Where Have All the “AIDS Babies” Gone? 
A Historical Memoir of the Pediatric AIDS Epidemic in New Haven and its Eventual Eradication

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S.L. was one of our first HIV-positive babies. He was born at Yale-New Haven Hospital (YNHH) in 1982. His mother was a sex worker who also injected drugs. He died at 3½ years following multiple episodes of opportunistic infection and metastatic lymphoma. In the years between 1986 and 1990, 163 HIV-positive mothers gave birth at YNHH. The mother-to-child transmission (MTCT) rate was 20 percent. Women represented 8 percent of all HIV cases in the US compared with 29 percent in New Haven. We had a six times greater proportion of children living with HIV. The mean number of HIV-exposed babies rose annually from 26 (1985-87) to 37 (1988-90). Our first team of caregivers comprised a nurse practitioner, a social worker, and me. We were, in time, joined by a growing number of colleagues. Enlightened and generous hospital administrators provided us with outpatient space and the promise of continued funding to support additional staff and in 1987, an independent Pediatric AIDS Care Program. We implemented the proven MTCT prevention guidelines articulated in the Pediatric AIDS Clinical Trials Group (PACTG) protocol 076 and by 1995, the MTCT rate at YNHH fell to 9 percent. Since 1996, the MTCT rate at YNHH has been zero percent. Combination antiretroviral therapy, cART, made its debut in the mid-1990s; five classes of drugs with multiple agents in each were licensed between 2003 and 2013. We designed individual treatment plans for each child and gradually entered an era when our clinic was populated with healthier long-term survivors. Our Program flourished, based on a multidisciplinary approach which honored interprofessional collaboration.

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Abbreviations: cART, combination antiretroviral therapy; CDC, Centers for Disease Control and Prevention; FDA, Food and Drug Administration; LTS, long-term survivors; MTCT, mother-to-child transmission; LIP, lymphoid interstitial pneumonitis; PACTG, Pediatric AIDS Clinical Trials Group; YNHH, Yale-New Haven Hospital; ZDV, zidovudine; CHA, Connecticut Hospital Association

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Note from the Author: All information, unless otherwise indicated, is culled from personal notes taken during lectures, seminars, or conversations. Some statistics are from unpublished pamphlets disseminated by local and state public health offices, and items in the medical literature, some of which are listed at the end of this memoir.
I. THE SHORT TRAGIC LIFE OF A NEW HAVEN AIDS' BABY AND THE START OF OUR MISSION

On the morning of January 15, 1985, a jolting banner headline appeared on the front page of the Journal-Courier (New Haven, Conn., 1973-1987): “Candida Lawler dies; autopsy due.” The newspaper’s publishers understood that their readers were already familiar with Ms. Lawler’s story; articles revealing her identity had been published in the New Haven Register as early as February 1984 [1]. Her story received national attention when the CBS television news magazine, 60 Minutes, revealed grave concerns about Ms. Lawler, a 29-year-old woman living with HIV, and whether she and others who were similarly afflicted, should be quarantined. City officials believed that their isolation would stanch the spread of deadly infection during high risk sexual liaisons with sex workers and sharing syringes during illicit drug use.

Shawn, Ms. Lawler’s son, was one of our first three “AIDS’ babies” and the earliest to whom that label could be applied with certainty. He was born in September 1982, and spent the first 2 months of his life withdrawing from heroin and methadone—drugs that had traversed the placenta.

Ms. Lawler had what are now known as significant risk factors for people living with HIV/AIDS, including drug use and engagement in sex work. Rehabilitation efforts had failed. At the time of her premature death from AIDS-related pneumonia, the Journal-Courier mourned the “once vivacious and beautiful woman with long black coal hair…who now appeared aged and emaciated.”

She might well have been designated New Haven’s “Patient Zero," the first publicly-named and shamed AIDS patient in the Elm City. However, a search of the medical records at Yale-New Haven Hospital (YNHH) would have revealed names of at least a dozen additional patients living with HIV. Lawler was one among many women living with HIV, but mother-to-child transmission was not yet widely recognized as a possible outcome of maternal infection. At age 2½ months, Shawn recovered uneventfully from a bout of bronchiolitis, but was re-admitted 5 months later, lethargic, malnourished, and covered with a disfiguring purpural rash. He had hepatosplenomegaly and marked lymphadenopathy. His discharge diagnoses included disseminated meningococccemia and failure-to-thrive. Months later, he developed intractable oral thrush and candida diaper dermatitis. He had suffered hair loss, seborrhea, and eczema. He was thinner. These striking clinical signs, particularly his multiple infections and skin diseases, ultimately suggested an immunologic deficit. A comprehensive diagnostic work-up was undertaken. Abnormal numbers of “atypical lymphocytes” were found in his blood and he failed to respond to skin test antigens. Lymphocyte subset enumeration revealed far too few CD4+ T cells, an aberration shared with his mother. We had recently learned that these abnormalities were characteristic of a new disease, referred to by some as “GRID,” or “gay-related immunodeficiency disorder,” “the gay plague.” In the early 1980s, the disease spread among men who had sex with men and intravenous drug users, including women. We wondered whether Shawn, a toddler, was similarly affected. Did Ms. Lawler pass HIV to her baby during pregnancy, at the time of birth, or perhaps, post-partum through breastfeeding.

Ms. Lawler’s blood was send to Max Essex’s lab in Boston. He had developed a test for human T-cell leukemia virus III, HTLVIII, the name of the virus thought to be the cause of the world’s newest immunodeficiency disease. Ms. Lawler carried antibodies to HTLVIII. (HIV was the name later assigned by an international congress.) Shawn’s blood came the same antibodies. Initially, we were unable to determine whether his antibodies were acquired from his mother in utero or were raised actively in response to his own infection.

Shawn followed an insidious downhill course, common in the early years of the epidemic. There were no antiretrovirals and few drugs to treat some of his multiple infections. At 9 months of age, Shawn was admitted to the hospital in respiratory distress. His chest X-ray revealed many large nodules and impressive mediastinal lymphadenopathy. Cultures for the usual suspects were negative, but a lung biopsy showed evidence of lymphoid interstitial pneumonitis (LIP), an entity only rarely reported in adults and almost never in children. LIP was, for the first 10 years of the epidemic, the most common AIDS-related illness in the pediatric population, an ominous predictor of advanced HIV disease. Nevertheless, it responded temporarily to steroids and during his second year of life, Shawn gained some weight, was less breathless and more playful.

Shawn presented with weakness of his left hand and face at age 21 months. A CT scan of his head revealed a mass lesion deep in the midbrain. Normal bone marrow was replaced by a B cell lymphoma. Several courses of chemo- and radiotherapy stabilized his condition for almost a year, during which time he had separated a crib in an isolation room with other infants infected with HIV. The final event was an unrelenting metastatic infection with Mycobacterium avium intracellulare (MAC), resulting in grotesque enlargement of his regional lymph nodes, liver, and spleen. Standard anti-infective agents and two experimental drugs donated by the CDC, ansamycin and clofazimine (neither of which is currently used), did nothing to change the course of the infection. Shawn died at 3½ years of age.

HIV-infected babies began to appear regularly in the emergency room and various clinics. The obstetricians
were caring for ever-increasing numbers of women testing positive for HIV. In New Haven, the mean number of HIV-exposed babies rose annually from 26 (1985-87) to 37 (1988-90). In fact, 20 percent of all babies born to mothers testing positive for HIV were also testing positive and in immediate need of complex and prolonged interdisciplinary care. We had moved into crisis mode.

Simultaneous with our need to devise an effective intervention, I had my first triennial leave, a mini-sabbatical during which I could devote myself exclusively to learning more about HIV and AIDS. Previously, I had been involved in research studying the ways in which the Epstein-Barr virus displayed its pathology in both healthy and immunodeficient children. But now we were witness to the debut of a novel disease caused by a puzzling new virus, one that snared mothers and infants, in addition to men. New diseases weren’t being seen that often—a rule that seems to have been broken with some frequency of late (viz. Zika, West Nile, MERS, SARS, COVID-19). I reasoned that this was my chance to enter a challenging clinical arena on the ground floor, to make this growing plague the center of my academic focus moving forward.

Descriptions of pediatric AIDS came to us from the earliest epicenters as graphic retrospective reports. Four of the “hot spots” were cities with large indigent populations, people who used drugs, men who had sex with men, and some of their female sex partners: New York City, Newark, San Francisco, and Miami. The majority of babies were infected intrapartum with infectious blood and genital secretions, less so in utero.

At the start of my explorations, I sought allies who could show me the ropes, introduce me to a few patients, and teach me some of the relevant clinical science. None of my usual teachers in the Pediatrics Department could help because they knew no more than I did, having read a few articles and listened to ominous stories on the news. So I made inquiries of colleagues in the Department of Internal Medicine who had been caring for most of the patients. They all came up with the same name, Leetha Fraulino, APRN. I was surprised to learn that Fraulino was a nurse practitioner who had come to YNHH from her previous position as a clinician with the Greater New Haven Visiting Nurses Association. Among her clients in the community were a handful of adult AIDS patients, some of whom had already spent some time in the hospital and some who were safely managed at home. She recognized the need for a place where the growing number of patients living with HIV could be followed in specialized settings, where they could receive both medical and much-needed psychosocial support. She imagined a place where preventive and supportive care, that included access to good nutrition and decent housing, would forestall the need for visits to the emergency department that frequently ended in moves to the ICU.

Hospital administrators, alarmed by the increasing numbers of uninsured, critically ill patients and the uncompensated costs incurred in their care, agreed to give Fraulino access to a few examining rooms in one of the ambulatory clinics for one afternoon a week. She was acquainted with many of her former clients and agreed to have me join her on her daily rounds. We reviewed X-rays, checked the results of laboratory tests, and shared insights we had gathered from the patients with the residents and nurses, including details of each one’s social situation, and relationships with significant others and family. Having anticipated a surge of HIV-positive babies, Fraulino welcomed the chance to have a pediatrician as her ally. We were among the first troops on the front lines, joined in battle against a powerful new foe. I was hooked and my professional life was forever changed.

II: RISING NUMBERS PORTEND A GRIM FUTURE

The histories shared by most HIV-positive mothers and their female kinfolk indicated that their babies had been born into “at risk families.” About half the mothers had used intravenous drugs which they often shared. Some were sex workers and still others reported that they did not consume illicit drugs but had had sexual relationships with men who had. Babies born addicted to drugs were immediately transferred to hospital units that were specially equipped to care for these irritable, tremulous, jittery newborns who sometimes spent weeks or months in isolettes at a distance from bright lights and disturbing sounds. They were swaddled and received round-the-clock feedings on demand.

Among a series of impediments, we faced one insurmountable problem: we were not able to discharge HIV-exposed babies to the care of mothers still battling addiction; and experienced foster parents refused to take “AIDS babies” into their homes for fear of infection. There was only one alternative—the nurses, doctors, and social workers became their de facto guardians. The babies stayed in the hospital for months, sometimes for more than a year.

In the early 1980s, we cared for an average of 26 HIV-exposed infants, born each year to HIV-positive mothers. We were obliged to track down a group of persons connected to each index mother, e.g. current and former sex partners, people who injected drugs, and older children. We invited them to meet with us to learn of their infection status. These meetings were long and excruciating. Most of the contacts never imagined they might be carrying HIV, complicated by the fact that they might have already spread the virus to unknowing partners. They all needed to be directed to healthcare centers—destinations other than emergency rooms or
“walk-in” clinics. Those with substance abuse disorders were transferred to drug rehabilitation programs. Women were given appointments with gynecologists who would provide access to birth control, cancer screenings, and treatment for sexually transmitted infections. We helped the homeless mothers, rejected by their families, to find housing and food stamps.

By the mid-1980s, we had access to reliable antibody assays and both antigen and nucleic acid-based tests that allowed us to measure accurately the present status and arc of the epidemic in children and women of childbearing age. We compared the demographic features of HIV infection in New Haven with the state of Connecticut and the entire country. We learned that New Haven was different! Cumulative data through December 1986, revealed that women represented 8 percent of AIDS cases in the US compared with 29 percent in New Haven.

Similarly, children represented 1 percent of all national cases compared with 6 percent of our local cases. New Haven had more than double the proportion of infected drug users compared with the rest of the country. In 1989, the Connecticut Department of Public Health reported that one in every 33 African American women giving birth in New Haven was HIV-positive, a proportion twice that of all women giving birth in the state, regardless of ethnicity. National statistics revealed that Connecticut ranked fourth per capita in the incidence of AIDS in women and first per capita in the nation in the incidence of AIDS in children. Intravenous drug use by the mother or her partner was the risk behavior that precipitated infection in 87 percent of the babies. In the US, the majority of patients were white (60% white, 38% Black and Hispanic) whereas in New Haven, HIV infection was far more common in people of color (61% Black, 14% Hispanic, 25% white and other). We lived and worked in a small American city (population estimated 125,000) with a disproportionate onslaught of AIDS. We were crippled by a dearth of antiretrovirals and effective anti-infectives for many of the opportunistic infections. We needed more clinicians and financial aid to support our efforts.

III. THE TEAM GATHERS STEAM AND BENEFACTORS COME TO OUR AID

Slowly, providers with a multiplicity of skills emerged from their quotidian workplaces and asked Fraulino and myself if they could help. June Holmes, MSW, was one of the first to volunteer. She already knew some of the patients through her work in other parts of the hospital. Like Fraulino and me, she believed she would be most effective if she could serve our patients even before they were hospitalized and, again, at time of discharge. Continuity of care was paramount, starting with the trust built during the first encounter, whether in the community, clinic, or hospital.

Physician specialists volunteered to help us in the clinics. They knew that AIDS was a growing epidemic, that they would soon be called upon. They wanted to be well-prepared, knowing they would become the teachers, transmitting their knowledge to the junior troopers who were gathering close behind. Well-concealed beneath the armor of denial and girded by their selfless efforts, there was sometimes a gnawing worry about the possibility of getting infected with HIV by accidental needlestick, a saliva or vomit-laden splash, perhaps by a urine, fecal, or blood-soaked bed, or maybe a bite or scratch by an agitated patient. (Other than by sex or needle-sharing, the risk posed by other behaviors or body fluids was still unknown.)

YNHH, the academic epicenter of medical care in southern Connecticut, was committed to serving the entire population of New Haven and the surrounding towns. Its promise of excellent care for all who presented themselves was being challenged by the financial burdens incurred in caring for those who required costly emergency and prolonged intensive care. Our team was called upon to educate an already receptive hospital administration. We were invited to present the facts of the epidemic, in all its alarming detail, to the hospital Board of Trustees. We reminded them that the uncontrolled demand for expensive care could be mitigated by creating a program devoted to longitudinal outpatient care for both adults and children, similar to those for patients with other chronic diseases. The caregivers would forge trusting relationships with their patients in a way that would ensure adherence to care and stimulate the creation of individualized care plans. We would introduce new treatments as soon as they became available. The social workers would focus their efforts on the financial, nutritional, and housing needs of the patients. Timely arrangements could be made for in-home nursing care. We would strengthen the education of parents, spouses, friends, and neighbors.

Our first formidable ally was Dr. John Fenn, a surgeon and the hospital’s Chief of Staff. He had heard of our work and already learned a bit about the clinical aspects of AIDS. He knew that the hospital was carrying a heavy burden and that babies and toddlers were beginning to fill isolettes in the nurseries and cribs on the wards. Dr. Fenn invited himself to make rounds with us a few times a week. He was deeply affected by what he saw and heard. After scrubbing, gowning, and masking, he would sometimes sit on the bed listening to patients’ stories. He thanked Fraulino and me and commended us for keeping abreast of every patient’s status and carried these stories and descriptions of our daily routines to the hospital president, the chairmen of Internal Medicine, Pediatrics, Obstetrics and Gynecology, and the Vice President for Nursing. In the wake of these meetings, Fraulino and I
met with the same leaders to provide first-hand accounts in all their startling details. We made clear our need for funding and asked for official promises by the hospital and medical school to establish an AIDS Care Program, in perpetuity, dedicated to the ongoing outpatient and inpatient care of HIV-infected patients of all ages.

We believed that health professionals on the front lines could be effective only with generous private and public support and the backing of two superlative academic institutions—YNHH and Yale Medical School. At the insistence of two successive Chairs of Pediatrics, Doctors Howard Pearson and Joseph Warshaw, the hospital agreed to support half my salary. The Pediatrics department would contribute much of the remainder to support my teaching efforts and a small percentage of my ongoing research projects. In a letter written in January 1988, Dr. Fenn agreed to relieve me of some of my responsibilities in the adult AIDS effort, by funding two new half-time physician slots. Both these physicians would serve the rapidly expanding adult population and I would be allowed to spend more time with the children who were HIV-positive and their families. The Hospital also assigned us pediatric clinic space for one, and then two afternoons a week. Full time RN and social service positions were added to the mix. Dr. Fenn penned an official note to Dr. Warshaw that fully acknowledged the work that Fraulino and I had already done. He wrote the following: “The goal in the recent expansion of the Program was to allow Warren Andiman and Leetha Fraulino some relief from their extraordinary burden and to make sure that the Hospital was supplying resources commensurate with the magnitude of the epidemic facing us. I am comfortable that we are doing our part and that we have now provided Dr. Andiman with the help he most certainly needed and the opportunity to engage in other academic activities.”

YNHH serves the entire city of New Haven, and with the University they are the city’s largest employers. As such, the hospital and medical school are obliged to foster cordial relations with the city’s leaders and provide them a voice in its stated missions. To keep these leaders apprised of the magnitude and severity of the “AIDS problem,” G. Harold Welch, the president of the Hospital, invited me to meet three city aldermen. After the dinner meeting, he wrote: “The three aldermen who attended are all members of the YNHH Board of Trustees.” The meeting was designed to foster “helpful communication between the city’s leaders, their constituents and the hospital. The hope was that the city would take appropriate action in the future.”

It did, in fact, “take a village” to support our Program and keep its accomplishments in the public eye. The media started to take increasing interest in our work and in the changing state of the epidemic. Fraulino and I were interviewed on multiple occasions for articles in The New Haven Register, the New Haven Advocate, Channel 8, the local TV station, and a few radio shows. I remember a few occasions when we chided reporters for having portrayed our patients in a light that may have stoked fear and derision among news consumers. It took some time to sensitize the media and other people of influence. In time, the Hospital’s Board of Trustees gave the go-ahead for the “official” creation of the “AIDS Care Program.” Soon the City of New Haven and local charitable organizations joined us in common cause.

Fraulino, now the AIDS Program Coordinator and Clinical Supervisor and B. Joyce Simpson, RN, MPH, once described in great detail the institutional response to the AIDS epidemic, using YNHH as the paradigm. They reminded us that public teaching institutions are responsible for making subspecialty expertise and state-of-the-art technology accessible to the public and local community needs and providing treatment with new antiretrovirals and anti-infectives. Fraulino continued to see all the adults and children with AIDS-related diagnoses and introduced me to them as the Medical Director. She assessed their needs and assisted patients and their families to gain access to necessary support services. She participated in discharge planning in conjunction with the nursing and medical staff and developed a long-term plan for each patient. She organized the outpatient clinics and acted as the primary liaison between the inpatient and outpatient settings. In response to a growing patient population, the hospital mounted a second phase of planning. Over the course of a year, we were introduced to additional subspecialists, with either adult or pediatric credentials. Simpson became our Pediatric Research Nurse and Pediatric AIDS Program Coordinator. She collected, organized, and analyzed data that fulfilled the specific aims of our various grants. We also welcomed an educator with a graduate degree in public health who oversaw HIV testing and counseling services and two HIV counselors with backgrounds in nursing. The social workers guided families through the onerous process of applying for entitlements, including Supplemental Security Income (SSI) and Medicaid. Finally, we developed cordial relationships with allies from pediatric and adult psychiatry, neurology, surgery, the Chaplain’s office, the Child Life Program (evaluates developmental milestones and provides play therapy), Nutritional Services, Respiratory Therapy, and Pharmacy.

The team recognized the importance of establishing collaborative relationships with community-based agencies and organizations. We were living in the midst of a public health crisis and we saw ourselves as the catalysts for change. Either individually or in pairs we educated leaders in the Visiting Nurses Association, the methadone maintenance programs, the Department of Children and
Families (DCF; formerly DCYS, Department of Child and Youth Services), community AIDS support groups, like AIDS Project New Haven, churches sympathetic to our philosophy of care, Connecticut Hospice, and other long-term AIDS residency facilities. The collaborations resulted in improved care and a modest reduction in costs that would otherwise have been borne by the Hospital.

**IV: AN INDEPENDENT PEDIATRIC AIDS CARE PROGRAM: BIRTH, GROWTH, AND DEVELOPMENT**

The pediatric AIDS epidemic in New Haven grew at an alarming rate. Along with the HIV-positive babies, who constituted 20 percent of our patient population, we decided early on to continue to follow, temporarily, the 80 percent of babies who had been exposed to the virus but were uninfected (some 130 infants by 1990). We had to guarantee their safe release either to their biological mothers or to foster parents, often close relatives. We found placements for those “new” mothers who required drug treatment and safe housing. The early development of the now independent pediatric program mirrored in many ways the genesis of the adult program. Therefore, we were not surprised when a willing group of talented, motivated, and energetic health professionals with diverse skills asked if they could help. We found assignments along the entire spectrum of their training—attendings, residents, post-docs, RNs, APRNs, social workers, nursing, and medical students. At the beginning, few of these assignments were designated as “official” and none was accompanied by bonuses or special treatment. These were professionals who incorporated their work with HIV-positive children into elective slots or a variety of required outpatient rotations.

By 1990, the Hospital recognized the need to split the AIDS Care Program in two: an adult medicine arm and a pediatric arm. It was obvious that the number of patients needing urgent care was growing too rapidly to remain under the aegis of one medical director who had other clinical, research, and teaching obligations. Also, my training as a general pediatrician with expertise in infectious diseases was no longer a good match for the enormous challenge posed by a population of seriously ill adults with life-threatening diseases and chronic conditions. The Hospital set out to hire two experienced, well-rounded primary care physicians to lead the adult program.

**Foster Care**

Most of our HIV-positive children had challenging home lives, including difficulties accessing food, transportation, and decent living conditions. Their lives were chaotic, lonely, and stressful. Some had already lost family members to AIDS and others faced the possibility of a parent’s incarceration or hospitalization. Following years of reluctance on the part of “professional” foster parents to bring babies living with HIV into their homes, we joined with the Connecticut State Department of Social Services and rolled-out intensive educational programs that featured infection control guidelines. The State increased payments to cover the costs of fostering a fragile, chronically ill child. These inducements encouraged some foster families to care for “AIDS babies.” For the most part, these placements proved to have positive outcomes. There were impressive gains in growth and development and increased adherence to clinic visits and prescription refills. The number of hospital “boarder babies” slowly decreased and by 1989, fell to zero. Sometimes the child remained in foster care temporarily, until the mother was released from prison or committed to a drug treatment program. Adequate housing was required for family reunification. Remarkably, some foster families adopted the children they had nurtured so successfully.

**Education**

The minority of HIV-infected children who reached school age, were consigned to a space in the basement of a municipal building and were “taught” by someone with little or no requisite educational background or training. No classroom in New Haven’s public schools found space for a child living with HIV. The task of righting this discriminatory practice fell to the Pediatric AIDS Care Program. Our nurses, social workers, and I became community educators whose principal goal was to share the evidence that HIV is not spread by casual contact and that minor incidents of bleeding, spitting, urinating, and even biting, could be managed by the simple application of standard precautions: gloves, soap and water, and the prudent use of diluted household bleach, as needed. At some point, as the abysmally inadequate education of our patients was deemed untenable, I was asked to serve as...
an expert witness in a complaint brought by the American Civil Liberties Union against the City of New Haven. Based on the preponderance of the scientific evidence and the recognition that the children were being discriminated against on the basis of physical disability, a clear violation of the American Disabilities Act, the presiding judge found in favor of the right of HIV-positive schoolchildren to an education equal to their same age peers. As a result, our children gained admission to the city’s classrooms with the promise that only the child’s teacher, the school nurse, and the principal would be informed of the student’s HIV status, an important concession that became operative in instances of accident or emergency.

**V: THE 1990s: A DECADE OF WONDROUS LIFE-SAVING EVENTS**

**Pediatric AIDS Clinical Trials Group (PACTG) Protocol No. 076**

The most basic principle of public health, prevention, had not been fulfilled. We were treating disease but not preventing it. The FDA approved the use of zidovudine (ZDV, AZT) to treat advanced HIV disease in adults. But we learned that ZDV, the first in a new class of drugs, reverse transcription inhibitors, provided only short-term survival advantage and its benefits lasted only a few months. Despite these disappointments, we convinced some of our pediatric pharmacists to create a syrupy concoction of ZDV powder that could be fed by mouth to infants and toddlers. (Once a drug is licensed, it can be used off-label if prescribers believe that the benefits outweigh the risks.) We knew of only two adverse reactions, mild anemia and liver dysfunction and monitored both by doing periodic blood tests that led to a change in dose or discontinuation of the drug, if necessary. As in adults, ZDV treatment resulted in only temporary clinical improvement—weight gain, greater alertness and activity level, and fewer life-threatening infections. Within a few years, the FDA approved the use of ZDV for children. We were buying time in the hope that more effective antiretrovirals would arrive.

Clinical relief is not prevention. Fifteen to 20 percent of HIV-positive mothers were still transmitting HIV to their offspring and with some exceptions, the infected babies died before the age of 5 years. Nevertheless, we witnessed a veritable miracle in 1994, when the results of the NIH-funded study, PACTG Protocol 076 was published. Until that time, strategies for reducing the risk of vertical transmission of HIV were limited to the avoidance of pregnancy altogether or refraining from breastfeeding, which was the most common cause of postnatally-acquired HIV. The double-blind placebo-controlled study, PACTG 076, investigating the effects of antiretroviral therapy during pregnancy, was initiated in 1991. The regimen was comprised of antepartum ZDV, given orally 5 times daily, starting at 14 to 34 weeks post-conception and continuing through the remainder of the pregnancy. ZDV was also administered to the mother intravenously during labor and delivery. The newborn received oral ZDV syrup, beginning at 12 hours postpartum and continuing every 6 hours for the first 6 weeks of life. Periodic HIV cultures were done to distinguish between infants infected in utero and those infected intrapartum or postpartum. Based on data derived from the 364 mother-infant pairs who completed the study, ZDV treatment was associated with a 68 percent reduction in MTCT (8% in the treatment group vs 26% in the placebo group). The drug regimen was well-tolerated. When the study results were published, the CDC recommended that the protocol be applied universally to all HIV-positive pregnant mothers. As per the CDC recommendations, we implemented the 076 protocol and by 1995, the MTCT rate at YNHH dropped to 9 percent, half the rate we witnessed previously.

Simpson, our pediatric research nurse made herself available, even at night, to attend the delivery of every HIV-positive mother. She guided the nurses and mothers through the steps of the PACTG 076 protocol. She met with each mother and learned about her social support system and living situation. She discovered whether there was money to buy formula, diapers, and clothing. The mother received her first 2-week appointment to the pediatric HIV clinic and a prescription for her child’s ZDV syrup. Before hospital discharge, the nursing staff judged whether the mother could provide a safe home for her baby.

**Combination Antiretroviral Therapy, cART, Makes a Debut**

The side effects associated with ZDV were easily managed, but the inevitable appearance of resistance convinced us that additional antiretrovirals were needed to use in combination with ZDV. Combination treatment met its earlier success with regimens for tuberculosis and subsequently, for other complex infections and cancer chemotherapy, diseases in which drug resistance had been a significant obstacle to cure. We participated in large multicenter clinical trials assessing the utility of combining non-nucleoside reverse transcription inhibitors (NNRTIs), e.g. nevirapine, with a growing number of newer nucleoside reverse transcriptase inhibitors (NRTIs) e.g. lamivudine. In time, the protease inhibitors, entry/fusion inhibitors, and integrase inhibitors were licensed sequentially in the decade between 2003 and 2013. Drug side-effects and resistance demanded that we follow the children closely and prepare to intervene with either temporary or permanent alterations in individual drug regimens. In good time, we witnessed varying declines in
viral loads and rises in CD4+ T-cell numbers to more normal levels. Many of the children felt better and returned to their regular activities, including school attendance.

As with adults, combination therapy with an ever-increasing number of agents, altered forever the natural history of pediatric HIV infection, changing it from a rapidly fatal to a chronic, manageable disease, including for some who had survived beyond early childhood. Despite these gains, our pre-eminent wish remained unshaken, i.e. to eradicate MTCT of HIV, a goal that would prevent the life-long morbidities and suffering that accompany pediatric HIV infection and its attendant limitations and stigma.

The State Legislature Votes in Favor of a Controversial Preventive Intervention

The PACTG 076 protocol, when practiced consistently, proved to be a lifesaver. For all mothers at risk who sought prenatal care and were not already being treated with antiretrovirals, HIV testing was offered. If the test results were positive, simple drug regimens were prescribed along with intensive counseling and admonitions to adhere closely to the instructions for drug compliance.

HIV care and obstetric care were linked. When close to term, the mothers were given explicit instructions to appear early in labor, so that ZDV could be administered intravenously before their baby’s birth. But routine HIV screening was not yet part of obstetric care and it soon became obvious that we were missing some women at risk: those who failed to receive prenatal care and those who did receive care but whose HIV infection status was unknown or not recorded. We posed an audacious question: Shouldn’t HIV testing be a mandatory part of obstetric care? In the early years, HIV testing was permitted only after a counseling session and signed consent.

Times change. Connecticut Public Act No. 99-2 became law on October 1, 1999 after much contentious opposition mounted by the Connecticut Civil Liberties Union Foundation, the Connecticut Hospital Association (CHA), and by editorials and harsh opinion pieces in local newspapers. The first part of the law read as follows: “(a) Each healthcare provider […] shall inform [pregnant women] […] that HIV testing is part of routine prenatal care and shall inform her of the health benefits to herself and her newborn of being tested for HIV infection. Such information shall be conveyed along with the counseling required […]. If the patient provides informed consent […] the health care provider […] shall perform or arrange to have performed an HIV-related test and document the result in the medical record […] either before delivery or within twenty-four hours after delivery and, in the absence of specific written objection, shall cause such test to be administered […] to every such infant […] consistent with any applicable confidentiality requirements [2].”

The parties expressing vehement objections argued that administering HIV tests by way of blood draw to newborns, absent informed consent and expressly against the will of the parents involved, constitutes an illegal search, forbidden under the Fourth Amendment to the US Constitution. The CHA filed a motion for a temporary restraining order enjoining the execution and enforcement of the law a mere “scant hours” before the law was scheduled to go into effect. Because the judge presiding over the US District Court concluded that the plaintiff had not proved the likelihood of success in demonstrating that the statute at issue was unconstitutional, the motion for a temporary restraining order was denied and the law went into effect.

Despite the law, by 1999 there was only limited evidence that providing antiretroviral therapy to the newborn would lessen the severity of infection, even if there was no prior treatment of the mother during the latter part of pregnancy, labor, and delivery. We now know that early postnatal treatment does lower the viral load in the infant and limits damage to the immature immune system. We also know that the discovery and treatment of HIV infection in a previously untested mother may be lifesaving and nearly always prevents vertical infection in all subsequent births, if the mother continues her treatment.

Connecticut Public Act No. 99-2 was the powerful tool we were waiting for. We went into the community and educated physicians who cared for pregnant women. We urged them to become familiar with the new statute and to call us with questions. Our nurses constructed detailed protocols for the labor and delivery floors. The mothers were given postpartum appointments to the High Risk Obstetrics Clinic and their infants made visits to the pediatric HIV clinic at 2 weeks of age, while still receiving oral ZDV.

We had foreknowledge of the impressive preliminary results of the PACTG 076 prevention study and had been following its guidelines, even before the study was published. This head start and our intensive educational efforts in the hospital and community resulted in a steady decline in the number of newborns testing HIV-positive. The last infant that tested HIV-positive was born at YNHH in 1996. For each of the past 24 years, we have screened and treated about twenty HIV-positive pregnant women, a significant decrease from earlier decades. None of the babies born to HIV-positive mothers between 1996 and late 2019 were infected.4 Nevertheless, we still care for a few HIV-positive children who have come to us from other parts of the world, mainly Africa, and for a handful of adolescent men who have had sex with older HIV-positive men.

VI: LOCAL, DOMESTIC, AND INTERNATIONAL RESEARCH ALLIANCES
After a half dozen years of familiarizing myself with the protean manifestations of pediatric AIDS, I began participating in research studies that would answer pressing clinical questions. I re-examined the statistics extracted from older studies conducted without benefit of appropriate study design and methodologies. Intending to correct these deficiencies, I set myself the task of embarking upon a prospective, longitudinal cohort study to determine the true risk of MTCT of HIV, the relationship between the degree of immunodeficiency and the incidence of AIDS-defining illnesses and survival, and the connection between specific gestational variables and transmission risk. Between 1987 and 2007, I was awarded an uninterrupted series of grants and contracts, the first few of which were designed to answer definitively the questions I had enunciated. The earliest of my grants coincided with the inauguration of two private foundations created to support basic and clinical research on HIV and AIDS: AmFar (the American Foundation for AIDS Research) and EGPAF (the Elisabeth Glaser Pediatric AIDS Foundation). We joined an international alliance of American and European academic centers and our collective data ultimately became the basis for what we now know about the epidemiology, pathogenesis, and natural history of pediatric AIDS.

Among the most important of our local and international collaborative findings were the following:

i). Among babies born to HIV-positive mothers and followed since birth at YNHH between the years 1986 and 2007, the overall risk of transmission of HIV was 9 percent (range 0-20%); ii). the risk of MTCT was 20 percent for mothers who received no antiretrovirals during labor and delivery versus 4 percent for mothers who received antenatal and intrapartum antiretrovirals and whose newborns received ZDV for the first 6 weeks of life (as per PACTG protocol 076); iii). among YNHH mothers who received antiretroviral therapy during pregnancy, the risk of MTCT was 6 percent for those whose CD4+ T-cell counts were ≥200 cells/ul versus 0 percent for those mothers with median CD4+ T-cell counts >500/ ul; iv). a meta-analysis of more than a dozen prospective cohort studies (including ours) by the International Perinatal HIV Group demonstrated that elective C-section before onset of labor and before rupture of membranes, resulted in a decline in the risk of vertical transmission from 19 percent to 10 percent. When C-section was combined with antiretroviral therapy during the third trimester, the risk of MTCT of HIV fell further, to 2 percent; v). among 733 HIV-exposed children enrolled in our prospective study (including those enrolled in collaborative studies during which they had received varying lengths and combinations of antiretrovirals), we recorded the range of clinical outcomes in 2007: a). 43 (5.8%) had been severely or moderately symptomatic; b). 21 (2.9%) had been mildly symptomatic or asymptomatic; c). 512 (70%) were seroreverters, i.e. they permanently lost all passively-acquired maternal antibody and were uninfected; d). 12% were deceased and 9.3% were lost to follow-up.

Once we had optimal practices in place for preventing MTCT of HIV and managing the care of children who survived without the burden of lifelong infection, we formally joined the PACTG. The PACTG (now IMPAACT) is a consortium of academic pediatric institutions charged with testing the efficacy of new antiretrovirals and anti-infectives. We also tested live virus vaccines for their safety in HIV-positive children whose immune function had been restored by antiretrovirals. Lastly, we participated in a detailed collaborative natural history study of HIV-infected and HIV-uninfected peers who were exposed to HIV perinatally, i.e. affected but not infected. Ultimately, between the years 1994 and 2007, we enrolled scores of children in one or more clinical trials each. The results of these studies meant healthier and more productive lives for thousands of infected and affected HIV-affected children worldwide.

VII. UNANTICIPATED OUTCOMES AMONG LONG-TERM SURVIVORS

Among HIV-positive children born prior to 1996, about half, our longer-term survivors, were healthy enough to attend school free of the bane of AIDS-related conditions. Many children were lucky to have found loving foster families who later adopted the children they had raised.

The number of “active” patients in our care fell by 50 percent in the decade ending in 2005. The 51 survivors met with our caregivers every 3 to 4 months. Eighty percent ranged in age from 8 to 18 years; 16 percent were older than 18, and 4 percent were younger than 8 years. Fifteen children died in the years between 1990 and 1995, half in the hospital and half at home or in hospice. There were only three deaths between 1996 and 2005.

Among our long-term survivors (LTS), adverse medical and social issues are common. Their outcomes have ranged from excellent to poor. Over 50 percent have maintained undetectable viral loads and CD4+ T-cell counts in the normal range. The number of emergency visits and hospitalizations has fallen precipitously. However, non-adherence to medical regimens, unprotected sexual intercourse, stigmatization, unchecked family discord, depression, and school drop-outs have stymied the realization of the fully successful social and physical outcomes we had hoped for. Many families failed to disclose the HIV diagnosis to their children for fear of precipitating untoward psychological repercussions, including long-term stigma. Some HIV-positive young
women and men became parents unintentionally, but all their offspring are uninfected (all the pregnant young women complied with their prenatal clinic appointments and took their medications). A minority of our LTS have completed high school, college, or job-training and a few have been successfully employed. A handful have been incarcerated on drug charges or acts of violence. One patient, lost to follow-up, died by gunshot.

**Transcending Patients to Adult Health Care Providers**

Those of us working in resource-rich countries encountered the “coming of age” of the first and largest cohort of HIV-positive children—those born between the early 1980s and the late 1990s. We confronted their need for a major health care transition. Data collected by the CDC in 2007, revealed that approximately 24,000 American youth, ages 13-24 years, were living with HIV/AIDS. This was a 25 percent increase from 2004, attributed to high-risk adolescent sexual behavior and increasing survival of children infected perinatally. Developmentally appropriate youth ought to receive care in adult health-care practices sometime in their early 20s. But there are numerous everyday tasks that represent major hurdles for many teens, in particular adherence to their medical regimens. Ultimately, with diligent guidance, most of them progress to a point where they can be safely transitioned. During the years 2006-07, under the guidance of Sostena Romano APRN, MBA, our longest-serving nurse practitioner, and Anne Murphy, MSW, we transitioned 30 patients, ages 15 to 26 years of age, to adult practices: 13 to Yale’s adult Nathan Smith Clinic, nine to other hospital-based clinics in Connecticut, and eight to private practices close to the patients’ homes. We have continued this practice as our patients enter late adolescence and young adulthood.

**CONCLUSION**

The eradication of MTCT of HIV in New Haven was made possible by the confluence of six nourishing streams: 1). The creation of effective antiretrovirals, anti-infectives, and sensitive diagnostic tests; 2). The flood of grants and contracts from federal, state, local, and private funding agencies; 3). Wise and generous support from Yale-New Haven Hospital and the Department of Pediatrics; 4). The passage in 1999 of Connecticut Public Act No. 99-2; 5). The creation of an effective multidisciplinary approach to care which honors respectful interprofessional collaboration; 6). The spontaneous and enthusiastic union in common cause of doctors, nurses, social workers, students, administrators, and volunteers to serve patients in need, their families and friends, in New Haven County and beyond.

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**FOOTNOTES**

1. Names of patients have been changed to protect their identity.
2. All babies born to HIV-infected mothers are “HIV-positive” until 7 to 15 months of age because they all acquire HIV antibodies transplacentally. But only a fraction are “HIV-infected.” Eighty percent are “exposed” to HIV and are temporarily HIV-positive, but remain “uninfected.”
3. Unfortunately, in late 2019, an HIV-positive baby was born at YNHH after a gap of 23 years. The teenage mother received prenatal care at a clinic unaffiliated with YNHH. She was non-compliant with the antiretroviral regimen that was prescribed for her. She was surprised to learn that her newborn baby was infected. The baby received antiretrovirals soon after birth, the mother’s regimen was re-started, and the baby’s biological father appeared for testing and treatment. All three have been adherent to their various regimens and, as of last report, all are doing well. Since the start of 2020 we have followed nine HIV-exposed babies, but no mother-to-child transmissions of HIV have occurred.

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