

Pediatric Hematology-Oncology

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Introduction

The following narrative represents an attempt to reconstruct from memory and a cursory review of several documents the history of the Pediatric Hematology-Oncology Program at UT Southwestern and Children's Medical Center Dallas during the past 50 years. Some of the specifics may lack accuracy, so readers are encouraged to respond with additions or corrections.

1950s

There was no organized hematology-oncology program at Children's or UT Southwestern during the 1950s. During this period virtually no treatments were available for children with cancer, and most hematologic diseases were poorly characterized. Pediatric hematology-oncology was not a distinct discipline. Most care of affected patients was delivered by general pediatricians, surgeons, radiologists and even pathologists. In fact, the two most prominent pediatric "hematologists" nationally at the time, Drs. Sidney Farber and Wolf Zuelzer, were trained as anatomic pathologists.

1960s

The pediatric hematology-oncology program at Children's had its genesis in the early 1960s. Dr. Teresa Vietti served on the teaching faculty for a year or two before going on to Washington University in St. Louis for her distinguished career in childhood leukemia research. Drs. Joan Windmiller and Joann Whitaker also served as faculty staff. One of the fellows in the early 1960's was Dr. Peggy Sartain, who joined Drs. Windmiller and Whitaker on the faculty (more about her later). By the 1960s chemotherapy had been introduced to treat childhood cancer, but there were few survivors and virtually no research protocols.



Joan Windmiller, M.D.



Joann Whitaker, M.D.



Peggy Sartain, M.D.

Early to Mid-1970s

By the early 1970s, Children's was in its new home on Motor Street, and the discipline of pediatric hematology-oncology was taking form both locally and nationally. Dr. Jo Ann Cornet came from the University of Illinois to join the faculty. Drs. Whitaker and Windmiller left the institution about that time, and Dr. Lon Rogers came on as fellow and then faculty member. However, within several years the lure of dermatology attracted him to a private practice career in that specialty. In those days the hematology-oncology clinic on the second floor at Children's was held in a small, cramped, tile-walled facility four or five mornings each week. It was unavailable in the afternoons since the general surgeons then had their clinic in the same space. Administrative staff consisted of a secretary and part-time social worker.



Jo Ann Cornet, M.D.



Lon Rogers, M.D.

By the mid-1970s the discipline of pediatric hematology-oncology nationally was defined. The American Board of Pediatrics established a sub-board, and a process for formal assessment of fellowship training programs was initiated a few years later.

Late 1970s

Dr. George Buchanan joined Drs. Cornet and Sartain on the faculty in 1977. He trained at Children's Hospital Boston and had particular interest in non-malignant hematology. Programs for children with sickle cell disease and hemophilia were initiated and grew rapidly. Notably lacking from the hematology-oncology program previously had been a focus on clinical research. At that time Dr. Buchanan began programs in sickle cell disease and bleeding disorders which eventually became nationally recognized.



George R. Buchanan, M.D.

Early 1980s

In 1980 Dr. Buchanan was named Division Director by Dr. Heinz Eichenwald, the Department Chair. Dr. Cornet retired in 1981. That same year Dr. Buchanan spearheaded entry of UT Southwestern and Children's into the nascent Pediatric Oncology Group (POG), a National Cancer Institute-supported clinical trials consortium. The timing was good since St. Jude Children's Research Hospital, Stanford, and other previously "independent" centers joined POG at the same time. However, lacking at UT Southwestern in the hematology-oncology program had been a laboratory research component. This was remedied in 1980 by the successful recruitment of Dr. Jonathan Ducore from the National Cancer Institute. He established a research program focusing on DNA repair and its application to the treatment of children with brain tumors.



Jonathan Ducore, M.D.

The early 1980s were also characterized by the development of two fundraising groups which have remained successful and loyal to this day raising money to support cancer research: A Weekend to Wipeout Cancer (later renamed Wipe Out Kids' Cancer) and the Children's Cancer Fund. The former was established by Cindy Brinker, a prominent community leader who had lost her mother to the ravages of cancer and the latter by parents of children with cancer treated at Children's.

The hematology-oncology program also literally moved "up in the world" by securing a new facility on the fifth floor of Children's, supported with funds donated by the Crystal Charity Ball. The area was spacious and nicely met the needs of the program for the next decade.

Mid-1980s

The mid-1980s were a period of rapid growth and increasing regional and national recognition of the program. The translational and laboratory research components of the division were strengthened greatly when Dr. Buchanan and Dr. Joseph B. Warshaw, the new Department Chairman, recruited Dr. Barton Kamen from the Medical College at Wisconsin. Dr. Kamen was widely known as a rising star in the area of cancer pharmacology, especially the development of novel agents to treat acute leukemia. It was the program's good fortune that he brought along with him an outstanding young fellow from Memorial Sloan-Kettering Cancer Center, Dr. Naomi Winick. After spending a year or two focusing mainly on laboratory research, she moved



Barton Kamen, M.D.



Naomi Winick, M.D.

to the clinical realm and, as described later, has over the ensuing two decades become one of the nation's leaders in childhood leukemia research. With generous support from A Weekend to Wipeout Cancer, a formal structured neuro-oncology program was developed under Jonathan Ducore's leadership. However, several years later (1987) Dr. Ducore moved to the University of California at Davis to become its Hematology-Oncology Division Chief.

By the mid-1980s the hematology-oncology program at Children's and UT Southwestern was receiving national notice, not only for its excellence in cancer pharmacology, administrative leadership and sizable patient accrual on POG protocols, but also for its emerging strengths in clinical sickle cell disease research. Much of the success in the latter area was fostered by the critical participation of superb advanced practice nurses, starting with Susan Smith, Betsy Jackson and Becky Morrison, who not only assisted with patient care but also contributed to establishment of patient databases and research projects.

The other major event of the mid-1980s was the establishment of a formal pediatric hematology-oncology fellowship program. The first fellow, in 1984, was Dr. Maxine Hetherington, a former resident. She is now director of the Pediatric Cancer Program at Children's Mercy Hospital in Kansas City. Starting in 1987 the program began taking on two fellows each year.



"Drs. Ducore, Kamen and Buchanan are engaged in exciting research projects they hope will provide some answers to hard questions about childhood cancers. Drs. Ducore and Kamen are heading a brain tumor research project, which is largely being funded by this year's "Weekend to Wipe Out Cancer." In 1983, "Weekend" monies went to a leukemia research project headed by Dr. Buchanan."

The Park Cities News
September 12, 1985

Late 1980s

The late 1980s were times of continued program growth and refinement. By this time the UT Southwestern/Children's program was one of the largest centers with regard to patient accrual in the Pediatric Oncology Group, with Drs. Kamen, Buchanan and Winick serving in major leadership roles. Another strong program component was the data management staff, headed by Bill Chappell, Ph.D. As the conduct of clinical research, especially in the multicenter setting, was becoming more complex with regard to data requirements and regulatory oversight, it was clear that the physicians were ill equipped to meet these mandates by themselves. By the end of the decade the program had one of the two or three most distinguished clinical research infrastructures in the country. These "data managers" were subsequently recognized as professionals and given the title of "Clinical Research Associates." The late 1980s were also a time of increased recognition of the unit's strengths in supportive care, both in oncology (e.g., characterization of the low risk febrile neutropenic patient) and hematologic disorders (outpatient management of febrile infants with sickle cell disease, optimal use of prophylactic penicillin, etc.).



William Chappell, Ph.D.

The late 1980s was a time a major program expansion. Dr. Perry Nisen, Director of Oncology Research at Long Island Jewish Medical Center, was recruited by the new UT Southwestern Department of Pediatrics Chair, Dr. Charles Ginsberg and Dr. Buchanan. Shortly thereafter Anne Bowcock, Ph.D., received her primary appointment in the program. Drs. Nisen and Bowcock had independently funded research laboratories focusing respectively on molecular characterization of brain tumors and neuroblastoma (Nisen) and gene mapping (Bowcock). Drs. James Roloff and Arlynn Mulne also served on the faculty at that time playing clinical roles, but both left the institution within several years.



Perry Nisen, M.D., Ph.D.



Anne Bowcock, Ph.D.

Early 1990s

The decade of the 1990s began with several major program changes. First, Dr. Peggy Sartain announced her retirement after 30 years in the clinical oncology "trenches." Her career was celebrated with much fanfare at a farewell banquet at the Westin Hotel. In 1990 the program moved from the 5th floor in the Ambulatory Building to partially renovated space (formerly "belonging" to cardiology and neurology) on the 6th floor at Children's. The new conference room/library in the clinic was named in honor of Dr. Sartain. Hematology-oncology also was given, for the first time, a dedicated inpatient unit consisting of 24 beds on the 6th floor of a newly constructed patient tower, currently known as Tower C. At this time the program somewhat belatedly initiated a bone marrow transplant program, having recruited Dr. Eric Sandler to direct it. Given these major steps in program expansion, the decision was made during this period to formally designate the Hematology-Oncology Program at Children's as the "Center for Cancer and Blood Disorders" (CCBD).



Eric Sandler, M.D.

The fellowship program also moved to the next level at this time, becoming the recipient of an institutional NRSA T32 Training Grant from the National Cancer Institute, which provided four full stipends for fellows each year. This funding continued uninterrupted for the next 20 years through three competitive renewal cycles. Three new first year fellows now joined the program each year, and a fourth year of training was offered to individuals with promise in clinical or laboratory research. A clinical research career development pathway for fellows was available, but was still somewhat unstructured in a "see one, do one, teach one" mode. Other faculty members coming on board at this time, but then departing a few years later, were Dr. Julie Katz (from Baylor) and Drs. Steve Weitman and Mahmoud Mustafa (both former fellows in the program). During these years the program's contribution to POG clinical trials was at its zenith. A clinical trials consortium was developed with Cook Children's Medical Center in Fort Worth, Texas, and later with the new private program at Medical City Dallas and called the "UT Southwestern Consortium." It ranked number one in patient accrual in POG for a three- to four-year period. Dr. Chappell led the Data Managers Committee and Dr. Buchanan was named chair of POG's Principal Investigators and Lymphoid Relapse Committees. Dr. Buchanan also made an unsuccessful (fortunately, in retrospect!) run for the position of POG Chair in 1993.

Shortly thereafter Dr. Buchanan became a member of the sub-board in hematology-oncology of the American Board of Pediatrics and later was its Chair for three years, during which he also served as leader of the national organization of Pediatric Hematology-Oncology Fellowship Program Directors.

The program gained cohesiveness during this period by administrative restructuring at Children's which allowed for formation of a leadership "troika" consisting of a physician, nurse and operations director. One of the reasons for the program's success at the time and to the present has been the excellent working relationship between Dr. Buchanan and his hematology-oncology leadership partners at Children's.

Mid-1990s

Drs. Nisen and Bowcock left the program at this time to pursue options in industry and at Washington University in St. Louis. However, the program's laboratory component continued, albeit smaller in size, with the expansion of Dr. Bart Kamen's laboratory to include a full time pharmacologist (James Greiner, Pharm.D) and organic chemist (Mary Kinsel, Ph.D.), both of whom were given research faculty appointments. Moreover, by this time, Dr. Gail Tomlinson had finished her fellowship and was developing a translational research program in cancer genetics (with emphasis on renal and liver tumors), as well as assuming the directorship of the Long-term Followup Program for Childhood Cancer Survivors (designated as the "After the Cancer Experience" Program). A young adult program component also came into fruition around this time, under the leadership of Dr. Kevin Oeffinger, a junior faculty member in the Department of Family Practice and Community Medicine, who later received a joint appointment in Pediatrics.

A major step forward during the mid-1990's was an increased focus on children with brain tumors, whose care had previously been directed by a private physician not part of the program. Following Dr. Perry Nisen's departure, Dr. Naomi Winick assumed leadership of these neuro-oncology activities and soon thereafter was recognized for her accomplishments in this area by being named the Lowe Foundation Professor in Pediatric Neuro-oncology at UT Southwestern.

The middle of the decade was also when emerging private competition brought challenges to the program. A group of pediatric hematology-oncology specialists, linked with a large multi-disciplinary adult oncology practice, launched a program at Medical City Dallas. Although it carved out a small "niche" in the metropolitan area, it has never represented a major threat to the program. However at the time, when managed care fervor reached its height in Dallas, there were serious concerns that our program could face major setbacks. The metropolitan area's other private program, at Cook Children's Medical Center in Fort Worth, was less of a competitive threat since it did not attempt to serve children in Dallas and points to the north and east. In fact many of its hematology-oncology specialists have been former fellows in the program, thus ensuring satisfactory relationships between us.

Late 1990s

The late 1990's were a time of major program change. Dr. Bart Kamen left the university to assume the directorship of the children's cancer program at the Robert Wood Johnson Medical Center in New Jersey. However, several important faculty appointments in the clinical realm added strength to the program. Dr. Patrick Leavey came from the University of Colorado (after training in Ireland and Australia) to begin a multi-disciplinary program for children with bone tumors and other sarcomas. Dr. Daniel Bowers – a former medical student and resident at Children's – returned to Dallas after a



Patrick J. Leavey, M.D.



Daniel C. Bowers, M.D.



Victor M. Aquino, M.D.

hematology-oncology fellowship at Johns Hopkins to take over the reins from Naomi Winick in neuro-oncology. Dr. Victor Aquino, previously a fellow in the program, and having served an additional year as bone marrow transplant fellow, assumed directorship of the Stem Cell Transplant Program following Eric Sandler's departure. And finally, Dr. Robert Bash, also a former program fellow who had initially embarked on molecular research involving T-cell leukemia and lymphoma, secured an administrative role in the clinical arena. All four continue on the faculty at present.

The end of the 1990's signaled major changes in national oncology research, with the merger of the four NCI-funded clinical trials group into a new organization, the Children's Oncology Group (COG). Dr. Buchanan served as co-chair of the Constitution/Bylaws Committee and chair of the Nominating Committee charged with identifying the first COG chair. With the oncology component of the program in the excellent hands of the existing faculty, Dr. Buchanan moved his clinical research interests virtually full time to non-malignant hematology.

Early to Mid-2000s

During the first five years of the new millennium, the Hematology-Oncology Program at Children's and UT Southwestern continued on a trajectory towards its desired position as one of the finest of its kind. A number of factors provided momentum. First, the senior administration at both UT Southwestern and Children's continued to exhibit strong support of the program. An example was the relocation of the Center for Cancer and Blood Disorders inpatient service to a 22 bed unit on the 10th floor of the expanded Tower C in 2003. However, the number of beds remained insufficient to fully support inpatient program needs, and the 1990 vintage outpatient clinic in the ambulatory building remains cramped and

congested. The years 2000-2005 also featured an impressive expansion of basic laboratory and clinical research performed by program faculty members. With donations from Children's Cancer Fund and Wipe Out Kids' Cancer – we were able to recruit three outstanding M.D./Ph.D. laboratory scientists from the Harvard system, Drs. Scott Cameron, Matthew Porteus, and James Amatruda. Two of them trained with Nobel Prize winners, and the superb research programs developed locally by each of them – focusing on programmed cell death, gene targeting, and molecular oncology using animal models including worms and zebrafish – helped to propel the program further towards a position of national excellence. In parallel with the strengthening of basic research, hematology clinical research program developed prominence is more than ever on the local and national “maps”. Drs. Charles Quinn, Janna Journeycake, Shelley Crary and Cindy Neunert, all former fellows in the program, received junior faculty appointments and became accomplished clinical investigators in their respective areas of hemostasis-thrombosis and sickle cell disease. All were participants in the American Society of Hematology's Clinical Research Training Institute and were among a select group of young clinical investigators at UT Southwestern designated as “Clinical Research Scholars”.



James F. Amatruda, M.D., Ph.D.



J. Scott Cameron, M.D., Ph.D.



Matthew H. Porteus, M.D., Ph.D.

This period also represented a time of continued growth of the fellowship program, with (in 2005) competitive renewal of the T32 training grant for another five year cycle and recruitment of outstanding fellow applicants through the National Residency Matching Program. In 2005 Dr. George Buchanan stepped down after 20 years as the fellowship training program director, with Dr. Pat Leavey taking the helm. During these years Children's and UT Southwestern maintained a position of preeminence in COG by means of strong patient study accruals well as Dr. Naomi Winick's position as vice-chair for clinical trials in the ALL committee. Drs. Gail Tomlinson, Kevin Oeffinger (who left the program in 2005 to assume a position at Memorial Sloan-Kettering Cancer Center in New York), and Pat Leavey also played major roles in COG research growth. Another major development at this time was the recruitment by UT Southwestern of Dr. James Willson as Director of the Simmons Comprehensive Cancer Center. His arrival in 2004 heralded a major expansion of cancer research and clinical care initiatives on the campus.

With Dr. George Buchanan serving as principal investigator, Children's and UT Southwestern reached the zenith of national recognition in sickle cell disease by being designated in 2003 as one of the 10 NIH-funded Comprehensive Sickle Cell Centers for a five year cycle. Prominent roles were played by Drs. Zora Rogers and Charles Quinn in the design and conduct of national clinical studies involving children and adults with sickle cell disease. During this time the program was also designated by the NIH as one of 17 clinical sites in the new Transfusion Medicine – Hemostasis Clinical Trials Network. In addition, investigator initiated research involving childhood ITP also fostered widespread recognition of the Children's-UT Southwestern hematology program.

2005-2006 to Present:

At this writing (May 2011), most would agree that the hematology-oncology program at Children's and UT Southwestern remains nationally preeminent, as measured by clinical care, publications in peer reviewed journals, and externally funded grants. The program ranks nationally on virtually everyone's “top 20” list and in some areas is among the top ten in the country. Within the next decade there is no reason that the program – like UT Southwestern and Children's as a whole – cannot achieve its goal of becoming among the world's finest.

The past five to six years have been highlighted by impressive program growth involving facilities expansion, recruitment of additional faculty, and implementation of new clinical and research programs. In late 2006 and early 2007 it was recognized that expanded outpatient CCBD facilities were required. Children's Board subsequently approved temporary relocation of the outpatient clinic to the third floor of the Bright Building, and we moved there in December 2007 following renovation of space formerly occupied by the ENT clinic. This provided to the CCBD a facility nearly three times as large as the space which they occupied since 1990, including separate clinic areas for oncology and hematology, new procedure rooms, and common waiting room and infusion area. Thanks to efforts by Children's Development Office and others in senior leadership positions, a commitment was made by the Pauline Allen Gill Foundation and several other major donors to support, design, and construction of an entirely new inpatient and outpatient facility for the hematology-oncology program, with ultimate plans for both the inpatient and outpatient components to relocate to and consume the entire 6th floor of the main hospital complex, encompassing the B, C, and D towers. This construction has progressed in several stages, with the opening of a 24 bed inpatient unit in Tower D in the summer of 2009. This facility includes 12 rooms especially designed for children receiving hematopoietic stem cell transplantation. With the usual inpatient census of 30 to 35, CCBD patients are also hospitalized on other floors, pending construction of an additional 10 beds in a renovated Tower C (expected to be available by 2014). This facilities expansion project will also include a new outpatient clinic in Towers B and C, for which construction began early in 2011. Ultimately, the new outpatient unit, with 20 examination rooms, a procedure and recovery area, pharmacy, and

satellite laboratory will be accompanied in Tower C by additional inpatient beds and a spacious day hospital/infusion area and expanded registration area and waiting room. The final stage of the construction will add administrative space and a new conference room. When completed the CCBD facilities will rank among the finest in the world.

The other new facility supporting the hematology-oncology program is Children's Medical Center at Legacy, 25 miles north of the main campus in suburban Plano. Hematology-Oncology elected to serve as an "anchor" program, and outpatient activities began there in 2007 and inpatient services in January 2010. At present, the Legacy hematology-oncology program –integrated fully with the program in Dallas – is staffed by four full time clinical faculty members (each of whom practices on the Dallas campus as well), and presently accounts for approximately 3,500 patient visits annually.

During 2006-2011 the number of full time hematology-oncology faculty members ranged between 25 and 30. Several key faculty (Drs. Scott Cameron, Matthew Porteous, and Charles Quinn) left the program during 2010, but we were fortunate in recruiting new colleagues, including Dr. Andrew Koh to direct the Hematopoietic Stem Cell Transplantation program in its new Tower D6 facility. Additional faculty have recently been recruited by Dr. Koh, and the transplant program has rapidly expanded in size and scope to become a regional center of excellence. The oncology component of the CCBD remains large and strong, with a record 325 new cancer patients being diagnosed and treated during 2010. The program ranked number 16 in the United States during 2010 by U.S. News and World Report, the highest position of any medical specialty program at Children's. Given the large population growth in the metropolitan area, it is anticipated that patient numbers will continue to rise in hematology as well as oncology, providing clear justification for facility expansion and faculty growth. Also fostering the pediatric cancer program's excellence has been formal designation of the Simmons Comprehensive Cancer Center at UT Southwestern by the National Cancer Institute. Children's CCBD therefore is the only NCI-designated pediatric cancer center in North Texas. Another major program enhancement was the recent formation of the Cancer Prevention and Research Institute of Texas (CPRIT) which provides millions of dollars of funding for cutting edge clinical and laboratory investigation involving cancer performed by faculty members. The hematology component of the CCBD remains strong as well, despite reduced funding from the NIH as a result of termination of the Sickle Cell Disease Centers program in 2008. Fortunately, active participation in other collaborative multicenter clinical trials involving sickle cell disease has kept the program visible on the national scene.



Andrew Koh, M.D.



George R. Buchanan, M.D.

As the second decade of the 21st century begins, new hematology-oncology leadership plans are being formulated. After 30 years, Dr. Buchanan has elected to step down as Division Director, and a national search has identified a highly qualified successor who will move the program forward to become one of the most distinguished in the nation, if not the world, during the decade ahead. Dr. Buchanan will remain on the faculty, with increasing focus on teaching, mentoring, clinical research, and patient care. There will be many challenges in view of major changes in the overall national healthcare landscape, alterations in trainee work hours, and other financial and logistical barriers. However, the outstanding faculty, support staff, and overall environment in the Department of Pediatrics and at Children's Medical Center will assure continued program excellence during the years ahead.