epidemic peaked in 1950 with 58,000 cases. Three thousand died and 21,000 suffered some permanent paralysis.

Spinobulbar and bulbar polio were admitted to the hospitals. As an intern on the Pediatric Service at the University of Michigan Hospital, I was assigned for a month to the Contagious Disease Hospital where we cared for acute infections, for example, meningitis, bacteremic sepsis and bulbar or spinobulbar poliomyelitis. We had a ward with thirty Drinker Respirators for our polio patients[4]. I quickly learned the technique of tracheobronchial aspiration so that there was little or no damage to the mucosa. Secretions and suffocation prevention were our major challenges.

The natural history of spinobulbar polio is that approximately fifty percent of patients recover completely; twenty five percent survive but have residual weakness and may need partial ventilator support for

some part of the day or during the night. The remainder dies or is ventilator dependent.

Spinal polio shows a similar course, half get better in 6 to 8 months, one-fourth have some residual paralysis and one-fourth are severely affected. Many of those with a residual paralysis show marked improvement with time. This improvement is due to hypertrophy of motor neurons that were spared. A normal motor neuron innervates about 200 muscle cells. The hypertrophied neuron sprouts new axons and it may control 1,000 muscle cells. These hypertrophied neurons tend to die prematurely giving rise to the "post-polio syndrome" that we internists are now seeing[5]. It should be appreciated that Intensive Care Medicine had its origin in the fight against polio.

The polio epidemic was ended with the development of vaccines. Salk grew polio virus in green monkey kidney cells in tissue culture. This system was developed by Enders, Robbins and Weller who received a Nobel Prize for their contribution. Initially, there was skepticism about Salk's inactivated polio vaccine because the protein content was very low, but fortunately polio protein is one of the most immunogenic. In a trial in 1955, Thomas Francis Study Panel validated the efficacy of the Salk vaccine[6]. It is of interest that it later was found that the initial vaccine was contaminated with an oncogenic virus SV_{40}. The CDC has detected no increased in cancer in the cohort who received the Salk vaccine.

In 1957, Albert Sabin developed an oral live attenuated polio vaccine which became widely used. The viruses replicated in the intestines and produced a high degree of herd immunity. It is now recognized that 1 in 750,000 persons who ingest the Sabin vaccine develop paralytic polio. This has led to a surge in the use of the Salk vaccine in developed countries recently.

B. Hypertension

Hypertension was a major problem in the 1940's and 1950's as we had no effective treatment.

For example, when Franklin D. Roosevelt attended the Yalta Conference he was reported to be severely hypertensive and suffered several lacunars infarcts, he was treated with sedatives. How different Postwar Europe might have been if Roosevelt had taken Churchill and his own advisors' advice and not given Stalin Eastern Europe.
On the "flip side", Stalin also had hypertension and died of a cerebral hemorrhage several years later. What if Stalin had lived, how would Kennedy's negotiations over the Cuban Missile Crisis with Stalin been resolved? The world or what was left of it might be quite a different place.

As a clinical clerk on the medical wards at Penn, I became very familiar with treating adrenal crisis. The standard therapy for severe hypertension at Penn was bilateral adrenalectomy[7]. In Boston, the treatment was radical sympathectomy.

At Duke, a charismatic physician Walter Kempner initiated a diet consisting of salt free boiled or steamed rice with some nuts and dates[8]. It was a tasteless, monotonous and unappetizing meal for treating hypertension. Patients stayed for months in a motel owned by the Department of Medicine at Duke. There was a spirit of almost religious dedication required to maintain this insipid diet. Blood pressure was reduced but it was of questionable significance although weight loss was significant. One had to live in this near religious experience to adhere to the diet. Patients relapsed when they left. The Kempner diet was the largest source of income for the Department of Medicine at Duke until the late 1950's.

The pharmaceutical industry realized that drugs to treat hypertension were a "gold mine". When I was an intern at the University of Michigan one of the first drugs— hexamethonium, a powerful ganglionic blocker-- was being studied[9]. Several patients died during these studies. The oral dose of hexamethonium was 20 times the subcutaneous dose. A student nurse was giving the evening meds and injected my patient with the oral dose of the drug. The patient developed irreversible shock and died. A second patient was titrated with oral hexamethonium and he improved. He went into a telephone booth to call his wife and had syncope secondary to postural hypotension. He was unable to fall and we found him dead, slumped in the phone booth.

Other early drugs for treating hypertension— for example, methyldopa, reserpine, pentaquine, and guanethidine—had significant adverse reactions so asymptomatic hypertensive patients refused to take them.

Diuretics were the first group of drugs to successfully treat hypertension. Sulfonamides were used to treat infections. In 1949, William Schwartz noted that, in patients with CHF who had infections, sulfonamides produced a brisk diuresis and lowered blood pressure. However, the side effects of sulfonamides were such that they could not be used for long periods of time. A chemist, Karl Beyer, by trial and error modified the sulfonamide formula and produced chlorothiazide, a safe and effective diuretic[10]. This diuretic also was effective in treating HTN. Beyer was awarded the Lasker prize for his discovery.

Beta Blockers were the next group of effective HTN drugs. They were developed by a physician pharmacologist, Sir James Black. He specifically designed the Beta Blockers based on his research of the B adrenergic receptors in the heart[11]. The first beta blocker was propanalol. James Block also designed the gastric-histamine H_2 receptor blockers. He was awarded the Nobel Prize for his discoveries in 1988.

We now have a potent armetarium of designed drugs Calcium channel blockers; ACE inhibitors; and new potent diuretics. But my experience in the primary care internal medicine clinic at Parkland reminds me of Hippocrates saying: "It is not enough for the physician to do what is necessary, but the patient must do their part as well and circumstances must be favorable".

C. Tuberculosis

I would now like to turn to tuberculosis which was the HIV of my generation. The standard of care was bed rest, fresh air and a good diet[12].

Sanatoriums were designated in every major hospital to care for the staff that had contracted TB. Sanatoriums were available all over the U.S. to isolate anyone with positive sputum for AFB or with an abnormal chest X-ray suspicious for TB. Climate was believed to play a major role in treatment. A famous sanatorium was the Trudeau at Saranac Lake, NY[13]. Cottages had open porches where patients in recliners were exposed to the frightful winters. The winters were so fierce that the Indians who lived in the Adirondacks retreated into Canada in the winter and returned in the spring, summer and fall to hunt and fish. William Osler founded a society, The American Clinical and Climatologic Association, to study climate effects. This distinguished association persists today as a forum for modern clinical investigations.

Trudeau was a legendary figure in TB medicine carrying out research and caring for his patients. He was beloved by his patients and a statue of him in a reclining bed is overlooking Saranac Lake. One of his patients carved on the base in French "To cure sometimes; to help often; to comfort always".

Patients had to be isolated until their sputum was negative. In the case of Cavitary Tuberculosis, this often required mutilating surgery. For example:

Thorocoplasty: removing several ribs leaving the periostium intact and then collapsing that segment of the chest to approximate the lining of the cavity so it was obliterated.

Phrenic nerve crush with pneumoperitoneum to collapse apical cavities.

Pneumothorax

Drugs that were available, streptomycin, para-aminosalicylic acid (PAS), and ethambutol, were not very effective.

As an intern in 1952, I admitted a 19 year-old woman with TB meningitis. We treated her with our three drug regimen and her systemic signs of fever, malaise, and sweats were relieved but she became paraplegic. We speculated that granuloma were compressing her cord or that the fibrosis of healing had compressed some spinal arteries and she had infarcted her spinal cord.

The next year, 1953, isonaizid (INH) became available and she was one of the first patients to receive the drug. It was a miracle, within a few months she regained the use of her legs and began to walk; INH was capable of penetrating into the central nervous system and cure CNS Tuberculosis.

With INH, for the first time, a cure for TB seemed reasonable[14]. The importance of INH, in addition to our three drug regimen, was reinforced when the VA Hospital in Ann Arbor opened in April 1954. Dr. Cyrus Sturges, Chair of Medicine, called Peter Barlow and me into his office. He said they were going to open two, 20 bed wards at the VA, but there would be no staff until July. He was sending us as Junior Residents to man the VA Hospital. One ward was General Medicine the other would be for TB. I lost the coin toss and got the TB ward. Within three weeks my 20 beds were full of Korean War veterans who had been POW's in

Chinese prison camps. The Chinese physicians had no drugs but they did thoracentesis on those with TB effusions so we had no bound lungs. Every morning Wynn Davie, Chief of Pulmonary Medicine, rounded with me and reviewed the chest X-rays. Our patients were all treated with a four drug regimen including INH. We were impressed by how quickly the sputum was cleared of AFB and by how relatively quickly TB infiltrates resolved on the X-rays. My primary assignment was to keep these battle-hardened veterans in bed. We were just learning how effective INH was as an addition to the older regimen[15]. As experience with INH was acquired, it became clear that Sanatorium and strict bed rest was not required. Sanatorium closed in late 1954 and 1955.

D. Role of a Test in Diagnosing Disease

Discoid Lupus was a disease described in antiquity.

Hippocrates recognized the deforming skin manifestations and called it the "bite of the wolf" hence Lupus. The distinction between discoid lupus and systemic lupus erythematosus was made by Moric Kaposi, a dermatologist, who described the malar rash, sun-sensitivity and arthritis in 1872.[16] However, the protean manifestation of SLE were not appreciated until Hargraves, a hematologist, serendipitously discovered the LE cell in 1948 while examining bone marrow of patients with classical SLE[17]. As clinical clerks, interns and residents, we drew blood on patients with puzzling diseases. We placed the blood in tubes with glass beads and let the blood clot. We vigorously shook the tubes, breaking the white blood cells and then let the tubes stand until the buffy coat formed. We smeared the buffy coat and used Wright's stain. The LE cell is a neutrophil or macrophage that has ingested denatured nuclear material of another cell. The denatured material is seen as an LE body.

Using the LE cell test, many of our puzzling patients—for example, a young woman with ITP, a second woman with pleuritis and pericarditis

and a third young woman with hemolytic anemia—all had positive LE cells. The spectrum of SLE manifestations was rapidly expanded. The LE cell test was an important diagnostic tool in the late 1940's and 1950's. It is rarely done today as we have much more sensitive and specific tests, but it was a god-send to us.

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