

**Perspectives in pathology****On being a pathologist—passing on the torch of knowledge****Lawrence M. Roth MD***Department of Pathology, Indiana University School of Medicine, Indianapolis, IN 46202, USA*

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Ours was a family that valued education. My father, Herman Moe Roth, was an engineer and physicist. Before marriage, my mother, Blanche Brown, was a high school English teacher in Canadian, Oklahoma, a small rural town in the southeastern part of the state. She had studied at Washington University in St. Louis for a year and then completed her education at the University of Oklahoma in Norman. My father obtained his undergraduate degree in electrical engineering from the University of Virginia in Charlottesville. He earned his PhD in astrophysics at the Mendenhall Laboratory of Physics of Ohio State University in Columbus during the great depression. He was the only surviving boy among 7 children and used to joke that he got the education and his sisters each got a dowry. Before World War II, he taught physics at what is now Oklahoma State University in Stillwater. During the war, he served in the US Army in the Corps of Engineers at Fort Belvoir, Virginia, and in Washington, DC. After World War II, he took a position with the Atomic Energy Commission in Oak Ridge, Tennessee, and later became director of research. He encouraged my brother, Sanford Irwin Roth, and me to pursue higher education. I followed my brother's footsteps and pursued medicine and ultimately the specialty of pathology. My maternal grandfather, Joseph Brown, was also pleased that we became physicians but would have preferred that we had become "real doctors," meaning that we would take care of patients.

I graduated from Oak Ridge High School and then Vanderbilt University in Nashville, the latter with a BA in

Chemistry. My first knowledge of the specialty of pathology came when my older brother, Dr Sanford Irwin Roth, accepted a position as an intern in pathology at the Massachusetts General Hospital (MGH) in Boston in 1956. Early in my fourth year of medical school at Harvard in 1959, I took an elective in pathology at the MGH and was first exposed to a number of eminent pathologists in Boston including Drs Benjamin Castleman, professor of pathology at Harvard and chair of the Department at the MGH; Robert E Scully; Austin L Vickery Jr; and Richard B Cohen.

I was not, however, convinced that pathology should be my career choice, so I subsequently accepted a rotating internship at the University of Illinois Research and Educational Hospitals in Chicago. There, during my elective month spent in pathology, I met Dr Seymour Rosen, who was a first-year resident and later became a well-known renal pathologist at the Beth Israel Hospital and Harvard Medical School in Boston. Dr Rosen showed an exceptional enthusiasm for pathology and a pursuit of excellence that I remember to this day. The long grueling hours and the many nights on duty spent on clinical rotations, especially the emergency department, helped convince me that pathology would be my career choice.

I chose Washington University and Barnes Hospital in St. Louis for my residency. The anatomical pathology residency program at that time was structured in an unusual way and consisted of 2 years in autopsy pathology followed by a year of surgical pathology. Dr Paul E Lacy assumed the chair of the Department of Pathology in 1961, the year I began my residency. The anatomical pathology faculty members were outstanding but most seemed mainly interested in their own research. There were, however, exceptions. Dr Margaret G

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Smith was an anatomical pathologist of the old school, and Dr John M Kissane could go through a box of autopsy slides in an incredibly short time but managed to observe much that I had missed. I vividly remember 1 autopsy that I performed. The patient previously had a hysterectomy for leiomyomas and died of metastatic benign-appearing smooth muscle tumors in the liver and elsewhere. This was not the usual “benign metastasizing leiomyoma” because the liver was massively involved. We interpreted the case as metastatic highly differentiated leiomyosarcoma based on the findings at autopsy and the clinical course. This was my first experience with benign-appearing neoplasms that were actually malignant, a subject that I have maintained an interest in throughout my career.

Half of the time during my first 2 years of residency was spent doing research on a topic of one’s own choice. I learned electron microscopy in the laboratory of Dr George D Sorenson. At that time, the residents had to cut thin sections using glass knives for their own research. After more than a month’s seemingly fruitless efforts, I achieved great success one day, and the sections seemed close to perfection in the electron microscope. Unfortunately, I was never able to duplicate that achievement and had to depend on the technicians completely for my thin sections after that. After much consideration, I professed an interest in the pituitary gland. Because study of the anterior lobe did not lead to any meaningful new observations, I began research with Dr Sarah A Luse, a noted neuropathologist, on the posterior lobe of the opossum, which has an unusually well-organized lobular structure.

During my second year of residency, I began attending some of the morning surgical pathology conferences usually moderated by the director of surgical pathology, Dr Lauren V Ackerman. It soon became apparent that he had become bored with the topic of papillary carcinoma of the thyroid, and if such a case were presented, he would simply declare, “Next case please,” and the conference would move on. When I first began surgical pathology the following year, Dr Ackerman gave the neophyte surgical pathology trainees the somewhat tongue-in-cheek advice, “For God’s sake, don’t make any mistakes.” I tried to follow his sage counsel but unfortunately was not always able to do so.

For my initial research project in surgical pathology, the topic suggested to me by Dr Ackerman was “Inclusions of non-neoplastic thyroid tissue in cervical lymph nodes,” a concept that originated with a noted French pathologist at the time, Gerard-Marchand [1]. These inclusions are typically found as incidental findings in lymph node dissections done for squamous cell carcinoma of the head and neck. I dutifully wrote up the 2 cases we had at the time, and an article was published in *Cancer* [2]. Several years later, my colleague at Tulane, Dr Richard J. Reed, let me know that he thought that the cases I had reported actually were metastatic papillary thyroid carcinoma. Thus, I learned early in my career that not everyone would accept my interpretations.

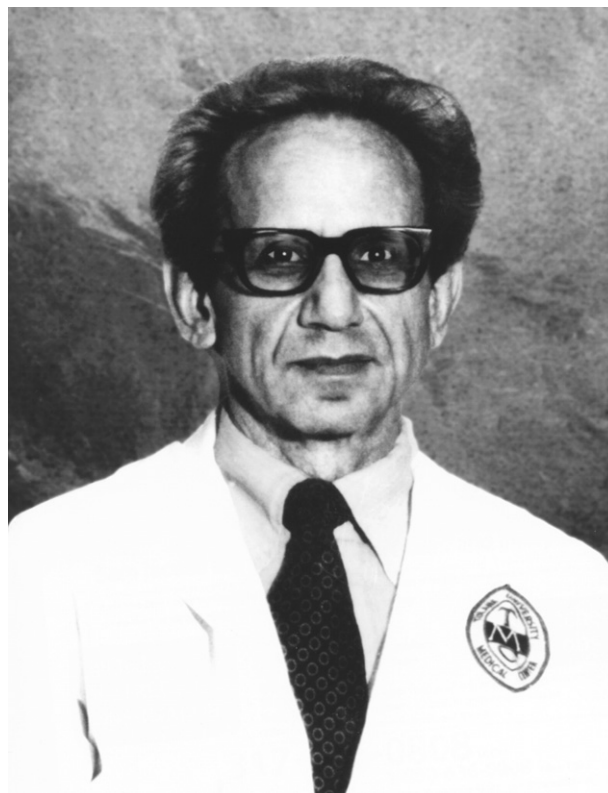
During my surgical pathology residency year, I became interested in gynecologic pathology and believed that my career would benefit from more basic research experience in that area. I decided on a fellowship in steroid biochemistry at the Karolinska Institute in Stockholm, Sweden. The director of the laboratory was Dr Egon Diczfalusy, a Hungarian endocrinologist. In his laboratory, steroids were separated by the rather laborious technique of countercurrent distribution. My main project was stymied when the director decided that my results were of interest but should be confirmed by examining the duplicate aliquots that had been stored in the cold room. Unfortunately, fungus had grown in the stored samples making them useless for analysis, thus ending my experience in basic research. During my time in Stockholm, I met my future spouse, Ann-Katrin Sundström, so the time was well spent.

After my stay in Stockholm, I served 2 years in the US Army fulfilling a prior commitment I had made by signing up for the Berry Plan to defer my military service until after completion of my specialty training. My initial assignment was at the Armed Forces Institute of Pathology (AFIP) in the Office of the Scientific Director. Colonel Joe M Blumberg, director of the AFIP, enjoyed giving tours of the AFIP to officers’ wives, and Ann-Katrin remembers him showing a specimen of an elephant’s heart. It was a pleasure meeting a high-level officer who was so kind to the troops and their wives. Blumberg later attained the rank of Major General, the highest rank ever attained by a pathologist in the US Army. The assignment at the AFIP, however, did not work out well for me because I was not allowed to attend diagnostic conferences in the gynecologic and breast pathology section, the research project I was assigned to did not seem relevant, and I was asked to sign up for another year of active duty. After I declined to sign up for a third year, I was told that I could no longer do research. Although this was at the time of the Vietnam conflict, I asked for a transfer and met with then Colonel Blumberg, and he kindly had me assigned to Japan where I was director of laboratories at the 249th General Hospital under the command of Colonel Martin Photenhauer in North Camp Drake, a US Army base just North of Tokyo. There I gained administrative experience, saw a limited number of surgical pathology specimens, and did some autopsies. A high point of my tour of duty in Japan was an inspection visit by General Blumberg to North Camp Drake. During my tenure there I was a Captain but served as director of laboratories since I was a pathologist. Because I had had no training in clinical pathology at the time, the position was a challenge. I had the able support, however, of 2 capable Medical Service Corps officers: Lieutenant Colonel Edward Koplan and Major James Allison. The only clinical pathology duty I was directly responsible for was reading crossmatches for transfusions that required a physician, and that was something I was able to learn. I remember particularly a difficult administrative decision I had to make soon after our arrival in Japan. There was a longstanding sergeant who had served in the Army loyally

for many years and was scheduled for retirement the following year. He had recently recovered from a stroke and unfortunately could no longer carry out his duties up to standards. The Medical Service Corps officers and the chief sergeant wanted to give him a disability discharge, so they could replace him with a more effective laboratory technician. This, however, would have involved a reduction in rank and would have severely impacted his retirement pay. It was ultimately my decision, and I let him serve out his time to receive his full retirement benefits.

After my tour of duty in the Army, I was still looking for adventure and decided to seek more training to obtain boards in clinical pathology. Instead of returning to St. Louis for a junior faculty position in surgical pathology at Washington University, I accepted a position as a resident in clinical pathology at the University of California, San Francisco. Clearly, Dr Ackerman was not pleased, but we continued to have a cordial relationship. The chair of the Department of Laboratory Medicine at that time was a well-known hematopathologist, Dr George Brecher, who had a grant to develop one of the first laboratory computer systems. He was extremely busy but very nice and a pleasure to work for; however, he soon realized that my main interest was in anatomical pathology. The following year, Dr Henry D Moon, the chair of Anatomic Pathology, offered me the position of chief resident, but I felt ready for a faculty position and decided to look elsewhere.

I accepted an assistant professorship at Tulane University in New Orleans with duties in anatomical pathology that began in August 1968 to begin my research in gynecologic pathology in collaboration with Dr William H Sternberg, an internationally renowned and highly regarded gynecologic pathologist (Fig. 1). Will, as his close colleagues knew him, had collected some excellent and often unique clinical and pathologic material but had not had time to publish much of it because of various departmental duties and perhaps also because of his keen interest in the arts. Some of his lifelong professional interests in addition to cytogenetics and the study of intersex patients were sex cord–stromal tumors of the ovary. He is now best known for his description of luteoma of pregnancy [3]. One of our major collaborations was the first description of Leydig cell tumors of ovarian stromal derivation, namely, stromal-Leydig cell tumor and nonhilar Leydig cell tumor. Both tumors are often clinically virilizing. The former arises in the ovarian stroma and has neoplastic components of ovarian stroma and Leydig cells containing crystals of Reinke [4]. It is considered analogous to partly luteinized theca cell tumor, now usually referred to as luteinized thecoma. The second tumor we described was Leydig cell tumor, nonhilar type [5]. It is a pure Leydig cell tumor containing crystals of Reinke that is located in the ovarian stroma rather than in the hilus. Another important contribution was our description of proliferating Brenner tumor, a cystic neoplasm with an epithelial lining composed of a noninvasive tumor analogous to low-grade papillary transitional cell carcinoma of the urinary bladder [6].



**Fig. 1** Dr William H Sternberg, professor of pathology, Tulane University School of Medicine.

Because of its intracystic growth and the absence of invasion, it is clinically benign.

The departmental chair was Dr Charles E Dunlap, who had a lifelong interest in radiation pathology. His knowledge of scientific writing was at a high level, and he corrected my English grammar and spelling whenever he had the opportunity, sometimes to my embarrassment. I learned a valuable lesson from him regarding the importance of clear and correct scientific writing. During my years at Tulane, I met a number of other professional colleagues who became lifelong friends. Because of space limitations, I will only discuss one, Dr Richard Reed (Fig. 2). Richard was trained at Tulane and spent a year as a surgical pathology fellow under Dr Ackerman in St. Louis 2 years before I did. He subsequently returned to Tulane, where he was the acknowledged expert in surgical pathology and dermatopathology in the New Orleans and gulf coast area. Although we did not collaborate on any clinicopathologic studies at Tulane, we continued our friendship after I left New Orleans.

Being young and inexperienced, Ann-Katrin and I stayed in New Orleans during hurricane Camille in August 1969, and that experience convinced us that we should eventually make a home somewhere else when the opportunity presented itself. After leaving Tulane, I continued working with Dr Sternberg on some projects started in New Orleans. I visited New Orleans and the Department of Pathology several times to see colleagues and old friends. For my most





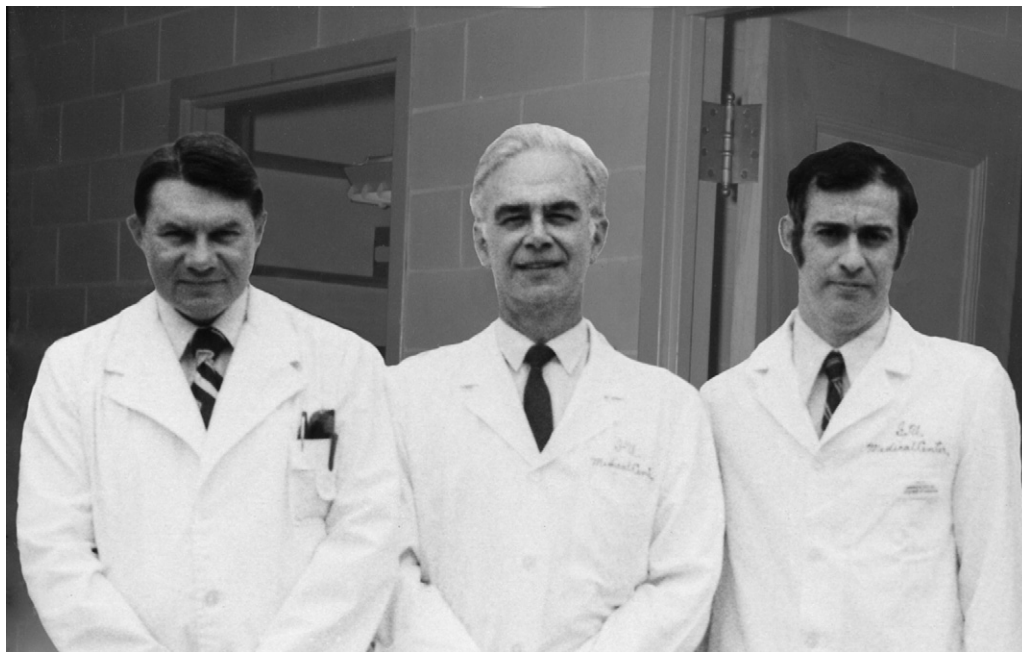
**Fig. 2** Dr Richard J Reed, professor of pathology, Tulane University School of Medicine.

memorable visit, Dr Michael A Gerber, the Departmental Chair, invited me to give the third annual William H. Sternberg Memorial Lecture at Tulane on May 1, 1992, in honor of my mentor. The subject was “Brenner tumors and

transitional cell carcinoma of the ovary.” It was a great honor and privilege to give that lecture. In 1997, Richard Reed and I published a tribute to Will in the *International Journal of Gynecological Pathology* as part of the “History of gynecological pathology” series [7].

After Will’s passing, Richard saved Will’s collected materials and shared them with me, for which I am deeply grateful. We decided to complete a project that Will was deeply interested in but never finished, perhaps because he did not want to report cases of any tumor or condition that he did not completely understand. This entity consists of an unusual benign smooth muscle tumor that has a tendency to grow through the uterine wall laterally and extend into the broad ligament. Because of its alarming macroscopic appearance, the surgeon may believe that he has encountered a malignancy. Will colloquially referred to these cases as the “red seaweed tumor.” In 1996, Richard and I reported Will’s original 4 cases as *cotyledonoid dissecting leiomyoma* based on its macroscopic appearance in the peritoneum in the vicinity of the broad ligament that often resembles the cotyledons of a placenta and its microscopic growth pattern within the uterus [8]. The earliest case of this entity in Will’s material was from 1946 and another dated from 1954. To acknowledge Will’s contribution, we included him as an author posthumously. We later learned that David et al [9] first described cases of this type as *grape-like leiomyoma of the uterus* in 1975. Since our original studies, I have received additional cases in consultation and exceptionally encountered them in my own surgical pathology material.

After I had considered several faculty positions, Dr Joshua L Edwards (Fig. 3), the chair of the Department of Anatomic Pathology at Indiana University School of



**Fig. 3** From left to right, Dr Carleton Nordschow and Dr Joshua L. Edwards, departmental chairs of Pathology at Indiana University School of Medicine, and Dr Roth in 1975.

Medicine (IUSM) offered me a position of associate professor of pathology and director of surgical pathology that I accepted after careful deliberation. I began the work in Indianapolis in September 1971. I became professor of pathology in 1975. During my time in Indianapolis, I served 4 departmental chairs, each of whom had their own personalities and administrative styles of leadership. After the anatomic and clinical pathology departments merged in 1979, I served under Dr Carleton Nordschow (see Fig. 3). After Dr Nordschow's retirement, Dr James W Smith served as the departmental chair from 1992 to 1998, followed by Dr John N Eble. During that time, the department and medical school underwent unprecedented development. In surgical pathology, I recruited Drs Thomas M Ulbright, Oscar W Cummings, and Helen Michael as young faculty members. They had previously trained at Washington University in St. Louis, and have since made significant achievements in the field. I also played an important role in the recruitment of Michael P Goheen as technical director of the Electron Microscopy Laboratory and Charles R Stine as program director of the Pathologists' Assistant Program. A number of our former residents in pathology at IUSM achieved academic distinction at our own or other institutions, including our current departmental chair, Dr Eble, Dr Jeffrey S Warren, Dr Daniel W Visscher, Dr Diane D Davey, and Dr Patrick D Walker.

I have worked with my colleagues in clinical departments throughout my tenure at IUSM, but particularly in the areas of gynecologic oncology and dermatology. Dr Clarence E Ehrlich, a gynecologic oncologist who I first met at Tulane, and I worked on a number of projects, most notably the study of Brenner tumors. I also worked closely with Dr Victor C Hackney, chair of Dermatology, and Dr Arthur L Norins, who later succeeded Dr Hackney as chair. In fact, we studied together for 6 months for the first Dermatopathology board examination. Happily, we all passed the examination.

During my time at Indiana, I observed a number of trends that I did not always initially embrace but eventually decided were inevitable. These include progressive subspecialization in surgical pathology, increasing governmental and organizational regulation, and the demands of complying with clinical protocols.

In 2001, after 30 years at Indiana University, I attained the rank of professor emeritus at Indiana University. I decided that I wanted to continue my research in gynecologic pathology, and I was offered an office in which to continue my work. I also decided to fund a professorship in my name at IUSM. The first holder of the Lawrence M Roth Professorship is Dr Ulbright (Fig. 4). In 2006, the Department of Pathology celebrated its centennial anniversary organized by Dr Eble. Current members of the department and pathologists who had been previously been members of the department or trained here returned for this festive occasion.

Most of my research has been in the area of gynecologic pathology, and I have been particularly



**Fig. 4** Dr Thomas M Ulbright, Lawrence M Roth Professor of Pathology at the centennial anniversary of the department in 2006.

interested in ovarian tumors. The importance of studying the pertinent literature cannot be overemphasized. I have had the greatest personal satisfaction from solving problems relating to histogenesis and classification of tumors. Nomenclature plays an important role in communication and should accurately reflect current knowledge. The applicable terminology should concisely and accurately describe the biologic behavior of the lesion to clinicians and pathologists. As information accumulates about an entity, new terminology sometimes needs to be introduced to reflect current concepts. When I believed it to be necessary, I have attempted to introduce new terminology with varying success. When discussing controversial topics, one should show the utmost respect for colleagues in the field, particularly when there are differences of opinion regarding scientific observations or nomenclature. All discussions should be carried out objectively based on the facts and should never reach the personal level. With regard to one's own practice and research, one cannot underestimate the importance of gaining familiarity with new techniques and understanding their benefits and limitations. One can adopt those that appear promising for one's research.

Nationally, I presented a short course on "Ovarian tumors and tumorlike conditions" at the annual meetings of the United States and Canadian Academy of Pathology from 1976 to 1981 with Drs Steven G Silverberg and William R Hart. In the final course, Dr Ulbright participated.

I was series editor for "Contemporary Issues in Surgical Pathology" published by Churchill Livingstone, Inc, New York, from 1983 through 1997. The volumes were edited by some of the leading authorities in the field. I edited 2 volumes in the series, volume 6 on "Tumors and Tumorlike Conditions of the Ovary" with Dr Bernard Czernobilsky and volume 7 on "Pathologists of Tumors of the Testis and its Adnexa" by Dr Aleksander Talerman and myself [10,11]. Professional collaborations with Bernard and Alek have continued throughout our careers.

I was chair of the Seminar Committee of the Indiana Association of Pathologists from 1976 to 1987. It was an honor to present the 34th Annual Indiana Association of Pathology Anatomic Pathology Seminar on lesions of the ovary with Dr Scully in May 1985.

I was a speaker at a symposium sponsored by the International Society of Gynecological Pathologists on New Techniques in Gynecologic Pathology at the meeting of the International Academy of Pathologists in Miami, Florida, on September 7, 1984. My topic was, "The application of electron microscopy to diagnosis in gynecologic pathology." Dr Daniel J Santa Cruz invited me to be a guest editor with Drs Ulbright and Talerman of an issue of *Seminars in Diagnostic Pathology* on testicular pathology published in November 1987. I was invited by the well-known German gynecologic pathologist, Dr Gisela Dallenbach-Hellweg, to be a speaker at the Robert Meyer Memorial Symposium at the Charité, Humboldt University of Berlin, Germany, on May 16, 1992. My presentation was entitled "Transitional cell carcinoma and Brenner tumors: Relationships revisited." This was a historic time in Germany since the Berlin wall had recently fallen and the country was reunited.

Because of the encouragement of Dr Ehrlich, I participated in the Gynecological Oncology Group from my early days at IUSM until my retirement and was a member of the pathology and ovary committees for many years. On 2 occasions, I was offered the chair of the Pathology Committee, but I declined because of my administrative and service responsibilities at IUSM.

I have served on the editorial board of the *American Journal of Surgical Pathology* since the founding of the journal in 1977 and on the editorial board of *Seminars in Diagnostic Pathology* since it was founded in 1984. I also served in the past on the editorial boards of the *International Journal of Gynecological Pathology*, *Human Pathology*, the *American Journal of Clinical Pathology*, and *Endocrine Pathology*. I am often asked to review manuscripts for other journals and do this whenever possible.

Reviewing manuscripts for journals is an important activity that is not much discussed. Although many investigators regard it as an inconvenience, it is a valuable function in support of the peer-review process. It can also be a learning experience and an aid in keeping up with one's own field of interest. In addition, it can help to improve one's own professional writing to critically examine the work of others. It is important to maintain

objectivity in a review and to allow for the development of new concepts.

After my official retirement from Indiana University, I was invited to serve as coordinating editor for the World Health Organization publication, "Tumours of the Breast and Female Genital Organs." This project was daunting and proved to be even more difficult than I initially thought. I originally was to spend 3 months at the International Agency for Research on Cancer in Lyon, France, but it stretched to 10. The volume was published in 2003 [12].

Professor Peter Russell asked me to contribute an article for a special theme issue entitled "Gynaecological Pathology" of the Australian journal, *Pathology*, that was published in 2007. Alexander Talerman and I collaborated on a publication titled "The enigma of struma ovarii" [13]. The research done for the article led to further studies regarding malignancy occurring in ovarian struma, and Dr Apollon I Karseladze and I described highly differentiated follicular carcinoma arising in ovarian struma, an entity that in some instances has been referred to as peritoneal strumosis, but we consider it to be an example of a malignant neoplasm that lacks histologic features of malignancy and usually cannot be diagnosed until it has extended beyond the ovary [14].

Recently, I have collaborated with Dr Liang Cheng and others, on immunohistochemical and fluorescent in situ hybridization studies of ovarian germ cell tumors, notably dysgerminoma and embryonal carcinoma [15]. The major thrust of my current research is in the area of ovarian stromal tumors, and I am currently doing research on the histogenesis of sclerosing stromal tumor and on the behavior of cellular ovarian stromal neoplasms.

Throughout my professional career, I have greatly benefited from collaborations in research on a national and international level. Many of these were mentioned earlier. I also worked with Frederick A Langley and Harold Fox in Manchester, England, and Drs Ulbright and Michael here in Indianapolis. Although we have not written any articles together because our research interests were divergent, my brother, Irwin, and I have had many fruitful discussions over the years regarding developments in pathology and more recently molecular pathology that have proved helpful in developing new topics for investigation and resolving specific problems.

A lesson learned early in my career was the importance of teamwork. When one first attains an administrative position, it is often necessary to motivate others to work together for the mutual benefit of the group as a whole. This is sometimes not easy and is best accomplished by setting a good example. If possible, one should do a share of the diagnostic work in addition to handling administrative responsibilities, and one needs to set a good example of diligence. Although clinical research has played an important part of my career, the diagnostic service was always my first priority.

In any organization, conflicts will sometimes occur because of limited resources and differing ideas as to the direction in which the department should move. It is



important that any conflicts be resolved in an equitable manner. Internal conflicts can be disruptive for the department as a whole and particularly for the individuals involved. Although one can never be sure of how an individual that one is recruiting will fit in, such should be a major consideration before offering an individual a position. Technicians and secretaries should be highly valued and treated with the utmost respect. They need to be supported when faced with unreasonable demands from others. Teaching medical students, residents, and fellows is of great importance and has always been an enjoyable activity for me.

Maintaining good relationships and an open line of communication with our clinical colleagues is extremely important. Remember, pathologists usually are not directly involved in patient care. One has to recognize the challenges that surgeons, oncologists, and other clinicians face and try to help them as much as possible for the patient's benefit. Try not to let strong personalities and egos interfere with the common goal of optimal patient care. It is also necessary to work together with your superiors, in my case the Departmental Chair, and to foster good relations with other departments. In dealing with a difficult administrative problem, one should try to be as objective as possible and weigh the pros and cons carefully before reaching a decision. When one is not sure how to handle a difficult situation, consultation with a trusted colleague is an important option.

It is worthwhile to maintain good relationships with pathologists in the community and elsewhere. So-called town and gown conflicts should be avoided, if possible, or resolved equably. Throughout my career, I received many cases in consultation and reviewed many outside cases on patients referred to our own institution. When there is a disagreement in diagnosis, one should word the report carefully and diplomatically. Great care should be taken to avoid pejorative or disparaging words or statements. When a case is considered difficult that should be stated in the report. One needs to recognize that as more information accumulates about a patient, a pathologic diagnosis that was not apparent earlier may become clear. In medicolegal cases, where one testifies after the fact, this point is especially important to remember.

In addition to my professional duties, I have always made myself available to supply informal medical advice to my friends and acquaintances and to recommend clinicians whenever asked. Occasionally, patients have located me through my publications and have requested information relating to the pathology and prognosis of unusual tumors.

Sometimes, they requested help in finding an appropriate clinician for their specific medical problems. I have obtained considerable satisfaction from aiding them under these circumstances.

On a more personal note, Ann-Katrin and I have 2 children, Karen Roth Hart and David Josef Roth, and 2 grandchildren, Robert Jonathan and Jason Scott Hart. The support and understanding of Ann-Katrin and our children allowed me to spend many hours outside of normal work time on research projects over the years.

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