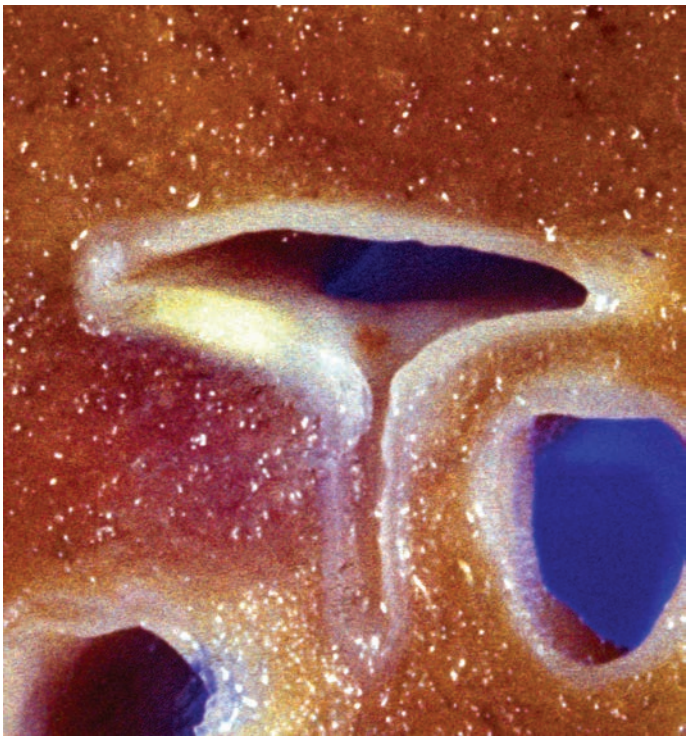
Explorations in Pathology

A Medical Autobiography

1944–2000



A yellow atherosclerotic plaque, seen in a cross-section of a pulmonary artery of a rabbit lung, was produced experimentally as the result of the organization of an *in vitro* thrombus introduced into the lumen of the artery three weeks previously (see Chapter Four).

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1944–2000

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CONTENTS

ACKNOWLEDGEMENTS

It is a truism that no one walks alone, not least when one is in the ever present company of those who went before. Lives impinge upon one another. The influences that first propelled me along from my earliest days are found in my family, teachers, and friends. As a young child, I was a passenger on a journey of discovery with Mr. Tom Sherman, assistant superintendent of schools in Richmond County. He took me along on his visits to the schools and nurtured my development as we rode around the county. Henry C. (Pop) Pearson took me under his wing at the Augusta YMCA, as he did countless other youngsters, always making sure that at one time or another we brought home a prize from sporting competitions. After he moved to the YMCA in Athens, I followed, and lived and worked there while attending the university. Many of the others who influenced my life are in the present volume.

This account was written with the advice and contributions of friends and colleagues who provided records and pictures as well as assisted in reviewing, correcting, and editing the manuscript. Over the past ten years this work has been in progress, helpful suggestions were received from classmates, in particular Drs. Harvey Newman, Alex Murphey, and Joe Chastain, and from several colleagues including Drs. Robert Baisden, Joe Bailey, Walter Brown, Alva Faulkner, and Helge Stormorken.

From the very beginning of this endeavor, Nora Freeman has assisted enormously by typing and formatting the manuscript, offering sound and useful advice along the way. This project could not have gotten underway without her contributions. Renee Sharrock, curator of historical collections and archives of the Robert B. Greenblatt Library, kindly facilitated access to numerous documents and other materials held by the section.

My older grandson, Bleak, III, did a magnificent job in digitizing the many photos that illustrate this volume. He then arranged the pictures into plates with exceptional skill and attention to detail. Phillip Jones, medical photographer at the college, utilized advanced technology to retouch some of the pictures and further enhance the plates.

Dr. Walter Brown, a fervent supporter of the college and treasured friend, reviewed an early version of the manuscript and made valuable suggestions. Walter had a keen eye and knew well how to express his thoughts. A superb physician, his premature death cut short an extraordinary life and career.

Dr. Helge Stormorken reviewed the account of my year at the Institute for Thrombosis Research in Oslo, Norway, where he was the director of research. We have had a happy reunion through correspondence, each exchanging thoughts and news about our projects, his being a history of the Institute.

Kathy Steele, an author in her own right, critiqued a later stage of the manuscript. Her admonition to "keep the narrative moving" helped me gather the courage to weed out the surplus, extraneous material. Hugh Connolly, erudite, long-time friend, and former board member of the Medical College of Georgia Foundation, was satisfied that the narrative carried the same tone and voice throughout.

I am grateful to Ellen Harris for editing the final manuscript. Her ability to rearrange my words to make them more readable is remarkable. It was amazing to see how a small change here and there could make such a big difference! Erin New capped off the project with her beautiful, elegant design and professional production of the book by her New Oconee Press.

It is a pleasure to acknowledge the support of the Department of Pathology of the Medical College of Georgia while this work was underway, and that of Dr. Stephen Peiper, my successor in the chair of pathology, Dr. Amyn Rojiani, who succeeded him, and Dr. John Steele, who served as interim chair.

The guiding light throughout this undertaking has been my wife, Jane Downing Chandler, whose astute mind and wise insight kept it on track. But more important, through her love and exuberant spirit she has kept me afloat and taught me what it means to serve.

—A.B.C., July, 2012

INTRODUCTION

My career in medicine and pathology began in the 1940s and extended over the second half of the twentieth century, primarily at the Medical College of Georgia. I witnessed and took part in the transition of the institution from a small provincial medical school to a full-fledged academic medical center with its own teaching hospital and associated schools, including a school of dentistry.

There are no physicians in my heritage; however, my attraction to teaching comes naturally, as many members of my family were in that profession. Pathology seemed to suit best my curiosity, love of books and history, and the opportunity to contribute to medical knowledge and society through research and teaching.

When this project was undertaken, I decided to write the last part first and the first part last out of respect for my short-term and long-term memory. As the manuscript progressed, it appeared that my hunch was correct. My short-term memory relied heavily on notes and documents, whereas my recall of medical school in the '40s was vivid and nearly flawless.

My early start in research was due entirely to the support and encouragement of my mentor, Dr. Edgar R. Pund, who succeeded Dr. Lombard Kelly as the second president of the college in 1953. The professors who taught me, Drs. Pund, Kelly, Hamilton, Sydenstricker, and their colleagues, paved the way for the Medical College to become what it is today.

Dr. Leland D. Stoddard followed Pund as the head of pathology and was part of the next generation of leaders who actually wrought the changes envisioned. I worked with Stoddard and others during this period of transformation and succeeded him as chair of pathology some twenty years later. The account that follows provides a glimpse from the inside by one of the spokes in the wheel.

"The time has come," the Walrus said,
"To talk of many things:
Of shoes—and ships—and sealing-wax—
Of cabbages—and kings—
And why the sea is boiling hot—
And whether pigs have wings."

—Lewis Carroll, 1872

PART ONE

Academic and Professional Life

CHAPTER ONE

Medical School in the Forties ~ 1944–1948

The nation was still at war in 1944, and most of the University of Georgia School of Medicine's Class of 1948 was in uniform, enrolled in one of the military training programs. A few of us were civilians in possession of draft deferral cards. Dean Lombard Kelly brought us together in July of 1944 at the University of Georgia in Athens, where we were registered. At that time, the medical school was officially a part of the university, even though it was located in Augusta, where we moved that September.

I had been at the university in a premed program since March of 1943, shortly after completing all requirements for graduation from the Academy of Richmond County. At that time, there were only eleven years of grade school in Georgia. I applied to the medical school in the spring of 1944, at the age of seventeen, and was interviewed by Dr. Kelly, who sent me a letter of acceptance a few weeks later. As did the others who were from Augusta, I lived at home but frequently joined in the activities of my fraternity, Phi Rho Sigma.

The military students originated from widely scattered parts of the country and gave the classes a welcome diversity. Many of them remained in Georgia after graduation. Standards were set inordinately high for those in uniform. If one of them failed a course, even in midyear, he was immediately shipped off to active duty. One other group of older students had transferred from the ill-fated medical school at Oglethorpe University, which closed for lack of a teaching hospital. They started over and repeated many courses. Only three women were in our class, which reflected the general attitude toward women in the profession at that time. Not only were they smart, they added to the spice of life in the class and were involved in all activities.

The heart of the school was the Newton Building, a wondrous place that almost had a life of its own. Together with the Dugas and Murphey Buildings, which

were erected in the late '30s, they constituted the entire academic campus. These newer buildings were used mostly for first-and second-year courses. The Newton Building housed the school library, anatomy hall, lecture rooms, student laboratories, dog surgery, Alumni Tavern, Stork Club, and administration, all squeezed into one huge structure. The recreation center, such as it was, could be found tucked away on the top floor in a small room with a billiards table and ping pong table. In addition, a couple of tennis courts were located in an area by the hospital. The school sponsored a highly successful basketball team in the local league, coached by Dr. John M. "Pepper" Martin. The University Hospital, which was owned by the city, was used as the teaching hospital. What follows is a brief sketch touching on the highlights of our years in medical school.

First Two Years

Medical school was a consuming life, especially for the first two years. We studied every night except Saturday, when we usually partied at one of the four fraternity houses until the early hours. We went back to the books on Sunday. There were a few notable exceptions to this pattern. Two of our classmates went to Athens practically every weekend to woo their future wives, sometimes not returning until Monday morning. One of the more daring students would at times simply disappear for a while. Only later did we learn that he had a part-time job in Savannah giving tennis lessons at a local resort.

Classes and laboratories were scheduled five and one-half days a week. There was great emphasis on laboratory work during the first two years. Each lecture was usually followed by a two-hour laboratory period. In gross anatomy, there were no lectures at all, only students and their cadavers for four hours most every morning. Harvey Newman, Joe Lee, Bob Shumate, and I were in charge of "Maggie."

A few courses such as psychiatry and osteology were confined to a lecture format supplemented by homework. For osteology, each anatomy team was supplied a set of skeletal bones from which we were expected to draw and label in ink each bone. Actually the drawings were traced from an earlier set handed down over

the years. In class Dr. Kelly would hand a student a bone and ask him to describe it with all its holes and notches before the whole class.

Dr. Hervey Cleckley, the head of psychiatry, had a different sort of challenge. At the beginning of the first year we were each given a fifteen-page outline as a guide for us to write an introspective self-analysis laced with numerous psychological queries. The paper was due at the end of the year. Writing these papers took an enormous amount of time and was taken seriously by most of the class. According to Dr. Cleckley's daughter Mary, he kept the papers locked in a safe and never read them. The real objective of the exercise apparently was in the doing.

Laboratory exercises provided an opportunity to change gears and learn from a different perspective, sometimes by performing experiments. Physiology is a good example. We measured everything imaginable, from nerve and muscle excitation to heartbeats in anesthetized frogs, cats, and dogs. All measurements were recorded on kymograph drums, which was a ritual in itself. First, the drum was coated with tracing paper and smoked black to record whatever was being measured, such as an electrocardiogram. Then the tracing was dipped in shellac to preserve it, and it was hung in an oven to dry: quite a procedure, but it worked.

In other laboratories, such as embryology, histology, and pathology, long hours at the microscope were devoted to drawing representative areas from the microscopic slides. We also spent a lot of time at the microscope in parasitology learning how to identify ova, from schistosomes to tapeworms. I can still see them in my mind's eye, but the ability to connect the right egg with its worm is lost in the sands of time.

With a class numbering around eighty, the professors knew the students very well and earned their respect by being demanding yet fair. The students, of course, also knew the professors very well and had a clever nickname for each one. Some of my favorite monikers were Morpheus Maryott, who it was claimed never read an exam; Rowdy Dow, who could wiggle his ears; Fog Hamilton, who seemed to be in the clouds; Bull Allen, who meant business when he headed your way in the anatomy hall. Dr. Pund, not to be outdone, had two names: the Great White Father and Hattie Pund.

Examinations were of the essay type and frequently unannounced. Blue books were the order of the day. In pathology we were usually given the choice of discussing one of two or three topics listed, enough to fill a blue book, sometimes two. There were also pop quizzes in other courses to keep everyone on their toes, as well as oral and practical exams. Multiple choice examinations did not appear in pathology until the '50s. Most of us considered the battle won when pathology switched from four to two days a week in the third quarter of the sophomore year. After that, it was clear sailing.

The most stressful examinations in the first year were in gross anatomy. At the conclusion of dissection of each area, we were subjected to an oral practical examination by either Dr. Allen or Dr. Kelly. While we sat on high stools around the cadaver, Dr. Kelly would draw up a stool and simply say to one of us, "Trace out the vagus nerve." He never wavered in his fixed expression nor did he say whether the response was correct or not. It is thus not surprising that he was known as the Great Stone Face. Dr. Allen was a bit more gentle and would help with a hint here and there.

Dr. Kelly was not as scary as one might think. Inside the classroom he was feared; outside he was revered. He was a friend of every student and nurtured each one along the way. Dr. Kelly probably knew more about me than others through our families, for he was taught the three R's by my great-aunts, Hattie and Maggie Bleakley, and was in high school with my uncle Edward Bleakley. Occasionally, Dr. Kelly would take Alex Murphey and me to visit Dr. Eugene Murphey at his home on Telfair Street, which is presently known as the Old Government House. We would listen to him reminisce about the time when he studied under William Osler at Johns Hopkins. I once asked Dr. Murphey what he most remembered about Osler. After a pause Dr. Murphey said, "He was always thinking."

Weekends usually brought some relief from the daily grind. There was always something going on at one of the fraternity houses on Saturday nights. Dr. Ray Ahlquist of alpha and beta receptor fame was very popular with the students and could be found telling jokes and stories with his dry wit at the Phi Chi house. Dr. and Mrs. Kelly were often at the Phi Rho house, where he liked to dance with the students' dates. The girls in attendance were both local belles and nursing

students. Around 10 P.M., one of the brothers who had a car would usually take Mrs. Kelly home while the Dean lingered a while longer.

The big celebration of the first year was the Freshman Brawl at the end of gross anatomy, when the course was put to rest until the next year. The entire school and professors were invited. Another annual event was the Student-Faculty Get-Together, otherwise known as Stunt Night, when each class presented a skit spoofing their professors. All classes participated except the freshmen, for whom it was deemed too risky. Afterward, everyone would meet in the hall or outside on the walk, and a keg of beer was consumed. The challenge of the evening was to get the profs to chug-a-lug a tankard as the students merrily sang.

PLATE I

First Year

1) *Newton Building.* Originally built as an orphanage, this vast structure on Railroad Avenue was occupied by the medical school in 1913, when the school's quarters were relocated there from Telfair Street. Visible in this view is the first floor, where the library was located. Gross anatomy was on the floor above and over that the dog surgery lab. The building was demolished in 1959.

2) *Anatomy profs.* From left, Drs. W. H. Waller, Lane Allen, and Lombard Kelly were responsible for the course in gross anatomy. In addition, Kelly taught osteology, Allen cross section anatomy, and Waller neuroanatomy. Dr. Kelly performed a dual role as head of anatomy and dean of the school.

3) *Gross anatomy quiz.* The quiz does not seem to be going too well. Dr. Kelly appears on the verge of losing patience with a frazzled student, which for Kelly was a rare event. More often, he sat in stony silence, living up to his nickname of the Great Stone Face.

4) *The librarians.* From left, Janie Turner and her assistant, Sadie Rainsford, held sway in the library. Miss Janie was a formidable figure whose strict rules were followed to a T. Sadie was younger and a nice balance to Miss Janie. The library also served as the bookstore. When a student went in to buy Dr. Kelly's *Sex Manual*, he would usually wait until Miss Janie was not around and deal with Sadie.

5) *The registrar.* Miss Mary B. Cumbus was much more than a registrar who kept track of student grades. The students would always go first to her before seeing Dr. Kelly, for they knew she had the dean's ear. She was a friend to all the students and especially to the women in the classes. The school annual was dedicated to her one year.

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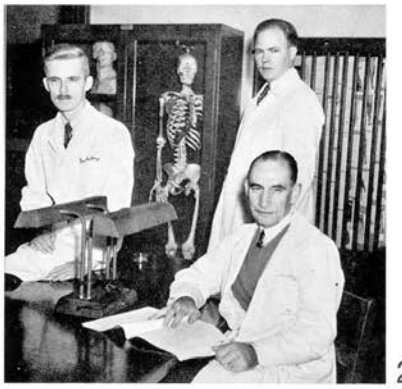

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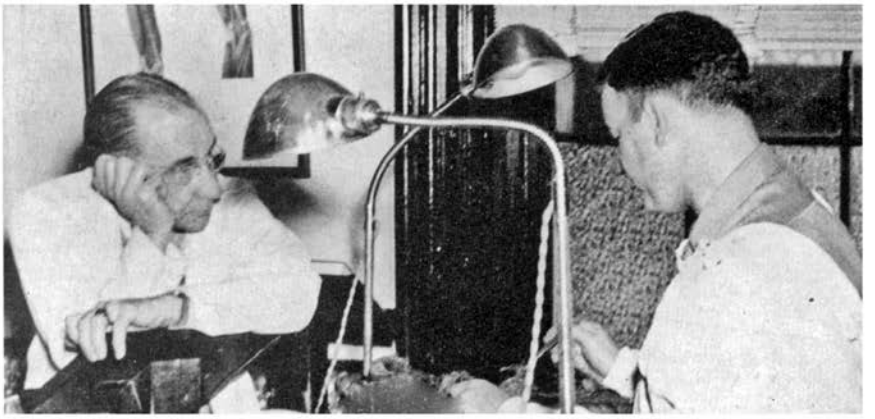

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PLATE II

First Year, Continued

1) *Dr. Hervey Cleckley*, who was chief of neuropsychiatry, taught in both the first year and the clinical years. Even though given on Saturday afternoon, his penetrating lectures on psychobiology were always well attended. His expressive hands were aided by an ever present cigarette, which he used as a prop to focus everyone's attention.

2) *Dr. Lester Bowles* taught histology. He was highly respected by the students and always available to them. Despite a severe physical handicap affecting his legs, he was unflappable. Most students rented their microscopes from the school, and it was Dr. Bowles who kept them in perfect condition.

3) *The Alumni Tavern* was located on the ground floor of the Newton Building, where lunch was available. Student servers got a free meal. The rustic décor with a stuffed deer head on one wall was complemented by pictures of campus scenes and caricatures of the profs, some of which can be seen on the opposite wall.

4) *Dr. Joseph Krafka* taught histology and embryology and had authored short textbooks on each subject. He was an entertaining and effective teacher. His description of the development of the stomach was unique. Dr. Krafka would remove one shoe and, while holding it up before the class, he would rotate the shoe into the stomach's correct position.

5) *Dr. William F. Hamilton* was head of physiology. He had made many significant scientific contributions to physiology and medicine. Here Dr. Hamilton is drawing his famous curve of a tracing of arterial blood pressure, which he was the first to measure directly in man. No student could ever forget this curve with its aortic notch created by the closing of the aortic valve as the curve slopes downward.

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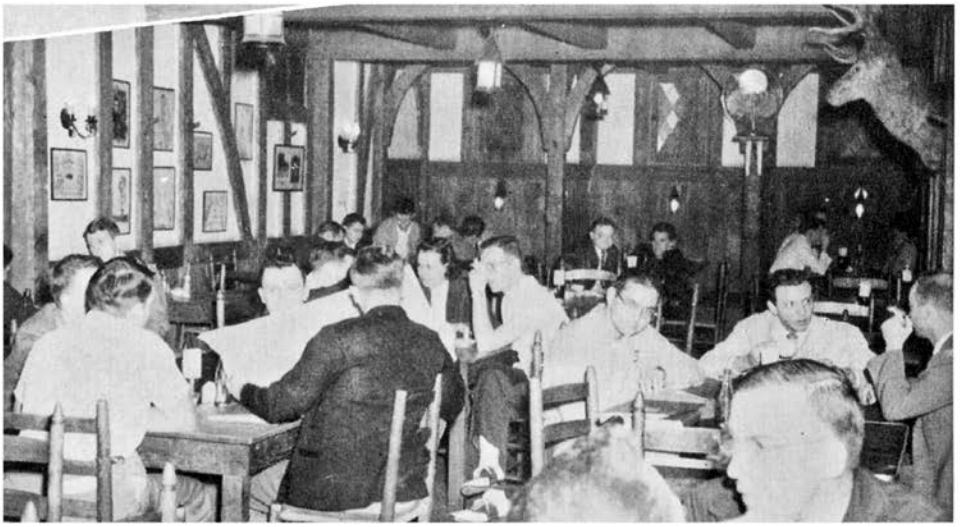

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PLATE III

Second Year

1) *Murphey and Dugas Buildings.* The Murphey Building, shown on the left, was erected in 1939, two years after the Dugas Building. The completion of the Murphey Building brought to a total of three the academic facilities on campus. Pathology and bacteriology occupied the Murphey Building, while physiology, biochemistry, and pharmacology were in the Dugas Building, which also housed the school auditorium.

2) *Campus scene.* Edwin C. "Stump" Shepherd, on the left, and two classmates walk across campus from the Newton Building to class in the Murphey Building, each carrying his books under arm. No student in those days would ever be seen wearing a backpack.

3) *Pharmacology profs.* From left, Drs. Raymond Ahlquist, George Child, and Robert Woodbury conducted their course in close tandem with physiology, having similar labs and format. Dr. Ahlquist had recently joined the faculty and quickly became the department's sparkplug and catalyst. He had a way of immediately connecting with the students by means of his dry humor and quick wit. He later became famous for his fundamental concepts that led to a whole industry devoted to beta blockers and related drugs.

4) *Pathology profs.* Lectures for the pathology course were shared between Drs. Stewart Auerbach, on the left, and Edgar Pund. In addition, Dr. Auerbach demonstrated autopsies to the class in the Murphey Building amphitheater, and Dr. Pund held a course in surgical pathology for senior students.

5) *Pathology student lab.* Each day the students were expected to draw the microscopic slides reviewed in class, but usually they procrastinated and there was a mad rush to finish them as the year drew to a close.

6) *A redraw.* Dr. Pund reviewed each drawing, and if acceptable it got a simple check mark. In this example, there were clear instructions to redraw and what to include in order to correct it.

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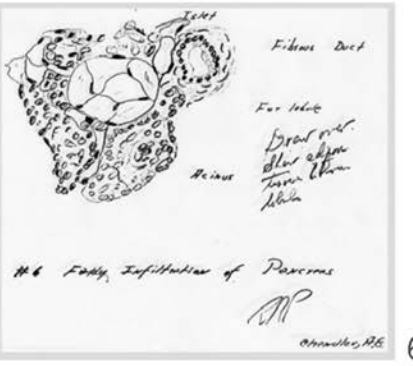

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Clinical Years

The third and fourth years were eagerly anticipated, for that was when we would get to test the knowledge gained from our first two years and start learning clinical skills on the wards and in the clinics of the University Hospital. We had been taught physical diagnosis by practicing on each other under the tutelage of Dr. Harry Harper, Jr., who was a pupil of the famous cardiologist Dr. Paul Dudley White. In the junior year, it was classes all morning and the out-patient clinics each afternoon. The senior year was devoted to work in the wards and clinics interspersed with some outside rotations. We were actively involved in the care of patients. Upon entering the hospital, one was greeted by the faint but distinctive aroma of ether wafting through the halls along with the equally distinctive voice of the switchboard operator, Mrs. Jennings, paging the doctors.

The Outpatient Clinic was located on the first floor of the relatively new Milton Antony Wing of the University Hospital. We worked in pairs and usually had one patient each afternoon. After obtaining the history, we conducted a physical examination and recorded our findings and diagnosis on the case. One of the residents or a faculty physician was then called to check on us. One day Alex Murphey and I landed the prize. When the door was opened there was the head of medicine, Dr. Virgil Sydenstricker, an imposing figure in any situation. When we introduced Dr. Sydenstricker to our patient, who was lying on the bench under a sheet, he immediately hopped to the floor, stuck out his hand and said, "Glad to meet you." He was buck-naked. While we were somewhat rattled already, we thought this was the end. Dr. Sydenstricker, naturally, was unperturbed, and after getting the patient settled back on the bench, proceeded to examine him. Leck and I breathed a sigh of relief.

The hospital formulary for 1944 reveals a lot about the state of medicine in the mid '40s. The formulary was published as a small four-by-six-inch booklet which listed some ten pages of medications. Such old-time remedies as Dobell's solution for a gargle, Brown mixture for cough, and Whitfield's ointment for the skin were included as well as a few medicines still in use today, such as nitroglycerin, phenobarbital, and digitalis. Penicillin was not listed, as the total production was saved for the war effort. Dr. Deas, the pharmacist, had a concoction reserved for

habitual clinic goers who would show up whenever the doors opened. Dr. Deas' anticlinic mixture was supplied in half-gallon bottles, Sig. "Take one teaspoon daily and return when empty."

The next big assignment was to see patients on the wards during the senior year clerkships. Open wards accommodated about six beds along each side of the room, each one separated by a draw curtain. The nurse's desk was in a large space in the center where all patients could be seen. Nurse Johnson, who was in charge of one of the wards in the Lamar Wing, was generally considered the best nurse around and was the students' favorite. She was always helpful to the neophytes. The original four-story hospital had a central core and two wings of equal size on each side: the Lamar Wing for black patients and the Barrett Wing for white patients. Even the nursing students were segregated up to a point. There were separate dormitories, but all students sat together in the classrooms.

In an era much different from today's litigious environment, we were in effect junior interns, working under the direct supervision of senior residents. We were responsible for the diagnostic workup of assigned ward patients, and our findings, including progress notes, were incorporated in the chart. At some point they were reviewed by a resident. Students and house staff also performed much of the laboratory work in a special laboratory next to the main laboratory, which was supervised by my aunt Berta Chandler. Blood work such as cell counts, urinalyses, and sputum exams for acid fast tuberculous organisms were routinely performed and recorded in the chart.

The class had a bit more time for diversions in the clinical years. A highlight of one year occurred on a Saturday afternoon when brother Louis E. "Pat" May commandeered a contingent of WAVES at the nearby Bon Air Hotel. They were navy women on leave from their station at the Women's College in Milledgeville. We first heard someone shouting a marching cadence, "one, two, three, four," as the contingent approached the Phi Rho fraternity house. They were welcomed with open arms, and a grand party indeed ensued that evening!

The most popular senior rotations were outside obstetrics and domiciliary or outside medicine. Four of us were on outside OB for a month. Prior to this service, we had worked in Labor and Delivery in the hospital, and Dr. Torpin, the head of the service, had pounded into our heads the four stages of delivery. We

were based in the Stork Club on the first floor of the Newton Building, where patients were brought when necessary. Otherwise, we would go into the community to deliver multiparous patients in the home, at first with a resident. We carried a small trunk with equipment such as sterile towels and instruments, and set up shop in the patient's bedroom and waited, and waited, as we invariably arrived much too soon. The patients usually delivered without much help from us, although on one occasion we did an episiotomy. An experienced midwife frequently was hovering in the background to offer advice, and a resident was always available if called. We were often asked to suggest a name for the new arrival. A favorite was Perry for Dr. Perry Volpitto, who was the head of anesthesiology. Not long after our rotation on this service, outside OB moved inside to the Stork Club.

These outside rotations required that we have transportation, and for those of us who did not have a car or did not team up with someone who did, it was necessary to rent one. I rented a car for the outside medicine rotation. This rotation was not as exciting or interesting as the OB experience but no less important, and consisted mostly of checking on medications or treating patients with various upper respiratory infections. Perhaps the most notable feature of this rotation was the fact that Dr. Curtis Carter, whom the students greatly admired, was the resident in charge of the service. Thirty years later he was dean when I became chairman of pathology.

In the summer of 1947, Bill Johnson, Ed Lockridge, and I prevailed upon Dr. Kelly to allow us to sell his *Sex Manual* to doctors for their patients in order to help us pay for a trip up the East Coast and to Canada. Business was good in the States; however, the Canadian authorities would not allow the manuals to cross the border. We continued on anyway, leaving the manuals behind, and saw the sights in Canada. A member of Dr. Greenblatt's family took us to lunch in Montreal and showed us around. When our funds started to run low, we slept in the car. In Quebec City we spent the night on the Plains of Abraham in view of the Chateau Frontenac, where we availed ourselves of the facilities. The full story is told in my wife Jane's biography of Dr. Kelly (83).*

* Numbers in parentheses refer to references in the Bibliography.

Out-of-town assignments were also a part of the curriculum. One novel experience occurred when Dr. Kelly sent the senior class members to the state colleges in Milledgeville and Athens to perform physical examinations on the incoming freshman classes. I was assigned to the Normal Campus for Women in Athens, where all University of Georgia women students lived during their freshman year. Our team conducted the physicals in assembly line style, each of us carrying out a different part of the exam. To say the least, it was a daunting challenge to maintain composure in a room full of girls, all young, giggly, and pretty.

A special feature of the junior year was dog surgery, when we operated on dogs two afternoons a week in the dog surgery room on the third floor of the Newton Building. The official name for the course was surgical technique. We learned aseptic sterile technique as well as such details as how to fold and drape towels and how to conduct ourselves in an operating room. Four students rotated in succession from anesthesiologist to surgeon to first assistant and nurse on four different procedures: a splenectomy, appendectomy, cholecystectomy, and resection and anastomosis of intestine. We were under close and constant supervision by a surgeon, Dr. Bowen, and anesthesiologist, Dr. Volpitto, who frequently tested our knowledge. It was an experience no one will soon forget, and one of the most valuable of the four years of medical school.

Some students who were surgically inclined would hang out around the emergency room on weekends in the hope of getting to suture a patient's wound and generally assist whenever the opportunity arose. They were usually not disappointed. This was a harmless way to spend Saturday night and educational as well. At night, if an old chart had to be reviewed the resident would simply crawl through the window of the adjacent record room to retrieve it. When a new patient arrived, one of the surgical residents would always ask, "Are you sick or are you hurt?"

When Dr. Sydenstricker returned from wartime leave in England and Europe, he resumed daily rounds with his residents precisely at 11 A.M. seven days a week. In the course of the rounds, he would select a patient for one of the residents to present before the class at noon several days each week. After the presentation, the patient would be returned to the floor, and Dr. Sydenstricker would discuss the patient's disease in remarkable detail without any prior preparation at all. He

did not need to do so, because it was said that he devoted a considerable part of each evening to reading and staying current. Another professor who mesmerized the students with his lectures was Dr. Robert Major, the head of thoracic surgery. His talks were spellbinding, and I would listen so intently that it was impossible to take notes.

Not many examinations were given during the last two years; however, one that captured our attention was given by Dr. Nathan DeVaughn, whose final examination in medicine was reminiscent of the kind that, according to legend, his predecessor Dr. Murphey gave to an earlier generation of students. Students were invited one by one to Dr. DeVaughn's office in the evening. He cordially greeted each student and then proceeded with the exam by offering a felt hat filled with slips of paper with the questions. After picking out a slip, the examination began: "Discuss typhoid fever." Usually if things were not going too well, the student got to choose another slip. Contrary to an evening with Dr. Murphey, we were not offered a drink of corn whiskey after the ordeal. We were left to our own ingenuity for that!

As the school began to emerge from the austerity of the war, the students introduced some new wrinkles. One of them was the start-up in 1946 of a student newspaper, *The Cadaver*. It had a long run until it went out of business in the 1990s at about the same time the school yearbook became defunct. One of the popular features of the newspaper was the annual evaluation of the courses and the professors, who pretended to ignore their grades. Profiles of the professors and occasional articles by them were an integral part of the paper. Dr. Kelly wrote about the early history of the school, and Dr. Greenblatt wrote a series on "The Doctor Looks at the Bible," which was subsequently published as a book. A classmate, Bill Johnson, created a memorable slogan as an ad for a nearby service station frequented by the students, "Adequate Therapy for Automobile Pathology."

Before we knew it, graduation was upon us. Because we were on a wartime accelerated schedule the first year, graduation was on March 22, 1948. Thomas Nolan and I would graduate with honors. Our class dinner was held a few days before in the Alumni Tavern on the ground floor of the Newton Building, where cartoon portraits of the professors adorned the walls. After dinner, as was the custom, Dr. Peter B. Wright appeared to let us know that the faculty had just met and

everyone would graduate. Pandemonium broke out and the party was continued at the AKK house. Around midnight someone decided that we should let everyone know of our good fortune, so the local police station was called, and an escort was provided for a parade down the middle of Broad Street. The escort was quite necessary, otherwise the new doctors would have spent the night in the pokey!

The class of 1948 sailed away in style.

PLATE IV

Clinical Years

1) *Dr. V. P. Sydenstricker* had been head of medicine since 1922 and was internationally recognized for his work in nutrition and sickle cell anemia. Although he was said not to be aloof, the students were in awe of him.

2) *Dr. Harry Harper, Jr.* The sophomore class appreciated his carefully composed, succinct lectures on physical diagnosis, which prepared the students well for their first steps into clinical waters. He respected the students, and they reciprocated in full.

3) *Dr. Curtis H. Carter.* When the students were on rotation on Outside Medicine they could always rely on his prompt advice when they got in a jam. Carter remained on the faculty for many years and became dean in 1972.

4) *University Hospital.* The teaching hospital for the school accommodated and involved the students in the daily routine, providing a truly rich learning experience under the guidance of the faculty and resident staff.

5) "*Spooky*" *Scaif* was a faithful and colorful member of the hospital staff who sometimes helped field calls for the students on Outside Medicine. It was said that she lived somewhere in the hospital. The origin of the name Spooky remains a mystery.

6) *Clinical Laboratory.* The laboratory was part of the medicine service under the direction of Dr. Sydenstricker. Shown here are laboratory technicians, from left, Catherine Shealy, Peggy Callahan, Berta Chandler, (assistant director), Elizabeth Martin, and Sarah Anderson. The caption under the original picture in the yearbook says, "Greatly over utilized and understaffed, this department has become an essential adjunct to medicine."

7) *Student laboratory.* Adjacent to the main laboratory was an important ancillary unit where much of the basic laboratory work on ward patients was performed and then recorded in the patient's chart by students and residents. Each student had a kit for finger sticks with equipment for counting blood cells and determining hemoglobin levels.

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PLATE V

Clinical Years, Continued

1) *University Hospital Formulary, 1944*. This small booklet contains ten pages of prescriptions that are largely outmoded today.

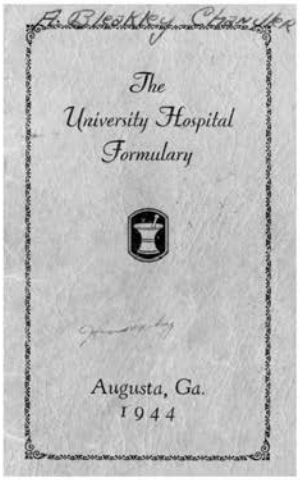
2) *A page in the Formulary.* Note the Latin terms still in use to describe the preparations that were available in the hospital pharmacy.

3) *Dog surgery.* The operating room was on the third floor of the Newton Building. Junior students operated in teams of four, each one having a designated task that was rotated in sequence for each of the four operations scheduled. Here at the front table is the student anesthetist at the head with the surgeon and first assistant on each side. The surgical nurse stands at the end of the table with the instrument tray.

4) *Dr. John Bowen* was the faculty surgeon who instructed the student surgeons and supervised all aspects of the surgery being performed. He also taught operating room protocol, including such details as the proper way to fold towels.

5) *Dr. Perry Volpitto* was the head of anesthesiology and taught the student anesthetists the different stages of anesthesia. He frequently interspersed his lesson with questions about the condition of the canine patient.

6) *Surgical anatomy.* A gaggle of students in the class of '48 are gathered around Dr. Emil Hummel as he demonstrates an anatomic feature in a cadaver. The anatomic structures involved in surgical procedures such as repair of an inguinal hernia were reviewed in this course.



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RESPIRATORY PREPARATIONS

Brown Mixture

Misturae Opii et Glycrrhizae Compositae ʒi v cc. 120.00
Sig: Shake. 1 teaspoonful,
p.r.n. for cough.

Brown Mixture with Ammonium Chloride

Ammonii Chloridi dr. iv. gm. 15.00
Mist. Opii et Glycyrr comp. q.s.ad ʒ iv cc 120.00
M.et fac. sol.
Sig: Shake. 1 teaspoonful p.r.n. for cough.

Creosote and Oil Mixture

Creosoti B. W dr. ss cc. 2.00
Olei Gossypii Seminis ʒ iv cc. 120.00
M. Sig: Shake. 1 teaspoonful for cough.

Codein Cough Syrup. (semi-narcotic)

Codeinae Sulfatis gr. iv gm. 0.25
Ammonii Chloridi gr. CLX gm. 10.00
Syrupi ʒ iv cc. 120.00
M.et fac. sol.
Sig: Shake. 1 teaspoonful for cough.

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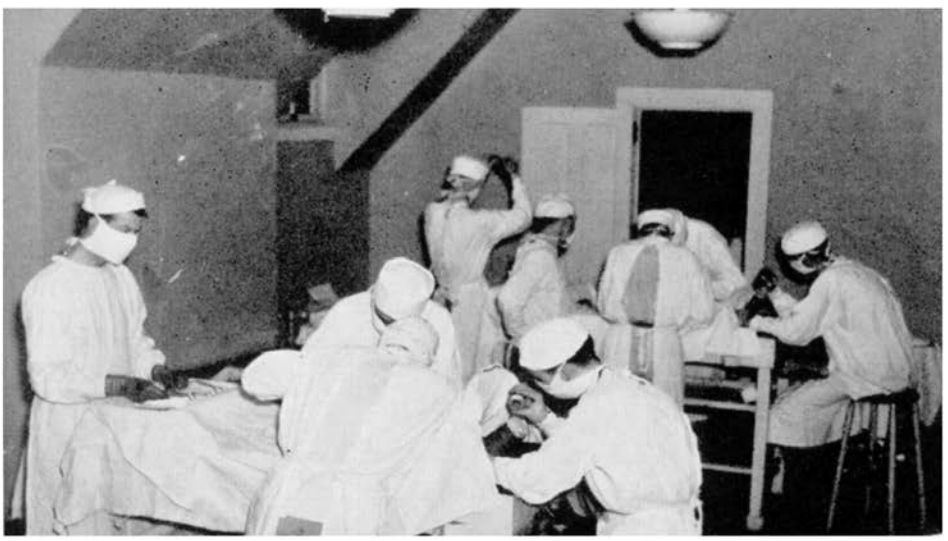

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PLATE VI

The Class of ’48

1) *Class of ’48 officers.* From left: David Hall, president; Charles Ramey, vice-president; Faust Durden, secretary-treasurer. Officers were elected for life. David Hall is the spokesman for the class and keeps everyone informed of coming events.

2) *Saturday night live.* It must be Saturday night at one of the fraternity houses, where a party is in full swing. Bill Johnson, ’48, is intently cutting a rug with the dean’s daughter Anne Kelly while classmates look on.

3) *The Phi Rho Sigma house* on Milledge Road was the scene of many happy Saturday night affairs as well as home to a close-knit group of brothers. The house was originally the home of a prominent Augusta physician.

4) *The graduate.* ABC with proud parents on Baccalaureate Sunday, the day before graduation on March 22, 1948. The baccalaureate service was held that year at the Sacred Heart Church in Augusta. Subsequently, the service was discontinued due to objections raised about a religious ceremony being an official function at a state school.

5) *Forty years on.* Theo Thevaos and ABC point to their pictures in the class photograph when they met in the 1980s, neither looking a day older!

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PLATE VII

Graduation and Beyond

1) *"The Cadaver."* The 1948 winter edition of the student newspaper highlights the recent stunt night. In the photo Dr. Cardwell, pathology, and Dr. Ahlquist, pharmacology, were portrayed as guests of honor invited to watch the students spoof the other profs. *The Cadaver* began publication in 1946 and after a successful run of fifty years went out of business in 1996.

2) *Rigor Mortis edition.* This issue of *The Cadaver* was a special edition to mark the graduation of the class of '48 on March 22, 1948. Final grades were rendered for all courses. Pathology got a respectable grade of B+.

3) *Twenty-fifth anniversary*. The class of '48 celebrated its twenty-fifth anniversary in Augusta in the spring of 1973. About 30 classmates attended. From left, kneeling: Newman, Burgamy, Daniel, Homeyer, Slappey, Waller, Carswell, Hancock; standing: Thevaos, Chandler, Moore, Kelly, Crandall, Dickey, unidentified, unidentified, A. Brown, unidentified, W. Smith, Barker, C. Smith, Pursley, Chastain, Hall, Tyson, Woodward, Mims. At the fiftieth reunion in Augusta in 1998, Bowdre Carswell taped interviews with all alumni who were present.

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THE CADAVER

Vol. III — AUGUSTA, GA., FEBRUARY, 1948 — No. 5

DR. BONNER NEW RESIDENT IN PEDIATRICS

THE STUDENT-FACULTY GET-TOGETHER---1948

IOTA SIGMA ALPHA ELECTS OFFICERS

DAMES MEET

School and Faculty News

2

THE RIGOR MORTIS

AUGUSTA, GA., MARCH 22, 1948

SENIOR CLASS GRADUATES!!!

A WORD TO THE WISE

ELECTION OF OFFICERS

TURN ABOUT

1. Manner in which course was presented.
2. Value of the course.
3. Limitation of the course.

Freshman Year

Histology	C+
Gross Anatomy	B+
Osteology	C+
Biochemistry	C
Embryology	D
Psychobiology	B+
History of Medicine	C
Physiology	B
Cross-Section Anatomy	D
Public Health	F

Sophomore Year

Physical Diagnosis	A
Physiology	C+
Pharmacology	C
Pathology	B+

The Mortis

Orthopedics	C–
Obstetrics	B
EENT	C
Gynecology	C
Urology	A–
Public Health	F
Surgical Anatomy	A–
Tuberculosis	B–
Neuro-Surgery	D
Dog Surgery	A–
Anesthesiology	A–
Thoracic Surgery	A
Infant Feeding	C

3

CHAPTER TWO

Graduate and Early Faculty Years ~ 1948–1975

The story has tracked me (it seems forever) that I was too young to obtain a medical license upon graduation. In fact, I was twenty-one and passed the state board examination shortly after graduation on March 22, 1948. Early graduation was brought about by wartime acceleration of classes. Our class had no summer break in 1945, which was just before the war ended. Graduating in March left a lot of time on our hands before internships started in July.

For the interim, Theo Thevaos and I landed jobs as volunteers at the Richmond County Health Department, which was housed in an old mansion on the corner of Fifth Street and Greene. We rotated through every aspect of the department, from inspecting drainage ditches with Albert Twiggs, the engineer, to inspecting restaurant kitchens with Mrs. Eugene Hoke. The purpose of the drainage ditches was to eradicate malaria by reducing the mosquito population, and it worked. Mrs. Hoke was a formidable inspector who would often appear unannounced at a local restaurant. Even so, she was well liked and usually found everything in order. The venereal disease clinic, which was conducted by Dr. Tom Phinizy, was a busy one. Irvin Connor, who was the head of the local vice squad, provided a steady supply of patients. Specimens were taken to the lab technician, Agnes Reese, for culture or other studies. Everything went smoothly until I had an encounter one day with the head of the department, Dr. Abe Davis. I had shown up several hours late for an assignment to help out in the mobile x-ray unit. I recall writing Dr. Davis an apologetic letter. He soon forgot about the incident, but I did not!

Internship, Baylor University Hospital, 1948–1949

At that time, almost everyone had a rotating internship. While we participated in the matching program, no one who applied to a distant place could afford to go for an interview, nor was it expected. Six of us landed spots at Baylor University Hospital in Dallas. Upon arrival, we learned that the medical school had moved to Houston the year before, leaving only the dental school in Dallas. This surprise, however, did not dampen our spirits, for there were plenty of good doctors on hand to guide our way. The other five nomads who traveled a thousand miles from home base were Charles Bruce, Bill Johnson, Harold Mims, Harvey Newman, and Thomas Nolan. We drove to Dallas in a caravan of two cars, one of which was mine, a graduation gift from the family. On arriving at the border, we stopped at a huge gas station to fill our tanks with the cheap Texas gasoline and to take photographs beside a granite monument proclaiming the great state of Texas. We knew we were somewhere different when a car pulled up, a man jumped out, and said, "It's great to be back from the States!"

A rotating internship assured us that we would never fall into a monotonous routine and provided the opportunity to refine our thoughts about the future. Each month's experience was different as well as rewarding for the nearly forty interns, all of whom were men. The pay was $37.50 a month. We lived in two old houses on Junius Street next to the hospital, where all meals were served. There were three or four bunk beds in each room. Everyone in our room got along fairly well except for a playboy in the group. He was a habitual gambler who came in late almost every night. He tried to get me to help him quit, but he was too entrenched.

Each month provided a new opportunity to decide on a specialty. I wavered between neurosurgery and pathology. I was attracted to surgery by one of the neurosurgeons, Dr. Albert D'Errico, who was gruff, yet unbelievably kind to the small children he operated upon. For interns on surgery rotations, the operating room lounge was a good place to hang out and have a cup of coffee. One day an orderly announced he was leaving to return to his home town. "Why?" I asked. He said, "They have discovered oil in my backyard." No one was particularly surprised.

The doctors as well as patients frequently did nice things for the interns. Dr. Jabez Gault, a young internist, at times asked me to substitute for him at the ice hockey games as the doctor for the home team. The players were predominantly French Canadian. I sat with them in the box. They were large and tough. After one period, I went back to the locker room, and one of the players asked me to sew up a cut in his finger. When I started to apply a local anesthetic, he stuck out his finger and said, "Here, Doc, just sew it up."

One of the patients gave me tickets to the Metropolitan Opera, which included Dallas on its tour each spring. The men gave their tuxedos a Texas flair with their boots and ten-gallon hats. One morning, I went by to see the patient who had given me the opera tickets at his saloon across from the Centennial Fair Grounds, where the theater and ice hockey rink were located. A group of boisterous hockey players were at a table drinking large tankards of beer. I asked my friend what was going on, and he said, "They are having breakfast."

In September 1948 Dallas was hit with the worst heat wave in decades, and all the hospitals in town were inundated with hundreds of victims of heat stroke/exhaustion. Even today, I have difficulty remembering the difference between the two, but at the time we had to figure out who needed saline or wet blankets and who needed other treatment. Temperatures in the area were around 107°F for many days. Patients were crowded into rooms and overflowed into the halls. Intravenous saline infusions were the order of the day. It is worth noting that isotonic saline was usually prepared in the hospital labs. The bottles and needles were reused after autoclaving. Disposable everything was still some years away.

Although pathology was not one of the rotations, I frequently dropped by the pathology laboratory to check on patients' lab results and also to attend autopsies. One case that has stuck in my mind showed how valuable an autopsy can be. A young girl who had died suddenly following a sternal bone marrow aspiration was found to have a ruptured aorta from the trocar, which had penetrated through the sternum. Dr. Joe Hill was the head of pathology. He was widely known for the blood bank he directed. In the spring of 1949, I had decided in favor of pathology and arranged with Dr. Pund to return to Augusta as a resident in pathology.

The year went by in a flash, with many memories still popping up from time to time: the man who had amputated legs from Buerger's disease rolling himself into the emergency room on a makeshift skateboard, chain-smoking cigarettes; the anatomist turned orthopedic surgeon whose precise operative dissections were almost bloodless; the brilliant yet corpulent cardiologist who was destined to precede many of his patients through the pearly gates; the burn patients whose stay was long and arduous, often treated without compensation by the plastic surgeons. Just before completing the year, I walked into a room with a doctor who was about to discharge a patient who he thought was malingering. He said to the nurse, "Give him a shocking dose of salts and send him home."

Residency and Fellowship, Medical College of Georgia, 1949–1951

In the summer of 1946 when I was a student, Dr. Pund let me spend a few weeks with him in pathology before resuming school. This experience, together with that during my internship, led me to pathology.

When I joined the Department of Pathology in July 1949, the only other pathology residents were Drs.William McCollum and Curtis M. Phillips. Phillips stayed on as a faculty member for the succeeding two years. Dr. Albert Bailey joined the resident staff in 1950, and McCollum transferred to Duke. The other residents were from either surgery or obstetrics and gynecology rotating through pathology for six-month stints. Dr. Alva Faulkner was one of them. She became my wife Jane's physician, and we have remained close friends. The faculty in 1949 consisted of Drs. Edgar R. Pund and George R. Lacy in the Murphey Building and Dr.Walter L. Shepeard in the clinical laboratory of the University Hospital, which was a short distance away. Pathology occupied the first floor of the Murphey Building and microbiology the second floor, where we shared a lecture room.

Life as a resident was pretty much as described in my book on the history of the department (77). There were some variations and improvisations on this theme, including research and outside jobs. My research during these years is described in Chapter Four. Dr. Pund encouraged residents to publish, usually

case reports. My first paper was coauthored with a surgeon, Dr. Frank Jones, and was on an unusual case of malignant melanoma of the stomach and intestine (1). An interest in illustrations of gross specimens led me to Orville Parkes, head of the art department, and he prepared a beautiful drawing. He was a pupil of the famous Max Broedel at Johns Hopkins and used Broedel's air brush technique. This paper was my only publication during my residency.

Residents performed most autopsies, but Dr. Pund did not allow us to dissect surgical specimens or render reports. When required, autopsies were performed at night and without any help. I recall a case one night that Dr. Robert Major requested and attended. Unfortunately, I did not properly prepare the body afterwards and the next day received my one and only dressing down by Dr. Pund, complete with a lot of "hell-damns," his favorite curse. As to surgical pathology, it was not easy to learn by watching someone else, even though Dr. Pund did spend a lot of time with us each day reviewing the microscopic slides and having us assist in minor ways with the gross surgical material. I kept copious notes, taking down his comments and pearls of wisdom on numerous subjects, and I still have them.

About once a week, I went on medicine rounds with Dr. William Agostas, a resident in medicine. In turn, he would come over to the Murphey Building, and I would review interesting cases with him. Many years later I tried to persuade our residents to get involved more with patients in this way, but as far as I know, none of them ever did.

Just before the first year was about to end, Dr. Cecil White, a surgery resident and cancer fellow, asked if I would like to be a fellow the next year. Dr. Hoke Wammock was the director of a National Cancer Institute educational and training program, which offered the fellowship. After learning more about it from Cecil and Dr. Wammock, I accepted the post. My duties as a pathology resident stayed the same, and other than attending some cancer conferences not much differed from the previous year. I received a stipend of three hundred dollars per month, which was substantially more than the fifty dollars per month in the first year. The windfall in funds was used to start a medical history and pathology book collection and to support my research, which included travel to other

laboratories. Some of these funds were used for a return visit to Dallas, where I met Dr. Walter Rice, who had just joined the pathology department there. In 1955 he moved to Augusta to head surgical pathology in the soon to open Medical College hospital.

OUTSIDE JOBS

Even though my actual experience had been limited in certain areas, Dr. Pund had enough confidence in me to arrange that I take a *locum tenens* on two separate occasions during the second year. I relieved Dr. Ingrid Sturgis for a week at Battey State Hospital for tuberculous patients in Rome, Georgia, where I performed one or two autopsies and rendered reports on the surgical specimens. Most of the specimens were ribs removed to collapse a lung. It was in Rome where I first met Dr. Rufus Payne, the superintendent of the hospital. I went on rounds with him one day, and he showed me a patient with acute tuberculous pneumonia. Dr. Payne said that if the patient recovered from this episode he would become immune to the disease. Payne later became the first superintendent of the Eugene Talmadge Memorial Hospital of the Medical College of Georgia in Augusta.

Another *locum tenens* was in Macon, Georgia, where I substituted for Dr. Max Mass for a week. He was in charge of both pathology and radiology at the hospital there. Upon my arrival, he showed me around and, just before leaving, told me I need not worry about radiology because the doctors read their own films. However, he said in regard to pathology I would be on my own. The week luckily went by without incident. The surgical cases were for the most part uncomplicated and readily handled.

In Augusta I had outside jobs of a different kind. Dr. Harvey Butler, the county physician, asked me from time to time to substitute for him and see the sick inmates at the county jail. If there was an examining room there, I never saw it. The jailer usually took me directly to the cell and then locked me inside with the inmate while the jailer waited outside. Amazingly, and probably foolishly, I felt safe. The only time I really felt uncomfortable was when I found myself in a holding cell with about ten inmates, all female.

While I liked pathology, especially the opportunity to conduct research, I still had the wanderlust. Early in my second year I learned about the American Hospital in Paris, which offered internships to Americans. I knew Dr. Henry Michel, a retired faculty member who served in the French army during World War I and later worked in the American Hospital. I would visit with him on Saturday afternoons and intently listen to his stories about the war, medicine, and life in general. My wife Jane has written a delightful sketch of Dr. Michel (84). He knew the American representative for the hospital in Paris, where they had worked together thirty-five years before. Dr. Michel recommended me, as did General R. O. Barton, who had led the Fourth Armored Division into France in the Second World War and was retired in Augusta.

I landed the job and immediately began studying French, as the ability to speak the language was a requirement. Alas, this much anticipated year abroad never came to fruition, for in the summer of 1951, when I was supposed to be in Paris, hostilities broke out in Korea, and I was invited to join the army. The American Hospital offered to postpone my internship; however, as events unfolded while in the army, this youthful splurge was soon forgotten, and I did not look back with any regret.[1] My career, no doubt, would have been radically different had I gone to Paris.

MILITARY LEAVE

As a resident, I was nominally listed as a member of the faculty in the school bulletin. In July 1951 I was formally appointed to the faculty in pathology. Upon joining the U.S. Army that September, I was granted a leave of absence for military duty. The first year was at the Army Medical Research Laboratory, Fort Knox, Kentucky, not far from Louisville. This year is described in Chapter Four. The second year was at the U.S. Army Hospital at Fort Belvoir, Virginia.

Before leaving to join the army, I suggested to Dr. Shepeard that funds be sought to commission a portrait of Dr. Pund in recognition of his contributions to pathology and to the school. Dr. Shepeard enthusiastically agreed and proceeded to solicit funds for the portrait, which when completed was placed in the Administration Building at the time Dr. Pund became president in 1953.

Fort Belvoir Army Hospital, 1952–1953

In June of 1952, I was transferred from the Army Medical Research Laboratory at Fort Knox, Kentucky, to the Army Hospital at Fort Belvoir, Virginia, where I served as chief of the Laboratory Service until my discharge at the end of August 1953. The commanding officer was Col. John McGibony, who was a 1927 graduate of the Medical College of Georgia. He welcomed me and took me under his wing, showing me all the ropes. I lived in the bachelor officers' quarters directly across the street from the hospital.

The hospital served not only the personnel at Fort Belvoir, but all army personnel in the Military District of Washington south of the Potomac River, which included the Pentagon and other smaller stations. The surgical volume was moderate and steady, and there were one or two autopsies per week. Since the patient population included the Pentagon, the age spread spanned from young soldiers to older military personnel. The clinical laboratory was also under my supervision, and I was fortunate in having the day-to-day operation of the laboratory handled by a Medical Service Corps officer, who was an experienced medical technologist. Under these circumstances, the year went by without any serious mishap, and I completed the year unscathed.

An unexpected duty that year was an assignment to take night sick call periodically for the troops at the fort. A long line awaited me each time. Having a knowledgeable sergeant at my side made the task relatively easy and, indeed, enjoyable. When one of the young men showed up with something serious, he was admitted directly to the hospital. At Fort Belvoir the hospital harbored some interesting characters. A grizzled old-timer occasionally would leave early and head into town for a game of poker at the White House with his old army buddy Harry Truman. I was told they liked to play on the new veranda Truman had built.

HELP CLOSE BY

Although I was the only pathologist at Fort Belvoir, there was plenty of help available at the Army Institute of Pathology (AIP) and at Walter Reed Army General Hospital in Washington, which was about fifteen miles away. Walter Reed was

at the far end of Sixteenth Street near the Maryland border. The Institute was downtown at Seventh and Independence in an old Smithsonian building. The Army Medical Library was in the same building as the Institute, which provided an extra incentive for going there. The library eventually became the National Library of Medicine in Bethesda, Maryland, and the Institute's name was later changed to the Armed Forces Institute of Pathology.

Colonel Joe Blumberg, who had been chief of pathology at Oliver General Hospital in Augusta, was in a similar capacity at Walter Reed. He was of enormous help when needed and vouched for my army experience when I stood the pathology board examination a few years later. During the year, I attended a week-long seminar on cytology at Walter Reed that was organized by Col. Blumberg. The course was taught by several leaders in the rapidly developing subspecialty.

The AIP staff was equally helpful, and I met quite a number of the section directors. It was there that I first met Dr. Robert Teabeaut, who was serving a tour of duty in the army as head of forensic pathology. He subsequently joined the department in Augusta. At times, Bob took call for me at Fort Belvoir when I went on weekend leave. All autopsy protocols and materials were shipped to the Institute for review. In most instances a form note was received stating that the case under review had been coded according to my findings. When appropriate, comments were added. In commenting on a forensic case of a man who died following a night of drinking, Teabeaut said, "A more complete toxicological examination may have been helpful." We had performed only a blood alcohol.

On one visit to the Institute, I met Drs. Bill Enos and Bob Holmes, who were preparing their report on coronary artery disease in young soldiers, which when published became an instant classic. Many years later, Bob was a representative for a medical laboratory company and would drop by the department in Augusta from time to time.

Washington was a quiet, easy-going, always beautiful place that seemed still to be recovering from the two great wars of the previous thirty-five years. Temporary office buildings along the Mall were a constant reminder. Other than the free concerts and exhibits at the museums and galleries, there was not a lot to do. A performance that sticks in my memory was a recital at the Corcoran Gallery by

the brilliant but inebriated Welsh poet Dylan Thomas, who had to be helped onto the stage. His readings were riveting.

Not infrequently, I took the train to New York for the weekend where I stayed with friends. On one of those trips, I had been asked by Dr. Pund to attend an invited lecture he was to give one evening at the New York Academy of Medicine. His talk was on carcinoma of the cervix. It was a formal affair, and Dr. Pund was decked out in a tuxedo. Although he had been a little nervous when I met with him and Mrs. Pund at the Plaza Hotel prior to his talk, it went over very well and was discussed afterwards by the renowned pathologist Dr. Arthur Purdy Stout.

A few weeks before my discharge, my replacement arrived. Dr. Don McKay, who was a few years my senior, had most recently been on the faculty at Harvard University. I learned a lot from him in those few weeks, and we maintained a friendship over many years. He subsequently became chairman of pathology at Columbia University in New York and later at San Francisco. Don originated the concept of disseminated intravascular coagulation and became famous for his research on this subject. When I became interested in thrombosis a few years later, I asked Don why he had not named the syndrome thrombosis instead of coagulation. He gave me detailed reasons for his choice of terms which are still valid today. We last met in the early '70s over an Irish coffee on St. Patrick's Day at a pathology meeting in San Francisco.

Before returning to Augusta and to the medical school, I had an important trip back to Louisville, Kentucky, where Jane Stoughton Downing and I were married on September 2, 1953. Jane's grandmother was born in Augusta, and there were still Stoughton family members in town, all of whom were friends of my family. We traveled to Augusta in August to meet everyone and to look around for a place to call our home. My future wife impressed everyone greatly, and afterwards my grandmother, Alice Bleakley, who was always outspoken, said, "That girl is not afraid of anything!" When my grandmother learned about my research, she often referred to me as a "rat doctor."

On another visit to Augusta that August, I met with Dr. Pund, who had succeeded Dr. Lombard Kelly as president of the Medical College that July. He

filled me in on activities at the school and discussed my pending return to the faculty. While driving out to his house for a drink, he also made an offer of salary. We were stopped at a red light at the corner near the site of the future Talmadge Hospital and, still looking straight ahead, he said, "Is nine thousand dollars all right with you?" Not knowing what else to say, I replied, "Yes," and we drove on.

An Interim Year, 1953–1954

The Department of Pathology in September of 1953 was a completely different environment from just two years before. Dr. Frank Mullins had been appointed interim chairman, and Curtis Philips had changed his career to surgery. Dr. Pund's former secretary, Juanita Sirmans, had moved to the old Wilhenford Hospital building, where she joined Dr. Payne to oversee construction of the Talmadge Hospital. The great bulk of the work fell on Mullins and me. He handled most of the surgical pathology cases, while I took on most of the teaching and autopsies. That year I gave some thirty lectures and demonstrated autopsies to the class in the Murphey Building amphitheater. Never having given a single lecture before, I resorted to reading to the class from my notes, which Jane had typed for me. In addition, I practiced my delivery ahead of time while sitting in my car parked on a nearby side street. I never really relaxed that first year, but the students, to their credit, stuck it out.

Mullins combined his outside practice, which he brought from Athens, with that of the department. When Mullins left the department in 1955, he took this combined practice with him. He continued an association with the department on the visiting faculty. Dr. Jim Clay was an intern, and Dr. Armour Sherrer was the only resident in 1953–54. Clay left in 1954 to complete his training in Miami with Dr. W.A.D. Anderson.

During the year, Dr. Pund and his newly appointed dean, Dr. Harry B. O'Rear, began the search for a permanent chair. By that spring of 1954, Dr. Leland D. Stoddard at the University of Kansas had been offered the post, and he accepted. I agreed to stay on, as his ideas about pathology and teaching were similar to mine, and it promised to be a good fit. In 1953–54, my faculty salary was supplemented

by Mullins from practice funds. However, beginning in July, I would be strictly full-time, and one of only a handful in that capacity in the summer of 1954.

The Stoddard Era, 1954–1973

During the first few years of Stoddard's tenure, I helped him implement his plans for new educational programs. In the spring and summer of 1954, prior to his arrival that September, we corresponded fairly often, especially about the second-year teaching program. I had read Forbus's pathology text and was familiar with his approach to pathology at Duke, where Stoddard had trained. In a letter from April 27, I said: "Though Dr. Pund is my preceptor, Dr. Forbus is my patron saint, for it is he who brings to pathology once again the holistic approach; the viewpoint I prefer."

By September, plans had moved well along for the introduction of a second-year program for case teaching in small seminar groups modeled after the one at Duke. The new program would be a radical departure from the past. A complete overhaul of all teaching materials as well as partitioning the large student laboratory into smaller modules were in the offing. Under Stoddard's leadership and with his advice, I designed and organized the program, which began in the fall of 1955. The case method of teaching pathology introduced the student to a realistic way of learning to make clinical-pathological correlations, so critical to the practice of medicine. Many times has a student said while presenting a case, "But the text says thus and so." The simple truth is that each patient is unique, whereas each description of disease in the text is a synthesis of many cases. As Osler said long ago, "The best medicine is taught by the patient."

Teaching by the case method was an enjoyable but demanding challenge. I asked a lot of questions. Most of the students seemed to understand this approach; however, teaching by the Socratic method was not appreciated by all. As one student wrote, "All he does is ask questions, why doesn't he teach us?"

For the first two or three years, I gave an introductory lecture on the history of pathology supplemented by a display of classic pathology books from the library and my personal collection. Later, we added a short film of William H. Welch from about 1930 in which he reminisced about the early days of pathology at

Johns Hopkins. Although the students were not especially enthusiastic, these offerings did set the tone for the course.

The pathology course was conducted in close concert with other second-year courses. The faculty as a whole acted as a promotion committee and considered the students' grades in each course before making recommendations for a student to go forward or to take remedial work. One of the more unusual episodes was the plight of a young student who was very much overweight. He was passed, but only on condition that he weigh in (literally) with Dr. Moretz, the chairman of surgery, until his weight was brought back in line. In today's environment, that would never happen, but if it did, there would be many more students tipping the scales.

TALMADGE HOSPITAL AND THE AUTOPSY SERVICE

By 1955 sufficient faculty had been recruited to accommodate the second year teaching program and get the new hospital service up and running. When the Eugene Talmadge Memorial Hospital opened in June 1956, the Medical College acquired its own teaching hospital and would no longer depend upon the University Hospital, the city hospital of Augusta.[2] The University Hospital pathology service had been taken over in 1955 by Dr. Menard Ihnen. He was joined by Dr. William Murphy in 1956. Drs. Albert Bailey and Walter Rice in surgical pathology and Walter Shepeard in clinical pathology formed the nucleus of the new Talmadge Hospital–based staff. A short while later, Dr. Hans Peters was added. Stoddard and I remained in the Murphey Building along with Dr. Floyd Skelton, who was mainly involved in his research program brought from Kansas in 1955. For the first six or seven years, my major effort was devoted to the teaching and autopsy programs.

The autopsy program was modeled after the one at Duke and was kept under Stoddard's tight control. Stoddard would not release a report until he had signed off. As a consequence, there was always a huge backlog of cases on his desk, which greatly aggravated the physicians on the floors. Taking a case to completion was a long and tedious process, including multiple gross and microscopic notes by faculty and lengthy write-ups by the prosectors. Sometimes a hundred or more

microscopic slides were prepared on a single autopsy. This overly thorough protocol was clearly unsustainable. Over the years it was progressively whittled away until by the end of the '90s, only the bare remnants remained. Nevertheless, these detailed studies are a valuable record and picture of the state of pathology in the middle of the twentieth century.

The Thursday night autopsy conference, introduced by Stoddard, was another hurdle for the resident, for each case had to be presented before completion. All residents and faculty were expected to attend. For years, many Thursday night social invitations were declined, much to the consternation of Jane and our friends, who finally stopped asking us out on a Thursday. But if truth be told, these sessions were very instructive. In addition, two of our research projects were an outgrowth of discussions on Thursday nights.

In the mid fifties, the pace was almost leisurely at the medical school. At the same time, there was much excitement and an enormous amount of energy concentrated on converting a provincial medical school into an integrated medical center. Everyone on the still small faculty knew each other. We got together for picnics at the Boy Scout camp and for scientific meetings of the Dugas Club, held at one of the fraternity houses or the Alumni Tavern in the Newton Building.

A long needed voice for the medical school was filled in 1951 when *The Proceedings of the Medical College of Georgia* was started by Dr. Shepeard. I was appointed an associate editor in 1956 and wrote a short update about the department for the *Proceedings* in 1958 (3). The P*roceedings* ceased publication that year and was continued for the next few years as *Foundation and Alumni News* under the auspices of the Medical Foundation of Georgia.

In the spring of 1956, Albert Bailey and I stood the American Board of Pathology exam in anatomic pathology in Boston. We traveled to Boston by rail, which gave us time to study Moore's pathology text, on which most of the written questions were based. Practical oral exams were part of the ordeal, and Don McKay was one of the examiners. I had been reluctant to take the exam, thinking it was a waste of time, but Albert and Jane convinced me it was the thing to do. They were right.

The 1957–58 year was a pivotal one for me. In the summer of 1957, I invented a method for producing a thrombus *in vitro*, which launched my definitive research career in cardiovascular disease for the next thirty-five years. The paper describing this research was submitted for publication in August of 1957, after Rice had reviewed and approved the manuscript in Stoddard's absence. My timing for submitting it was intentional, for just as with autopsy protocols, Stoddard frequently held up release of manuscripts for weeks at a time, which I do believe drove some faculty to refrain altogether from writing papers. This practice was dropped when I became chairman in 1975. Publications, however, continued to be recorded in the department's annual report.

When the department was awarded a National Institutes of Health research training grant in pathology in 1958, I became more involved in the training program as my operational role in the teaching program receded. Hans Peters took over as director of the course in 1961. In the meantime, several new faculty members had joined the department: Drs. Robert Teabeaut, Holde Puchtler, Titus Huisman, and William Boring. Teabeaut and Puchtler would stay the course.

DR. PUND'S SUCCESSOR

In January of 1958, I was invited by Dr. Pund to attend a dinner with Drs. Sam Singal, George Smith, and, I think, John Sherman, the former head of surgery. After dinner Dr. Pund announced his plans to retire that July and assured us there would be a smooth transition in leadership. In retrospect, he probably had notified the Regents of his intentions and wanted to get the word out quietly. Indeed, in looking back, he may very well have had a premonition of a rough transition, which it turned out to be.

Dr. Harry B. O'Rear, who had been dean, moved up a notch to become acting president. He then appointed Dr.Walter Rice as acting dean. Their status remained thus for about one and one-half years while the Regents' search committee floundered. The atmosphere at the school was tense. Unrest was developing among the faculty. Finally, it was arranged for a delegation from the school to address the search committee at one of its meetings in Macon.[3] I was a member of the delegation along with Drs. Alex Vaughan, Sam Singal, Claude-Starr Wright,

and perhaps one other. An alumnus from Macon, Dr. Milford Hatcher, was also in attendance. The meeting was held in the evening after dinner in the Dempsey Hotel, and Chancellor Caldwell presided. Each of us spoke and made a case for permanent or full-time appointments for O'Rear and Rice. During the course of the discussion, one of the committee members asked, in effect, What's wrong with having an acting president? I piped up and said, "How would you like to have an acting wife?" Despite this rude and brash remark, Rice and O'Rear were confirmed soon thereafter.

ACTING CHAIRMAN

In 1960 Stoddard appointed me the co-director of the training grant in anticipation of his taking a sabbatical leave in 1961–62. Prior to Stoddard's leaving, I agreed to serve as acting chairman, which I took as a challenge and only on the condition that he recommend me for a sabbatical year on his return. Since I had not given up any other duties or my research, it soon became evident that the most expedient way to handle the job entailed arising at 5 A.M. and arriving early to get a head start on the day.

We had the largest contingent of residents and fellows ever that year, with thirteen residents and five full-year student fellows. There were far more fellows than either before or since, and far too many. One of the major disappointments, yet a forceful lesson, was the almost complete failure of our requirement for all residents and fellows to become involved in research in order to justify the funding provided by the research training grant. Even an intriguing proposal by the former dean, president, and respected authority on sexual disorders failed to elicit any interest. Dr. Lombard Kelly appeared at my door one bright summer day, smartly dressed in a crisp white suit as was his custom, and proceeded to tell me that he thought impotence could be caused by arteriosclerosis. He asked my help in exploring this idea. Even though his idea lacked details, it seemed reasonable and ideal for a resident to undertake, but there were no takers. Subsequently, we backed off from this rigid approach and used most of the grant money to support student fellows who worked in ongoing faculty-directed research projects in the department. This part of the program was very successful.

In the meantime, I began to receive inquiries about my interest in chairmanships at other institutions. While I expressed interest in some positions and visited two of the institutions, nothing serious ever developed, nor was I that interested. Before his return in 1962, Stoddard had proposed my promotion to full professor, which was effective that July. I was thirty-six.

The following year, 1962–63, was a quiet one. There was time to seek funding and secure a place for a sabbatical year in 1963–64, which was at the Institute for Thrombosis Research in Oslo, Norway. The year in Norway is described in Chapter Five. The family returned home refreshed and recharged, and I had a pocket full of ideas for future research. There is much to learn from the Norwegians and their zest for life. If there is any one maxim we brought home, it is "Do it now."

The year after Norway was devoted to getting back in gear and preparing for an expanded round of research. At about the same time, Stoddard appointed me as director of the residency and fellowship program in 1966. While the student fellowship program continued to operate at top speed, the residency program had begun to dwindle in size, reaching a low point in the late '60s. It did not fully recover until the late '70s. The reasons for the decline were complex, coming on when the nation was in a terrible war in Vietnam that affected everyone, including the young physicians who were being called up for duty.

In this decade I became involved in various civic organizations and served on the boards of the Young Men's Library Association, the historic forerunner of the Augusta City Library; the Augusta-Richmond County Museum; Historic Augusta; and the Greater Augusta Arts Council. The Library Association at the time managed a trust fund, which supported the Augusta Library. Participation in the affairs of the museum was the most rewarding. A small committee developed plans for a medical exhibit. It came to fruition, in a different format, many years later after I was off the board.

The full-time faculty was enrolled in the Teachers Retirement System, a program originally designed for public school teachers. At that time, twenty years' service was required to become fully vested. With the help of friends in the state legislature, a bill was passed that allowed me to count my sabbatical year of leave

toward retirement, which I think permitted others to do so as well. Also, I was able to convince the head of the retirement system to include my two years of residency toward retirement. So in 1969 I became fully vested in the retirement program and felt free to view my options against the background of a deteriorating situation in the department. Not only had the residency complement dwindled, but the faculty strength had declined as well, and the future seemed very uncertain.

INTERLUDE IN GENEVA

An unexpected set of circumstances landed Jane, our son Bleak, and me in Geneva, Switzerland, for about two weeks in the summer of 1970. I was attending the first congress of the International Society on Thrombosis and Haemostasis in nearby Montreux, where Bleak suffered a fractured arm and concussion from a fall while hiking alone in the surrounding hills.

Fortunately, I was sitting next to Dr. Claude Bouvier in the lecture hall when I was informed of the accident. Bouvier, who was from Geneva, immediately took charge, and shortly thereafter we were in an ambulance on our way to the University Hospital in Geneva, about thirty miles away.

During Bleak's hospitalization I had the opportunity to visit Bouvier in his hematology laboratory and also to visit the pathology department, where I met a young pathologist, Dr. B. Bouchardy, who had just published an interesting paper on myocardial infarction. The director of the hotel where we stayed in Geneva was very gracious, providing us with a small, affordable room overlooking the parking lot and amenities such as fruit baskets from time to time. Switzerland was just about as expensive then as now. Cokes in the hotel were a dollar fifty. We consumed a lot of Swiss yogurt.

Prior to leaving for Switzerland, I had developed an interest in the work on heart disease underway in East Africa and found my way to the cardiovascular disease section at the World Health Organization headquarters, which was located on a hillside on the edge of Geneva. There I met the head of the section, Dr. T. Strasser, a physician from Yugoslavia. I inquired about the possibilities for work in that region of Africa and in particular at the British-run medical school

in Kampala, Uganda. I knew that Dr. Jerry Shaper from England was there conducting research on thrombolysis. Strasser was very attentive and then politely let me know that the public health problem in heart disease in Africa is not arteriosclerosis but rather rheumatic fever, which takes an enormous toll. Needless to say, I did not get very far with that meeting. I was left with the memory of lunch in the dining room on the top floor of the building, which provided a spectacular view of Mont Blanc!

As the seventies rolled into view, leadership changes were on the horizon in both the department and the school. In 1972 Dr. O'Rear stepped down as president and was succeeded by Dr. William H. Moretz. The following year, Stoddard resigned as chairman. Events leading up to this change of leadership in pathology dated back to the late '60s. At a time when there was insufficient faculty and few residents, Stoddard instituted what he considered to be a reform movement to meet the changing times. He correctly foresaw that medicine was rapidly becoming a business and losing its characteristic strength as a learned profession. I strongly disagreed with this view and gave a rebuttal at one of the departmental meetings.[4] Notwithstanding this annoyance, Stoddard brought in a quasi psychological motivator who was actually a chemist by trade. This approach backfired and led to further discord in the department. When Stoddard resigned as chairman in June 1973, a search committee was immediately formed with Dr. J. Graham (Skee) Smith, chairman of dermatology, as its head.

Dr. Curtis Carter, who had recently been appointed dean, asked me if I would serve as interim chairman pending the naming of a successor. I declined, saying that I had already served some eighteen months in the '60s as acting chairman, but if he wished to consider me for the post of chairman I would be receptive. Curtis thereupon appointed Skee Smith as interim chairman. This arrangement worked very well, as Skee was an effective and sensitive administrator. In addition, being a Duke man like Stoddard and Teabeaut, he was able to identify easily with them and their concerns. The search would last one and a half years, until it was concluded by my appointment to the chair in March of 1975.

NOTES

1. As noted in Chapter Four on research, all of this correspondence, along with other papers and research records, was destroyed in the fall of 2000 by an overzealous clerk in the department.

2. The origin of the name University Hospital seems to have been forgotten. From the earliest days of the medical school, the city hospital served as its teaching hospital. After the name of the Medical College of Georgia was changed to the Medical Department of the University of Georgia in 1873, a new city hospital built in the early 1900s was renamed the University Hospital in recognition of its teaching role. However, the justification for this name ceased to exist when the name of the medical school reverted to its earlier name of the Medical College of Georgia in 1950 and acquired its own teaching hospital in 1956.

3. Bob Hand, a student fellow in pathology, played a role in arranging this meeting through his relative, Howard (Bo) Callaway, who was a member of the Board of Regents.

4. In retrospect, it is clear that the advent of Medicare in 1965 was a major turning point. Many indigent patients became paying patients and the gradual commercialization of medicine followed. From that time forward the practice of medicine in this country was irrevocably changed.

PLATE VIII

Internship, 1948–49

1) *En route.* In June 1948 the Augusta contingent headed for a year's internship at Baylor University Hospital in Dallas. Dr. Harvey Newman stands beside a giant granite marker as we cross the border and stop to fill up on the cheap gasoline.

2) *Outpatient clinic.* ABC in front of the clinic, which was located in an old house across the street from the hospital. The hospital clinic was a charity service provided mostly by the housestaff.

3) *Clinic staff.* Assignments in the clinic were rotated. This group was on duty in the clinic at the time of the photo. From left: Drs. Henry Winans, C. G. King, Frank Ryburn, and ABC.

4) *Dr. Joe Hill* was chief of pathology and director of the Wadley Blood Bank, for which he was best known. Pathology was not one of the rotations, but there were several residents in pathology. One of them, Dr. C. E. (Flash) Gordon later established a pathology practice in Rome, Georgia.

5) *Work and some play.* Every third night on call followed by two free nights allowed some time for leisure activities. This picnic probably was held at a nearby lake with interns, residents, and dates. From left: Bob Jordan, Frank Ryburn, Mazie Hall, Will Turner, J. A. Mclean, and Meg Carr. The photo of the outing could be an ad for a well known Georgia product—in the home town of Dr. Pepper!

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PLATE IX

Residency, 1949–51

1) *Dr. Edgar R.. Pund* was the head of pathology at the Medical College of Georgia and director of the residency program, which was basically an apprenticeship. He reviewed the microscopic slides of all cases with the housestaff each afternoon but did not render a final report until the next morning, in sharp contrast to the rush of today's practice.

2) *Miss Juanita Sirmans* was the pathology secretary and had the only telephone on the floor. A buzzer system notified those in other rooms of incoming calls. When the Talmadge Hospital opened, she became director of the medical records department. After her retirement around 1980, she helped organize the first pathology alumni reunion.

3) *First publication, title page.* The residents were encouraged to publish, usually consisting of case reports. This paper on an unusual case of malignant melanoma of the stomach and intestine was published as part of a special issue of *The American Surgeon* with contributions by members of the hospital staff (1).

4) *Illustration of melanomas.* This drawing by medical artist Orville Parkes for the case report paper in fig. 3 illustrates multiple melanomas growing from the inner wall of the stomach. A cross section of one of the tumors is shown on the left.

Fort Belvoir Army Hospital, Fort Belvoir, Virginia, 1952–53

5) *Officers' mess.* The table decorations and garland around the neck of one of the nurse officers suggests a festive occasion in progress. Col. Robert Hardaway, chief of surgery, is at the head of the table. ABC is in the middle on the left.

6) *Colonel Joe M. Blumberg, MC,* was chief of pathology at Walter Reed Army General Hospital in Washington, D.C. He was a much appreciated advisor and resource to ABC when he was stationed at nearby Fort Belvoir.

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Malignant Melanoma of the Gastrointestinal Tract
A Case Report

A. B. Chandler, M.D.
G. Frank Jones, M.D.
Augusta, Ga.

Reprint from The American Surgeon,
August, 1951, *Vol. XVII*, No. 8, *pp.* 719-721

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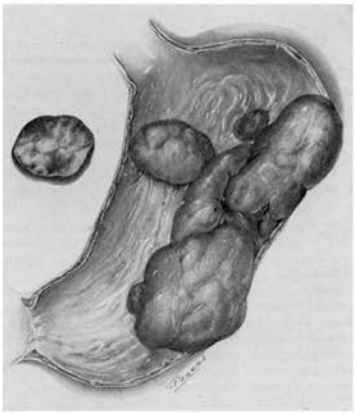

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PLATE X

Transition, 1953–1955

1) *First home.* Jane Stoughton Downing and Arthur Bleakley Chandler were married on September 2, 1953, in Louisville, Kentucky, and shortly thereafter arrived in Augusta, where ABC resumed his position on the pathology faculty at the Medical College of Georgia. Their home for a year was a small rented house in the Summerville area.

2) *Jane and ABC* on the doorstep of their first home.

3) *Surgical pathology.* ABC at the surgical pathology bench. The student looking on is Harold Ramos. ABC and Dr. Frank Mullins handled the pathology service for University Hospital during the 1953–54 transition year before Dr. Leland D. Stoddard arrived in October 1954 to be head of pathology.

4) *Dr. Armour Sherrer*, who was a resident in pathology, and ABC conducted an experimental research project on hematopoiesis during this transition period. Sherrer later joined a pathology practice in Marietta, Georgia.

5) *Pathology faculty, 1954–55.* From left, first row: Drs. E. V. Hastings, N. Thornton, L. D. Stoddard, and A. B. Chandler; second row: Drs. F. G. Stephens and A. W. Bailey. Hastings and Stephens were on the visiting faculty based at St. Joseph Hospital and the Veterans Administration Hospital, respectively. Thornton was a pediatric intern assigned to pathology.

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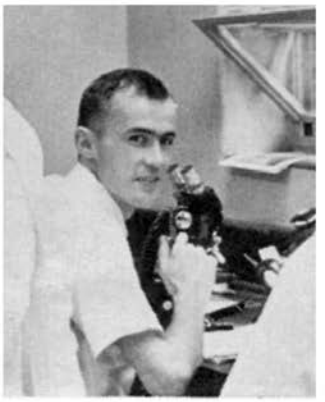

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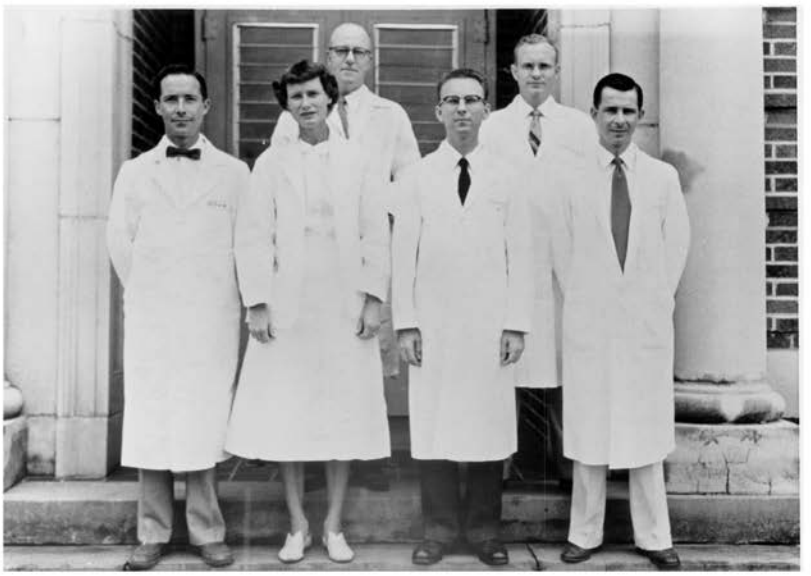

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PLATE XI

Talmadge Hospital Opening, 1956

1*) Pathology Department, 1955–56.* The pathology faculty, residents, and staff had grown considerably since 1954. This photo was taken on the eve of the opening of the Eugene Talmadge Memorial Hospital in June 1956. From left, first row: J. E. Eubanks, B. R. Logan, E. W. Blackstone, J. H. Hatch, M. A. Dye, B. J. Wilson, D. F. McNure; second row: *W. G. Rice, M,D., E. R. Pund, M.D.*, I. R. Brown, M. S. Hawkins, B. S. McDonald, M. Kennedy, J. Stringer, *D. F. Mullins, Jr., M.D., H. J. Peters, M.D.;* third row: *F. G. Stephens, M.D., M. Ihnen, M.D.,* M.E. Blutinger, *A. B. Chandler, M.D., A. W. Bailey, M.D., L. D. Stoddard*, *M.D., W. A. Sherrer, M.D., F. R. Skelton, M.D.*, *W. L. Shepeard, M.D., E. V. Hastings, M.D.*, H. M. Conner; fourth row: A. Thomas, M. Henry, A. Young. (*Faculty and residents in italics*)

2) *Eugene Talmadge Memorial Hospital.* The teaching hospital of the Medical College was opened in June 1956. It was named in memory of the former governor by a unamimous vote of the state legislature. The two buildings on each side are part of the hospital complex. The row of buildings immediately behind the complex are, from left: the Richmond County Health Department, Dugas Building, Murphey Building, Administration Building. The University Hospital can be seen in the distance.

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PLATE XII

The Fifties and Sixties

1) *Case teaching.* The new case teaching program in small seminar groups was introduced in the 1955–56 year. Dr. Menard Ihnen of the University Hospital, third from right, is shown reviewing a case with a group of sophomores. It would have been nearly impossible to get the program underway without the participation and support of the visiting faculty based at the hospitals in the area.

2) *Summer student fellows.* Each summer the teaching materials were reviewed and updated with the assistance of student fellows. Here, Melvin Hirsch on the left and Larry Cohen, class of 1962, are attending to some isolated museum specimens used in the teaching program.

3) *Weekly CPC.* Students and faculty gathered in the large auditorium for the clinical-pathological conference each week to watch the pitched battle between clinicians and pathologists as the clinicians did their best to unravel the case. In this photo Dr. Albert Bailey is next to ABC, who has turned to greet Drs. Ed Wood and Curtis Carter of the medicine faculty.

4) "*The Cadaver*" mocks pathology. This cartoon by Sherrill Kelly in the student newspaper showing the pathologists blasting away at medicine, surgery, etc., is a takeoff on the then popular television series about Chicago gangland wars in the 1930s entitled *The Untouchables*.

5) *Christmas party.* In the '60s, some great "bring a tray" parties were held at Christmas in the mezzanine hallway of the Research Wing. Cathryn Cox, on the left, and Marion Hutson are enjoying the festivities. Cathryn was the secretary for ABC and the residency program, and Marion was based in the thrombosis lab in the Research Wing.

6) *Dr. Robert Teabeaut and Betty Barton* enjoying one of the Christmas parties. Betty worked with Dr.Walter Rice in his immunology laboratory and was instrumental in the success of one of our research projects involving antibodies that she produced. Teabeaut was mainly involved in the autopsy service and teaching.

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January, 1961
THE CADAVER
PEDIATRICS
MEDICINE
SURGERY
THE UNTOUCHABLES

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CHAPTER THREE

Pathology Chairmanship ~ 1975–2000

Swimming with Sharks in Academic Waters

Keep your sense of humor.
— Curtis Carter, 1975

After a year and a half search for a successor to Lee Stoddard, the Board of Regents approved my appointment as chairman of pathology, effective March 13, 1975. Several outside candidates had visited during the search, and a good catch was in sight, only to be lost, when the candidate, Dr. William Shelly, died in a tragic airplane accident. After a few more candidates were interviewed, Dr. J. Graham Smith, the search committee chair, approached me one day in November and asked if I would be interested. I said yes and proceeded to develop a plan based on the assumption that I was being offered the post, an offer that Dean Curtis Carter later confirmed. Over the next two months, I met with all chairmen, most section chiefs, the search committee members and pathology faculty. Finally, Curtis became exasperated with my nitpicking and called me one day in February to ask if I intended to accept the offer, and I said that I was ready.*

Shortly after my appointment, I attended a retreat for new chairmen at Quail Roost, North Carolina, not far from Chapel Hill. The retreat was sponsored by the Association of Pathology Chairs, and several seasoned chairmen from southern schools were on hand to offer the fledglings advice. I recall Fred Lucas from Vanderbilt telling me privately that the best strategy for keeping deans at bay is to prepare a five-year plan. Later, I did just that and kept it updated through 1994. During those early days, advice was easy to come by. Dr. Kenneth Brinkhous told me that recruitment is like picking ponies and that I should expect some losers

*It is the intent of this chapter to complement the formal narrative in my history of the department by giving background and insight into events as well as express personal views (77). Repetition is kept to a minimum.

as well as winners. Events bore him out. One other person, whose name I do not recall, said I should expect to give fully and unselfishly of myself if I were to succeed. I interpreted that thought to mean that I worked for the faculty, not the other way around.

Congratulations came from friends and colleagues, and announcements of the appointment appeared in the *Archives of Internal Medicine* and the *Archives of Pathology*. Letters were received from former pathology teachers including Dr. Stuart Auerbach and my mentor Dr. Edgar Pund, who offered no advice but did send warm congratulations.

Getting Started

The operational and organizational plan is described in detail in my history of the department (77). In brief, the plan was based on the tried and true premise that function is subordinate to structure. Anyone who doubts the validity of this concept has only to look at the structure of DNA. The basic organizational structure of the department was by no means unique, consisting of well-defined sections of anatomic pathology, clinical pathology, and the Veterans Administration Laboratory Service, each with a chief. Curtis Carter's predecessor, Dr. Christopher Fordham, had split off clinical pathology into a semi-autonomous unit. Part of my plan stipulated that clinical pathology be fully reintegrated into the department. There was also a division of general pathology based in the chairman's office to give general direction to research and educational programs that embraced all areas of the department. I retained directorship of the residency program, which allowed me to influence the educational programs of each section and thereby help maintain high standards.

Stoddard shifted to a part-time appointment and assumed limited service responsibilities in anatomic pathology. He devoted considerable attention to the affairs of the International Academy of Pathology in his role as executive secretary. As time went on, he became more and more supportive of the direction I was taking the department.

I had barely begun when Curtis announced his intention to retire in September 1975; I had unwittingly helped him reach this decision. Albert Bailey was being

prevailed upon to rejoin the faculty, and one of the inducements was that his residency years could count toward retirement. This information was shared with Curtis, who looked at his own record of service and decided he could retire at once, and he did. My first encounter with him was as a medical student when he was a resident in charge of domiciliary or outside medicine. Curtis was a superb physician and teacher who was idolized by all who knew him. His departure left a gaping hole.

THE NEW DEAN

Dr. Fairfield Goodale arrived the next April from Richmond, Virginia, where he had been chairman of pathology. Goodale was helpful in recruitment and in restoring full accreditation to the residency program. In one instance, however, he went too far, in my opinion, when he tried to place one of his friends from Richmond in the open slot of chief of clinical pathology. Eventually the offer in Augusta was declined. After that, Goodale more or less left me alone, and I dealt primarily with his business manager and Dr. Joe Bailey, the associate dean for clinical sciences. Goodale was a well-educated, tweedy academic. He was also a Yankee. Joe, on the other hand, was a true southerner who kept a large portrait of Robert E. Lee in his office in the dean's suite, in case any callers should lose their bearings. Joe and I had known each other since childhood, and we had maintained close family ties. If it had not been for Joe's insight and advice, my term as chairman would have been a short one indeed.

Recruitment of faculty was an ongoing, arduous task. I soon learned to expect disappointments and high turnover, especially among younger faculty, but by 1980 a solid, dedicated team was in place. Dr. Paul Milner was of enormous help in the recruitment effort, as was Dr. Walter Shepeard, who had just retired. At times, I traveled from Augusta to meet prospects. My first meeting with Dr. Robert Baisden was in the Baltimore airport. He accepted the position of chief of clinical pathology in 1979. Dr. Raghunatha Rao was already on board, and he was named chief of anatomic pathology in 1979. An alumnus put me in touch with Dr. Richard Chamberlain, who was appointed chief of the laboratory service at the Veterans Administration Hospital in 1978.

I was equally fortunate in building a superb, loyal staff to assist me in my role as chairman. Tom Broome became the departmental manager in 1977. He stayed for over twenty years and soon knew everything about the operation of the department and school. After two or three false starts with secretaries, who were all quite capable, Marie Hiller joined the staff in 1980. Both Marie and Tom were consummate diplomats. They kept me informed of the many minor crises in the department and frequently attended to them with my complete confidence. Mary Cobb was a long-time office member who handled much of the filing and other related duties. The weekly calendar was never released until it had been checked for errors by her sharp eye.

As the '70s turned the corner, I could rely on highly competent associates running the show in the clinical arena of the Talmadge Hospital. Rao and Baisden had the complete respect and support of their clinical colleagues and, in addition, relieved me to a large extent of having to deal with the hospital administration. Baisden accurately pointed out that the people in the administration produce nothing but claim credit for everything. His style of management by "walking around" was very effective.

The clean-cut separation of the anatomic and clinical pathology sections at the Medical College worked well, and everyone knew to whom they were accountable. On several occasions, we attempted to organize a subsection with a combined immunopathology service, but it never got off the ground. A few years later we took another tack and successfully integrated hematopathology, this time without the formality of a subsection. In the end, what works is what people decide will work. Even though our organizational structure was rigid, we demonstrated its adaptability to need. As Calhoun Witham once said to me, "Do not organize beyond your capacity"—good advice to heed.

The department's connection with the VA Laboratory Service was mainly through educational and research programs and a few shared services. Chamberlain ran a tight ship at his bailiwick and always managed to stay two or three paces ahead of his administrative brethren. Dr. Pund had sensitized me to government bureaucrats long ago. In the '40s residents would perform autopsies at the VA Hospital and leave the brains with the diener, Mr. Coastline, to fix in formalin for later dissection. Usually, however, the fixed brains accumulated on a

shelf in the autopsy room, which led Dr. Pund to say that Mr. Coastline had more brains than all the bureaucrats in Washington!

EDUCATIONAL PROGRAMS

When Skee Smith took over as interim chairman, he placed Dr. Robert Teabeaut in charge of the second-year pathology course. After being offered the post of chairman, I asked Teabeaut if he would continue to direct the course. I proposed that he head a new division of undergraduate education in pathology, and he went along with this plan. Teabeaut and I had known each other since 1952, when we were both in the army. He was a brilliant, charismatic teacher who had his own idiosyncratic ways, which did not always sit well with students, faculty, or the administration. It seems I was continually bailing Teabeaut out of scrapes, which incidentally he immensely enjoyed—seeing his plights become mine!

Teabeaut also had a humanistic side that was highly individualized. Each year an honorarium check was cut for Dr. Hobbs, who continued to teach long after his retirement. Rather than simply sending him a check with a note, Teabeaut insisted that we do something special to thank him by taking him to lunch, so each year we did. Giving Dr. Hobbs his honorarium was as easy as passing the biscuits.

The residency program was governed by a departmental committee comprising the chiefs of services, which I headed as the program director. Practically all of our residents became boarded and were placed in good positions upon completion of the program. More residents were graduated between 1975 and 2000 than in all the previous years since the program's inception in 1940. Postgraduate programs were also an important part of our educational offerings. The regional pathology society from the '60s was revived, and we initiated an annual pathology symposium. An added dividend of the symposia was the opportunity to visit with our returning alumni each year.

Faculty evaluation. Following the Board of Regents' edict in 1979 that each unit of the system evaluate its faculty, the pathology senators developed an open-ended format that included personal documentation and a narrative assessment of each

faculty member's progress by section chiefs and the chairman. Checklists were not used inasmuch as they lead to false quantification by giving subjective opinions a number. Their use avoids the true question: Is the evaluator capable of putting into words a thoughtful analytical opinion?

WHO DID WHAT TO WHOM

Relations with other chairmen were generally cordial and mutually supportive. Occasional turf wars erupted, but everyone managed to stay on speaking terms. Pathology was by no means immune from these rifts. Dermatology became a big headache whenever we lost the services of a specialist in this area, and its chairman would threaten to obtain these services elsewhere, preferably from a dermatologist. The pathologists could hardly complain. The pathology board had shot itself in the foot in the 1970s when it allowed dermatologists to become certified in dermatopathology after only six months' training. Drs. Jim O'Quinn and Steve Mullins, both pathologists with this expertise, usually came to the rescue when we were in need.

In 1975 there were about thirty satellite laboratories based in other departments, often providing services that duplicated our own. The administration was of little help and usually refrained from forcing incorporation of these laboratories into pathology. Our solution for this inefficient system was long-range. We accepted these laboratories only when offered and as long as all personnel and other resources were part of the package. The number of satellite laboratories was reduced at least by half through this approach.

In the spring of 1983, one of those curious "It could only happen here" incidents occurred. Quite by chance our son Bleak informed me that he would attend a hooding ceremony one evening at a local country club the week before his graduation. I learned that the dean and one or two other chairmen had arranged a dinner for the graduating class, to be followed by the hooding, and that neither I nor other faculty members, with few exceptions, had been invited to this academic function. I was incensed at being excluded, but it was too late to do anything other than to crash the party, which I refrained from doing. This affront to the faculty, students, and families was discussed with Dr. Harry O'Rear, vice

chancellor for health affairs, and I urged him to take corrective action by moving this academic function to an appropriate venue open to all faculty and families. A year or two later this change was made, and the ceremony became a daytime function at a local church. As president of the alumni association in 1997, it was my privilege to address the class at the hooding ceremony that year, but without cocktails and dinner beforehand!

The social occasions when we got together at one another's homes were a more enjoyable aspect of the chairman's life. Goodale started these gatherings in the '70s, and they were continued for several years.

A Short Term President

When Dr. Moretz retired as president in 1982, there was a clutch of local candidates to replace him, including Drs. Fair Goodale, Lois Ellison, and Joe Bailey. I supported Joe in his bid, as did others; however, the Board of Regents decided to go outside and picked Dr. Jesse Steinfeld, who was dean of the medical school in Richmond, Virginia. Steinfeld made a broad impact during his brief stay of three and one-half years, from 1983 to 1987. Goodale resigned in 1984 and left Augusta. After Goodale departed, Steinfeld named Dr. Paul Webster as interim dean for the 1984–85 year.

In the spring of 1985, the second-year students rebelled and submitted a petition to Webster and Steinfeld demanding an investigation of the pathology course. They claimed that Teabeaut used unfair and inequitable evaluations and grading. Webster appointed a review committee. It was difficult defending Teabeaut when I knew some of his practices could be questioned. Nevertheless, as recounted in my history, the course survived. Despite the efforts of many, and two in-depth faculty teaching conferences, the course did not regain its previous credibility and luster under Teabeaut, which was a reflection on my leadership as well. The whole matter was brought to a satisfactory conclusion when the course director was changed for the 1992–93 year. Dr. John Steele, whom Teabeaut had taken under his wing in the teaching program for several years, agreed to take over the directorship. Teabeaut strongly endorsed Steele and the changeover took place without missing a beat. Steele immediately gained the respect of the students and

support of the faculty and turned the course around, garnering for the department the students' award as the Outstanding Basic Science Teaching Department for six years in a row.

The Buzzards. From the mid '60s into the '80s a group of faculty known as the Buzzards met every day for lunch in a small alcove of the main hospital cafeteria, at a long table that was once in Rufus Payne's palatial office. Faculty from all departments were there, and much business as well as gossip transpired each day. Occasional evening meetings were held at a member's house. Especially memorable were those at the hospitable home of Barbara and Bill Quillian. Moretz would regularly have lunch with the Buzzards when he was chairman of surgery. He continued to do so whenever possible after he became president in 1972. In contrast, Steinfeld seemed reluctant to have lunch there. Sad to say, the alcove was not retained when the cafeteria was remodeled around 1990. Moretz knew its value, but he was gone.

RENOVATION AND CONSTRUCTION PROJECTS

From 1975 to 2000, the space available to the department was more than doubled. Two large renovation and building projects were completed in the 1980s. Later, in 1994, the scattered blood bank components were centralized in a new facility in the Sydenstricker Wing of the hospital.

Murphey Building renovation. The Murphey Building renovation was held in abeyance for most of Goodale's and Moretz's tenure. The project was scheduled to start in 1976, but all of a sudden, it was postponed, and the funds were diverted to build the Radiation Therapy Center, which admittedly was a worthy project. For several years thereafter, our project was given a low priority by the Board of Regents. But unknown to me, a surprise was in the making. Joe Bailey had occasion to mention the need for the renovation to his neighbor, Toby Ivey, who was a member of the Board of Regents. In due course, Ivey became vice chairman and then chairman of the board. One day in the spring of 1982, I received a call from him. He said, "Do you want the Murphey Building?" I was almost speechless, but quickly recovered and gave him an unequivocal yes.

It was apparent that it would take several years to acquire enough research to utilize the two-story building fully. Now the stark reality was upon us to make certain all space would be accounted for; otherwise it would be siphoned off. To make certain the building's identity became widely known, the word "PATHOLOGY" was included on the outside lettering. By the time the building was occupied in the spring of 1986, every inch of space had been taken into account for current and intended use, so that when Steinfeld was taken on a tour of the building, he was pleased. My successor, Dr. Stephen Peiper, who is a prominent cancer researcher, converted more of the space to research, as originally intended.

Anatomic pathology wing. We had worked with the architects for some time on a major renovation and expansion in the hospital for the anatomic pathology area, which was bursting at the seams. Once the plans were drafted, the architects met with Steinfeld for a final review, but without any warning whatsoever, he refused to sign off on them and sent us back to the drawing board. That was a lucky turn of events, for we ended up in 1988 with a two-story wing to the hospital plus a basement with its own elevator, which was named the Jesse Steinfeld Elevator in recognition of his unexpected benevolence.

A New Beginning Once Again

The cycle for naming the next president of the Medical College began precipitously in 1987 after Steinfeld's early departure. I decided to become a candidate and submitted a letter of intent to the chancellor. There were at least four other local candidates, including Dr. Francis Tedesco, who was then serving as interim dean. At the urging of the Alumni Association, the alumni candidates were asked to prepare a plan for leading the institution. But forthwith we received a letter from the chancellor saying he would not accept any such documents. Despite strong support and endorsements from faculty, alumni, and other colleagues including Drs. Rufus Payne and Harry O'Rear, I was not invited for an interview. My plan, for what it's worth, adopted the basic theme that the institution must become a truly statewide asset with education as its focal point. In the end, Tedesco was chosen.

As a new regime geared up under Tedesco in 1988, the pathology faculty was implored to stay on course and to maintain high standards of academic achievement and clinical services. The faculty was reminded of the true purpose of the hospital as stipulated by the Board of Regents in 1955:

> Resolved further, that the Board of Regents shall and it does hereby direct that the primary purpose of the Eugene Talmadge Memorial Hospital shall be to serve as an auxiliary of the Medical College of Georgia in the development of medical knowledge and skills through organized programs of teaching. The development of such knowledge and skills is, of necessity, dependent upon the proficiencies developed while engaged in the care of patients under proper supervision and in observing and participating in medical research programs.
>
> —Minutes of the Board of Regents, March 9, 1955.

Shortly after Tedesco was appointed, I asked him if the portrait of Dr. Pund in the Administration Building could be moved to the Murphey Building since the funds that paid for it were raised when Dr. Pund was head of pathology. Tedesco instead provided funds for a second portrait to be painted, which was displayed in the lobby along with portraits of Drs. Murphey and Lamar, and later of Stoddard in 1993.

Tedesco named Dr. Gregory Eastwood, a fellow gastroenterologist, as his first dean. When Eastwood arrived in October of 1989, I informed him of the situation in pathology and told him about future plans. Eastwood was a kindly, sensitive person with a philosophic bent who in some ways reminded me of a graying hippie, but that may be too harsh a judgment. An anecdote may help. When I told him of the need for a dress code, including the use of name badges, for the students in the first two *basic science* years similar to the one for the students in the last two *clinical* years, Eastwood asked if I thought they would respond. The school, of course, continued on its merry way as essentially two separate schools, each with its own style of dress, curriculum and promotions committee.

I enjoyed working with Eastwood, who left in 1992 to become president at Syracuse. He had a human touch with a dash of humor. It was not all peaches and cream, however, for an isolated flap occurred when Eastwood brought along uninvited and disruptive students to a teaching conference organized by the department. I took exception to this interference. The end result was two articles

in the student newspaper,[1] one favorable to Teabeaut, the pathology course director, and the other castigating both the dean and the department. Afterwards, Eastwood and I quickly settled our differences and moved on.

THE ADMINISTRATION KNOWS BEST

It was my fate to serve on many bylaws committees, at times as chairman, which included the Alumni Association, Medical Staff, and Physicians Practice Group. I was named chairman of the PPG committee shortly after Tedesco became president. He wanted a number of changes and made it a point to attend practically every meeting. The members soon found that even if Tedesco was insistent about an issue, if we tabled it for a while and returned later, he would often have second thoughts. Controversial issues were soon resolved and the overhauled bylaws were adopted. In the process the organization's original name of Medical Research Foundation of Georgia was changed to the Medical College of Georgia Physicians Practice Group Foundation, thus incorporating the working title of Physicians Practice Group.

For years, evaluation of teachers and courses by students has been the gold standard for gauging effectiveness of these activities. The professors usually dismiss these evaluations as irrelevant—unless they are favorable! The administration listens to the students. It seems that regardless of a program's success or lack thereof in terms of scholastic achievement, the important criterion is popularity. In the mid '90s, this point of view became more embedded as the term "teaching effectiveness" crept into the academic vocabulary of the school. The Pathology Executive Committee decided to challenge this flawed view and prepared a position paper that was forwarded to the administration.[2] In essence, we said that while student evaluation of a teacher's ability to communicate and inspire one to learn is important, the evaluation is meaningless without corroborative evidence that the student has indeed learned what is expected. Too often it is assumed that the two modes of evaluation are the same and the only evaluation used is that of the student.

One of the battles I fought virtually alone for many years concerned discriminatory advertising or, by its newer name, marketing. My position was one of

opposition to a state institution's advertising locally without doing so throughout the state. No one ever listened. The Medical College physicians were determined to compete locally, while the physicians in town did not seem to care as long as they could send their nonpaying patients to the Medical College hospital. This situation came to a head at a departmental level in the mid '90s when Baisden, who was director of the department's outside service program, and I decided to announce throughout the state our specialized services in dermatopathology. Prior to that announcement, with the help of Dean Eastwood, an agreement had been reached with the hospital administration to expand our outside services and share in the income. We, therefore, thought it appropriate to proceed, only to be thwarted by an anonymous opponent who had contacted the Board of Regents objecting to our program.

The stand-off was ultimately resolved in our favor when it was made clear that our program had the backing of the dean and hospital director. This episode was a searing reminder of a visit over dinner in 1973 with Professor D. Sinapius in Washington, D.C. I asked Sinapius how he accomplished so much research and yet managed to direct a large pathology department in Göttingen, Germany. He replied that he arose early in the morning to conduct his research and then left the rest of the day for the inevitable "imponderables."

Excursions

During my tenure as chairman, I became involved in a number of activities and organizations not directly related to the position, which on occasion benefited the department. The organizations other than those referenced in other chapters included medical organizations from local to national in scope, the Alumni Association of the School of Medicine, and the Trustees of the Academy of Richmond County.

In the early '80s, an initiative was undertaken once again to rehabilitate the Old Medical College Building on Telfair Street, which was erected in 1835. This time the alumni took the lead. I succeeded Dr. Dan Sullivan as chairman of the alumni committee which worked with other groups to raise the necessary funds, most notably with the Medical College of Georgia Foundation, headed by Dr.

Gordon Davis. Jack Hagler represented the foundation in this endeavor, and before long, sufficient funds had been raised or committed to begin the project in 1988. I was one of the Trustees of the Academy of Richmond County, who had custody of the building, and along with the other trustees, we negotiated a long-term lease of the property to the foundation. Craig Cranston, president of the trustees, strongly supported this project and worked closely with Jack Hagler and the alumni. The historic structure was reopened with a ribbon-cutting ceremony in 1990. The occasion was marked by an article in *MCG Today* and one by my wife Jane in the *Journal of the Medical Association of Georgia* (85).

I served on the Alumni Association board from 1984 onward and as president of the organization in 1996–97. Serving as president provided an opportunity to travel around the state to attend regional meetings and visit the many loyal alumni of our school. Our thrust that year was to promote the scholarship fund, which had grown substantially since Gordon Davis established it in the early '80s. Prior to serving as president, the association honored me in 1994 as a distinguished alumnus. Past presidents serve on the board for life. It has been enlightening over the years to hear the reports of various presidents and deans.

The Richmond County Medical Society had held its meetings in the Old Medical College Building for years, and upon the reopening of the building after its renovation they resumed meeting there. The society contributed $25,000 to the renovation. I served on the Board of Trustees from 1984 through 2002. In 2000 the society honored me with an achievement award, which was followed by the Lamartine Hardman Cup of the Medical Association of Georgia for contributions to the science of medicine. The latter award was presented on the same date that my predecessor, Edgar Pund, received it forty-nine years before.

In 1984–1985, I was president of the Georgia Association of Pathologists and remained on the board for several years thereafter as the academic representative. When the department prepared to embark on a postgraduate educational program offering an annual symposium, the association accepted an invitation to cosponsor this annual event, which began in 1987. This union was a successful educational venture for both parties. The Georgia Association is an affiliate of the College of American Pathologists, and through my former faculty colleague, Dr. Hans Peters, I became involved in the activities of the college, serving on its

Autopsy Committee from 1987 to 1993. Hans was chairman of the committee at the time of my appointment, and we worked together on a number of projects and publications in this field (68, 69). Later on, Dr. Grover Hutchins from Johns Hopkins became chairman, and the committee issued two practice guidelines for autopsy pathology (71, 73).

"A Nice Little Southern School"

No new dean worth his salt could begin without a slogan. The slogans of various deans with whom I have served go like this: "This school has great potential," "The school is a sleeping giant," but the most memorable one is by Dr. Darrell Kirch, Tedesco's new dean, who proposed a paradigm shift from "A nice little southern school" to "The best." [3] All deans since Curtis Carter have been imports, and most of them have seemed compelled to be patronizing. Eastwood was an exception. He said that upon reflection, "We will know in our hearts that we are the best." [4]

Kirch, a psychiatrist, arrived in February 1994. He waited until August 12th to give what I called his "nice little school" address to the assembled chairmen, at which time he presented his agenda. His vision was to "achieve excellence by mastering change." [3] At the end of the speech, he challenged the chairmen to get on board. The chairmen's reaction appeared restrained and cautious. Not long afterward, the clinical chairmen began to meet on their own. Weekly meetings led by the chairman of surgery became largely a debating society, for without the authoritative presence of the dean, who rarely attended, little was accomplished.

In the fall of 1995, I gave a presentation on the current status of the department at a meeting of the Faculty Senate as a prelude to an external department review scheduled for March of 1996. We had amassed a large amount of data and documents for the review, which was conducted by a panel of distinguished pathologists. In their report, the reviewers commended the department for its highly regarded educational and clinical programs and for the prudent management of its financial resources. They concluded that the department was well positioned to meet the challenges of the future. We were well aware that research should be

expanded, which was reflected by our recently launched internal research grant program (77).

On my seventieth birthday in 1996, a turning point was reached. Rao, the chief of anatomic pathology, had indicated his desire to retire in the near future; however, I was not quite ready to do so, which was poor timing on my part. I had hoped to retire before him, as it would be easier to find a new chair that way. But I procrastinated and Rao proceeded to retire in 1998. I was then faced with the dilemma of deciding on my own retirement date versus maintaining the integrity of the anatomic pathology service. By this time, the dean was leaning on me, asking when I intended to retire. I told him my plan was to leave as soon as anatomic pathology could be made secure.

Rao kindly agreed to continue on a part-time basis during the recruitment period for a new chief. Not surprisingly, there was little interest in the position, since it was generally known that I was near retirement. However, several good candidates were interviewed. In rapid succession, my retirement was set to begin January 1, 2001, as part of a large-scale early retirement program, and two prospects with good credentials were identified. In early 2000 the candidate from Arkansas, Dr. Stephen Bonsib, was selected. Just prior to that, an extraordinary series of events began to unfold.

RAW POWER IN ACTION

And I expect you'll all agree / That he was right to so decree, /
And I am right, / And you are right, / And all is right as right can be!
—The Mikado [5]

Since several chairmen would take early retirement in the months ahead and one would soon leave for another post, the clinical chairs wrote the dean in January 2000 urging him to appoint search committees without further delay. Later, I met with Kirch and told him the pathology faculty was concerned that no search committee for the chair had been formed. Several members of the pathology faculty drafted a letter to him, but I prevailed upon them not to send it, as it would only make matters worse. What I did not know at the time was that Kirch, exercising his authority as dean, had met separately with each of four pathology

faculty members to discuss departmental issues and determine each one's interest in serving as interim chairman.[6] Each one implored him to quickly appoint a search committee, which would help allay the concerns of the faculty.

When Dr. Bonsib returned for a second visit in February 2000 as a candidate for the chief's position, he met for the first time with the dean on a Friday. By the following Monday, Bonsib had accepted my verbal offer to be chief of anatomic pathology, and I notified the dean. It quickly became apparent that during or shortly after their brief meeting, Kirch had offered and Bonsib had accepted the interim chairmanship to begin in June. I told Kirch that Bonsib had not been recruited or interviewed for that purpose, and since anatomic pathology was a huge job in itself, it would be unfair to him. I urged that he be brought on board instead as associate chairman and work with me to effect a smooth transition. Kirch listened but would not go along with my recommendation. A few days later, he informed the pathology faculty of his decision at a departmental meeting on March 7.[6]

After several inquiries from alumni that spring, I attended a meeting of the alumni board on Saturday, April 29, 2000, and explained the situation in an executive session. By then, I had decided that my reputation and standing in the Medical College and medical community were under attack and that it was time to defend myself. The board was attentive and concerned. Whether a coincidence or not, the dean announced at a meeting of the chairs the following Monday that he would be leaving to assume a post elsewhere.

Subsequently, the alumni president sent Tedesco a strongly worded letter conveying the sentiment of the board that I remain as chairman until my retirement.[7] As early as March, one former alumni president had written Tedesco citing the lack of protocol and propriety in addressing the issue of the chairmanship.[8] The chancellor was sent copies of these letters. At a garden reception on May 5, Tedesco told Jane and me that he would take care of my situation and urged me to be patient. He also said that when the chancellor called to ask what he should do about the calls and letters received from alumni, Tedesco told the chancellor he would take care of the matter. Tedesco's main concern seemed to be a strong desire to maintain good relations with the alumni, which, as an alumnus, I was glad to hear. Finally, however, a divergent note sounded when

another former alumni president related that when he called to inquire about my status, Tedesco told him he was waiting on a recommendation from the dean.

Dr. Betty Wray, a member of the pediatric faculty and graduate of the Medical College, entered the picture in early June in preparation for becoming the interim dean in July 2000. Wray had ties with the pathology department extending over many years, having worked with me as a student fellow in 1959, with Stoddard on a part-time basis after her graduation, and more recently with other pathology faculty. Two senior members of the department wrote her on June 9 to express the deep concern of the pathology faculty regarding the appointment of an interim chair.[6] They urged Wray to appoint a search committee and to ask that I remain as chair until a permanent replacement could be recruited. At about the same time, two of the clinical chairmen offered their support and met with Tedesco. A senior faculty member met with both Wray and Tedesco. As the new year got underway, four residents left the department and two faculty members resigned.

After discussions with Wray and Bonsib in June and early July, Wray sent over a letter on July 5 to be signed by me and Bonsib which specified that I would serve as chairman through August with Bonsib as associate chairman. I signed the letter with reservation and so informed Wray and Tedesco. It was thus quite a surprise to be given a *second* contract a few days later, signed by Tedesco on behalf of the Board of Regents appointing me as professor *and* chairman from July through December 2000, which I signed on July 10. This action led me to believe, mistakenly, that the matter had finally been resolved by Tedesco along the lines I had originally proposed. Actually, I had been duped by my own credulity.

A few weeks later, Wray informed me by letter on August 28 that the Board of Regents had approved a change in my status from professor and chairman to professor, effective September 1. No copies were shown. It would seem to follow that the second contract from Tedesco that I had signed on July 10 would have been revised to reflect this change in status; however, a revised contract was not issued. In addition, the contracted financial commitment was continued. This clever, and generous, maneuver became known around the house as the Tedesco gambit. One might say I had been scuppered, but only by half!

No doubt, much of this saga would never have unfolded had I gone away quietly. What remained to be fathomed after this year of unbridled power was a web of machinations that was about as easy to disentangle as a slippery Gordian knot. The underlying tenor of these events, which at times bordered on the ludicrous, is perhaps best conveyed by the lively verse from *The Mikado*[5] quoted at the beginning of this section. *The Mikado* is about power and intrigue from another era. In the ivory tower of today, power usually is cloaked in a thin veneer of academic freedom. Moreover, as Lord Acton said, "Power tends to corrupt, and absolute power corrupts absolutely," which is the ugly side of the equation. The days ahead were viewed with uncertainty, mixed with hope, for the department's successful transition to a new era and prosperous future.

Transition

In the fall of 2000, Dr. Baisden solicited and obtained funds from generous pathology alumni and colleagues for my portrait to be commissioned. It was painted by Lamar Wood and presented at the annual pathology symposium in April 2001. The portrait, along with portraits of Baisden and Rao, was placed on display in the Murphey Building beside other departmental leaders of the past. In addition to attending to the portrait that fall of 2000, I put the finishing touches on my history of the department, which was published by the end of the year (77). It was thirteen years in the making.[9]

A search committee for the chair was finally convened in August 2000, some eight months after I had announced my plans to retire in January 2001. In order to give some perspective for the future, a statement was prepared for the search committee, the pathology faculty, and others, which laid out the major accomplishments of the department from 1975 through 2000. I reviewed my prior presentation to the pathology faculty that the time had come to embark on a carefully planned research expansion, while referencing the substantial research

output of the department since the 1930s. Once the search began in earnest, I was invited to meet with each candidate and submit an opinion.

As the search progressed, a topic that received attention during the year was the undergraduate educational program in pathology. The pathology course had been led by a physician since its inception in 1837. Now, at a time when several well-qualified physician pathologists were on the faculty, a clinical laboratory supervisor and member of the medical technology faculty with an Ed.D. degree was jointly appointed to the pathology faculty and designated the course director for the '01–'02 year.[10] Despite my concerns, I decided to continue teaching in my capacity as emeritus professor. While the students at times complained about the lack of a pathologist director with whom they could relate on a professional level, they were undeterred and finished the year in stride.

For the following '02–'03 year, the hands-on case teaching program that Stoddard and I started in 1955 was scuttled by the incoming chairman and replaced by a lecture-oriented course. I gave one lecture that year and then decided to bow out. I had taught at the Medical College since 1949 and participated in the education of some seven thousand students. It was time to stop.

The prospect for the appointment of a new chair brightened the scene as the summer of 2001 turned into fall. The field was narrowed to two external candidates with outstanding research records. At a pathology faculty meeting on December 12, 2001, the interim dean introduced Dr. Stephen Peiper of the University of Louisville and announced that he had accepted the offer of the chair in pathology. Peiper was well qualified to move the department forward. The faculty offered their support in anticipation that he would meet the challenges of the future and usher in a new era for pathology at the Medical College of Georgia.

But the tenure of the new chair was short-lived. In the summer of 2008, Peiper announced he would be leaving to assume the pathology chairmanship at Thomas Jefferson Medical College. Peiper successfully introduced new programs, changed others, and rebuilt the faculty in a short span of six years. The search for a new chair with all its attendant unknowns would soon begin anew.

Conclusion

The chairmanship was unrelenting in its demands and consisted mainly of keeping several balls in the air at the same time all the time, which no doubt was the experience of many other chairs. Giving proper recognition and being fair to everyone was a constant challenge, especially when faced with decisions that were not easy to make. Success of leadership occurs only when common goals and challenges are met. Overall, the record of accomplishments far outweighs the disappointments. Indeed, little would have been accomplished without the strong support of the pathology faculty, housestaff, and staff, whose dedication to the goals of the department, the school, and to the profession were unsurpassed.

NOTES

1. *The Cadaver* (student newspaper) April, 1990.

2. Memorandum dated January 8, 1997, from Dr. A. B. Chandler, (for the Pathology Executive Committee), to Dr. Barry Goldstein, Vice President for Academic Affairs, with attached letter dated June 21, 1996, from Dr. John Steele to Dr. Ruth-Marie Fincher, Vice-Dean for Academic Affairs.

3. Memorandum dated August 15, 1994, from Dean Kirch to department chairs with enclosed copies of overheads shown at the meeting of August 12, 1994.

4. *Student Pulse* (student newspaper) November 8, 1989.

5. *The Mikado* by W. S. Gilbert and A. S. Sullivan, 1873.

6. Memorandum dated June 9, 2000, from Drs. John Steele and Ross Gerrity to Interim Dean Wray. (Copy of memorandum provided by Dr. Gerrity.)

7. Letter dated July 3, 2000, from Dr. David Cohen, President of School of Medicine Alumni Association to President Francis Tedesco. (Copy of letter provided by Dr. Cohen.)

8. Letter dated March 23, 2000, from Dr. Walter E. Brown, Past President of the Alumni Association, to President Tedesco. (Copy of letter provided by Dr. Brown.)

9. A bibliography of the department from 1838–2000 was published in 2006 (78) as a companion volume to the history of the Department of Pathology (77).

10. Newsletter, Department of Pathology, September 2001; Memorandum dated June 26, 2001, from Interim Chair of Pathology to Pathology Faculty and Residents.

PLATE XIII

Residency Program

1) *Dr. John Shippey,* a former surgeon, was the first chief resident. He was appointed for the 1973–74 year. His experience added a perceptive dimension to the residency program and to his meticulous studies. New residents were often referred to his work as an example to follow.

2*) Housestaff, 1974–75.* From left, seated: Derene Akins (full-year student fellow), Drs. Bertha Morales, Rose Badaruddin; standing: Drs. Frank Winecoff, Masato Hanada, David Lehmiller (chief resident), Mehboob Fatteh, and Prawat Nitiyanant. On the suggestion of Lehmiller, the department held its first dinner in honor of the graduating residents that year, which was continued each year thereafter.

3) *Resident schedule.* Before the days of computer programs that could create a rotation schedule with the click of a mouse, Marie Hiller, the residency program coordinator, resorted to a board with colored markers to arrange the year's rotations. Marie also served with distinction as the departmental secretary from 1980 to 1998.

4) *Visiting Arab.* Dressed in Arabian garb, Dr. Robert Baisden presents graduating resident Dr. Osama Abdelatif a star from the East that he had acquired on one of his foreign trips as an inspector for the College of American Pathologists. His wife, Helen, on the left and Osama's wife, Rory, are having a good laugh as well.

5) *The lecture.* Graduating resident Dr. Barbara Amaker gives ABC the lecture, admonishing him about his aversion to the overuse of abbreviations and acronyms. At times residents' protocols (and faculty, too) read like a Chinese menu.

6) *Resident poster.* Each year at the annual pathology symposium, members of the housestaff and faculty presented scientific posters of their work. A prize was awarded the resident with the best one. Here, Drs. Greer Falls and Regina Chorsky stand beside her poster on primary pulmonary hypertension.

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PLATE XIV

Old Medical College Restoration

1) *Rededication.* From left, President Francis Tedesco, Dr. Gordon Davis, and John Hagler rededicated the restored Old Medical College Building at a ribbon-cutting ceremony in 1990. Davis and Hagler represented the Medical College of Georgia Foundation, which provided most of the funding.

2) *Restoration* of the Old Medical College Building included reopening the central rotunda, which had been sealed for many years. The Alumni Association of the School of Medicine was involved in the restoration through its committee for this project, first headed by Dr. Daniel Sullivan, followed by ABC. The story of the restoration, which included the photos shown here in figs.1 and 2, was recorded in 1991 in an article by Jane D. Chandler in the *Journal of the Medical Association of Georgia* (85).

Pathology Endowments and Departmental History

3) *Pathology endowments pamphlet.* In the late 1970s the Pathology Department began a concerted and successful drive to establish endowments for the department. Endowed chairs were started in memory of Drs. Pund and Shepeard. A library fund was established in memory of Dr. Frank Mullins with substantial funding assistance from his brother, Dr. William Mullins.

4) *Fund raiser.* The first effort to raise funds was facilitated by luncheons throughout the state for the Pund endowment. From left, Drs.Volpitto, Payne, and Engler attended one of these luncheons in Augusta.

5) *Departmental history.* Elizabeth McDaniel with her husband, Ed, and ABC at McDonalds Restaurant in Washington, Georgia. She designed and published the history under the imprint of her Stratford Press in Athens, Georgia (77). Frequent meetings were held at our halfway house in Washington as the project neared completion.

6) *Title page of "Pathology at the Medical College of Georgia."* Publication of the history in 2000 was sponsored by the D. Frank Mullins, Jr., Library Fund and by many pathology alumni and friends of the department.

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Pathology Endowments
MCG Foundation, Inc.
Medical College of Georgia

At this time of year it is natural that our thoughts turn to those who have affected our lives. Alumni of the Medical College of Georgia remember especially outstanding pathologists, Dr. Edgar R. Pund and Dr. Walter L. Shepeard who gave many years to the Department of Pathology, and Dr. D. Frank Mullins who served the Department and doctors throughout Georgia and the Southeast.

PUND

At a recent Pathology Alumni Reunion held here their influence was apparent; speakers, though not pathologists, referred many times to the contributions to the professional lives of graduates made by these devoted and beloved teachers.

Within the MCG Foundation there are special funds which receive gifts and pledges to each.

SHEPEARD

The "Edgar R. Pund Memorial Fund" now contains approximately $82,000; the goal is $250,000 with which to establish a Chair in Pathology in his memory.

The "Walter L. Shepeard Clinical Pathology Fund" contains over $11,000 which will be used to support educational endeavors at the Medical College.

MULLINS

The "D. Frank Mullins, Jr. Library Fund" contains over $22,000, the income from which will be used to purchase educational materials and support scholarly pursuits within the Department of Pathology.

To make a contribution to any or all of these endowments, please use the enclosed gift card and return envelope. Your gift will be credited to the appropriate fund(s) within the MCG Foundation.

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PATHOLOGY
at the
MEDICAL COLLEGE
of GEORGIA
A Chronicle, 1837–1997

A. Bleakley Chandler, M.D.

STRATFORD PRESS ATHENS, GEORGIA
2000

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PLATE XV

Inner Workings

1) *Chairman's office staff.* From left: Dorothy Parker, Christina Jones, ABC, Marie Hiller, and Tom Broome. Photo is from the '90s.

2) *Annual Report.* An important project each year was to publish a departmental annual report as a permanent record of accomplishment, along with plans for the future. Bound copies of these reports dating back to the 1930s are housed in the Medical College Library. This photo of the cover page of the 1997–98 edition shows the Murphey Building in the center and the departmental logo in the upper left.

3) *Tom Broome* carried out his role as department manager with great skill and sensitivity, dealing with many personalities and challenges on a daily basis. Tom served the department and school with distinction for over twenty years.

4) *Mary Cobb* had worked in the department for more than thirty years, most recently in the chairman's office, where she provided innumerable services. Here, at the time of her retirement in 1995, she is shown with ABC, who had worked with her from the beginning.

5) *ABC* plotting his next move.

Bibliography

6) *Nora Freeman* worked with Dr. Gerrity and was coordinator for the department's participation in the multicenter project on atherosclerosis in youth, known as PDAY. She also helped greatly in producing the bibliography of publications emanating from the department.

7) *Title page* of the bibliography of publications of the Department of Pathology, 1838–2000, which was published in 2006 (78).

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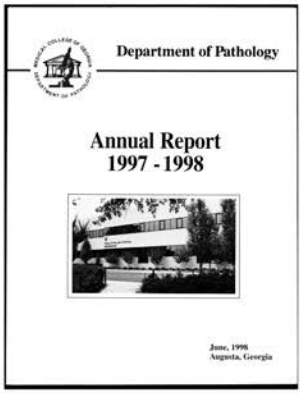
Department of Pathology
Annual Report
1997 - 1998
June, 1998
Augusta, Georgia

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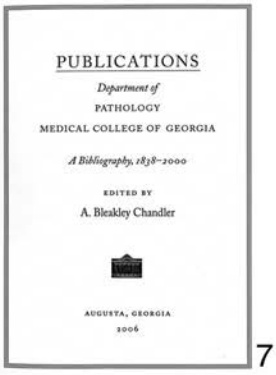
PUBLICATIONS
Department of
PATHOLOGY
MEDICAL COLLEGE OF GEORGIA
A Bibliography, 1838–2000
EDITED BY
A. Bleakley Chandler
AUGUSTA, GEORGIA
2006

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PLATE XVI

Some Milestones

1) "The Pathfinder." The department's newsletter was published twice a year from 1989 through 1997. The name was thought to be unique until it was learned that an automobile had the same name, and later another pathology department unknowingly adopted the name. Photo shows Dr. Greer Falls presenting a framed collage of pictures to Harold Conner on the occasion of his retirement in 1990.

2) *First chiefs.* From left: Dr. R. N. Rao, first chief of anatomic pathology at Talmadge Hospital (1977), and Dr Walter Rice, first chief of surgical pathology (1956). Initially, the surgical pathology and autopsy service were stand-alone services until they were consolidated in 1977 as a single program under anatomic pathology.

3) *Chamberlain retirement*. Dr. Luther Mills, standing on the left, presents Dr. Richard Chamberlain with gifts on the occasion of his retirement in 1993 as chief of pathology at the Veterans Affairs Hospital. Mills succeeded Chamberlain as chief. Emeritus President Dr. Harry O'Rear looks on. After he retired, O' Rear kept a small office in the Murphey Building and attended departmental meetings from time to time.

4) *Portrait presentation.* Artist Lamar Wood on the left and ABC at presentation of his portrait of ABC to the department during the annual pathology symposium in April 2001. The portrait was sponsored by colleagues and pathology alumni.

5) *The hand-off.* Dr. Stephen Peiper on the right succeeded ABC as chair of pathology in 2002 and quickly put his stamp on the department with new programs and faculty. His stay, however, was short, for he left for another post in 2008.

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The Pathfinder

July 1990 — Department of Pathology, Medical College of Georgia — No. 4

GAP Elects President

Dr. C. Robert Baisden, chief of the clinical pathology laboratories and professor of pathology at the Medical College of Georgia, was elected president of the Georgia Association of Pathologists for 1990-91.

Dr. Baisden has been active in the parent organization College of American Pathologists inspection and accreditation program for several years and is currently the program's commissioner for Georgia.

Harold Conner: Friend of Students

Mr. Conner (left) receives a pictorial history of his years at the Medical College from Dr. Greer Fallis.

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PLATE XVII

Friends and Family

1) *Life-long friends.* From left, Drs. Joe Bailey and ABC, both Augusta natives, wound up in similar careers at the Medical College but in different fields. Bailey was serving in the dean's office as associate dean for clinical sciences when ABC became chairman of pathology.

2) *The Buzzards*. This sketch of two buzzards out on a limb was drawn by one of the artists of the comic strip *Steve Canyon,* as a special gift for Dr. Marty Frank, who shared it with fellow Buzzards. The Buzzards were a diverse group from all departments who met for lunch in the alcove of the hospital cafeteria to share each other's company and news of the day. Drs. Marty Frank, Joe Bailey, and ABC, to name a few, were charter members.

3*) Mountain visit.* After the O'Rears moved to the North Carolina mountains in the '90s, we had an enjoyable visit with them. From left: John Chandler, ABC, Jane, and Harry O'Rear.

4) *Small reunion.* Dr. Hillery (Sandy) Newland visits Augusta in 2002. Sandy conducted thrombosis research as a student fellow and resident in pathology. Later, he joined the pathology group at Athens General Hospital, where Bleak, Jr., worked part-time in the lab while attending the university. From left: Bleak, Jr., Sandy, and ABC.

5) *Ewell farm.* Jane and ABC visited Dr. Walter Brown and his wife, Alice, in 1993 at their home in Tennessee, which had been the home of a famous confederate general. Walter maintained close ties with his alma mater throughout his career and was a special friend to the pathology department. From left: Jane, ABC, and Walter Brown.

6) *Old classmates.* Dr. Harvey Newman returns to Augusta in 2006 for a short visit and a chance to reminisce. He moved to Oregon not long afterward to be with family.

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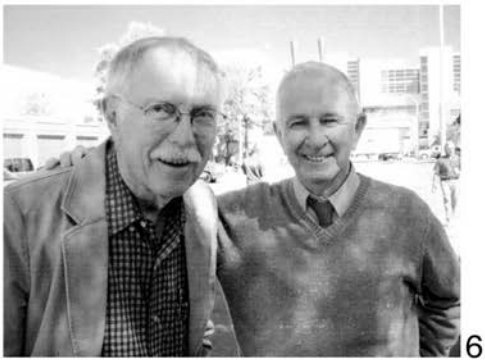

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PART TWO

Research

CHAPTER FOUR

Research Initiatives ~ 1949–1963

Residency Years, 1949–1951

My career in research began in 1949 while I was a resident in pathology; it was for the most part self-started. From 1949 until 1951, when I entered the U.S. Army, I initiated several projects prompted by comments and the work of Dr. Pund, who was engaged in the study of preinvasive carcinoma (carcinoma-in-situ) of the uterine cervix. In order to demonstrate that the lesion has neoplastic properties, a notion not generally accepted at the time, I decided to test the idea of autonomous growth of the tissue by means of guinea pig eye implants and tissue culture. Dr. Pund gave me a grant of five hundred dollars, which was a large sum indeed, and I proceeded first with the guinea pig project.

carcinoma of the uterine cervix

Anterior chamber implants. Harry Greene at Yale University had shown that autonomous growth could be demonstrated for melanomas and some other human tumors by implanting the tissue in the immunologically protected anterior chamber of the guinea pig eye. Tissue for my experiments was obtained in the operating room at the time of hysterectomy or partial removal of the cervix on cases proved to be preinvasive or invasive carcinoma by prior biopsy. Surgical residents helped in collecting the material and would call me when the specimen was removed. Drs. Joe Mulherin and Ed Roundtree were especially helpful. These experiments, however, were unsuccessful, for most of the implants soon became infected or were already infected when implanted. Having failed with this approach, I next tried tissue culture.

Tissue culture. Although Alexis Carrel, Ross Harrison, and a few others were well recognized in this field in the first half of the twentieth century, it was not yet fully adapted to research because of the bugaboo of bacterial infection. But in 1949 antibiotics were changing things rapidly, and within a few years there was widespread application of tissue culture in research.

I was fascinated with this technique. In addition to reading all the books available, of which there were precious few, I visited laboratories on the East Coast in the fall of 1949 and spring of 1950: Drs. Wilton Earle and Virginia Evans at the National Cancer Institute, George Gey at Johns Hopkins University, and Margaret Murray at Columbia University. Each of them had made important advances in the field. One incident I vividly recall was my visit with Dr. Gey. When I told him I was attempting to culture preinvasive carcinoma, he said it would be difficult and tried to dissuade me from this project. This advice, though sound, made me all the more resolved to proceed. Many years later I learned that it was Gey who subsequently cultured the cervical cancer from which the famous line of HeLa cells originated. The other investigators I met were most encouraging, especially Margaret Murray.

One of the highlights of the trip in 1950 was a visit to the Rockefeller Institute for Medical Research in New York. Dr. Sydenstricker had arranged for me to meet Dr. Tom Rivers, the director, who was from Georgia. He had one of the fellows take me on a tour of the Institute, where among many other things I saw the tissue culture laboratory of Alexis Carrel, which was preserved as a shrine exactly as he left it some years before. Later, I attended the first American workshop on tissue culture in Cooperstown, New York, where I met other workers in the field.

In my experiments several techniques were used, mostly with the Carrel flask and the roller tube apparatus of Gey. Tissue samples were obtained as before, and upon implanting the cells, antibiotics were added to the culture medium. Infections still occurred, but some cultures survived for several days to a few weeks. Growth of preinvasive carcinoma was intermediate between that of normal epithelium and invasive carcinoma. I was somewhat at a disadvantage, because the only incubator available was in the bacteriology laboratory in the University Hospital. The results of this study were reported in January of 1951 at the faculty research club, otherwise known as the Dugas Journal Club. The presentation was

supplemented by microscopic demonstrations of the actual cultures set up in a student laboratory.

OTHER EXPERIMENTAL STUDIES

During this two-year period of my residency, I also became involved in two other experimental studies on cancer: one utilizing cell fractions and the other an attempt to create immunity to transplanted animal tumors. Dr. Pund contracted tuberculosis in the 1920s and after recovery remained relatively inactive physically. He frequently commented that those individuals who had tuberculosis seemed to be immune to cancer and referred me to an article published around 1930 by Raymond Pearl, a biostatistician at Johns Hopkins. After reading Pearl's article, I decided to try out his hypothesis on an experimental basis.

Tumor transplantation. Dr. Esmond R. Long at the Henry Phipps Institute at the University of Pennsylvania had described the biological and chemical properties of fractions of the tubercle bacillus. He and others proposed that the lipid fraction of the organism was responsible for eliciting resistance by the infected host. Taking that as a clue, I decided to test susceptibility of mice to a transplantable tumor after subcutaneous injections of lipid. Lecithin was used at first, and later Dr. Long kindly supplied the lipid from the organism. The tumor was an easily transplantable, rapidly growing sarcoma. Although I tried to give control and test animals an equal dose of tumor, the method used was crude. Portions of tumor were suspended in saline, and the cells were counted in a hemocytometer. Nevertheless, the injections of the lipid had no effect on the test tumors, which grew rampantly, just as they did in the controls. The idea was fairly decent, but the experimental design was flawed.

Cell fractionation. Another project that was educational yet produced no results was conducted in collaboration with Dr. Sam Singal in the Department of Biochemistry. The ultracentrifuge had recently been developed, and Singal was using it to prepare various cell fractions by differential centrifugation. He prepared both nuclear and cytoplasmic fractions of an animal tumor. My idea, based

on the concept of plasmagenes, was to see if tumors could be induced by one of the cytoplasmic fractions called the x-fraction. Injections of this material into animals of the same species did not induce tumors, nor did other cell fractions that were tested.

Endocrine studies. Dr. H. E. Nieburgs, who conducted cytological studies with Dr. Pund on carcinoma of the cervix, had previous experience in experimental endocrinology in England, and he continued some of these studies in Augusta. A couple of nights each week for several months I assisted him in performing thyroidectomies, adrenalectomies, and several other operations in the mouse such as transplanting ovaries into the spleen. This was interesting work and stood me in good stead when I was called to join the army.

The army calls. Soon after the war in Korea began in June of 1951, I was called to active duty and served for two years. My first assignment was at the Army Medical Research Laboratory at Fort Knox, Kentucky, beginning that September.

Army Medical Research Laboratory, 1951–1952

In the summer of 1951, when the Korean War began, it was apparent I would be called for active duty in the military service. One day the head of physiology, Dr. William Hamilton, who was a noted scientist with wide contacts, called me over to see him. Dr. Hamilton was a man of few words and got right to the point. He wanted to know if I would be interested in joining a research program in the Army, and I said yes. Evidently, my research over the previous two years had not gone unnoticed. In a few days, I received a telex from Washington telling me to report for active duty at the Army Medical Research Laboratory in Fort Knox, Kentucky, to join a frostbite research team, probably in anticipation of frostbite problems in Korea. A few days later, however, I received another telex instructing me to join a radiation biology unit instead and to report first to the Army Institute of Pathology in Washington, D.C., the end of August 1951, and attend a one-week course on radiation biology and injury.

The course was an eye-opener to an area I knew absolutely nothing about. Pathology luminaries, including Drs. Burt Wolbach, Shields Warren, Averill Liebow, and others, spoke on their particular area of experience. It was impressive to hear Dr. Wolbach, who was dressed immaculately in a dark suit with a starched white shirt and high collar, as he precisely recounted his work on radiation injury in 1909—at once conveying how much and how little was known about the subject. I also recall a talk by Dr. Lalla Iverson, a member of the Institute, who spoke on radiation injury to the lung. Twenty-five years later she joined the pathology faculty in Augusta, shortly after I became chairman. Col. Carl F. Tessmer, director of the Army Medical Research Laboratory and a pathologist himself, was also in attendance. We hit it off right away, and he was most supportive during my stay at the laboratory.

The Army Medical Research Laboratory (AMRL) was under the direct control of the surgeon general in Washington. The physical facilities were in a separate complex on the grounds of Fort Knox. They consisted of the original two-story concrete block building where the commanding officer, Col. Tessmer, was located and about ten temporary style renovated barrack structures scattered along each side of the road leading to the headquarters building. Each remodeled barrack housed one of the research units.

I lived in the bachelor officers' quarters for the hospital at Fort Knox. A classmate, Paul DeWitt, was chief of the pathology laboratory at the hospital, and, along with his wife Liz, we occasionally got together socially. I also took call for him a couple of times at the hospital. Although there was a small library at the AMRL, I would occasionally go to Louisville, about thirty miles away, to visit the library at the medical school there. I also attended the scientific meetings of the Louisville Pathology Society, which provided an opportunity to keep informed as well as meet pathologists in the area.

The AMRL, which was established in 1942, took on an entirely new personality after World War II. In the final stages of the war, German scientists were captured by the Allies, and quite a number of them ended up at the laboratory in Fort Knox. While I was there, they were kept under constant surveillance and were made to live in Elizabethtown, a small town nearby. Although most of them kept their political persuasions to themselves, one of them was an ardent Nazi who

frequently made bellicose statements about the superiority of the Aryan race. The director of the radiation biology unit where I was assigned was Dr. A. T. Krebs, a German scientist who had worked in or in connection with the uranium mines in Czechoslovakia. I did not like him and did not get along with him at all. If it had not been for Col. Tessmer, I would have left sooner than I did.

Whole body radiation. Notwithstanding the tense atmosphere, I proceeded to become involved in a project on whole body radiation and thermal injury simulating the biological effects of the atomic bomb explosion. We were familiar with the work of Leon Jacobsen at the Argonne National Laboratory in Chicago, which showed that lead shielding of the spleen in rabbits protected them from a lethal dose of whole body radiation. A few years later, after Stoddard had arrived in Augusta, he told me that this idea had originated with him and his colleague Bernard Black-Schaffer, and that Jacobsen learned about it on a visit to Duke University. The reason for the protective effect of shielding is that in small animals there is considerable hematopoiesis, or marrow production, in the spleen in normal states. In addition to my prior experimental work as a resident, I read extensively, especially historical material. In this context, I proposed an experiment with whole body radiation in splenectomized animals, quoting Claude Bernard in his 1865 treatise, *Introduction a L´Étude de la Médecine Expérimentale,* who said that every proof should have a counterproof if at all possible.

The radiation and thermal burn experiments, which were performed on mice, resulted in no difference in lethality between the splenectomized group and a control group. In the splenectomized animals, there was a marked shift in hematopoiesis to the bone marrow. A striking feature of these experiments was the occurrence of hemoglobinuria (blood in urine) shortly after the induction of thermal burns, which lysed red cells coursing through the burned area of the skin. Col. Tessmer reviewed progress of this work by meeting with me in his office about once a week in the evening. He was quite knowledgeable about radiation injury, having served as the first director of the Atomic Bomb Casualty Commission in Hiroshima. This work was probably reported through channels to the surgeon general, but it was not published in a medical journal.

Transfer to Fort Belvoir. Despite the support, advice, and encouragement of Col. Tessmer, I grew weary of working under the supervision of the German scientist. In the spring of 1952, I decided to take action, so one day I called Col. Joe Blumberg and asked if he could have me moved to another post. Col. Blumberg was chief of pathology at Walter Reed Army Hospital at the time. I had known him when he held a similar position at Oliver General Army Hospital in Augusta during my residency. In a few weeks, orders were cut for me to report for duty that June at the army hospital at Fort Belvoir, Virginia, where I would become chief of the laboratory. Col. Tessmer, of course, had been consulted by Col. Blumberg, and the transfer was supported by Tessmer, who seemed to understand and wished me well. He was a true gentleman. My year at Fort Belvoir, where I served until my discharge in August 1953, was devoid of research and is described in Chapter Two.

PLATE XVIII

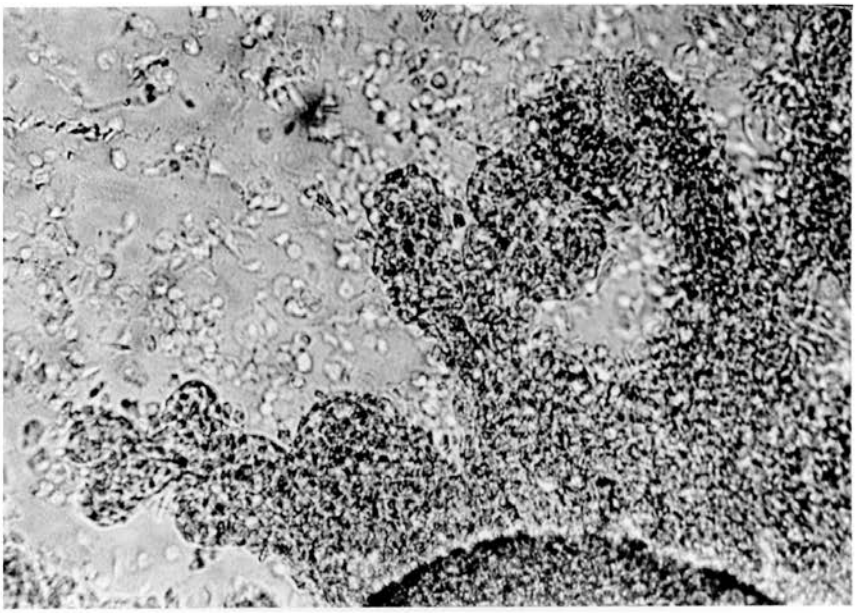
Tissue Culture

1) *Culture of invasive carcinoma, microphotograph.* At eight days' growth the carcinoma has extended out from the initial explant at bottom of photo to produce multiple branching fronds. The Gey roller tube apparatus was used to culture the cells.

2) *Carrel flask.* Photo from original article in 1923 showing the flask Dr. Alexis Carrel designed for tissue culture. The flask was awkward to use because the tissue cells had to be viewed from below with an inverted microscope. Carrel's laboratory at the Rockefeller Institute for Medical Research was painted black and the benches were draped with black cloth to highlight dust and other contaminants so important to avoid in the pre-antibiotic era.

3) *Roller tube apparatus.* Tissue cells were planted in test tubes that were then placed in slots of the apparatus, which was rotated to bathe the cells with the culture medium. The roller tube wheel was housed in an incubator as depicted in this photo. The apparatus was designed by Dr. George Gey in the 1930s.

4) *Dugas Journal Club.* A talk on the history of tissue culture and report of experiments on the culture of cancer cells was given by ABC at a meeting of the club in January 1951.



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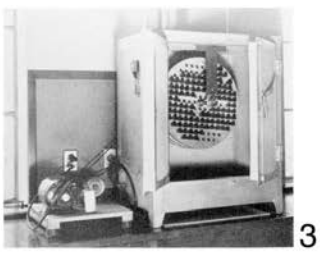

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JANUARY MEETING - January 31, 1951

The Dugas Journal Club of the Medical College of Georgia held the fourth meeting of the year on Wednesday, January 31, in the Anatomy lecture room following a dinner in the Alumni Tavern. Dr. Bleakley Chandler told of his work with tissue cultures, including some history of the technique, the methods used, and some of the difficulties he has encountered and overcome in his work here. Numerous questions led to interesting discussion. Dr. Chandler had several demonstrations of his cultures of normal and neoplastic tissues for observation with microscopes.

4 The dinner was attended by 25, the meeting by 28.

PLATE XIX

Army Medical Research Laboratory, Fort Knox, Kentucky, 1951–52

1) *Research program.* The booklet describes the various units of the laboratory and the staff assigned to each program. *Inset*: ABC was assigned to the radiobiology department.

2) *Colonel Carl F. Tessmer, MC,* was a pathologist who served as commanding officer of the AMRL. He had most recently served as director of the Atomic Bomb Casualty Commission in Hiroshima and was very familiar with the pathology of radiation injury. Col. Tessmer was of enormous help to ABC in his radiation injury studies.

3) *AMRL complex, aerial view.* Col. Tessmer and administrative staff were located on the second floor of the white two-story building in the foreground, which was the original structure for the facility. Laboratories for environmental studies were located on the first floor. The radiobiology laboratory and other units were housed in renovated barracks along the road leading to the headquarters building.

ARMY MEDICAL RESEARCH LABORATORY

FORT KNOX, KENTUCKY

RESEARCH PROGRAM

RADIOBIOLOGY DEPARTMENT

Krebs, A. T.	GS-14	Dept. Head (Radiobiologist)
Vacant	GS	Secretary
Ionizing Radiation Section		
Krebs, A. T.		
Puckett, N. L.	GS-7	Biochemist
Parr, W. H., Jr.	GS-7	Radiobiologist
Dixon, E. H.	GS-1	Technician
O'Neill, T. A.	Pvt.	Technician
Bush, S. G.	Pvt.	Technician
Hatfield, W. H.	WB-2	Laborer
Cellular Research Section		
Vacant	GS	Cytol st
Chandler, A. B.	Lt., MC	Pathologist
Vacant	MSC	Biochemist
Czerwonka, O. H.	GS-7	Biophysicist
Czerwonka, L. J.	GS-7	Biophysicist
Ransom, B. G.	Cpl.	Technician
Geuger, C. M.	PFC	Technician
Vacant	EM	Technician

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Research During Early Faculty Years, 1953–1957

I returned to Augusta from military leave and resumed my position as a faculty member at the Medical College in September 1953. Relatively little research was conducted during the first three or four years as I was more involved in getting settled again in the department and in Augusta with my family. However, two small projects were initiated, one concerning splenic arteriolosclerosis and the other on induction of hematopoiesis in transplanted bone.

Splenic arteriolosclerosis. It is well known that arteriolosclerosis is common in the spleen and, unlike that in the kidney, cannot be correlated with hypertension. Less well known is its occurrence in infants and young individuals. I studied a number of spleens from young people and tried to figure out by microscopic examination why arteriolosclerosis is apt to occur at this age only in the spleen. My observations did little more than confirm its occurrence in the young. I was left with the premise that the change occurs in relation to the little understood pattern of circulation in the spleen, whereby the rapid diminution of the arterial lumen places the arterioles under a large head of pressure, similar to that in the afferent glomerular arterioles of the kidney observed in the nineteenth century by Bowman.

Bone marrow induction. A recent article caught my eye that described how active hematopoiesis, or the production of marrow cells, could be induced in the normally inactive marrow in the tail vertebrae of rats by curling back the tail and implanting it beneath the skin. This simple procedure, which raised the temperature of the vertebrae, induced active hematopoiesis, leaving behind in the proximal tail a nice inactive control. Dr. Armour Sherrer, who was a resident in pathology, and I decided to amputate the terminal tail of some rats, remove and dry the vertebrae to kill the cells, and then implant them into the same animal subcutaneously. Since the presence of bone and its structure is obviously related in some way to hematopoiesis, we postulated that the bony

environment of the implanted vertebrae might induce fat tissue to grow in the marrow spaces and become actively hematopoietic. Although tissue did grow into the marrow spaces, for the most part it was fibrous and no hematopoiesis was detected.

IN VITRO THROMBOSIS

> *Why do you call him Lord "Thrombosis," Sir Winston? Because he is a Bloody Clot!*
> —As recounted by Dr. Charles H. Best, 1963, Toronto.

In the spring of 1957, another idea popped into my head. After having only sporadic success in research for the first few years, albeit learning a lot along the way, I finally hit pay dirt. Soon after Stoddard arrived in September 1954, he initiated the Thursday Night Autopsy Conference. One evening the discussion got around to the subject of thrombosis. Stoddard had said before that a thrombus is not the same as a blood clot, but this time he explained that a thrombus always forms in flowing blood. This statement got my wheels turning again.

It occurred to me that flowing blood could be simulated by partly filling a circular tube with blood and then rotating it so that the blood would "flow" relative to the movement of the tube. If a cotton thread was placed in the lumen secured to the collared joint of the circular tube, rotation of the tube would allow the blood to flow past the foreign object and induce the generation of a thrombus at that site. So far, so good.

So, in the first experiment, a large segment of clear polyvinyl tubing was half filled with several milliliters of fresh venous blood without anticoagulants, and the tube ends were closed by a collar to form a circle with a thread in the junction. The circular tube was then rotated on a slanted turntable at 17 rpm, which happened to be the speed of my record player commandeered from home. After several minutes' rotation, no visible change had occurred on the thread. Serendipity then entered the picture. I decided to continue rotation, and after a few more minutes, a burst of turbulence was noted in the advancing end of the blood column and a spinning, bobbing mass then appeared as the turbulence subsided. The contents of the tube were poured into a dish to expose a cylindrical solid mass about 2 cm long in a pool of liquid blood, which did not clot.

The cylindrical structure was fixed in formalin and slides prepared. Microscopic examination revealed two distinct components. The leading end was composed of aggregated platelets connected by strands of fibrin with entrapped leukocytes and variable numbers of red blood cells. This area strikingly resembled an *in vivo* thrombus. The trailing end of the mass consisted almost entirely of a fibrin mesh with entrapped red cells. Not only was the liquid residual blood incoagulable, it was completely devoid of platelets, which had been incorporated into the platelet-fibrin head of the thrombus. The whole structure was later designated as an artificial thrombus or *in vitro* thrombus.[1]

By the end of the summer of 1957, sufficient experiments had been performed to confirm the validity of the technique, and a paper was prepared for publication. It was entitled "In Vitro Thrombotic Coagulation of the Blood: A Method for Producing a Thrombus." The manuscript was submitted to *Laboratory Investigation* and it was published in the March–April issue of 1958 (2), exactly ten years after my graduation from medical school. My research career had gotten off to a rocky start, but at this juncture, at the age of thirty-one, the future seemed promising. As soon as this paper was accepted in the fall of 1957, research grant applications were prepared, one for the Georgia Heart Association and one for the National Institutes of Health. In the meantime, a paper entitled "A Method for Producing a Thrombus *In Vitro*" was presented at the annual scientific meeting of the American Association of Pathologists and Bacteriologists in Cleveland in April 1958.

In the ensuing months, both grants were awarded. The Georgia Heart Association grant was awarded first, to begin in July 1958. Then, in July, word was received that the NIH grant was awarded to begin in September. So in accordance with the stipulation in the Georgia Heart award, this grant was rescinded. The NIH grant was to continue for seventeen years while research and other funding based on this *in vitro* thrombus technique continued into the mid 1980s.

Initial Grant Years, 1958–1963

My grant was initially funded in direct costs for $10,485, which allowed me to employ a research assistant and occasionally an additional person. I was fortunate

to recruit a well-qualified person with a B.S. degree then living in Tennessee. Marion Hutson was a superb research assistant who worked in the program with me for some twenty years. She had superior technical skills and assumed more and more responsibility as the work progressed over the years. Other technical assistants from time to time during this period were Dorothea Fortson, Anne Fulghum, and Teresa Klett.

Shortly after Stoddard arrived in September 1954, the first floor of the Murphey Building was renovated, and a research laboratory was created in the northeast corner of the building, which I used initially. For the first two years, a satellite laboratory was set up in one of the examining rooms of the outpatient clinic on the first floor of the hospital. Blood samples were obtained mainly from obstetric patients with the guidance of Mrs. Murphy, who was the head nurse for the clinic and provided liaison with the patients' doctors. In 1961 the thrombosis laboratory was moved from the Murphey Building to the new Research Wing of the hospital where most experiments were performed thereafter.

For the first several months, the technical aspects of the method for *in vitro* thrombosis were adjusted and refined. For example, we found that occasional occlusion of the circular tube by a forming thrombus and cessation of thrombus formation could be prevented by simply increasing the slant of the turntable. It was also found that pH of the blood could be more accurately controlled by replacing the air in the tube with 5% CO_2. The description of the tube designed for this purpose was published in 1960 (4) and subsequently it was patented. This patent came in handy a few years later when a small company in New England started marketing what was called a thrombo-wheel. An attorney was engaged to restrain this company inasmuch as the apparatus was essentially a copy of the method for producing an *in vitro* thrombus. I was concerned that commercialization of the technique would thwart other investigators from using it. Indeed, the method began to be widely used, especially in England, but elsewhere as well, and became known as the Chandler loop or Chandler tube. The method continued to be used into the twenty-first century.[2]

Another by-product of the initial phase of this work was the observation that when blood is collected in polyvinyl tubing without exposure to air, it does not coagulate for up to two hours and the red cells settle out as in a sedimentation

rate tube with anticoagulated blood. Since we employed fresh venous blood in our experiments, setting aside some of the blood in a sealed segment of tubing served as an indicator of whether the blood collected was contaminated with tissue juice, or thromboplastin, for if it had been contaminated, the segment would quickly coagulate and the red cells would not settle. This observation of sedimentation of blood *in vitro* without anticoagulants was published in 1960 (5).

In vitro thrombi were also used to study thrombolysis by means of human plasmin, a fibrinolytic enzyme. The effects could be correlated with dosage, and it was noted that blood of lysed thrombi contained numerous clumps of platelets that could be broken up by adding more plasmin. These experiments indicated the resistance of platelet clumps to lysis, a finding that was studied in more detail during my fellowship in Norway a few years later. This work was reported in abstract form only (79).

In the early '60s, I returned to my original idea, but instead of inserting a thread in the loop, we placed a small gelatin plaque on the inner wall. Since gelatin is composed largely of collagen, which has an affinity for platelets and causes them to aggregate, it was not surprising to find that small platelet thrombi had developed on the plaque after a few minutes' rotation of the loop. We briefly tried mixing other ingredients in the gelatin, such as thrombin, before making a plaque, but even though the idea looked good, we never developed any traction with this approach.

THROMBOATHEROSCLEROSIS

In the 1958–59 year, the department offered student fellowships under the auspices of our recently awarded research training grant from the NIH. Bob Hand was appointed a full-year post-sophomore fellow to participate in the autopsy program in Talmadge Hospital. During the year, he joined me in the thrombosis research program and studied the fate of autologous *in vitro* thrombi in the rabbit. This study was prompted by a discussion at one of the Thursday night conferences after Stoddard had insisted that arterial thrombi are organized by adventitial vessels growing through the arterial wall. Bob and I thought this question

would be worth investigating, so we worked out a plan for following the fate of *in vitro* thrombi introduced as emboli in the pulmonary arteries of rabbits. I distinctly recall Bob calling me into the laboratory one day at the time of autopsy of a rabbit embolized three weeks before. He had not found any thrombi but instead found a perfectly formed small eccentric yellow plaque in one of the arteries.

This single observation dramatically changed the course of this study. Reconstruction of events from earlier thromboemboli showed that the occlusive emboli could eccentrically retract, become organized by cells from the intima, or inner wall, and undergo complete transformation to a fibrofatty plaque identical in every respect to a human atherosclerotic plaque. In animals followed for one year, calcification, bony change, and spaces typical of cholesterol clefts—all features of advanced atherosclerosis—developed in the plaques. No dietary manipulations to produce hyperlipemia were employed.

Further study revealed that the likely source of the lipid was from the lipid-rich platelets that had been engulfed and digested by monocytic white blood cells within the thrombi. Correlative studies of incubated human *in vitro* thrombi confirmed that monocytes can phagocytose platelets and undergo transformation to lipid-filled foam cells. Similar observations were made on human *in vivo* thrombi. While the work on rabbit thrombi was being completed and prepared for publication, the observations on human thrombi were reported in *Science* in 1961 (6). In addition, both the animal and human studies were reported at national pathology meetings in Chicago in the spring of 1961. Bob's work was published in 1962 in *The American Journal of Pathology* (8), for which he was awarded the Bausch and Lomb Medal of the American Society of Clinical Pathologists. Forty years later, these two papers were recognized in an article in *Nature Medicine* as two of ninety-six landmark papers on atherosclerosis published in the twentieth century (86).

These studies were amply confirmed by other investigators, particularly in England by Drs. John Poole and John French and in Australia by Drs. Neville Ardlie and Colin Schwartz. The latter investigators conducted similar studies of thromboemboli in hypercholesterolemic rabbits which intensified the lipid and calcium components of the atherosclerotic plaques that formed (87). While studies on the fate of experimental whole blood clots, which lack a platelet-fibrin

head, had been previously reported by other investigators, the plaques induced from the clots lacked significant lipid, thus supporting in a different way the importance of platelets in experimental thromboatherosclerosis.

Shortly after the experimental thromboatherosclerosis project with Bob Hand was completed, Dr. Hans Peters, the department's neuropathologist, approached me with an attractive idea to look at plaque development in cerebral arteries. He proposed that autopsy cases be surveyed to identify cerebral arteries with only one plaque located at a site where an organized thrombus could account for an observed old infarct. Nine cases out of almost four hundred surveyed met these criteria. Most of the plaques identified were fibrous, but one of them was a typical fibrofatty atherosclerotic plaque. I had little to do with the actual investigation, but Hans included me as a coauthor when the article was finally published in 1971 (31).

In October of 1961, the studies of phagocytosis of platelets were once again reported, this time at the American Heart Association annual meeting in Miami. This meeting provided an opportunity to meet several investigators involved in the renaissance of research on thrombosis as did a symposium on the platelet in Detroit in 1960, where I had met some other researchers. I particularly recall meeting Dr. Kenneth Brinkhous, head of pathology at Chapel Hill, who was to show me many kindnesses in the future.

Dr. Fraser Mustard, who had recently established a laboratory for the study of platelets and thrombosis at the University of Toronto, was also in attendance in Miami, and he was intrigued by our work. He and his wife Betty visited us in Augusta the following February. We became good friends over the years, both socially and professionally, and visited each other's family from time to time. Fraser developed a large research program and became one of the leading workers in the field.

ADENOSINE DIPHOSPHATE AND PLATELET AGGREGATION

Mustard's visit to Augusta in early 1962 was indeed fortunate, for it was Fraser who told us about a report that was about to turn the thrombosis world on its

head. Fraser was already widely traveled and knew about the remarkable discovery reported in *Nature* in November of 1961 by Dr. Anne Gaarder and her associates at the University of Oslo and the Institute for Thrombosis Research in Oslo, Norway (88). They had found that the platelet aggregating agent derived from red blood cells described by Dr. Arvid Hellem (89) at the same institute and known briefly as Factor R of Hellem is adenosine diphosphate (ADP), a compound that in minute amounts induces platelet aggregation. This discovery opened the door to numerous investigations as researchers around the world jumped on board.

In our laboratory we began immediately to study the effects of ADP on platelets and thrombosis both *in vitro* and *in vivo*. We found that ADP greatly accelerated the onset of *in vitro* platelet aggregation, but not thrombus formation. I commented on these effects of ADP in an invited presentation in May 1962 at a National Academy of Sciences conference on the pathogenesis of thrombosis in Washington, D.C.

In order to investigate further the effects of ADP, we injected ADP in progressively increasing doses intravenously in the rabbit, but no thrombi were observed in the lungs or other organs in autopsied animals. Surprisingly, however, we found that ADP greatly enhanced the effects of thrombin on the formation of typical platelet-fibrin thrombi. This work extended into 1963 and was presented at a haematology congress in Lisbon that August (80).

The discovery of the effects of ADP on platelets helped further elucidate the steps in thrombotic coagulation and the formation of *in vitro* thrombi. Thrombotic coagulation via the generation of thrombin outside the body probably results from contact of blood with a foreign surface such as the plastic tubing used, which sets off a series of complicated but well worked out enzymatic steps that convert prothrombin to thrombin. While it is has long been established that fibrin is formed by the action of the enzyme thrombin on fibrinogen, in 1955 it was shown by Zucker and Borelli that thrombin in minute amounts also causes platelets to aggregate (90). It remained for Kaser-Glansmann and Luscher in 1962 to demonstrate that thrombin aggregates platelets by causing them to release ADP, thus tying the whole process together (91).

FATTY ACIDS AND THROMBOSIS

Fred Marschalk joined the laboratory as a student fellow in the summer of 1962 and began a project on the effects of fatty acids on *in vitro* thrombosis, which was continued in the summer of 1963. Earlier studies by Connor and Poole (92) had shown acceleration of *in vitro* thrombus formation by saturated fatty acids suspended in saline. They speculated that the acceleration was due to incompletely dissolved acids that formed negatively charged particles or micelles. Fred demonstrated that this was indeed the case, for when he dissolved the acids in an albumen solution that was micelle-free the effect was abolished. This study was reported in a progress report to the NIH but was not published.[3] Follow-through with publication is always a difficult task, and so often when student fellows moved on, especially after graduation, preparing their work for publication became a lost cause.

Plans for Sabbatical Leave

During 1961–62, I had been serving as acting chairman for Stoddard, who was on a sabbatical year of leave, and in accord with my stipulation to which he had agreed, I began plans for a sabbatical year on his return. I had previously looked into going to England to work with Dr. John Poole at Oxford, but at this juncture it seemed logical to go where the action was, the place where the effects of ADP on platelets had been worked out—Oslo, Norway. The Institute for Thrombosis Research there was already widely known for discoveries and advances in the field of coagulation under the leadership of Professor Paul A. Owren, who had discovered the blood coagulation Factor V under adverse conditions during the wartime German occupation (93). After receiving word from Owren of my acceptance to work in his laboratory for the 1963–64 year, I applied to the Commonwealth Fund of New York for financial support. I had already written Owren that whether or not I obtained this support, he could count on my arrival the following July. Little did I know that my thoughts on this matter almost came true.

The director of the Commonwealth Fund, Dr. Roderick Heffron, invited me for an interview in New York in late December 1962. Heffron was very cordial,

and he asked a lot of questions about my research. I recall telling him about the absence of lymphocytes in artificial thrombi. We both thought that lymphocytes could be isolated by this method, and I decided to pursue this idea at a later date. After lunch, Heffron told me that the Fund usually gave awards to more experienced investigators in their forties. I was thirty-six. I became quite livid and told Heffron I was fully capable of a successful fellowship and that furthermore, I had gotten an early start in my career, which made me equivalent to someone in his forties. We managed to part on amicable terms, and I returned to the hotel, where I told Jane I had just blown my chances of getting the fellowship. I was asking for one-half my salary of $18,000 plus travel expenses. The school would pay the other half. Needless to say, I was quite surprised to hear from Heffron in February of 1963 telling me I was to be awarded the full amount requested and wishing me a successful year. The assurance of full funding made it much easier to begin planning in earnest for the year ahead. All the family—Jane and I along with our sons Bleak, Jr. and John—would embark from New York in July.

NOTES

1. At a meeting a few years later, Harry Goldsmith, a Canadian hemorheologist, informed me in all good humor that the Canadian paper mills had for years used a similar gigantic wheel to separate out the sludge from the paper pulp.

2. In 2008, an article on thrombolysis that used the method for *in vitro* thrombosis was published by Dr. Nuala Booth and colleagues in Aberdeen. As it was the fiftieth anniversary of the publication of the method, I sent her an original reprint of the paper. She replied to thank me, saying she had never before received a reprint fifty years old!

3. When I looked for these accounts in the fall of 2001, I discovered that an overzealous clerk in the department had destroyed all of my research grant records through 1975. In the process, all of the original departmental annual reports from 1933–2000 were also destroyed. Fortunately, I had the foresight to preserve copies of all annual reports before my retirement. These reports helped greatly in the review of unpublished studies during this period.

PLATE XX

In Vitro Thrombosis

1) *Title page* of reprint from article describing a method for producing a thrombus *in vitro* (2). The method is based on the premise that a thrombus forms in a moving stream of blood, as opposed to a blood clot, which forms in stagnant blood.

2) *Thrombogenerator.* The apparatus first used was a simple motor-driven slanted turntable on which a closed circle of plastic tubing half filled with blood was mounted and then rotated at 17 rpm.

3) *Close-up of circle.* The blood flows relative to rotation of the circular tube and the thrombus forms at the leading edge of the blood column, as depicted in this drawing.

4*) Stages in thrombus formation.* This sketch is based on observations in platelet-rich plasma showing the initial aggregation of platelets into small clumps throughout the plasma column. The clumps then collect at the leading edge of the column just prior to thrombus formation, which is accompanied by the conversion of fibrinogen to fibrin.

5) *Snowstorm effect.* This view of platelet-rich plasma in rotating circles shows the initial stages of platelet aggregation forming clumps throughout the column to give the appearance of a snowstorm quite like that in a small ornamental globe.

6*) Mrs. Murphy* was the head nurse in the outpatient clinic of the Talmadge Hospital, where a room was used as a satellite lab. Mrs. Murphy very kindly arranged with the patients in liaison with their doctors for blood samples to be drawn for the *in vitro* thrombosis studies, mostly from prepartum patients.

1

In Vitro Thrombotic Coagulation of the Blood

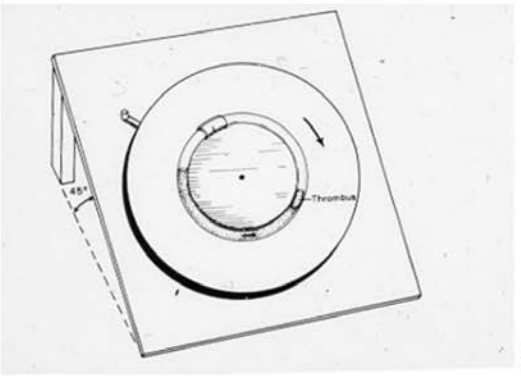
A Method for Producing a Thrombus

A. B. Chandler, M.D.

Reprinted from

LABORATORY INVESTIGATION

VOLUME 7, NUMBER 2, MARCH-APRIL, 1958



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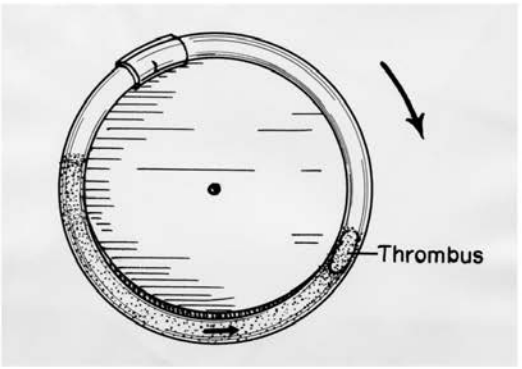

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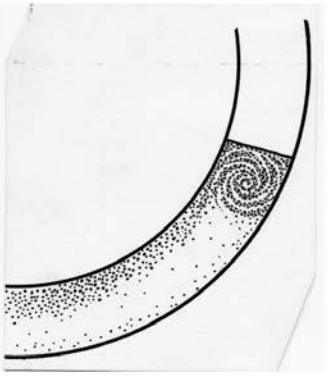

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PLATE XXI

In Vitro & *In Vivo* Thrombi & Blood Clot

1) *In vitro thrombus, gross photograph*. The platelet-fibrin head at the right end of the thrombus is contiguous with the fibrin–red blood cell tail.

2) *Bisected in vitro thrombus, gross photograph*. The thrombus head is white due to the collection of platelets and white blood cells at this site. This part is most typical of an arterial thrombus, which early pathologists often described as a white thrombus.

3) *In vitro thrombus, microphotograph*. Aggregated platelets form clumps connected by fibrin strands colored black. Many white blood cells, appearing as black dots, are trapped between the platelet aggregates.

4) *Blood clot, microphotograph*. In contrast to a thrombus, this blood clot consists of a sea of red blood cells entrapped in a fine meshwork of fibrin. The well-known hematologist Dr. T. H. Spaet likened a blood clot to a bucket of paint and a thrombus to a work of art.

5) *In vivo thrombus, microphotograph*. This thrombus obtained at autopsy and the *in vitro* thrombus depicted in Fig. 3 closely resemble each other. The *in vivo* thrombus is not quite as well preserved, causing the platelet aggregates to be less compact.

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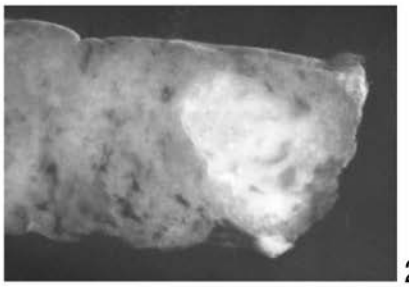

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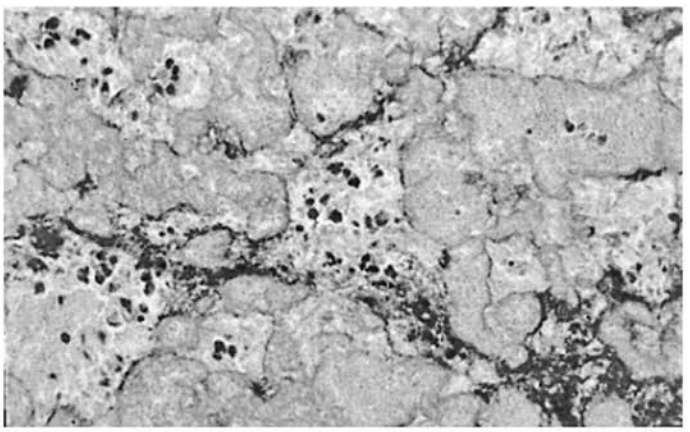

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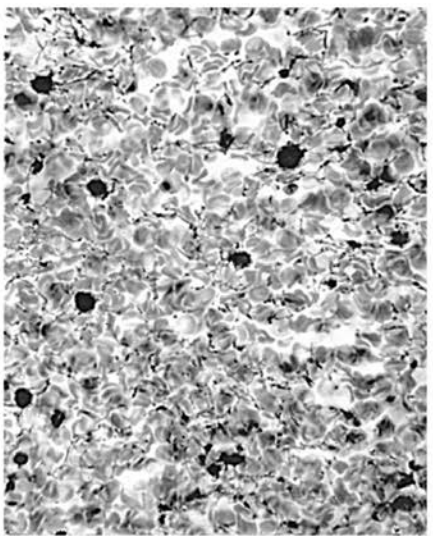

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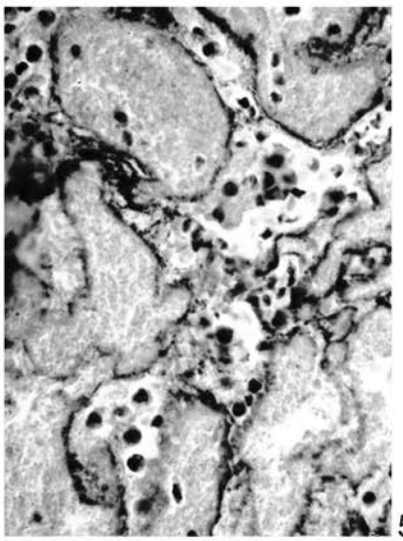

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PLATE XXII

Experimental Thromboatherosclerosis

1*) Bobert Hand.* As a full-year student fellow in pathology, Bob investigated the fate of autologous *in vitro* thrombi in the rabbit (8). Here, he has exposed the jugular vein of a rabbit for injection of thrombi, which lodged in the pulmonary arteries as emboli. The platelet-rich part or white head of the *in vitro* thrombi was used for the emboli.

2) *Recent embolus, gross photograph.* The thromboembolus in a pulmonary artery on the right has begun to retract from one side of the artery to create an opening for blood to pass through.

3) *Atherosclerotic plaque, gross photograph.* Another thrombus at three weeks post-embolisation has retracted and condensed to become incorporated into the arterial wall and transformed by organization into an eccentric atherosclerotic plaque (arrow). The plaque had a distinctly yellow hue.

4) *Atherosclerotic plaque, microphotograph.* A microscopic view of the same plaque as Fig. 3 shows an inner layer of fibrous tissue next to the lumen and beneath that layer a collection of foam cells with clear spaces where there had been lipid that was dissolved by processing the tissue. The foam cells are macrophages derived from monocytic white blood cells in the thrombi.

5–7) *Phagocytised platelets, microphotographs.* The source of the lipid in the foam cells was shown to be due to phagocytosis and digestion of lipid-rich platelets by macrophages derived from monocytic white blood cells in the thrombi (6,8):

5) Swollen platelets seen inside a large macrophage in the center of the photo of an experimental thromboembolus in a rabbit,

6) A human *in vitro* thrombus from a tissue culture experiment showing a macrophage filled with phagocytized platelets.

7) Phagocytised platelets in macophages of a human thrombus obtained at autopsy, showing macrophages filled with platelets. A foam cell is seen on the left.

Landmark papers: The two papers describing this work (6,8) were cited by an article in *Nature Medicine* as two of ninety-six landmark papers on atherosclerosis published in the twentieth century (86).

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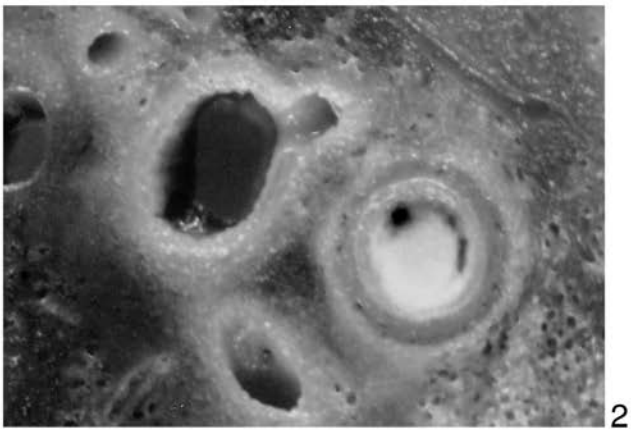

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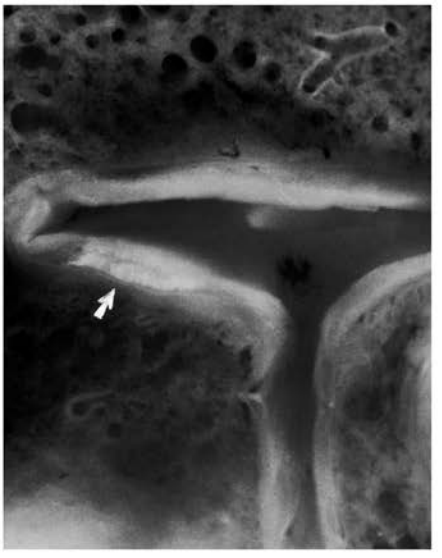

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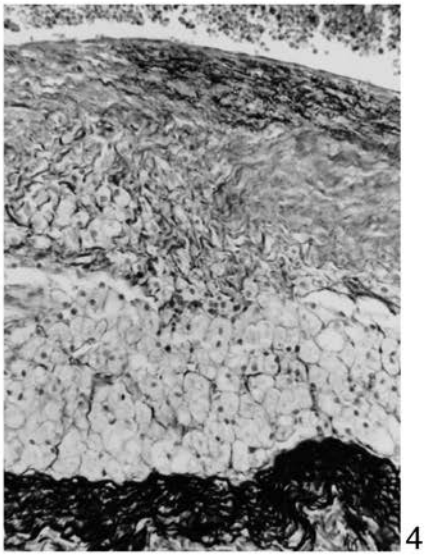

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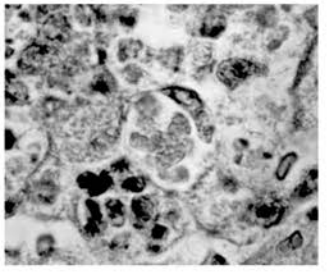

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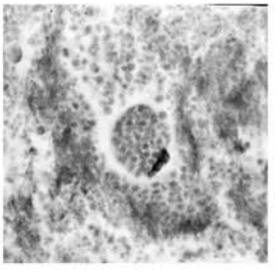

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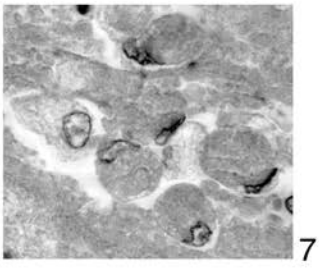

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CHAPTER FIVE

The Year in Norway ~ 1963–1964

We arrived in Oslo in early July after an eleven-day voyage from New York on the Norwegian liner *Oslofjord,* stopping on the way in Bergen, Stavanger, and Copenhagen. As the ship glided silently along the fjord leading to Bergen, all the cottages along the shore had their Norwegian flags waving to the passengers, many of whom were returning home. The Viking spirit is still alive in this proud nation, and I recall standing at the rail next to a Norwegian colonel whose eyes welled up as the national anthem was played on the ship's loudspeaker. We next stopped briefly in Stavanger and climbed an observation tower to look around. Before we knew it, a newspaper reporter was interviewing young Bleak, who gave a very good account of his impressions thus far and our reason for traveling to Norway. The article was published in the local paper, and the reporter kindly forwarded a copy to us. The ship pulled into port and docked in Oslo on a cold, rainy day in July. After the long voyage, we knew we were far from home. Our new home for a year awaited us.

Dr. Helge Stormorken, the director of research at the laboratory, greeted us at the dock and took us to Blommenholm, a village near suburban Sandvika, where we would live. As we headed out of Oslo, he waved to Dr. Carl Jacobsen on a street corner, with whom I would soon find myself engaged in research. Helge picked up some bread and cheese and a few other items on the way to the house. He then introduced us to the way to eat bread and cheese in Norway: first, spread a thick layer of butter on the bread. Later in the year when I studied Norwegian coronary arteries, I remembered that first day. Professor Owren had arranged for us to rent Dr. Peter Hjort's house, a few doors away from his own. Hjort was an internist and coagulationist who would be on a sabbatical year in California.

The Institute for Thrombosis Research occupied one floor of one wing of Rikshospitalet, the University Hospital, which was located in downtown Oslo.

The Institute's facilities consisted mainly of a large research laboratory of about fifteen hundred square feet with open bays at the end of a hall along which there were offices for faculty. Also along this hall was another large open laboratory of about six hundred square feet, which was the hematology and coagulation laboratory for the hospital. This laboratory was staffed by nurses, or sisters, who had been trained to do this specialized work. The famous ice skating queen Sonja Henie occasionally visited the laboratory for blood work, but I always managed to miss seeing her. The Institute was part of Medicine Department A, headed by Professor Owren. He was the most prominent physician in Norway and was the king's personal physician.

Owren conducted ward rounds almost every day and would stop by the laboratory with his entourage, one of whom was the granddaughter of Gerhard Hansen (of Hansen's disease). I was never invited to join them, but I am sure he would have allowed me to do so, had I asked. The Norwegians are very reserved, but always courteous, and I suppose I did not ask to go because I would have understood little of what was said.

Everyone worked a full five and one-half day week, but from the outset I decided not to come in on Saturday, so that my family could travel on weekends. This arrangement was perfectly acceptable to Stormorken. I was given about six feet of bench space, a sink, and a water bath. Stormorken attempted to teach me how to measure clotting times of plasma by tilting test tubes, but he soon realized this was not my cup of tea. Not much else happened for the first few weeks other than becoming familiar with the place and people. Practically everyone was fluent in English.

I usually took the train in from Blommenholm to Oslo, a thirty-minute trip. From the train station in Oslo, it was about a ten-minute walk uphill to the hospital. Occasionally, my neighbor Dr. Gunnar Eskeland, who was at a nearby hospital, and I would share either his car or mine. Early on, Dr. Arvid Hellem told me to put several sacks of sand in the trunk to keep the car from sliding on the icy roads. These sacks probably saved our lives when we swerved around a dangerous mountain curve on a skiing trip. I was told that during the war a Norwegian bus driver drove off this curve with a busload of German soldiers.

Haematology Congress in Lisbon

In August we traveled by sea, car, and rail to Lisbon, where I presented our work from Augusta on the potentiation of thrombin-induced thrombosis in the rabbit by adenosine diphosphate at the IXth Congress of the European Society of Haematology (80). Dr. Robert Wissler was at the meeting, stopping off on his way back to Chicago from Switzerland. He had written a letter of recommendation for me to the Commonwealth Fund. Our paths would cross many times over the years, to culminate in our participation in a nationwide study of atherosclerosis that he organized and directed.

On the return trip, the train got behind schedule because of a long stopover in the border town of Hendaye. When we reached Bayonne, we decided to wire the Mackies, our friends in Dordrecht, Holland, that we were delayed. So being the expert in French, Jane went into the station while I stayed on board with the luggage. "Le chemin de fer est retarde!" she wrote. Before Jane could get back to the train, it was pulling out of the station, so I jumped off without the luggage, and we were momentarily stranded. We caught a later train and, fortunately for us, a French IBM executive was in our compartment. Besides entertaining us with stories about Napoleon and Josephine, he helped us retrieve our baggage in Paris and took us to the St. Anne Hotel, where we had stayed a few nights before. They welcomed us back.

Projects at the Institute

After Lisbon my research assistant, Marion Hutson, arrived, and we promptly set up shop studying *in vitro* thrombosis under a variety of conditions. Customs inspectors were puzzled by the strange apparatus she brought with her, and Stormorken had to go to the authorities to explain! She was supported by my NIH grant for this travel and work in Oslo over the next six months, returning to Augusta the following April.

During the year I became involved in several projects ranging from *in vitro* thrombosis with Drs. Stormorken and Jacobsen, to experimental animal studies

with Dr. Nordöy, and, lastly, to studies of human coronary artery thrombosis with Drs. Jörgensen and Borchrevink at Ülleval Hospital. One of the projects at the institute evolved from discussions with Stormorken about the role of the von Willebrand factor in platelet aggregation.

Platelet aggregation and the von Willebrand factor. Following the discovery by Gaarder, et al., of the effects of adenosine diphosphate (ADP) on platelet aggregation (88), a crude mechanism for cohesion of platelets was proposed that required a chemical molecular bridge in which calcium and fibrinogen were somehow involved. Another idea was the possibility that the von Willebrand factor also participated in this bridge. The factor is a plasma protein produced mainly by endothelium. In order to proceed, washed platelets were suspended in heat-inactivated plasma and tested for ADP-induced platelet aggregation against normal and abnormal plasmas. Von Willebrand–deficient plasma gave the same degree of aggregation as normal plasma, which offered no support for a pro-aggregative effect of this factor. In contrast, aggregation was much reduced in the presence of fibrinogen-deficient plasma, thus adding weight to the role of fibrinogen in aggregation (13). Subsequently, it was shown by Timmons and Hawiger (94) that the von Willebrand glycoprotein can compensate for a deficiency of fibrinogen in ADP-induced platelet aggregation, which could explain the low level of aggregation in afibrinogenemic plasma recorded in our study.

The von Willebrand study was conducted with Stormorken, Solum, and Gaarder. Not long after it was published, Dr. Anne Gaarder died in a tragic automobile accident returning to Oslo from a vacation. Years later I learned she was Owren's niece. Drs. Nils Solum and Stormorken followed up this report with detailed studies on the influence of fibrinogen on platelet aggregation (95).

One morning around 10 A.M., I was told it was time for coffee, and everyone went to the hematology laboratory, where the sisters served coffee and usually some kind of coffee cake. Every few weeks we would enjoy this treat.

Thrombolysis in vitro. Shortly after Marion arrived, a study of thrombolysis *in vitro* comparing urokinase and streptokinase in health and disease was undertaken

with Dr. Carl Jacobsen. He was a research fellow working on his thesis for the M.D. degree. In the European tradition, this degree was awarded only after years of study, both during and after postgraduate residency-type training, and the successful completion of a thesis. The *in vitro* thrombosis technique was ideally suited to the study of thrombolysis. When the effects of streptokinase and urokinase were tested on *in vitro* thrombi it was found that the fibrinous tail was most susceptible and the platelet-fibrin head was most resistant to lysis. It was noted that one explanation for the difference could be that platelets possess antifibrinolytic activity as shown previously by Johnson and Schneider (96). We postulated further that the tight structure of platelet aggregates also may have inhibited lysis. It is now known that the antifibrinolytic activity of platelets is due to their production of a potent inhibitor of the activation of plasminogen, which is the precursor of the fibrinolytic enzyme, plasmin.

The von Willebrand (13) and thrombolysis (14,15) studies could not have been completed without the expert assistance of Marion Hutson. They were published in 1965 in a Festschrift honoring Owren on his sixtieth birthday.

One day I was taken to meet Professor Kreyberg, the head of pathology, who had at his door a three-light system—red, "stop"; green, "enter"; and yellow, which meant "watch out!" He was a gruff but kindly man whom we met up with a while later on a train trip. In January I was invited to give a presentation at a meeting of the Norwegian Pathology Society. All I recall is that several of the old hands there were quite astonished to find that I was a full professor, which carries an entirely different connotation in their part of the world. Nevertheless, the paper was well received, and I met several pathologists from around Norway.

ADP-induced experimental thrombosis. It was not until our return from Lisbon that I met Dr. Arne Nordöy, who had been on vacation. Arne was a fiery redhead from Tromsö, north of the Arctic Circle. I learned that Nordöy means "north island." He had been studying injury-induced venous thrombosis in the rat, again working on his thesis. When I told him about my failed attempts to induce thrombosis in the rabbit with ADP alone, we decided to give it a try in the rat. After much trial and error, we finally figured out that platelet thrombi were produced but were very transient.

Upon injection of ADP in the vena cava there was almost immediate, usually transient, respiratory arrest. Larger doses of ADP led to persistent arrest. Immediate fixation of the lungs within a few seconds or a minute or two after injecting ADP revealed in microscopic sections numerous platelet thrombi filling small arteries, arterioles, and alveolar capillaries. Only rarely was fibrin noted in the thrombi. In other experiments, it was determined that the ADP-induced thrombi produced respiratory arrest by simple mechanical obstruction of the pulmonary arteries. It was perhaps fortunate we chose the rat, which has a normal platelet count of around 900,000 per cubic millimeter of blood, twice that of the rabbit and human count. Once the dosages and other details were worked out, it allowed us to embark on a series of studies utilizing this experimental system.

The report on the method was published in issue number one of the *Scandinavian Journal of Haematology* in 1964 (10). For the rest of the year, we studied ADP-induced thrombosis under various conditions (11, 12, 16). In one of these studies, we investigated the effects of dietary fats (12). High dietary saturated fat but not unsaturated fat increased thrombosis. This work gave marginal support to another ongoing project in the laboratory conducted by Dr. A.E. Ödegaard. He was finding that dietary linseed oil, which contains a highly unsaturated fatty acid, inhibited platelet adhesiveness. The work on dietary lipids was continued and expanded during a subsequent fellowship by Nordöy in Augusta. Throughout his career, he conducted experimental and clinical studies on the effects of dietary fats on thrombosis and platelets to become one of the recognized authorities in the field.

During the winter there would be an occasional *fernluft,* or warm air blowing in from across the sea. On one of those days, Arne and I walked down to the dock in front of City Hall and bought a bag of shrimp, which had been boiled on the boat as they were caught. We sat on the dock in our shirt sleeves and peeled and ate the delicious shrimp.

Atherosclerosis Meeting in London

In late November we went down to London, where I had been invited to participate and give a presentation at the British Atherosclerosis Discussion Group. Jane

and I departed by rail late on the afternoon that Kennedy had been assassinated; Marion Hutson stayed with the children. As we left the house, Marion ran out to tell us the news she had just heard. The next morning as we rode through Sweden all of the flags were at half-mast. We had booked a compartment on the sleeper car and were quite surprised to find that instead of two bunks as in American trains, there were three. We mistakenly thought we had the compartment to ourselves, so one can imagine how surprised we were when Professor Kreberg walked in and graciously took the top bunk. We talked, and I think he vaguely remembered meeting me. He asked how many children we had, and I told him two boys. Kreberg said, "You are a rich man."

After a full day of rail travel, overnight on a train ship across the channel, and a further two hours by rail, we arrived in London. We stayed at the Strand Palace, a kind of poor man's Savoy, which was across the street. When we arrived at the hotel, we both had on Norwegian boots and felt a little out of place, but nonetheless undaunted. On the Monday after Thanksgiving Day we went to a memorial service for President Kennedy at St. Peter's Church in Notting Hill, which was apparently favored by Americans. The church was jammed and the service solemn.

One evening, we attended a performance of Handel's *Messiah* with 400 voices at the Royal Albert Hall and learned to stand during the Hallelujah Chorus, which is a tradition from the time of George II. He stood when the chorus began and the audience rose with him. It is not known whether the king was inspired or simply wanted to stretch his legs.

While in London, I had the opportunity to meet Dr. Gustaf Born in his laboratory at the Royal College of Surgeons. As a pharmacologist/physiologist is wont to do, he was using the cat to study the effects of ADP. Gus was very cordial, and we subsequently met at meetings over the next thirty years. He was a transplant from Germany and the son of the physicist and Nobel Laureate Max Born, who emigrated to England before the war. While at the College, I saw John Hunter's anatomical museum, much of which had been destroyed during World War II.

The meeting was held at the Ciba Foundation House in Portland Place. Many of those in attendance I had known by reputation or through correspondence. Drs. John Poole and John French were there from the Dunn School of Pathology

at Oxford. Poole was one of the early investigators who used the *in vitro* thrombosis technique. The English like their words and after my presentation he came up and in jest said I should use the term *in plastico* not *in vitro*, which means "in glass." Later that day, he took me to a nearby pub for a pint of warm beer.

Others in attendance were Drs. Colin Schwartz and J. R. A. Mitchell from Oxford along with Dr. George Pickering, the Regius Professor of Medicine there. Drs. John Gordon and Alex Gresham were there from Cambridge. Fraser Mustard, who was also at the London meeting, visited us in Oslo afterwards for two or three days. A sumptuous dinner was held that evening at the Ciba House. Before dinner, I met Dr. Hugh Sinclair, a nutrition expert from Oxford. He asked if I knew Dr. Sydenstricker, who had stayed with him during the war. Sydenstricker had been brought over by the British as a consultant on nutrition. I told Sinclair I did know him, and on my return to Norway, I wrote and told Sydenstricker about meeting Sinclair. Dr. Sydenstricker replied that while in England, Hugh Sinclair was his "mother and father."

Dr. Theodore Crawford, professor of pathology at St. Georges, was at the head table, and in due course, as everyone stood, a toast was raised to the queen. Both Pickering and Crawford were knighted or soon would be. Pea-soup fog was still the order of the day in London and after dinner, Dr. Kevin Carstairs, who worked in Crawford's department walked me part of the way back to the hotel before peeling off for the tube. The return home to Norway was uneventful. The clear, fresh air was a welcome change.

Christmas in Norway

Christmas was a festive time in Norway. At the hospital the entire staff gathered in the auditorium to sing Christmas carols. There was even a special beer sold in the markets called Juleøl, which was delivered to our door by our friendly grocer, Mr. Kirkibe. In Blommenholm the neighborhood children came by to exchange greetings, one of whom, dressed as Nisse, carried a lantern to show the way in the early afternoon darkness. Our younger son John brought in a small tree that he had cut down in the adjacent woods to decorate with Norwegian

ornaments. Luckily he was not apprehended for his contribution to the Christmas celebrations!

Project at Űlleval Hospital

Coronary artery thrombosis and anticoagulants. In the spring of 1963 at a Federation meeting in Atlantic City, I met Dr. Christian Borchgrevink, an internist who was working with Dr. Judith Pool in California. He had recently completed his thesis at the Institute for Thrombosis Research. He returned to Norway that summer to work at Ülleval Hospital in Oslo. Soon after our arrival, Christian invited us to their cottage on the Oslofjord, where I found myself, without choice, swimming in the iciest water ever. Later, I was introduced to Dr. Leif Jörgensen, who was in the pathology department at Ülleval Hospital. Borchgrevink was interested in the effects of coumarin anticoagulants on coronary artery thrombosis, and before long a clinical-pathological study was launched.

All patients in the study who died were autopsied, and the coronary arteries and heart were examined in detail by Jörgensen. I was the blinded observer, not knowing which patients had been anticoagulated. Anticoagulant therapy appeared to inhibit thrombosis on dense fibrous plaques but had no effect on the frequency of thrombosis associated with plaque rupture, and if anything, intensified the hemorrhage in these lesions (30). The coronary arteries were the most severely sclerotic I had ever seen before or since, which brought back to mind my first day in Oslo and the encounter with the butter and cheese combination. A year or so later, Leif went over to Canada to join Fraser Mustard and his group for a year. In a state-run system such as in Norway, faculty sabbaticals, at least then, were relatively easy to come by.

An incidental finding in this study was the observation of an occasional platelet thrombus in small myocardial arteries and arterioles. Dr. Jörgen Haerem, who was in the same department as Jörgensen, was just beginning to work on his thesis, and he further investigated the nature and significance of these small thrombi. By 1968 he had shown that the microthrombi in the myocardium could be associated with sudden cardiac death. A preliminary report included

Jörgensen, Borchgrevink, and me as coauthors, even though we had little to do with the actual study (21). Ten years later, I was one of the judges at Haerem's *disputas* in Oslo when he successfully defended his thesis. At the banquet that evening, which was an elaborate dinner and festive celebration, one of the speakers, Dr. Hans Prydz, credited me with helping at least three of my Norwegian colleagues obtain the M.D. degree.

Winding Down

The last days were full as we prepared to finish the year and return home. As the year was winding down, a curious meeting was held with Dr. Sverre Blix and a few others connected with Nygaard and Company. They were about to market linseed oil as a cure-all for heart disease. Earlier, Ödegaard at the Institute had demonstrated that a daily dose of linseed oil greatly diminished platelet adhesiveness. Nordöy and I had shown a slight but not significant inhibition of platelet thrombosis by linseed oil in our experimental animal studies. I could only relate to this group our findings, but it was obvious they had some reservations—and rightly so, for some months after the linseed oil was brought on the market as Aurol (gold oil), it was discovered that the original results on platelet adhesiveness could not be confirmed. Owren then had to issue a formal retraction in a medical journal. Now after some forty years, omega 3 and 6 unsaturated fatty acids are gaining credence again as healthy fats. Nordöy has continued to be in the forefront of these studies on dietary fats and thrombosis.

As the year drew to a close, Prof. Owren gave a magnificent farewell banquet at the Grand Hotel in Oslo. The main course was rype, an arctic game bird. We had met earlier in the evening at his house for cocktails. I admired the thick publication in which he described his discovery of factor V, and without hesitation he reached up to the shelf and gave it to me.

But the most memorable occasion was in the laboratory itself. One morning the word went around that in a few minutes there would be coffee in the sisters' hematology laboratory. It was then that someone said, "They are going to talk about you." After everyone assembled and was standing in a circle around the room, Stormorken made remarks in Norwegian and then in English and

presented me a small pewter Viking ship. I managed to respond by saying that someday that ship in spirit would bring me back to this land and then went around the room thanking each person individually. The simple dignity and sincerity of the occasion made an indelible impression.

PLATE XXIII

Sabbatical Year in Norway, 1963–64

1) "*The Augusta Chronicle*" ran a story on April 10, 1963, about the forthcoming sabbatical in Oslo, Norway. The purpose of the year was to work at the Institute for Thrombosis Research of the University of Oslo, which at the time was one of only a few such centers in the world.

2) *Stopover.* During a brief stopover of the passenger liner Oslofjord in Stavanger, Norway, Bleak, Jr., was interviewed atop an observation tower in town. The interview was reported in the *Rogalands Avis,* Stavanger. He gave a good account of his plans to go to a Norwegian school, learn to speak Norwegian, and make new friends, all of which were accomplished.

3) *Oslo harbor.* Oslo is nestled at the head of the Oslofjord, surrounded by low-lying hills. The large building on the water's edge is the city hall. Its great hall is filled with modernistic murals and sculptures. Rikshospitalet, the main teaching hospital of the University of Oslo, is nearby on the side of a hill in downtown Oslo.

4) *Rickshospitalet campus.* One of the many clinic buildings that made up the hospital campus. The small sculpture of mother and child in the foreground was a gift of the great opera soprano Kirsten Flagstad. Other statues are in the background.

DR. A. B. CHANDLER AND MARION HUTSON WATCH EXPERIMENT
Augusta pathologist invented the thrombo-generator at Medical College

Will go to Norway

Dr. Chandler plans year's study abroad

Dr. Bleakley Chandler, professor of pathology at the Medical College of Georgia, will sail from New York July 1 to spend a year in Norway.

He will work at the University of Oslo in the Institute for Thrombosis Research. This is considered one of the finest medical centers in the world in this field.

Dr. L. D. Stoddard, professor and chairman of pathology at the Medical College, said it had become increasingly important today for men of science to travel and exchange ideas.

1

Rogalands Avis
Stavanger, Norway

Mandag 15. juli 1963

gram fra Stavanger

terd mot natt

nettet. Da han fikk oppdraget burde han tenkt på dette, og lagt programmet opp, akm som han lørdag sier han kunne tenke seg å gjøre det. I samme intervju sier han at «dette har ikke vært noen heksekunst».

Det var kanskje heksekunst det burde ha vært!

kleng.

Dagens tvist

Gå på ski og snakke norsk i Oslo

Gutten hadde vist funnet noe av stor interesse i sportsforretningen. Han snudde seg mot faren og forklarte noe viktig på hurtig engelsk med amerikansk drei. Vi forsto det ikke, men så at klikket igjen rettet seg mot skistativet inne i forretningen.

— Vil du ha ski med hjem til Amerika?

— Jeg skal ikke hjem til Amerika jeg. Jeg skal til Oslo og bo der et år, forteller Bleakly Chandler, vi skal ikke tilbake til Georgia før neste år. Far skal være doktor ved Rikshospitalet i Oslo et år først.

— Og du skal gå på skole i Oslo?

— Ja, jeg skal begynne på skolen og lære norsk. Så skal jeg få mange norske venner og lære å gå på ski. Det gleder jeg meg aller mest til. Far og mor har gått på ski før, og de sier at det er veldig moro. Bare vent til snoen kommer, så skal vi gå på ski alle sammen. Utenfor Oslo kan vi gå på ski, har far sagt, og i fars ferie og i skoleferien kan vi reise høyt til fjells og gå på ski. Det skal bli frykteleg moro.

— Du tror ikke det blir vanskelig å snakke norsk?

— Jeg må jo lære det for å kunne snakke med alle de nye kameratene jeg skal få. Guttene her forstår vel ikke engelsk når de bare er 9 år. Så skal jeg jo gå på skolen og lære det ordentlig der. Jeg må skynde meg å begynne på skolen og få mange venner, i stedet for alle hjemme i Georgia som jeg ikke skal se igjen på et helt år.

— eth.

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PLATE XXIV

Institute for Thrombosis Research

1) *Professor Paul Owren* was head of Medicine Department A and of the Institute for Thrombosis Research. His discovery of blood clotting factor V was an important key contributing to our knowledge of hemostasis and thrombosis.

2) *Professor Helge Stormorken* was the research director of the Institute. ABC had the opportunity to collaborate with him, and they have maintained a close friendship ever since the year in Norway.

3) *The scholar.* Dr. Olav Egeberg returns from the library with a stack of books when working on his thesis. Egeberg is credited with discovering the first abnormality in the coagulation system associated with a propensity to thrombosis.

4) *The Thrombosis Institute* was at the end of the second floor of this building in which Medicine Department A was also located.

5) *Dr. Anne Gaarder* unlocked the door to platelet adhesiveness when she and her colleagues discovered that Factor R of Hellem is adenosine diphosphate, a plentiful substance in red blood cells and other cells as well. While studying platelet stickiness at the Institute, Dr. Arvid Hellem found the effects of this substance in red blood cells before it was known to be ADP.

6) *Hematology and coagulation laboratory.* This laboratory for the Institute and Medicine Department A was staffed by nurses or sisters, who had been trained in this specialized field. The head of the laboratory, Sister Solveig, stands third from left, surrounded by her coworkers. Inga Fossen, the secretary of the Institute, is on the far left.

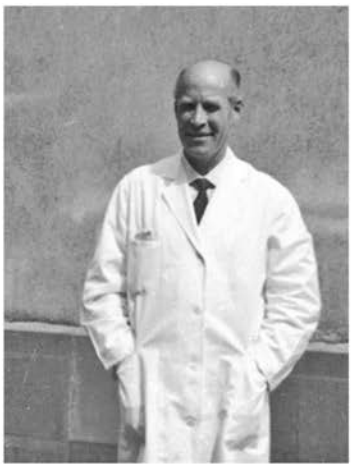

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PLATE XXV

Thrombolysis

1) *Dr. Carl Jacobsen* was working at the Institute on his thesis studying fibrinolysis. He and ABC investigated the effects of urokinase and streptokinase on the lysis of *in vitro* thrombi (14,15).

2) *New design for in vitro thrombosis.* Jacobsen designed an apparatus that would allow many samples to be tested simultaneously by constructing a spindle on which multiple loops could be placed and then rotated by an attached motor. The spindle was immersed in a constant-temperature water bath to further standardize the experiments.

3) *Streptokinase.* The fibrin tail of an *in vitro* thrombus in this microphotograph is being lysed in a ragged manner from the surface inward after introduction of streptokinase into the medium.

4) *Urokinase.* The platelet-rich head of an *in vitro* thrombus in this microphotograph shows lysis of fibrin by urokinase between platelet clumps, but black-stained fibrin remains stuck to the surface of some clumps, indicating resistance to lysis in these areas. In the upper right, fibrinolysis has released entraped white blood cells, which have pooled together.

In Vitro Thrombosis in Disease

5) *Afibrinogenemia (absence of fibrinogen in blood).* Microphotograph of an *in vitro* thrombus produced in this condition resulted in the formation of a large mass of platelets equivalent to the white head of a thrombus, but lacking distinct clumps of platelets separated by fibrin, which is typical of thrombi formed in blood that contains fibrinogen (18).

6) *Afibrinogenemia.* In this high power microphotograph from the same case as Fig. 5, platelets are clearly delineated and loosely arranged. The lack of fibrinogen in the blood may have prevented the platelets from being closely packed together, which occurs when fibrinogen is present. The small scattered black-stained objects are white blood cells.

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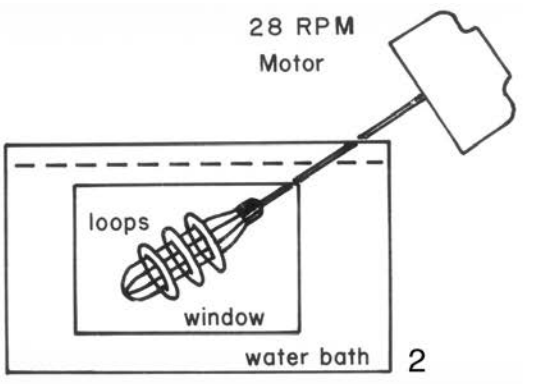

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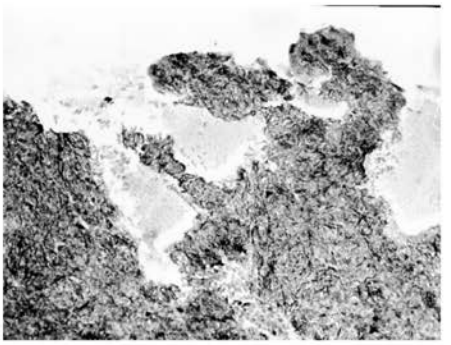

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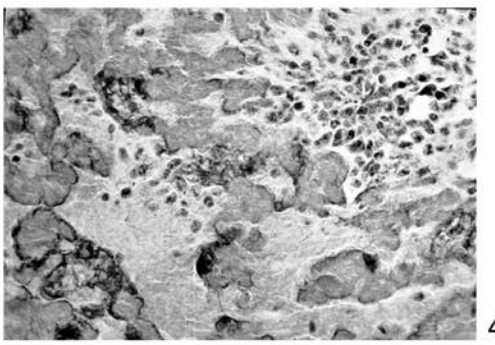

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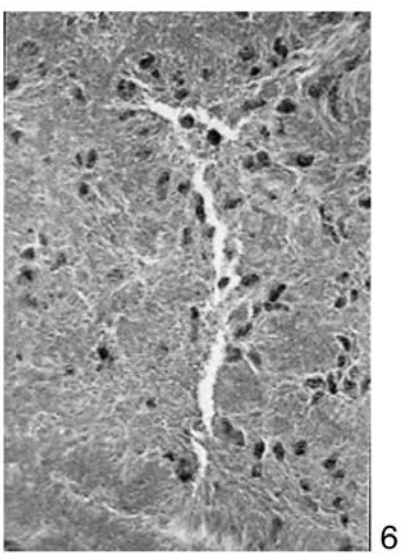

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PLATE XXVI

Experimental Thrombosis

1) *Dr. Arne Nordöy* was the only fellow at the Institute studying thrombosis in the experimental animal. In follow-up of prior work by ABC in Augusta, he and Nordöy devised a method for inducing thrombosis in the rat with adenosine diphosphate (ADP). The method was published in 1964 (10).

2) *Inga Fossen,* the secretary for the Institute, was an invaluable resource to all the researchers. She prepared the typescripts, including numerous tables and figures, with great skill and precision.

3) *Thrombin-induced thrombus.* Prior to the year in Norway, ABC studied the effects of intravenous thrombin and ADP in the rabbit (80). This microphotograph shows a platelet-fibrin thrombus in a pulmonary artery induced by thrombin. Platelet clumps are stained gray, and fibrin is black.

4) *Thrombin plus ADP- induced thrombus.* ADP alone failed to produce detectable thrombi in the rabbit; however, when it was combined with thrombin in small amounts, thrombi were produced that were composed mostly of platelets. The microphotograph shows a largely platelet thrombus with a few strands of black-stained fibrin in a pulmonary artery that extends into a small branch to the right.

5) *ADP-induced thrombi.* In the rat it was possible to induce platelet thrombosis with ADP alone, which Arne and ABC studied under a variety of experimental conditions (10–12, 16). In this microphotograph, a branch of a pulmonary artery extending to the left contains several small pale-stained platelet thrombi, some obstructing smaller branches. Red blood cells are stained black.

6) *ADP-induced thrombus.* In this microphotograph, a small pulmonary artery in a rat is filled by a platelet thrombus in which the individual platelets are faintly delineated.

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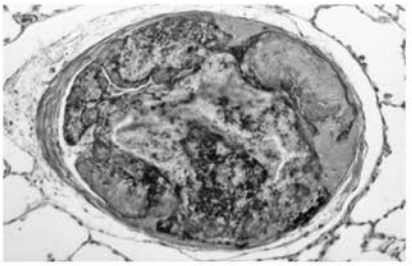

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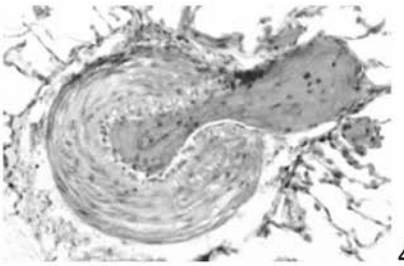

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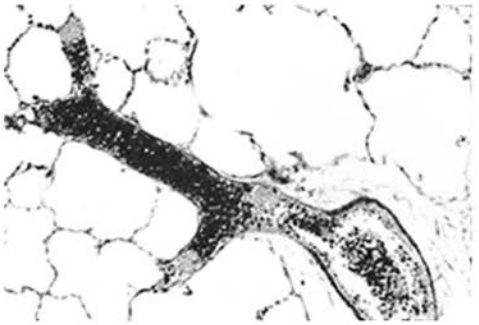

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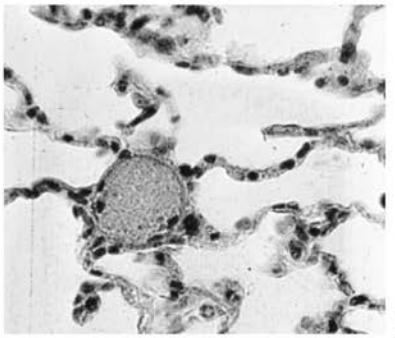

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PLATE XXVII

Norway Scenes

1) *32 Bjerkasen.* We were fortunate to rent Dr. Peter Hjort's house in Blommenholm near Sandvika, where we made many friends, most of whom were professional people working in academia or for the government. Dr. Hjort was on sabbatical in California.

2) *Jane and ABC.* This photo was taken during the year outside our home in Blommenholm.

3*) Dr. Fraser Mustard's visit.* In the fall of 1963, Fraser Mustard visited for a few days when he came by on what turned out to be a successful recruiting trip for his thrombosis laboratory in Toronto. Here, he is on the doorstep of 32 Bjerkasen with our sons, John and Bleak, Jr.

4) *Ringkollen.* Jane, Marion Hutson, Bleak, Jr., and John at a nearby skiing lodge on a beautiful sunny day.

5) *Easter holiday.* Helge Stormorken and Jane skiing in the hoifjell (high mountains) near Stormorken's cabin in the Rondane region.

6) *Farewell party.* Our neighbors the Eskelands gave a wonderful farewell party at their home next door before our departure in June 1964. From left, first row: Betty Laland, Eva Nordland, Jane Chandler, Mrs. Nordahl, and the Eskelands' daughter, young Benedicte; second row: Dr. Per Laland, Benedicte Eskeland, Dr. Gunnar Eskeland, Dr. Nordahl, and Dr. Odd Nordland.

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CHAPTER SIX

Research and Related Activities ~ 1964–1994

We left Oslo in late June of 1964 and traveled by car through Norway, Scotland, and England to embark from Southampton on the Statendam. On the way, we stopped over in London, where I visited Drs. Neville Woolf and Kevin Carstairs at the old St. George's Hospital across from Hyde Park. They were studying thromboatherosclerosis in the pig aorta and were using *in vitro* thrombi to test the antibodies they had raised for tracing platelet and fibrin antigens. While there, they showed me the couch in a hallway where in 1793 John Hunter died in a fit of anger after leaving a heated boardroom meeting. The famous anatomist and surgeon had suffered from angina pectoris for years and was said to have predicted that his coronary arteries would be ossified, and they were.

Return to Augusta

When we arrived in August, the laboratory was in order and running smoothly, thanks to Marion. She had been assisting Dr. Walter Stern and a student fellow, George Rinker, in their studies with Dr. Robert Ellison of *in vitro* thrombosis in open-heart surgery (97). Walter had administered the research grant in Augusta during my absence. In time, the year in Norway resulted in ten papers working with four different research groups.

Shortly after our return, Dr. Armour Sherrer called from Atlanta to say that Sir George Pickering, whom I had met in London the year before, would be in Augusta for the Georgia Heart Association meeting in September 1964 and would like to visit our laboratory. Pickering had been invited to the meeting by Dr. Joe Wilber, who had worked with him in Oxford. Dr. Wilber brought Sir George by the laboratory for a brief visit, and he showed considerable interest in our work. While Pickering was mainly known for his work on hypertension, he had been

involved in the first observation of transient monocular blindness due to platelet emboli in the retinal circulation.

During the first year back from Norway, I gave a talk before the Dugas Club on my research and another one before the Richmond County Medical Society. After my talk at the Dugas Club, Dr. Harry Harper, Jr., a prominent cardiologist in Augusta, was curious enough to come by the laboratory to have his platelets tested. My astute former professor was ahead of his time as these studies were in progress some years before the advent of platelet inhibitors such as aspirin for the prevention of coronary thrombosis.

IN VITRO THROMBOSIS IN HEALTH AND DISEASE

Part of the research effort over the next year was devoted to clinical studies of *in vitro* platelet aggregation and thrombus formation. Adenosine diphosphate in low doses was found to induce platelet aggregation in platelet-rich plasma followed by deaggregation so that the duration of platelet aggregation could be measured. The ADP aggregation phase was followed by a second wave of irreversible thrombin-induced aggregation and thrombus formation. In a few conditions such as hypothyroidism and third trimester prepartum patients, there was prolonged duration of platelet aggregation. In studies using whole blood, thrombus formation time was shortened in acute thrombophlebitis and in women taking oral contraceptives, while it was normal in coronary heart disease and peripheral vascular disease.

A by-product of the work in Norway with Carl Jacobsen was an examination of the structure of *in vitro* thrombi produced from some of the patients in the thrombolysis study. Carl shipped the fixed specimens to Augusta for histological preparation. Highly abnormal structures were noted in Glanzmann's thrombasthenia (a platelet disorder), hemophilia A (Factor VIII deficiency), and afibrinogenemia (lack of fibrinogen in blood). The microscopic features of thrombi made from normal blood were also described in more detail than before. This work was published in 1967 (18).

ELECTRON MICROSCOPY OF ADP-INDUCED THROMBI

While in Norway, I had applied to the NIH for a grant to study the ultrastructure of platelets in thrombogenesis in anticipation of the opening of the long-sought electron microscopy laboratory in the department. A departmental grant was also sought for funds toward the purchase of an electron microscope. Both grants were awarded to begin in September 1964. My grant was for two years. At the same time, two electron microscopists, Drs. Eddie and Dorothy Nathaniel, joined the department.

Over the next two years, in collaboration with Eddie Nathaniel and later also with Arne Nordöy, we studied the ultrastructure of ADP-induced thrombi in the rat. In rats on a normal diet, the thrombi consisted of closely approximated platelets with junctions similar to those between epithelial cells, which is the usual pattern for aggregated platelets (23). However, in animals fed saturated fat diets, we found that in many areas of the thrombi, platelets in small clusters of three to four platelets were adhered to each other by *tight* junctions identical to those between endothelial cells (34). Animals on unsaturated fat diets had far fewer similar clusters. While ADP could have induced the tight junctions, we postulated that these changes could have existed in the blood prior to thrombus formation. Similar tight junctions had been observed by other investigators in experimental thrombosis in the mouse, unassociated with fatty diets (98).

Thrombosis Research Group, 1965–1966

The 1965–66 year was a productive time for the laboratory. Two research associates and one full-year student fellow were part of the group that year. Hans Knieriem arrived first.

ANTICOAGULANTS AND PLATELET AGGREGATION

Dr. Hans Knieriem joined the department in February 1965 as a research associate following several months at the University of Chicago with Dr. Wissler. Knieriem was a pupil of Meesen in Dusseldorf and was rounding off his training.

He investigated the effect of the anticoagulant warfarin sodium on ADP-induced platelet aggregation. The duration of platelet aggregation in platelet-rich plasma was measured in response to ADP in a group of healthy adult volunteers given warfarin in therapeutic amounts for four to sixteen days. During the first two to three days of medication, the duration of platelet aggregation was prolonged; however, at no time was it shortened (9). These results agreed with one other investigation, but in general, studies of platelet aggregation in response to anticoagulants such as warfarin were and are inconclusive.

EXPERIMENTAL ANIMAL STUDIES

In the summer of 1965, two additional fellows joined the laboratory. Hillery (Sandy) Newland joined the program as a full-year post sophomore student fellow working in the thrombosis laboratory and autopsy service. Sandy did a prodigious amount of work during the year, ending up with five publications as author or coauthor to his credit. In September 1965 Arne Nordöy arrived with his family from Norway. Arne had received an award from the NIH as an international postdoctoral research fellow, and his entire year was devoted to research.

With Arne on board, we embarked on several projects. We first reinvestigated the effects of dietary fats on experimental thrombosis. Luckily for us, Dr. James Hamlin, who had expertise in the chemical analysis of lipids, had recently joined the faculty in the Department of Medicine. Jim agreed to participate in the proposed project and after detailed planning of the experimental design, we were off.

Dietary fats and ADP-induced thrombosis. The incidence of ADP-induced thrombosis was compared with plasma and platelet lipids in rats fed various dietary fats. A high saturated fat diet was compared with two other diets of saturated fat, each supplemented by an unsaturated fat: linseed oil, which is rich in linolenic acid, and cottonseed oil, which is rich in linoleic acid. Linolenic and linoleic acids of the omega 3 and omega 6 series respectively are the two recognized essential fatty acids supplied only by the diet. Much lower doses of ADP, from 1 to 5 mg, were used than before, because the high dose of 17 mg used in our earlier experiments with dietary fats in Norway may have masked subtle differences between

the groups. While both cottonseed and linseed oil in the 1 mg group reduced the incidence of thrombosis compared with the pure saturated fat diet, only linseed oil showed a significant reduction in the higher 5 mg group (24). It soon became apparent that another important factor that was unknown at the time probably was at play in these experiments.

The discoveries in the 1970s of the role in thrombosis of a class of fatty acid derivatives known broadly as prostaglandins helped clarify much of the earlier work by ourselves and others, particularly in regard to platelet aggregation (99). A pro-aggregative substance called thromboxane A_2 can be synthesized in stimulated platelets from arachidonic acid which is a metabolite of *linoleic* acid. Many agonists including ADP and thromboxane A_2 itself, once produced, can initiate synthesis of this potent but unstable substance.

It was therefore relevant to our study to revisit the analyses of platelet lipids in the three diet groups. The most striking finding was a marked reduction in the content of arachidonic acid in the platelet membrane phospholipids of the linseed oil group. Linseed oil primarily contains Omega 3 *linolenic* acid, which does not break down to arachidonic acid. Therefore, if thromboxane A_2 was involved in the production of the ADP-induced platelet thrombi, as would seem most likely, the least amount of this compound would be synthesized by the platelets in the linseed oil group, the group which had the least number of thrombi. Obviously, were this study to be conducted today, the experimental design would be quite different.

Two additional experimental studies from this year are described below. Sandy and Arne investigated the interrelations of uric acid and thrombosis, especially in regard to gout. Before completing his fellowship, Arne undertook one more study, which was on Factor XII and its potential role in the pathogenesis of thrombosis.

Uric acid and thrombosis. Two separate but connected experimental animal studies were performed (100,101). In a series of elegant experiments, Sandy and Arne found that high blood levels of uric acid increased the incidence of ADP-induced thrombosis, whereas thrombosis was decreased when uric acid levels were lowered. They proposed that uric acid levels influenced the rate of breakdown of ADP in the blood, whereby high levels impeded and low levels accelerated the rate of breakdown. Despite the relevance of these studies to gout and the pathogenesis

of thrombosis, other investigators have paid them little attention. It was indeed a well-deserved honor when Sandy received the Sheard Sandford award and Bausch and Lomb Medal from the American Society of Clinical Pathologists for this work.

Factor XII and thrombosis. Ratnoff and Crum reported in 1964 that the intravenous administration of ellagic acid, a derivative of tannic acid, could activate Factor XII *in vivo,* a blood clotting factor that leads to the generation of thrombin (102). Even though Factor XII in plasma was activated, it did not induce thrombosis. In view of the scarcity of fibrin in ADP platelet thrombi, Arne and I posed this question: Will prior activation of Factor XII by ellagic acid facilitate the conversion of ADP-induced platelet thrombi in the rat into more stable platelet-fibrin thrombi? This procedure resulted in the formation of many platelet-fibrin thrombi. The generation of thrombin and consequent precipitation of fibrin from entrapped activated plasma within the thrombi appeared to be the critical factor (20). This work was submitted for publication as Arne completed his fellowship year and returned to Norway.

After the Storm

After such a whirlwind year, it was time for a breather and for a while the laboratory was remarkably quiet as papers were prepared for publication. Sandy had returned to medical school but would rejoin the laboratory a few years later, after his internship. One short project was completed with Dr. Luther Mills, who was a resident at the time.

Isolation of lymphocytes. Remembering my conversation with Dr. Heffron of the Commonwealth Fund in the fall of 1962 about the lack of lymphocytes in thrombi, Luther and I devised some simple experiments to isolate lymphocytes from whole blood (22). We prepared platelet-rich plasma from whole blood and produced *in vitro* thrombi, which selectively incorporated most granulocytic and monocytic white blood cells to leave a lymphocyte-rich serum from which concentrated cell suspensions were prepared. This method was pursued by a few

other investigators but it never caught on, as more automated procedures became available. The overriding question, however, remains: Why are granulocytes and monocytes incorporated into thrombi but not lymphocytes?

CONFERENCE ON THROMBOSIS

During this year I also began to become involved on the national scene. The National Academy of Sciences had formed a small task force comprising Drs. Kenneth Brinkhous, Edward Genton, Sol Sherry, and James Stengle to look at the problem of thrombosis at a time of rapid development in the field. It was decided to have an international conference on the subject, and I was invited to be a member of the planning committee. The conference was scheduled for the fall of 1967. In the interim, several planning meetings were held. I recall meeting with Drs. Irving Wright and Sol Sherry at the O'Hare Airport in Chicago, where Wright spoke enthusiastically about coronary bypass surgery just being introduced and about its long-range implications for thrombosis research.

My section was to be on the nature of a thrombus. Dr. James Paterson of London, Ontario, was invited to speak on the pathology of venous thrombosis, and Dr. John French of Oxford on the ultrastructure of experimental thrombi. My paper was on the anatomy of a thrombus, which included a historical review (25). The conference was held at the National Academy of Sciences in Washington and was attended by about one hundred investigators. The proceedings were published in 1969 in a book entitled, simply, *Thrombosis*. After the conference French flew to Augusta to visit for a few days before returning to England.

In addition to French, several other visitors came by about that time, including Drs. Helge Stormorken, Jack Hoak from Iowa, J. R. A.(Tony) Mitchell from Oxford, and Leif Jörgensen. Leif and I completed the manuscript for the paper on coronary thrombosis (30). Dr. Walter Rice, who was then dean, and I proposed to Tony that we establish a student exchange program between Oxford and Augusta, but numerous bureaucratic obstacles got in the way and prevented us from implementing the program. Other investigators who visited a few years later were Drs. Neville Woolf from St. George's Hospital, and John Poole from Oxford.

Smoking and in vitro thrombosis. In the fall of 1968, I attended an International Congress of Hematology in New York, where I met Dr. Hyman Engleberg, an internist in Beverly Hills. He had shown acceleration of *in vitro* thrombosis after cigarette smoking (103). While many clinical studies have shown a relation between smoking and thrombosis, very few experimental studies have demonstrated this effect. In a later study, he offered additional evidence that thrombin generation is the key to *in vitro* thrombus formation (104). Hy blended his research with an active practice in Hollywood, where he was personal physician to many stars, including Danny Kaye, Rita Hayworth, and Marilyn Monroe. Being a former New Yorker, Hy knew a good delicatessen nearby, where we went for lunch.

Ultrastructure of Platelet Aggregates

When Stoddard was on leave in Japan in the fall of 1966, he arranged for a Japanese pathologist/electron microscopist to come to Augusta as a research fellow. Dr. Kenjiro Shirasawa had been investigating the ultrastructure of platelets, so it was a good fit for him to join our laboratory. It was a happy and profitable union that led to new insight into the structure of platelet aggregates. Shirasawa and his family had intended to stay only a couple of years, but it eventually became four years, long enough to bring forth another Augustan, young Shinichi. Shirasawa was a careful, meticulous investigator who worked long hours and usually could be found on Saturday afternoons at the scope.

Structural bond between aggregated platelets. While it had become apparent that fibrinogen is involved in platelet aggregation, little was known about the structural aspects. Shirasawa examined this question in a two-step approach. In the first study, it was observed that the cell coat of platelets formed structural bridges of an amorphous substance between aggregated platelets (26). In some areas the structural bridges merged with fibrin at the edge of aggregates, suggesting that they are composed, at least in part, of fibrinogen. While structural bridges had previously been noted by several investigators, the observation that they might contain fibrinogen provided additional insight.

In a second study, antibodies to fibrinogen/fibrin were raised by Betty Barton in Walter Rice's immunology laboratory and tagged with ferritin, which is a small electron-dense molecule. This tagged antibody marked the structural bridges between aggregated platelets, which provided even stronger evidence of the role of fibrinogen in aggregation (35). As research by others advanced over the next several years, these observations were confirmed. It is now known that specific receptors on the platelet surface become available when platelets are activated by ADP and other stimulants so that fibrinogen binds to the receptors to effect a structural bond between aggregated platelets.

Writing these reports for publication took about as long to complete as the studies. Language barriers intensified as we struggled to write an accurate account. I maintained that Shirasawa thought vertically, Japanese style, instead of left to right as in English. Despite our joint efforts, this conundrum persisted but did not prevent ultimate accuracy in our writings and publications. Shirasawa returned to Japan in 1971 and continued his studies of platelet ultrastructure. He was following a long family tradition in medicine. I once asked him how long doctors had been in his family and without hesitation he said, "five hundred years." Now, his son Shin is a doctor.

Reviews of Thrombosis and Related Studies

During the late '60s and early '70s, I wrote several reviews of thrombosis and atherosclerosis in connection with invited presentations, some of which included reports of our research.

Needle puncture wounds. One of these presentations at a meeting of the International Committee on Haemostasis and Thrombosis in Bath, England, in October 1969 included a report on healing of needle puncture wounds in arteries (27). These wounds are ideal for study, for they can be precisely timed. Crawford had reported in 1956 that fibroblasts provide the collagen for healing of puncture wounds(105). More recent observations indicated that smooth muscle cells are responsible for synthesizing collagen in arteries, which prompted renewed interest in this subject.

When Sandy Newland returned as a resident in 1969, we collected at autopsy carotid artery needle puncture wounds from angiogram procedures that ranged in age from a few hours to eight months. The rate of healing previously described by Crawford (105) was confirmed. In addition, we found that smooth muscle cells from the inner arterial wall (intima) rather than fibroblasts, as Crawford had stated, were responsible for collagen formation and healing of the wound. There was no evidence that smooth muscle cells of the arterial media (middle layer) participated. While many workers in atherosclerosis research had promoted the idea that medial smooth muscle cells migrate into the intima to produce fibrous atherosclerotic plaques, our results do not support this concept.

While in Bath, we drove to the nearby house in Berkeley where Edward Jenner lived and where he vaccinated the young boy James Phipps in 1796. Cows grazing in the surrounding fields were a present-day reminder of Jenner's great discovery. After the meeting, we traveled to Scotland, and I had the opportunity to visit Dr. A. S. Todd in Dundee. He had found that a principal source of tissue plasminogen activator is the endothelium, especially venous. He was using *in vitro* thrombi in his studies of the activator but did not localize its inhibitor in platelets, which is now known to exist.

Coronary artery microthrombi. Another autopsy study, which concerned observations of coronary arterial microthrombi in young individuals, was presented in Philadelphia in 1971 at a symposium on atherosclerosis and coronary heart disease published in 1972 (33). This work was reported in more detail in 1974 at a meeting in Tromsö, Norway (37). Serial sections of the left coronary artery in nine individuals ranging in age from twelve to thirty years revealed a few microthrombi, most of which were on existing fibrous plaques. Covered or endothelialized thrombi were found only in the three cases over twenty-five years of age. I wrote Professor J. B. Duguid in Aberdeen, who had previously described small, or fine, thrombi in the aorta and in coronary arteries, and told him about my findings. Duguid had revived Rokitansky's thrombogenic hypothesis of atherosclerosis in the 1940s. His reply was succinct: "I would not expect to find microthrombi very readily in the coronary arteries. Their existence must be very short before they are incorporated into the vessel walls and changed beyond recognition. I

think that, if they were so frequent as to be easily found, our coronary arteries would soon be in a sorry mess."

Thrombosis in Sickle Cell Anemia

Around 1970, shortly after President Nixon established a sickle cell anemia initiative as a line item in the budget, Drs. Titus Huisman and Larry Lutcher approached me about joining a proposed grant application to the NIH to develop a sickle cell center at the Medical College. I accepted the invitation, and an application was prepared for a subgrant on thrombosis in sickle cell anemia. The subgrant and center grant were awarded. We investigated sickle cell anemia patients on two fronts: *in vitro* thrombosis and by means of an extracorporeal flow unit Marion Hutson and I devised.

In vitro thrombosis. In sickle cell anemia *in vitro* thrombi were invariably two to three times larger than control thrombi, with a large white platelet head and long fibrinous tail. We were quite puzzled by this finding until we realized it was merely a reflection of the low hematocrit (ratio of red blood cells to plasma) accompanied by considerably more plasma and its fibrinogen in a given quantity of whole blood being tested, plus the usually elevated platelet count in this disease. But do these giant thrombi reflect what might happen in patients?

Extracorporeal flow unit. It was current dogma at the time that much of the cellular damage and pain in sickle cell anemia patients is the result of sickled red blood cells blocking the microcirculation. We investigated this question by devising an extracorporeal flow unit made of plastic tubing with the smallest lumen achievable by compression of the tubing, which was about 100 micra, the size of a small arteriole. The flow unit was attached to tubing with a venepuncture needle at the other end, which when placed intravenously would allow blood to flow through the unit until flow spontaneously ceased, thus giving an extracorporeal bleeding time. The contents of the flow unit were processed for electron microscopy, which revealed a thrombotic hemostatic plug composed entirely of aggregated interlocking platelets (42).[1]

In studies of sickle cell anemia patients, few sickled red blood cells were observed in these plugs even in the presence of low oxygen tension, nor was there any fibrin seen. In fact, in patients with a very low hematocrit, the unit would not occlude at all and the procedure had to be stopped after a few minutes. While these experiments did not suggest one way or the other that sickled red cells may cause obstruction of the microcirculation, it did demonstrate that effective hemostasis by a thrombotic platelet plug could develop without fibrin.

Fate of Experimental Coronary Arterial Thrombi

Terrell Pope joined the department as a full-year student fellow in 1972 upon completion of his third year. He knew his way around the hospital, and before long Terry and I had teamed up with Drs. S. K. Asokan and D. Pollard in cardiology. Asokan had recently worked with Dr.Timothy Regan's group in New Jersey, where investigators had studied experimentally induced coronary thrombosis in the dog. Thrombosis was induced by inserting a wire electrode into an artery and reversing the normal negative charge of the inner wall, utilizing the principle worked out by Sawyer and Pate (106), which is mentioned here to note that Dr. James Pate is a graduate of the Medical College of Georgia and well-known cardiothoracic surgeon. We employed this method in the dog to study the fate of occlusive coronary artery thrombi formed *in situ*, or in place, in contrast to Bob Hand's study, which utilized *embolic* occlusive thrombi. Duguid had concluded earlier from his autopsy studies that an occlusive thrombus formed *in situ* can retract and undergo transformation to an atherosclerotic plaque. Dr. Allen Weisse, in Regan's laboratory had reported a study similar in some respects to the one we planned (107).

The experiments were performed in the cardiac research laboratory of the hospital, which was fully equipped for electrocardiographic and radiographic monitoring of the procedure. Induction of an occlusive thrombus was confirmed by angiograms and the animals were followed up to twelve weeks. Most thrombi retracted eccentrically to reopen the lumen, which was followed by their conversion to sclerotic fibrous plaques with very little fat as early as three weeks after the artery was occluded. The plaques were derived from largely fibrinous thrombi, with few platelets, which might explain the paucity of lipid in the plaques. The animals were normolipemic.

This work was reported at American Heart Association meetings in 1973 (81) and 1974 (82) and at a symposium on heart infarcts in Vienna in 1977 (46); however, a full-scale manuscript was not prepared before Terry graduated from medical school. The symposium in Vienna was chaired by Professor Schettler, who was known as "the pope of heart disease" in Germany. He asked me to prepare a color plate for the proceedings, which I gladly did. Here I included some of the pictures from Terry's work. While in Vienna, we were entertained royally, including attendance at the opera and a formal dinner afterwards at the Hotel Sacher. At the conclusion of the dinner and after the famous Sacher-Torte, I responded for the North American contingent.

During his fellowship year, Terry also prepared a comprehensive table that surveyed the frequency of incorporation of thrombi into human atherosclerotic plaques, which was presented at a meeting in Holland in 1974 and published in 1975 (43). This table proved to be useful shortly thereafter, when an initiative got underway with the American Heart Association to organize a workshop on the relation of thrombosis to atherogenesis. It complemented a table I had prepared earlier on experimental thromboatherogenesis, which was presented at a Gordon Conference in 1973.

Excursion from Vienna. The trip to Vienna allowed us to take an excursion to Italy, which got off to a rollicking start when we were bumped from Austrian Air to an Alitalia flight in Zurich and placed in first class. As soon as we were seated, the stewardess came by and poured champagne. She then proceeded with the bottle to the cockpit. We were already nervous, and, needless to say, we were happy to arrive safely in Rome. After a few days, we took the express train to Florence. Standing on the platform near us was a stylishly dressed woman who was also waiting to board. When Jane and I found our compartment, we were greeted by this same woman with her husband and young son. They spoke Italian. She kept fiddling with her passport and pulling press clippings from her purse. We remained silent. Finally, they decided to go to the diner for tea. At this point, Jane informed me I had been sitting next to Audrey Hepburn and was astounded I did not know it was she!

PLATE XXVIII

Thrombosis Research Group

1) *Thrombosis research group, 1965–66.* From left, seated: Dr. A. B. Chandler; Hillery Newland, full-year student fellow; and Marion Hutson, research assistant, standing: Dr. Arne Nordöy, NIH research fellow; Dr. Hans Knerium, visiting fellow.

2) Dr. *Kenjiro Shirasawa* was a research fellow in pathology from 1966 to 1970, studying the ultrastructure of platelets by electron microscopy.

ELLAGIC ACID AND THROMBOSIS

3) *Ellagic acid and thrombosis.* Nordöy studied the effects of ellagic acid on thrombosis in the rat (20). When injected intravenously, ellagic acid activates factor XII, starting a molecular sequence toward the generation of thrombin. Ellagic acid alone did not induce thrombosis; however, when injected under conditions of disturbed flow, typical platelet-fibrin thrombi developed, as shown in this microphotograph of a thrombus in the right ventricle of the heart.

4) *Adenosine diphosphate and ellagic acid.* When ADP was injected intravenously in the presence of ellagic acid, fibrin developed in ADP-induced platelet thrombi, as shown in this microphotograph of a platelet-fibrin thrombus in a pulmonary artery. The strands of black-stained fibrin were thought to be caused by thrombin generated within the thrombus.

STRUCTURAL BOND BETWEEN AGGREGATED PLATELETS

5) *Structural bond.* In this electron micrograph by Shirasawa of an ADP-induced platelet aggregate, amorphous threads can be seen connecting adjacent platelets to provide a structural bond between the aggregated platelets (25).

6) *Nature of structural bond.* In this electron micrograph of an ADP-induced platelet aggregate, antibodies to fibrin/fibrinogen attached to iron particles appear as fine black grains between adjacent platelets, which supports the concept that fibrinogen is a constituent of the structural bond between aggregated platelets (30). The larger black dots within the platelets are glycogen granules.

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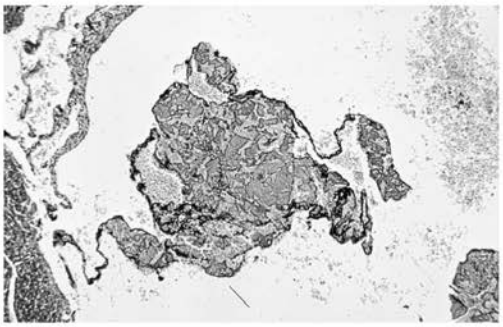

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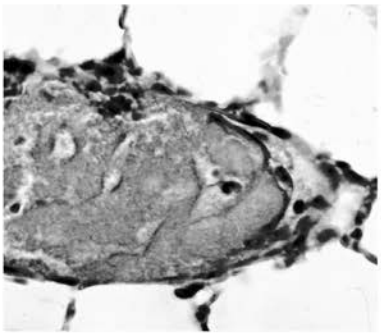

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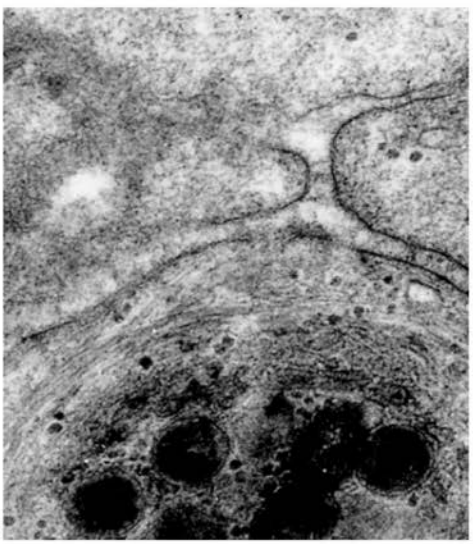

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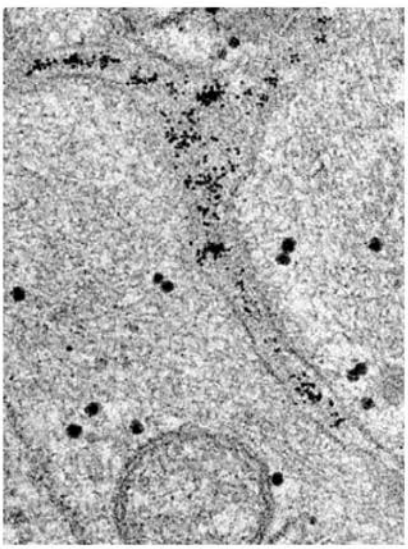

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PLATE XXIX

Extracorporeal Flow Unit and Sickle Cell Anemia

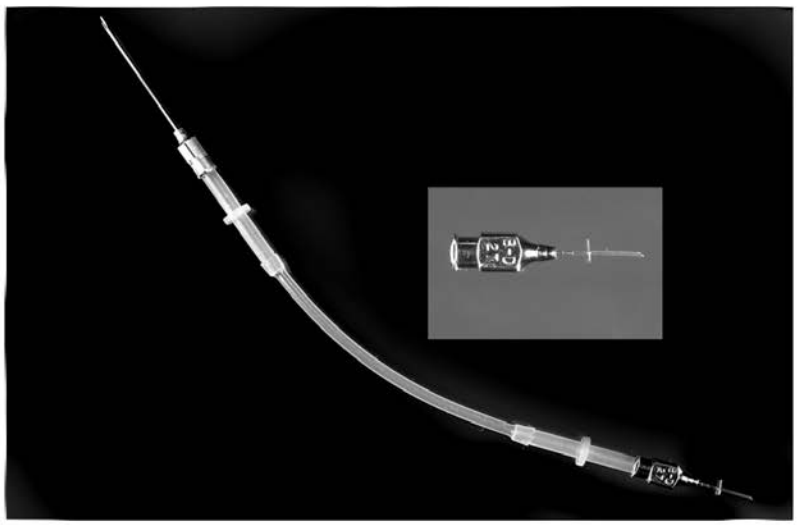
1) *Flow unit.* The extracorporeal flow unit depicted here was designed to study thrombosis in sickle cell anemia. Blood drawn intravenously was allowed to flow through the unit until flow ceased. The inset shows detail of the terminal end of the unit, where a constricted tube with an opening about the size of an arteriole is attached. Sickled red blood cells did not obstruct, but instead a platelet plug formed (42).

2) *Cast of occluded unit.* Depicted in this microphotograph is a cast of the unit at its narrowest point, which is composed almost entirely of aggregated platelets forming a thrombotic hemostatic plug, as shown in figure 3.

3) *Electron micrograph of hemostatic plug.* The thrombotic hemostatic plug shown here is composed of closely packed platelets, which stopped the flow of blood through the unit. No fibrin is seen. The empty spaces were caused by the processing of the sample.

4) *In vitro thrombosis in sickle cell anemia.* The upper *in vitro* thrombus in this gross photograph was made from normal blood. The *in vitro* thrombus below was made from the blood of a patient with sickle cell anemia. It is almost three times longer due to its increased content of fibrin. In this anemia, there are fewer red blood cells relative to an increased amount of plasma, which provides more fibrinogen for fibrin formation in a given volume of blood being tested.

5) *Dr. Paul Milner* was a member of the pathology faculty and of the school's Sickle Cell Center. He supported the objectives of this project and provided both insight and assistance in facilitating the studies that involved patients in the center's clinic.



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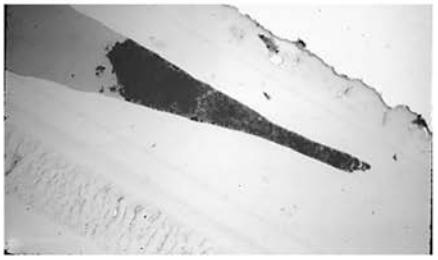

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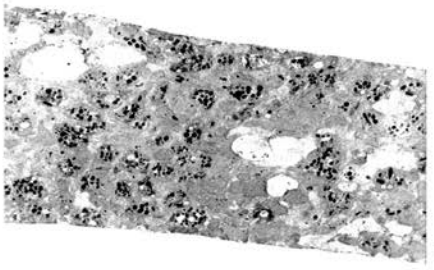

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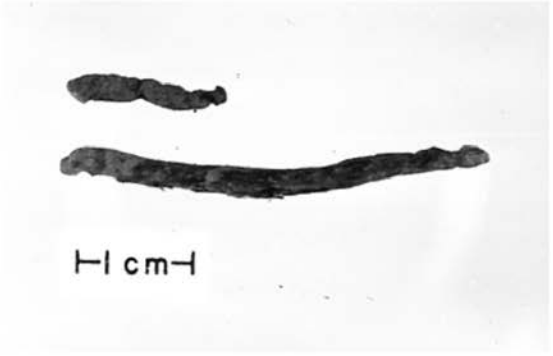

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PLATE XXX

Experimental Coronary Thromboatherosclerosis

1) *Terrell Pope.* As a full-year pathology student fellow in 1972–73, Terry investigated experimental thromboatherosclerosis of canine coronary arteries in collaboration with cardiologists in the Department of Medicine (81,82).

2) *Coronary arteriogram.* After induction of a thrombus, an arteriogram was performed with radiopaque dye to confirm occlusion of the coronary artery, which is shown in this contrast X-ray film as a blunted image at the site of occlusion.

3) *Retracted thrombus, microphotograph.* One week after induction of an occlusive thrombus, this thrombus has retracted from the arterial wall to open the lumen and is undergoing organization by fibrous tissue. A one-cell layer of endothelium can be seen on the left growing over the surface of the thrombus to incorporate it into the arterial wall.

4) *Fibrous plaque, microphotograph.* By six weeks this thrombus has lost its identity and has become converted by organization into a largely fibrous atherosclerotic plaque. The paucity of lipid in these plaques reflects the initial largely fibrinous composition of the thrombi and the presence of only a few lipid-rich platelets in them.

Hemodynamic Localization of Atherosclerosis

(*Text description in next section on external collaborative research*)

5) *Derene Akins.* As a full-year pathology student fellow in 1974–75, Derene investigated the hemodynamic localization of atherosclerosis in cerebral arteries in collaboration with Dr. Fred Cornhill in Ohio and Marion Hutson (50).

6) *Basilar cerebral artery.* This drawing from Spaltholtz shows the convergence of the two vertebral arteries from below to form the basilar artery. The vertebral arteries are the only medium-sized arteries in the body that converge and direct their blood flow into a single artery.

7) *Hemodynamic localization of plaques.* This photograph shows two small atherosclerotic plaques localized at the vertebral-basilar junction where the vertebral arteries and their blood flow converge. The plaques are seen through the translucent arterial walls. The one on the left is smaller and only faintly visible. In the natural state, the plaques were distinctly yellow. No other plaques are present in this segment.

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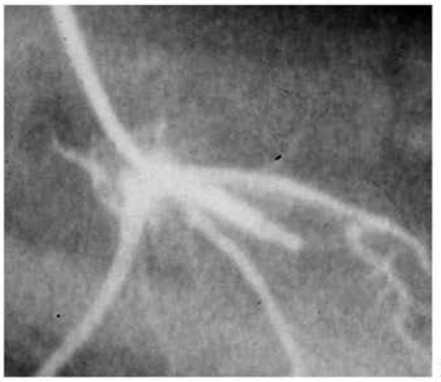

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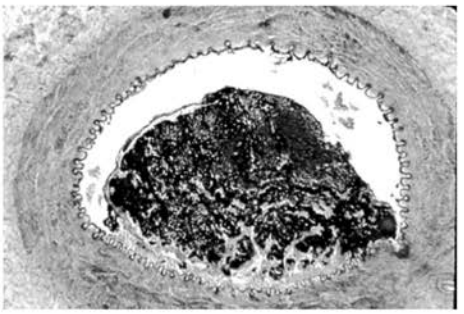

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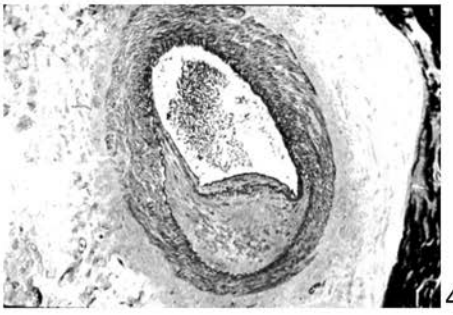

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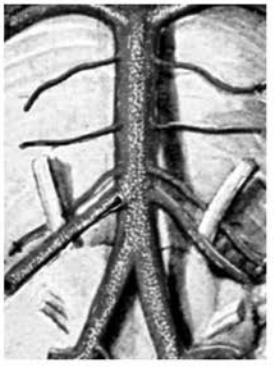

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The second half of this chapter concerns external collaborative research and my involvement in national organizations. The main organizations are the American Heart Association and its Scientific Councils on Thrombosis and Arteriosclerosis, and the National Institutes of Health and its National Heart, Lung, and Blood Institute.

NIH Committees

Between 1969 and 1993, I served on numerous ad hoc NIH review committees mostly for program projects or specialized centers of research in connection with atherosclerosis and thrombosis. On one occasion I was the chairman of a site visit committee at Chapel Hill. It was a daunting task to evaluate Brinkhous and his troops, who gave strong presentations. But when the committee huddled that night, problems arose and despite my and Colin Schwartz's efforts, we did not prevail. After the dust settled, the outstanding issues were satisfactorily resolved. I had the opportunity to speak with Brinkhous at a later date, and he was gracious as always.

Dr. James Stengle, the head of the thrombosis and blood diseases desk at the NIH, appointed me to a thrombosis advisory committee for a four-year term in 1970. I soon found myself on a blood diseases panel and one of its task forces on thromboarterial disease, which first met in 1972. Dr. Stanford Wessler chaired the task force and panel. A comprehensive multi-volume report was sent to the president and Congress in 1974 recommending that the National Heart and Lung Institute be reorganized to become the National Heart, Lung, and Blood Institute, which was accomplished in 1976 (36).

WORKSHOP ON CORONARY THROMBOSIS

At one of the task force meetings, the raging controversy over coronary thrombosis and its relation to myocardial infarction was discussed. Dr. William Roberts, a cardiac pathologist at the NIH Clinical Center, was claiming that contrary to conventional wisdom, coronary arterial thrombosis is the result, not the cause,

of myocardial infarction. Drug makers were in a tizzy, and the hysteria was spilling over to the public in health newsletters. Something had to be done. Wessler proposed that I organize and chair a workshop on the subject, bringing all the diverse parties together to hash out the evidence and clear the air. I went along with the proposal provided someone would co-chair the workshop with me, and Dr. Sol Sherry agreed to do so.

The workshop was held at the NIH in May of 1973 and was jointly sponsored by the Thrombosis Advisory Committee of the NIH and the Thrombosis Council of the American Heart Association. An international group of investigators, mostly from the U.S., were invited to participate and present their work. It was an extraordinary session. Here was a recognized cardiac pathologist from the NIH strongly suggesting on the basis of his studies that coronary thrombosis is a consequence rather than a cause of acute myocardial infarction. The other pathologists invited to speak gave an opposing view. They listened and then, one by one, presented evidence in support of the long-standing classical concept of coronary thrombosis as a cause of transmural infarction. One other speaker, Dr. Leif Erhardt, an internist from Stockholm, supported Roberts; however, he hedged his opinion by saying that a small nidus of primary thrombus could antedate infarction.

It remained for me to collect the individual reports and prepare an analysis for publication in *The American Journal of Cardiology* in 1974 (38). The paper concluded that the classical concept had the weight of evidence on its side. The report did clear the air and served to calm the troubled waters for a while (39). But it was Dr. Marcus DeWood, and his colleagues who in 1980 conclusively demonstrated by means of angiograms that coronary artery thrombosis develops prior to infarction (108). Their observations once and for all paved the way for widespread thrombolytic therapy in the treatment of myocardial infarction and justified the use of other antithrombotic modalities.

Thrombosis and the American Heart Association

In the early ’70s Dr. Sol Sherry spearheaded a successful drive to establish a Thrombosis Scientific Council in the American Heart Association and became its first chairman. I was appointed to the nominating committee, which met in

Atlantic City in the spring of 1973. During the meeting someone proposed that I be nominated to serve on the executive committee of the new council. Although I raised questions about the propriety of this action, others insisted it would be appropriate, so I went along with the nomination. This was my introduction to national politics, which are no different from the local scene. I served on the executive committee from 1973 through 1975 as an at-large member. In 1975 Dr. Fletcher Taylor called from Oklahoma to say I had been nominated as vice-chairman of the executive committee and council. By then, I had been thoroughly indoctrinated and told Fletcher I would accept the two-year appointment for 1976 and 1977, to be followed by the chairmanship for the next two years. There was a heavy predominance of hematologists on the committee, and I was the only pathologist.

WORKSHOP ON THE THROMBOTIC PROCESS IN ATHEROGENESIS

The council participated in the annual meetings of the association by sponsoring scientific sessions and joined hands with the American Society of Hematology for special sessions on thrombosis at their meetings. Among other activities, there was the opportunity to organize workshops such as the one on coronary thrombosis in 1973. The time seemed ripe to organize a workshop on thrombosis in relation to the pathogenesis of atherosclerosis. To my knowledge, such a conference had never been held. At the October 1975 meeting of the executive committee of the council, I laid out my proposal. Stan Wessler was the chairman by that time, and he enthusiastically endorsed the idea and urged that we seek cosponsorship from the Arteriosclerosis Council and the NIH, to which everyone agreed.

This decision set in motion an almost endless series of meetings and negotiations before the workshop was finally convened in October of 1977. Dr. Gardner McMillan, chief of the Arteriosclerosis Branch at the NIH, moved first by holding two small informal seminars on the subject in late 1975 and early 1976 in Bethesda. It was at this juncture that Colin Schwartz became involved. He knew Gardner well and was able to exert a positive influence on him and the arteriosclerosis faction, which was composed mostly of lipidologists.

Stan Wessler, who was then at New York University, held planning meetings there, mostly with people in the area to conserve costs.[2] At one of these meetings, Dr. Harvey Weiss solved a dilemma that had been a stumbling block—what to name this workshop. He coined a phrase that clicked and has served well to this day: "Thrombotic Process in Atherogenesis." Meetings were also held in Bethesda into the summer of 1977. At one point, the Blood Diseases Branch raised questions about funding, but the problems were soon resolved and the workshop went off as scheduled with full sponsorship by all concerned.

The workshop, which lasted two and a half days, was held in Reston, Virginia, near Dulles Airport, with about one hundred investigators in attendance. Many vested interests had a hand in the program. For example, one speaker gave a review of lipid metabolism, but not once was any connection with thrombosis mentioned. Stan and I co-chaired the meeting. Colin Schwartz gave a paper on arterial thrombosis and embolism and included me as one of the coauthors (48).

I had learned earlier that the Broadway show *Chorus Line* would be playing at the Kennedy Center and arranged for a bus to take the group to see it one evening. Betty Mustard and Jane, who were staying in town, met Fraser and me for the show. Notwithstanding a few ruffled feathers in Bethesda, everyone enjoyed the performance and returned to Reston in high spirits.

The workshop achieved its purpose, which was best expressed by Gardner McMillan (118):

> In my view, what is happening today in research on atherogenesis is that two major theories are being found not merely to be debatable alternatives, but that rather they are being found to be compatible and to share common phenomena at the most basic initiating stages of atherogenesis.

The proceedings were published in 1978 (47).

Flushed with success, I found the remainder of my term as chairman of the Thrombosis Council, in 1978 and 1979, anticlimactic. There was, however, one episode worth recounting. In the late '70s, the Arteriosclerosis Council was preparing to launch a new American Heart Association journal to be named *Arteriosclerosis,* with the first issue to be published in 1981. Stan Wessler and I attempted to persuade the Arteriosclerosis Council and the publications

committee of the association to include "thrombosis" in the title, but in vain. Ten years later, after a decade of many thrombosis-related articles in the journal, its name was changed to *Arteriosclerosis and Thrombosis*.

THE LESIONS COMMITTEE

Parallel to my involvement with the Thrombosis Council, I also served on the Coronary Artery Lesions and Myocardial Infarctions Committee of the Arteriosclerosis Council. The committee was free-wheeling and for many years had a life of its own with very little direction or funding from the council. Occasional symposia supported by outside sponsors were arranged. The committee was known as the Lesions Committee. (Lesion refers to a pathologic change in cells or tissues.) Its cumbersome name was officially changed to the Vascular Lesions Committee in 1982. Pathologists made up the largest group on the committee. I served on the committee from 1972 to 1994 and in 1980 and 1981 as its chairman. I became chairman in a manner befitting the relaxed atmosphere of the committee. At a meeting in Anaheim, California, when only two or three members were present, the chairman, Dr. Aram Chobanian, casually said, "I think you are going to be the next chairman." Aram seemed anxious to be relieved. What he did not tell me was that he needed a clean slate, for he would soon take on the formidable task of chairing an NIH study section.

Dr. Gene Bond was the catalyst for the group. He proposed that we organize a workshop on quantitative evaluation of atherosclerosis, especially at the clinical level. Procedures such as ultrasound and angiography were beginning to be used in clinical trials to follow the effects, if any, of therapy on regression of atherosclerosis. The committee agreed that a workshop on this topic would be timely. Gene was the driving force in planning and obtaining funds for the workshop, which was held in Silver Spring, Maryland, in February 1982. Other than planning, my participation was limited to writing the preface for the proceedings, which were published in 1983 (55, 56).

A short while later, the Lesions Committee under the leadership of Dr. Seymour Glagov organized a comprehensive symposium entitled "Pathobiology of the Human Atherosclerotic Plaque," which was held in September 1986 in Rockville,

Maryland. I gave a review on thrombosis and the platelet in atherogenesis (67). The proceedings were published in 1989. At the banquet I was presented a plaque from the American Heart Association for scholarly and dedicated leadership, which came as a complete surprise and spoke to the ingenuity of my secretary, Marie Hiller, who kept mum about providing biographical data. While serving on the Lesions Committee, I got to know Dr. Fred Cornhill, who was developing methods for analytical topography of arteries with Dr. Margot Roach in London, Ontario. This association led to a collaborative long-distance project on cerebral atherosclerosis.

Hemodynamics and Cerebral Atherosclerosis

The influence of fluid mechanics on the localization of atherosclerosis has been known for a long time. In observing cerebral arteries at autopsy, I had noticed that sometimes a single plaque would be located on the ventral (under) side of the basilar artery at the confluence of the vertebral arteries. Here was an opportunity to study a unique configuration where flow converges into a curved artery as it courses under the brain. Derene Akins joined the department in 1975 as a full-year student fellow, and she was recruited to join in a study designed to explore this observation in more detail. Fred Cornhill agreed to participate in the study, and he came to Augusta a couple of times to work out the research plan. Cerebral arteries were collected at autopsy from older adults fifty-one to seventy-one years old and the basilar-vertebral segment was opened and stained for fat by Marion Hutson. Tracings were made by Derene. Fred, who by then had moved to Columbus, Ohio, then subjected the data to computer analysis, which clearly demonstrated the localization of atherosclerosis in relation to the convergent flow and curvature of the basilar artery. This study was published in 1980 (50).

Thrombolysis Japanese Style

The cerebral artery project was performed without specific research grant funding, which had expired by 1975. The grant hiatus lasted four years, until in 1978 I heard from Dr. Toru Miyaji in Osaka, who was head of the department where

most of our Japanese fellows originated. He had arranged for Jane and me to visit Japan under the auspices of the Green Cross Corporation. This company was interested in collaborative work involving the fibrinolytic agent urokinase, which was one of their products.

We traveled to Osaka in March 1979.[3] There I attended a symposium sponsored by Green Cross and gave a talk on coronary arterial thrombosis, which was repeated the next day in Tokyo. During our brief stay in Tokyo, we had the opportunity to visit with Ken Shirasawa and his family. Toru Miyaji seemed to serve as the broker who explored the idea of Green Cross sending one of their researchers to Augusta to work on thrombolysis in my laboratory using their brand of urokinase. The researcher was Yoshiro Iga, who had been studying the effects of urokinase on *in vitro* thrombi. I accepted the proposal and stipulated from the outset that all results of our research would be disseminated through regular scientific channels. The company went along with my caveat and in September of that year, Iga and his family arrived in Augusta.

Iga brought a thrombogenerator for producing *in vitro* thrombi similar in concept to Jacobsen's design (18). It was a box-shaped incubator with transparent plastic walls that housed a rotatable spindle long enough to accommodate eighty loops.[4] Iga employed a sensitive method for estimating thrombolysis (109), which was based on measuring the rate of release of radioactivity from lysed radiolabelled fibrin in the thrombi (52). Sylvia Greenwald (later Stella) joined the laboratory as a research assistant in 1980, and a series of projects were undertaken over the next four years. Iga stayed two years and returned to Japan. We continued to collaborate and communicate by telex. He returned for short visits a couple of times.

We first investigated the uptake of radiolabelled plasminogen by *in vitro* thrombi during and after formation, and found that most of it was bound to fibrin (58). Plasminogen is a constituent of blood and a precursor of the fibrinolytic substance plasmin. As might be expected, plasminogen-enriched thrombi were more sensitive to lysis by urokinase than were controls (62).

In view of these ongoing studies, we next investigated the flux of substances between thrombus and plasma by means of radiolabelled molecules such as water, plasminogen, and albumin. Water quickly established equilibrium with

the fluid medium and also albumin but at a slower rate, while plasminogen did not equilibrate to any extent. These observations clearly indicate that thrombi exist in a dynamic state with the surrounding medium, which has implications for resolution of thrombi as well as their growth (60).

Lipids and thrombolysis. Dr. John Steele joined the faculty in 1981 upon completion of his residency at Louisiana State University, where he had worked with Dr. Jack Strong's atherosclerosis group. He had previously studied the effects of plasmin on lipoprotein as part of his Ph.D. thesis at Duke University, so it was a natural next step to study the effects of lytic agents on lipoprotein-enriched *in vitro* thrombi. Plasma lipoproteins isolated from healthy donors were used. The lipoproteins, which were highly purified, had no effect on lysis, but preliminary experiments with less purified fractions did show inhibition of thrombolysis (65). This finding suggested that other studies, especially like those of McNicol and colleagues (109), who found resistance to lysis using hyperlipemic plasma, must consider the possibility of inhibitory factors other than lipoproteins. Dr. Maciej (Mike) Speidel, a research fellow in the department, also worked on this project.

In 1982 Jane and I attended an international meeting on fibrinolysis in Venice and traveled in the area. It was a moving experience to visit the University of Padua and the great hall where Harvey, Copernicus, and Galileo once stood, and then to see the anatomical theater of the celebrated pathologist Giovanni Battista Morgagni. An added dividend was the nearby seven-hundred-year-old Scrovegni Chapel with its glorious frescoes by Giotto. Whatever sins Scrovegni was supposedly paying for, he was surely amply rewarded in heaven. The next year, Iga and I presented some of our work in Stockholm, which lived up to its reputation for dullness, except for the beautiful women.

I returned to Japan in January 1983 to seek additional funding, but Green Cross had apparently achieved its objective and no further funding was forthcoming after 1984. In retrospect it is clear that the most original aspect of much of our research was the use of a special brand of urokinase. Nevertheless, some interesting observations were made, particularly in regard to molecular exchange between blood and thrombi, and the lack of effect of purified lipoproteins on thrombolysis.

While in Japan, Toru Miyaji arranged for a wonderful reunion with former fellows. I also gave a talk on thromboatherogenesis at the Japan Atherosclerosis Society meeting in Osaka. Before the meeting that afternoon, I met with Professor Tanaka from Fukuoka and was served what must have been an expedited green tea ceremony in the middle of the hotel lobby. We discussed possible collaborative studies comparing atherosclerosis in our two countries, but our plans did not get very far before I became involved in an epidemiologic study in the United States.

NIH Recommendations for Arteriosclerosis

In 1981 Gardner McMillan appointed me to a small task group on atherogenesis assigned to write part of a ten-year update of the National Heart, Lung, and Blood Diseases program initiated in 1972. We worked in a cramped room in an old building on Wisconsin Avenue near the main campus. Dr. Tom Clarkson led the group as we created long lists of recommendations. In addition to writing much of the background material for the thrombotic process in atherogenesis, I contributed to formulating the recommendations for future research from 1982 to 1987 (59). Thrombosis kept its hat in the arteriosclerosis arena. More global objectives were to advance knowledge of the epidemiology and natural history of the disease. The complete report was transmitted to the president and the Congress in 1982.

Epidemiology of Atherosclerosis

In the United States serious epidemiologic research on atherosclerosis began in the New Orleans area, based at Louisiana State University. I recall an article in *Time* magazine in the late '50s showing a picture of Dr. Russell Holman, head of pathology at LSU, holding a lipid-stained aorta.[5] Already the group in New Orleans was drawing widespread attention with a publication in 1958 on the natural history of atherosclerosis by Holman, McGill, Strong, and Geer (110). This group was the nidus for the formation of a multicenter international autopsy study of atherosclerosis. The project had barely started when Holman died, and

it remained for Drs. Jack Strong, Jack Geer, and Henry McGill to carry on. The major findings of their project amply affirm that atherosclerosis begins in young people and progresses subclinically for years until it rises above the clinical horizon as stroke, gangrene, aneurysms, and related maladies (111). The question of the significance of the fatty streak in the origin of atherosclerosis was addressed, but not fully answered.

As early as 1973 at Lesions Committee meetings, I began to hear about the riddle of the fatty streak, which appears at a young age as a yellow streak on the inner surface of an artery. Pathologists naturally try to equate the microscopic picture with the gross appearance of a lesion; however, it had been known for some time that the fatty streak has several different compositions microscopically. It had also long been thought that some fatty streaks progress to atherosclerotic plaques while others may regress and disappear (112). But how does one discern which ones are apt to go which way? As Virchow said, one must distinguish between the "mere form and true nature" of a lesion.[6]

At the meeting on the thrombotic process in atherogenesis in 1977, Bob Wissler mentioned that a group in West Virginia was seeking to organize a collaborative study of the fatty streak. This effort fell through the cracks. Not long afterward I heard from Wissler that he was getting together some investigators in Chicago to consider launching a multicenter project on atherosclerosis. I attended the meeting in the fall of 1983 and was invited to participate. After consultations both with Wissler and colleagues in Augusta, I agreed to join the project, which became widely known as PDAY, the acronym for Pathobiological Determinants of Atherosclerosis in Youth.

Pathobiological Determinants of Atherosclerosis in Youth

The overall plan was to conduct a prospective multicenter study of atherosclerosis based on autopsies of young individuals who died suddenly, mainly as a result of trauma. The aorta, coronary arteries, and other tissues would be collected and processed according to a strict NIH-approved and legally acceptable protocol. The project was designed to study systematically the natural history of atherosclerosis from fifteen through thirty-four years of age (113). Core center

investigators would study the evolution of the disease in relation to known adult risk factors, while the investigators at the special studies centers would assess other possible determinants by means of modern technologies then available. The material would be shared by all centers. Georgia would become one of fifteen centers, nine of which would also be collection centers. Much of the material was later made available to other investigators in the scientific community. Studies would continue well into the twenty-first century.

Each center submitted separate but coordinated grant applications to the National Institutes of Health in the spring of 1984. Awards were made to begin in June of 1985. A trial run was conducted for two years to get the kinks out of the system, which was followed by a five-year definitive collection and study phase. The entire project, which was directed by Wissler, was highly and effectively organized with internal and external monitors. From the outset, Henry McGill and Jack Strong were intimately involved in the design and overall operation. Strong became director in 1996. Regular meetings were held with the NIH monitors, which were often followed by scientific meetings of the investigators. Over the seven-year period of the grant, there was frequent productive interchange between groups, and lasting friendships were engendered. Dr. Ross Gerrity, who was a member of the data review board for PDAY, joined the department in Augusta and the atherosclerosis project in 1990. Our studies at Georgia are outlined below.

We organized two special studies, one led by Ben Spurlock and the other by Dr. R. N. Rao. Spurlock surveyed the inner surface of the left coronary artery and the aorta by means of scanning electron microscopy. Rao and Dr. Greer Falls studied connective tissues of the aorta by means of histochemistry. Collection of cases in Augusta was led by Falls. Dr. Kailash Sharma and his associates at University Hospital in Augusta and Dr. Joel Sexton, a forensic pathologist in Newberry, South Carolina, participated with Falls in the collection of cases. The assistance and cooperation of Leroy Simms, the coroner for Richmond County, was invaluable, inasmuch as most of the cases were coroner's cases.

Spurlock searched for microthrombi in the plaque-prone abdominal aorta and in the resistant thoracic aorta and in similar areas in the left coronary artery. He found a few fresh microthrombi comprised of platelets, leukocytes, and fibrin,

which were about as frequent in the thoracic as in the abdominal aorta. A few thrombi were also observed in the left coronary artery (63, 66). In addition, scattered single platelets were adhered to the endothelium. An unexpected finding was the presence of leukocytes, mostly monocytes, adhering to the endothelium and arranged in clusters beneath the endothelium, with almost twice the frequency in the thoracic compared with the abdominal aorta. Blood monocytes have long been implicated in the pathogenesis of atherosclerosis; however, this is not the place to review the subject except to note that Ross Gerrity made significant contributions in this area before his untimely death in 2008.

Rao and Falls obtained more meaningful results in relation to progression of the disease. They found that synthetic smooth muscle cells were more heavily concentrated in the innermost intimal layer in the atherosclerosis-prone abdominal aorta than in the resistant thoracic aorta (114). In these same sites, the thickness of the inner layer was correlated with the production of connective tissue by the synthetic smooth muscle cells, both of which increased with age.

CORE STUDIES

As one of the collection centers, Georgia contributed cases to the core and special studies investigations. Grading and mapping of the gross arterial lesions took place at core centers at Louisiana and Ohio State Universities. A core statistical center was located at the University of Texas in San Antonio. The major known adult risk factors of smoking, serum lipoprotein levels, hypertension, obesity, and hyperglycemia and the immutable risk factors of age, sex, and race were correlated with the frequency, extent, and types of gross lesions observed. In essence, these risk factors for clinically manifest atherosclerosis were associated with the subclinical disease in varying degrees beginning in the age bracket of fifteen through nineteen years (115,116).

The observations on the evolution of the fatty streak, however, were not so different from earlier studies until McGill and his colleagues provided a critical breakthrough in 2000 (117). They separated fatty streaks into flat and raised subsets and then correlated these distinct gross lesions with the known adult risk factors. Raised fatty streaks are associated with risk factors and increasing extent

of the lesion through all age groups beginning in the fifteen through nineteen-year age group, whereas the flat fatty streaks progress in extent up to the twenty-five through twenty-nine-year age group and then level off. The more advanced fibrous plaques are associated with the risk factors in the twenty-five through thirty-four-year age group.

In addition to being thicker and more cellular than the flat fatty streak, the raised fatty streak has small microscopic pools of *extracellular* lipid—all features of an intermediate lesion that is also grossly identifiable. Flat fatty streaks with mainly *intracellular* lipid are commonly fond in the less disease-prone area of the thoracic and upper abdominal aorta. While it would seem reasonable that flat fatty streaks can become raised and committed to advance, especially in disease-prone areas, it remains impossible to know if a flat streak is likely to progress except by its location. Thus, the riddle of the fatty streak is only partly solved. Earlier it was the subject of extensive debate in Lesions Committee meetings in the late '80s and early '90s.

The Lesions Committee Classifies Atherosclerosis

Dr. Herbert Stary at LSU succeeded Glagov as chairman of the committee in 1987. He proposed that the committee define the lesions of atherosclerosis based on current knowledge and create a modern workable classification of the disease. The committee accepted his proposal and drafted a series of papers beginning with an introductory article on the normal intima in 1992 (70). This paper was followed by one on the early lesions in 1994 (72) and then on advanced lesions in 1995 (74).

The committee devised a scheme for classifying the lesions from the earliest microscopic change to advanced complicated plaques, which were numbered I–VI. For most types, the gross and microscopic features of the lesions were consistently matched; however, this was not the case for Types II and III. Type II was equated with the gross fatty streak even though the variable microscopic appearance of the fatty streak did not always match the narrowly defined microscopic description of Type II. As to Type III, which was considered an intermediate or transitional lesion, there was no matching gross lesion identified. Although this

aspect of the scheme was obviously flawed, I was unable to convince the committee to address the issue.

It remained for the PDAY core research group to come to the rescue and provide the missing link, albeit too late for the committee's consideration. McGill and his colleagues as noted above reported in 2000 that the fatty streak can be subdivided into two distinct components: a flat streak equivalent to Type II and a raised streak equivalent to the intermediate Type III (117). A brief statement from the American Heart Association officially amending the classification to include the two subsets of the fatty streak would make it a more useful and accurate guide.

THE COMMITTEE MOVES ON

By 1994 my twenty-two years of service on the Lesions Committee was nearing an end. Dr. Valentin Fuster became the new chairman, and he proceeded almost at once to organize a conference on "Syndromes of Atherosclerosis: Correlations of Clinical Imaging and Pathology," which was held in Orlando in 1995. It was, in part, an update of Gene Bond's 1982 workshop. Colin Schwartz and I gave a paper on coronary atherosclerosis (76). All members of the committee helped edit the proceedings, which were published in 1996 (75).

Conclusion

My research career began in 1949 and, for all practical purposes, ended in 1994, some forty-five years later. During this period, my research was supported by various NIH research grants and subgrants for thirty-one grant years and by one other research grant for five additional years. Throughout this period, it was my good fortune to work with innovative collaborators and to have superb research assistants. Eight of the projects described herein were autopsy studies, which now seem to be from a bygone era. In retrospect, it is easy to see a progressive drift of my research from bench to armchair. Research is tedious, and advances come slowly, but the rewards are many, not least of which are the friendships that arise through collaboration and common interests.

A FINAL REFLECTION

In early correspondence with a colleague, I commented that research is a respectable way for adults to have fun. For me, that turned out to be not far off the mark. I enjoyed research. Ideas were easy to come by and plentiful, but I soon learned that the doing is in the details. As Ben Hogan said, "It's in the dirt!"

NOTES

1. By a bit of luck, we found that the plastic tubing of the flow unit would swell during processing so that the contents would slip out. Phyllis Brewer, the electron microscopy technician, figured out this technical problem, which greatly facilitated the ultrastructural studies.

2. One day when only Stan and I were present, he said, "Let's go to the cafeteria for lunch." With that, he pulled out a bottle of claret from his desk and off we went. In addition to being extremely intelligent and articulate, he was urbane with a distinctly continental flair. We became good friends over the years, for which I am grateful.

3. Luckily, we stopped overnight in Honolulu, for when we got to the gate to board for Japan we were told that a visa was required. After a mad dash to the Japanese embassy, we made it back to the plane in time. No one seemed surprised at what must be a common event.

4. Once again I had to call on my patent attorney friends in Washington, this time to restrain Green Cross from commercializing the machine. It is a wonder the company awarded me the grant.

5. According to Henry McGill, the aorta is that of an African baboon, which demonstrates the natural occurrence of the disease in a primate other than man. (Telephone call, November 25, 2002.)

6. Rudolph Virchow, *Cellular Pathology*, 511, 514, Translation of 2nd German Edition of 1859 by F. Chance, New York: Robert M. DeWitt, 1860. Virchow illustrated his comment by the sad fate of a man whose penis was amputated when the surgeon mistakenly thought a simple wart was a verrucous cancer.

PLATE XXXI

Thrombosis Conferences

1) *Dr. J. R. A. Mitchell* visited Augusta in December 1966 after he and ABC had attended a meeting on thrombosis and hemostasis in Chapel Hill, North Carolina. In this photo, he is on the left of Dr. Walter Shepeard. Mitchell was an internist at Oxford and had coauthored a monograph on arterial disease with Dr. Colin Schwartz.

2) *Dr. John French* visited Augusta after he and ABC presented papers in Washington, D.C., at a National Academy of Sciences conference on thrombosis in December 1967. French was at Oxford University and had extensively investigated experimental thrombosis, especially by electron microscopy. From left: Drs. Chandler, French, and Stoddard.

3) *Montreux, Switzerland.* The first Congress of the International Society on Thrombosis and Haemostasis was held in Montreux in the summer of 1970. Stalwarts of the society on the front row are from left: Drs. Verstraete, Duckert, Brinkhous, Koller, Sherry, Stengle, and Surgernor. ABC is third from left on the back row. Leif Jörgensen is on his right, and Dr. Claude Bouvier of Geneva, wearing dark glasses, is on his left.

4) *Tromsö, Norway.* This poster announces a conference organized by Dr. Arne Nordöy on lipids and thrombosis scheduled for June 1974 at the University of Tromsö, the northernmost university in the world. The modern church seen between the arches of the bridge is known as the Artic Cathedral. It was designed by Jan Inge Hovig, the brother of the electron microscopist Dr. Torstein Hovig.

5) *Jacket front: The Thrombotic Process in Atherogenesis.* The publication contained the proceedings of the conference of the same title held in Reston, Virginia, in October 1977 (47,48). Dr. Stanford Wessler and ABC were co-chairmen of the conference.

6) *Dr. Colin Schwartz* visited Augusta in the '80s when he was a member of the pathology department in San Antonio. Schwartz was of great help in organizing the Reston conference through his wide contacts and expertise in the field of arterial disease. In this photo with ABC, he is on the right.

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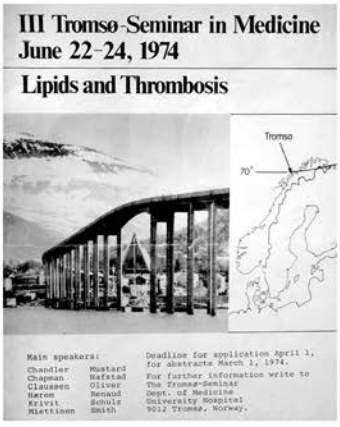
III Tromsø-Seminar in Medicine
June 22-24, 1974
Lipids and Thrombosis
Tromsø
70°
Main speakers:
Chandler Mustard
Chapman Nafstad
Claussen Oliver
Haron Renaud
Krivit Schulz
Miettinen Smith
Deadline for application April 1,
for abstracts March 1, 1974.
For further information write to
The Tromsø-Seminar
Dept. of Medicine
University Hospital
9012 Tromsø, Norway.

4

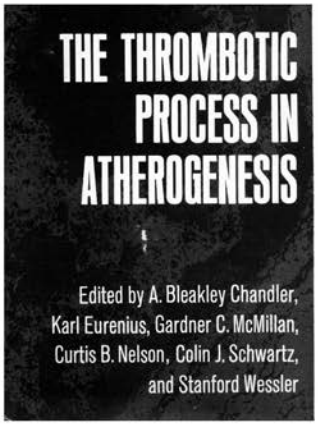
THE THROMBOTIC PROCESS IN ATHEROGENESIS
Edited by A. Bleakley Chandler, Karl Eurenius, Gardner C. McMillan, Curtis B. Nelson, Colin J. Schwartz, and Stanford Wessler

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PLATE XXXII

Japan, 1979 and 1983

1) *Lecture in Tokyo, 1979.* The Green Cross Corporation, which sponsored the trip, organized a symposium where ABC gave a talk on the pathogenesis and fate of coronary thrombi. The talk was simultaneously translated into Japanese.

2) *Jane Chandler and Dr. Toru Miyaji.* The visits to Japan were arranged by Dr. Miyaji, the head of pathology at the University of Osaka.

3) *Reunion in Osaka, 1983.* Many former pathology fellows in Augusta attended a reunion in Osaka. From left: Drs. Chandler and Miyamoto, Mrs Yutani, Drs. Shirasawa, Morisue, Yutani, Kikui, and Miyaji. Dr. Morisue was an officer in the Green Cross Corporation.

4) *Geisha house gala in Osaka, 1983.* An elaborate banquet was held at a geisha house after a meeting of the Japan Atherosclerosis Society where ABC was one of the speakers. Having dinner seated on the floor was made less taxing by the geishas in attendance. From left: a geisha, Miyaji, Chandler, a geisha, the president of the society. When the president shed his jacket, ABC followed.

Congress in Stockholm, 1983

5) *Stockholm, 1983.* In July, Iga and ABC attended the International Congress on Haemostasis and Thrombosis, where a poster on molecular exchange between blood and *in vitro* thrombi was presented. At a reception, old friends met. From left: Drs. Jack Hoak, Arne Nordöy, A. B. Chandler, and Yoshiro Iga.

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PLATE XXXIII

Coronary Artery Microthrombi

1) *Microthrombus.* In this microphotograph of a cross-sectional view of a coronary artery, a microthrombus is on the surface of a fibrous atherosclerotic plaque. Small dots on the surface are platelets (37).

2) *Covered microthrombus.* In this microphotograph of a cross section of a coronary artery, a microthrombus on the surface of an atherosclerotic plaque is covered by endothelium as it undergoes incorporation into the underlying plaque.

Pathobiological Determinants of Atherosclerosis in Youth (PDAY)

3) *Ben Spurlock* was a member of the department's PDAY team. By means of scanning electron microscopy (SEM), he searched for microthrombi on the surface of the aorta and coronary arteries (63,66).

4) *Platelet carpet.* In this SEM view, numerous single platelets are adhered to the surface of a coronary artery.

5) *Single adherent platelet.* The platelet in this SEM view of the aortic surface appears to be a space ship that has just landed.

6) *Microthrombus, coronary artery.* The microthrombus in this SEM view appears to be composed entirely of platelets. No fibrin is seen.

7) *Raised fatty streaks.* In this gross photograph of the aortic surface taken by Dr. Greer Falls for PDAY, fatty streaks can be seen as raised ridges, which in the natural state were yellow. These raised fatty streaks are thought to be precursors of atherosclerotic plaques.

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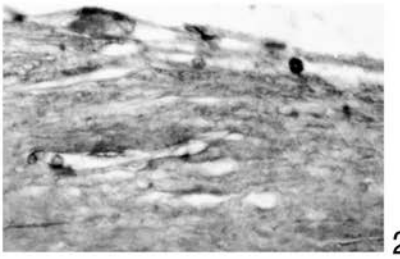

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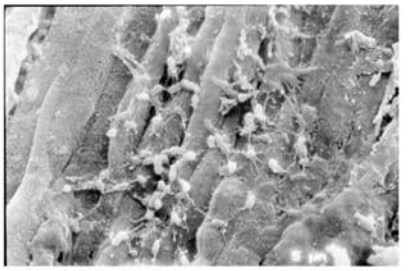

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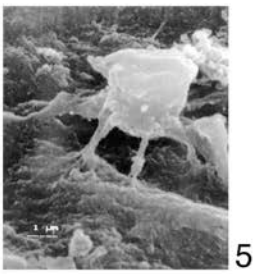

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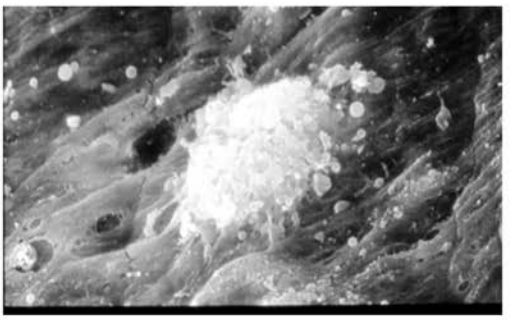

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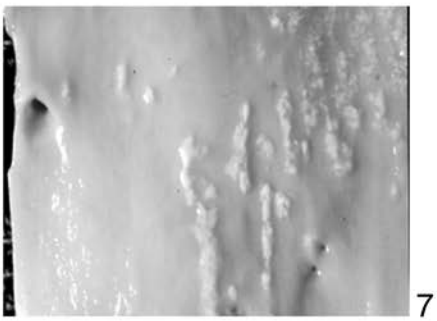

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EPILOGUE

Be not the first to cast aside the old,
Nor the last to try the new.
—adapted from Alexander Pope

The foregoing account records my experience from 1944 to 2000, first as a student and then as a resident and faculty pathologist engaged in research, education, and service primarily at the Medical College of Georgia and its teaching hospital, serving as pathology chair for the last twenty-five and one-half years of this period. While it is difficult to gauge the success of one's teaching, my accomplishments as chairman are a matter of record. Our research has been corroborated and extended over the years by many investigators in other laboratories.

My career extended over a half century of medical and scientific progress. During this time, medical practice evolved from a hands-on approach into a highly specialized technological system, which by its very nature became increasingly fragmented and impersonal. As medicine moved in this direction, it also became overtly commercialized. While the individual patient often feels confused and neglected, the American people are generally healthier and living longer. On balance, the medical profession has succeeded in adapting to a technological world.

Where does the future of pathology fit into this picture? Pathology has also become intensively commercialized amidst rapidly advancing technological transformation. As a result, more and more of the analytical work in the laboratory is being deferred to technologists and doctoral scientists. This is a daunting picture for the pathologist, who has devoted years of study to a specialty that is seemingly slipping away.

Pathologists are not likely to become extinct. As the specialty evolves, pathologists can be expected to maintain their educational, managerial, and professional roles in the laboratory and as consultants to other physicians. Furthermore, they will have the opportunity to continue studying disease in individual patients and remain in the forefront of integrating and advancing medical knowledge across many areas.

Education in pathology has reached a crossroads. Although graduate and postgraduate education prospers, students in undergraduate programs have lost a great deal of practical and personal contact with the discipline. Larger class sizes have led to courses with a heavy lecture format supplemented by computer-driven virtual programs. Pathologists have accentuated this trend by increasingly letting staff other than pathologists replace them in the classroom. This approach appears to be the wave of the future. But the question remains: Will the students emerge from this environment with a thorough understanding and knowledge of disease in their patients?

What Then?

"The work is done," grown old he thought,
"According to my boyish plan;
Let the fools rage, I swerved in naught,
Something to perfection brought;"
But louder sang that ghost, "What then?"

—William Butler Yeats, 1938

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Figures 3 and 4: Reproduced by permission from: A. B. Chandler and G. F. Jones. *The American Surgeon* 17:719–721, 1951.

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Figure 2: The July 15, 1963, issue of *Rogalands Avis*, Stavanger, Norway probably carried this article; however, the newspaper cannot verify its publication because several pages of this issue are missing from the paper's archives (email from >rogalandsavis.no< May 7, 2012).

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