PEDIATRIC HISTORY CENTER
American Academy of Pediatrics

ORAL HISTORY PROJECT

William A. Silverman, MD

Interviewed by
Lawrence M. Gartner, MD

June 10, 1997
Greenbrae, California

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PREFACE

Oral history has its roots in the sharing of stories which has occurred throughout the centuries. It is a primary source of historical data, gathering information from living individuals via recorded interviews. Outstanding pediatricians and other leaders in child health care are being interviewed as part of the Oral History Project at the Pediatric History Center of the American Academy of Pediatrics. Under the direction of the Historical Archives Advisory Committee, its purpose is to record and preserve the recollections of those who have made important contributions to the advancement of the health care of children through the collection of spoken memories and personal narrations.

This volume is the written record of one oral history interview. The reader is reminded that this is a verbatim transcript of spoken rather than written prose. It is intended to supplement other available sources of information about the individuals, organizations, institutions, and events that are discussed. The use of face-to-face interviews provides a unique opportunity to capture a firsthand, eyewitness account of events in an interactive session. Its importance lies less in the recitation of facts, names, and dates than in the interpretation of these by the speaker.

ABOUT THE INTERVIEWERS

Lawrence M. Gartner, MD

Lawrence M. Gartner was born and grew up in Brooklyn, New York. His undergraduate education was at Columbia University, followed by medical education at Johns Hopkins University, where he received his medical degree in 1958 and pediatric internship from 1958 to 1959. Returning to New York, he continued his pediatric residency at the Albert Einstein College of Medicine, where he was Chief Resident in Pediatrics from 1961-62. He continued at Einstein, doing a fellowship in hepatology, neonatology and research. In 1964 he became a faculty member, rising to Professor of Pediatrics and Director of the Divisions of Neonatology and Gastroenterology and of the Pediatric Clinical Research Center. During this period he carried out a major research program in neonatal bilirubin metabolism. In 1980, he became Professor and Chairman of the Department of Pediatrics at The University of Chicago and Director of Wyler Children's Hospital. In 1998, Dr. Gartner retired from the University of Chicago. He now lives and works from his ranch in Valley Center, California (San Diego), continuing lecturing and writing in neonatal jaundice, breastfeeding and history of neonatology.

In 1956, he married Carol B. Gartner, who subsequently became Professor of English at Purdue University and Dean of the College of Arts and Sciences at the Calumet campus. She also writes and lectures on the history of medicine, sometimes with her husband. She also assists in the oral history project, with specific responsibility for the video recording and photographs that accompany each oral history. They have two children, Alex Gartner, a movie producer, and Madeline Gartner, a breast and endocrine surgeon.

Interview of William A. Silverman, MD, FAAP

DR. GARTNER: This is Dr. Lawrence Gartner interviewing Dr. William Silverman on June 10th, 1997, in Greenbrae, California, in Dr. William Silverman's home.

Bill, we are really delighted that you've agreed to do the oral history on neonatology for the American Academy of Pediatrics. The purpose of this neonatology oral history program is to record for future historical research the information contained in the memories of those who founded the field of neonatology and contributed to its direction and development. In addition we are interested in recording personal information about these leaders so that we can better understand the nature and origins of their contributions as leaders. You're among the group of those who created neonatology as an academic, clinical and scientific discipline within pediatrics. I am most grateful to you for agreeing to share your ideas, memories and analyses of the field of neonatology with all of your colleagues and students.

We will start with personal background and career development, and then move into the broader area of development of the field of neonatology. There is no time limit for this interview; we want to be as complete and comprehensive as possible. Please let me know whenever you want to take a break. The primary recording for archival purposes is the audio-taping. The audiotape will be transcribed into a print version, which will then be edited for accuracy by both of us. The editing process is not intended to delete or alter any components, but only to ensure accuracy in transcription of names, dates and other information. If there is any segment that you feel is so sensitive that you would not want it to be revealed until a later time, that section can be sequestered. But we hope that all of the transcription will be made available now without restrictions.

The video-taping is an enhancement to enable those who use the oral history to see the individual and the setting in which the oral history was recorded. We would also like to video a portion of your house, photographs in the room and artifacts that would provide useful orientation to your personal and professional history. We'd also be most grateful to you if you could provide us with photographs or slides from your own collection, which would be copied for retention in the Academy's historical archives.

All of the recorded, transcribed and copied materials will be made available to appropriate scholars through the Pediatric History Center of the American Academy of Pediatrics. It will be indexed and listed in the national and international historical reference resource catalogues. Since we are trying to assemble a data set for future historical research, we are trying to gather a parallel series of responses from all of those interviewed. Therefore, I will use a script and will ask you to respond to these questions. However, please do not feel

constrained by this process. Add whatever comments you wish and feel free to expand beyond my specific questions. Also feel free to add your own questions. Please relax and enjoy the interview.

I would like to begin with some background and perspective on your life and career. Tell me first about your origins, birth, parents, siblings, family life, and early schooling.

DR. SILVERMAN: Well let me say first, Larry, my friend of 38 years, I am delighted to have you come and interview me. You and Carol have taken the time to do this, I'm very grateful to you. Well, let me say that I was born in 1917, I'm going to be 80 years of age this October. I was born in Cleveland, Ohio at the time of the great influenza epidemic, and my mother, who had rheumatic heart disease as a child, had a worsening of her condition during the pregnancy. So for the first 3 years of my life in Cleveland, I was raised by my grandparents, who did the child care. My mother was virtually an invalid at this point. My father was advised to take his wife and new child to a healthy climate, and that's how I immigrated to Los Angeles in 1920. And my mother lived for 2 more years, and then died of a cerebral embolus, a complication of her mitral [valve] heart disease. And I was a sickly child. I'm afraid that's my interest in medicine, this long association with one doctor after the other, I had childhood asthma and so forth.

My schooling, the public schools in California in the 1920s, were very good, very well supported. I went through the Los Angeles school system, and it was always sort of understood that I was going to go into medicine. I graduated from high school in 1935 and went to UCLA [University of California, Los Angeles], where I was a pre-med for 3 years, and took the usual grind subjects for medical school. And at the end of the third year, I applied to the University of California, San Francisco, UCSF, as it's now called, and began medical school here in San Francisco. This was 1938, and I graduated in 1942. I had pretty much decided that I would go into pediatrics; and I suspect again, it was [the influence of] my childhood. There was one episode of a friend of the family whose child died under particularly tragic circumstances. All of this I think sort of made it understood. I don't really remember when the epiphany occurred.

I had an internship here in San Francisco at the University of California Hospital, then a residency. I had never been out of, consciously out of California, for all of these years, when someone urged me very strongly to get some "foreign" experience. So I applied to Columbia [University] Babies Hospital. In 1944, I had my [pediatric] residency at Babies. It was an amazing place in 1944 and 1945. Names like Hattie Alexander [1901-1968; New York] and Jack [John H.] Caffey [1895-1978; New York] and Beryl Paige, Mac [Donovan] McCune [1902-1976, New York], one luminary after another, the only luminary who was not there at the moment was Dick Day

[Richard L. Day], and I was closely associated with Dick Day, so I didn't get to see him, in about a year, year and a half after I arrived at Babies. And it also became very clear that this small town hick from Los Angeles was just bowled over by New York. New York was just such an exciting place, and Columbia was a very exciting place. Babies Hospital, 350 beds. When I had my internship here at UC [University of California, San Francisco], we had 18 children on the pediatric ward; it was a very small service. And the pathology and the wide range of illness at Babies, it was very, very exciting. The first summer I was there, 1944, New York City had its largest polio epidemic. And it was an incredible experience. We set aside an entire ward, entire floor, for polio of all ages. We had four of these huge [Drinker] respirators that were all filled for a period of 6 weeks, many deaths. And that was quite an experience, there was an epiphany at that time I would like to tell you about.

On one particular night, this was late summer, it was before air conditioning, just steaming hot in New York. We had 2 deaths in the respirator, our spirits were low, our jaws were slack, and the nurses were putting on these Kenny packs, Sister Kenny packs for poliomyelitis, steaming caldrons of hot water, taking these wool pads to put on, the wards were just incredibly hot. And the nurses were gliding back and forth to the patients, wearing these long dresses; it looked like a scene out of Florence Nightingale in the Crimean War, unbelievable. And at 3:00 a.m. in the middle of the night, our attending arrived to make rounds. Drunk, his tie tied perfectly, but not in front, in back. He was lucid, and very dignified, and matter-of-fact, and with flashlights we made rounds on this polio ward at 3:00 a.m. under these unbelievable conditions. Interesting enough, his theme, patient after patient, is, how do you know that the Kenny packs are doing any good? Fifty percent of these children get better without paralysis, and this method of treating polio has never been really evaluated. How do you know that you're not making them worse? I was so insulted by this, you know, it's unbelievable; here's this drunk who comes up and accuses us of maybe making our patients worse. As time went on, months and years later, I realized that this was probably the most important learning experience of my entire medical training career, including pediatric training, after graduation from medical school. It was quite something. And I think this summarized the whole experience at Babies Hospital. I was with a group of people who were willing to say "how do we know;" this was very different from my educational experience up to that time.

DR. GARTNER: Thank you, that is quite an experience. Do you remember any particular physicians in your early life who might have influenced you to go into pediatrics?

DR. SILVERMAN: Not particularly, as a matter of fact. As I say, I was a sickly child going from doctor to doctor. The one who made the most

important mark was a man whose name I can't even remember at the moment. My stepmother was pressing him to do something for this child, and in desperation he reached for a most unbelievable treatment. There was a new preparation made in France called Lipiodol. Lipiodol, iodized oil, was used for the treatment of asthma. And I recall, coming to his office over a period of weeks he cocainized my pharynx, put a catheter into my throat and dripped Lipiodol into my lungs, if you can imagine. [laughs] Following that, my chest film horrified everyone. That medical encounter was very disastrous. No, I had no specific guidance. I came into pediatrics as the vague result of my childhood experiences. This was during the Depression, you understand, these were horrendous times in southern California. California was particularly hard hit during the Depression; nonetheless, the state schools were marvelous. There was only one state medical school in California, and the tuition was $125 per semester. I remember, how much difficulty I had getting that $125 together.

DR. GARTNER: What did your father do?

DR. SILVERMAN: My father was a very skilled cap maker, and a union organizer; he led a large strike in Los Angeles just as the Depression hit. They lost the strike, and he was blackballed and could not get a job. Just as the Depression was getting worse, we were saved by my stepmother. She was a very good cook, and opened up a little coffee shop. First it served coffee and doughnuts; later it became a restaurant, and we made it through the Depression. Many of my friends were losing their homes, I mean, it was horrendous. We squeaked through as a result of my stepmother's cooking ability. My father and my stepmother worked, slaved at this little restaurant, all during the Depression and we made it.

DR. GARTNER: Your stepmother became your…?

DR. SILVERMAN: My mother. In fact, my stepmother was my mother's first cousin, so there was a close family tie, but it was not an easy relationship for me. The early loss of my mother, as I look back on it now, made me very angry. Somebody did that to me. It was a very rough childhood.

DR. GARTNER: I can imagine. Do you have any siblings?

DR. SILVERMAN: Yes, I have a stepbrother, my stepmother brought a child into the marriage. And then my father and stepmother had a child who is my youngest brother, half brother, actually, so there were three boys in this family.

DR. GARTNER: What was that relationship like, the 3 of you?

DR. SILVERMAN: Very rough, as you can imagine. I was the oldest, and

there was a lot of sibling rivalry. It has taken us years to get close. We're all now back in California, and see one another probably more than we did when we were children.

DR. GARTNER: What are the brothers doing?

DR. SILVERMAN: My stepbrother was a salesman. He is now deathly ill, unfortunately. My youngest brother is an electrical engineer and got into computers early in the game. He had a rather successful career in computers.

DR. GARTNER: So they didn't go into medicine.

DR. SILVERMAN: No others in medicine.

DR. GARTNER: And no one else in the family in medicine.

DR. SILVERMAN: Not at all; all 3 of my children I think have avoided medicine. [laughs] As a result of my experience.

DR. GARTNER: Now tell me a little bit about your marriage to Ruth, and your children.

DR. SILVERMAN: Well, Ruth and I met at Columbia when she was a student nurse. We met during that polio epidemic. She was on night duty, and, I can remember very well, I was doing a lumbar puncture in the middle of the night. Our faces were very close together. I asked her if she would show me around New York on the next opportunity, So, we went out and saw New York. We also had a very interesting experience which I think cemented the relationship. We cared for an extremely small, premature infant. This, you understand, was 1945 when we had a 4 bed premature nursery at the Babies Hospital for outborn [extramural] premature infants. It was empty most of the time. A 620-gram premature infant, born in the Bronx, was brought into this little 4 bed ward on her second day of life. The obstetrician was amazed that this infant breathed spontaneously; he was even more amazed the next day when the infant was still alive. He then asked to transfer it to our hospital. This was the smallest premature infant I ever saw, and, as a matter of fact, the smallest infant alive at that age in all of the Babies Hospital history. This became a rather celebrated case. I had absolutely no experience with an infant of this size. I quickly looked up Sam [Samuel Z.] Levine and Harry Gordon's classic 1943 article on the handicaps and care of premature infants, and I followed their advice just like a cookbook. The infant did surprisingly well. We used an old Davidson incubator, an enormous cast iron affair, good heat sink. Once you got it up to temperature, it held very well. We maintained, not normal body temperature, but according to the cookbook recipe, stabilized incubator

temperature. We fed a high protein low-fat formula [Alacta] proposed by Dr. Harry Gordon to deal with the steatorrea of premature infants. I also read about an intriguing possibility that carbonic anhydrase deficiency in the red cells might be the cause for the recurrent apnea and cyanosis of immature infants. This is exactly what I was looking for: something exciting, something new, something never tried before! And I began to transfuse this infant with my blood every day to increase carbonic anhydrase. The infant did well and I felt like a hero! The child was presented at Grand Rounds; she regained birth weight and for 3 months the survival of this infant was a sensation. I realized only later, and of course even more painfully now, that the parents were horrified. They were in their middle 40s, this was an unplanned, unwanted pregnancy, and here was this young whippersnapper not only keeping this baby alive, but using untested methods to do so. I could not understand why they didn't see this as a glorious adventure. They were looking into the future, and I was looking at the present, and it was a very exciting present. Ruth was a student nurse at this time; she was assigned to the small premature nursery. Our relationship blossomed and became closer. Then the infant died quite suddenly. I suspect the cause was cardiac because at that point a loud murmur appeared, probably a patent ductus. The family refused a post-mortem examination. Their attitude, their good sense, and my immature "rescue fantasy," is so clear now, but at the time I was very puzzled. That amazing episode sharpened my interest in newborns and, more specifically, extremely premature infants.

DR. GARTNER: This was an important period in your life.

DR. SILVERMAN: As a matter of fact, we have photographs of that infant lying on the nurse's outstretched hand to show how small this baby was, it was taken at about two weeks of age. I used that picture on the dust cover of the third edition of *Dunham's Premature Infants*, published in 1961.

DR. GARTNER: That's wonderful, an interesting experience. What about Ruth's career?

DR. SILVERMAN: Yes, Ruth graduated from Smith College in 1942. She came to Columbia-Presbyterian [Medical Center] for her nursing, 2-1/2 years. When she graduated in 1945 we were married. She went to work first as a research nurse with Paul di Sant'Agnese [1914-2005, New York] who later became well known as a researcher in cystic fibrosis. At that time he was interested in a new scheme for multiple immunization of all infants with diphtheria and pertussis, DPT. The early trials of DPT were conducted by Di Sant'Agnese with Ruth as the research nurse for that pioneering project. She worked at Babies when I was there. Our children began to arrive in 1948. After the birth of Dan, our first child, Ruth left nursing to be at home during the infancy and childhood of all three of our children. Our daughter, Jenny, was born in 1950; now, my God, 47 years of age, it's unbelievable, she

just had her birthday two days ago. Our youngest child, David, was born in 1953. Ruth went back into nursing when the kids were back in school; she was a research nurse at the Albert Einstein College of Medicine working with Dr. Helen Ranney [1920-2010]; internist/hematologist; New York and San Diego] to establish, with Helen and Dr. Ruth Gross, the first heredity clinic at Einstein. This turned out to be a marvelous job; she could leave at any time if the kids were sick, since the job didn't involve bedside nursing. It turned out to be a wonderfully educational experience.

DR. GARTNER: What about the children's involvement with your career or your career's involvement with the children?

DR. SILVERMAN: With my children?

DR. GARTNER: Yes, your children.

DR. SILVERMAN: I think my children got a rather negative view of medicine, as a matter of fact. One, their father was usually not there at dinner… I was involved with somebody else's kids. I, as you know, have been a critic most of my life, and I think my children were aware of my views about medicine's shortcomings. My children didn't get a positive picture: their father was an overworked man who was grumbling most of the time. [laughs]

DR. GARTNER: Tell me a little bit about Babies Hospital during the time you were there during the war, when you were there as a resident. This was war time, and things must have been affected by that.

DR. SILVERMAN: Right, Babies Hospital was short-staffed, so that I was on duty every-other night, and I was very busy. In those years, pediatrics dealt with acute disease. We had very little chronic disease. Babies was a very exciting place. Since we were short-staffed, it was an awful lot of work, but a wonderful experience. The most important element was the teaching staff: people like Rusty [Rustin] McIntosh [1894-1986; New York], Mac McCune, Hattie Alexander, Dorothy [H.] Andersen [1901-1963; New York] and Jack Caffey. They were just bubbling and critical. All not team players – each independent and skeptical.

An incident took place in 1944 that led to the "discovery" of a new disease: infantile cortical-hyperostosis. The experience was instructive. When I was a resident at UC San Francisco, I saw a 3 month-old infant who came in with this mysterious swelling of the jaws, and swelling over the clavicles, scapulae and forearm; these were tender to the touch. The infant had a low grade fever. The x-ray appearance of the long bones was that of infantile scurvy: the periostium of the cortical bone was elevated and thickened. The infant was treated with orange juice, but this failed to relieve signs and symptoms.

This led to a diagnosis of "Vitamin C resistant scurvy," an unheard of illness! About six months after I arrived at Babies Hospital, I saw an identical example of this "unheard-of illness." I became very excited and I rushed to the radiology department to speak to Dr. Jack Caffey. I was surprised that Jack Caffey wasn't the least bit excited. He said "Oh I have other patients with these findings," and he went into his file and showed me sets of identical films taken in 1938 and published in 1939. Jack Caffey was a very good observer, and he had a photographic memory. He pigeon-holed cases that he wasn't sure of. He pulled out a folder of x-rays with similar bone lesions. Some were associated with congenital syphilis, others with Vitamin A intoxication, and still others were unexplained. The "unexplained" infants had a benign course, low grade fever for a few weeks; pain and tenderness gradually subsided and temperature returned to normal. Jack suspected this mysterious "disease" was a viral infection. When I told Jack I saw an identical example in San Francisco and thought the new disease might be reported in a joint publication, he could see I was very naïve. Jack Caffey was a master at competing for priority. He arranged to have a public presentation as quickly as possible. The New York Academy of Medicine had an upcoming program in which residents in the various hospitals in New York City presented interesting cases. Jack saw to it that I was put on the roster, and we presented and recorded the new disease before anyone else. The first publication in July 1945 by Caffey and Silverman coined the new name "infantile cortical hyperostosis." As you can imagine, this first paper, the discovery of a new disease, was a thrill. We subsequently had five cases of it.

I learned about the rough and tumble of academic rivalry from this experience as well as the importance of a label. When the term "infantile cortical hyperostosis" appeared in print other cases suddenly came out of the woodwork. Poor Francis Scott Smyth [1895-1972; San Francisco], Chairman of the Department of Pediatrics at UC San Francisco, reported the San Francisco case in 1946, but, no one remembers his article. Smyth's title was a "Periosteal Reaction, Fever and Irritability in Young Infants. A New Syndrome," in the *American Journal of Diseases of Children*. The paper sunk like a stone. "Infantile cortical hyperostosis" became a well-known entity; Jack Caffey made it so.

DR. GARTNER: Also known as Caffey's disease.

DR. SILVERMAN: Caffey's disease.

DR. GARTNER: But it should have been Caffey-Silverman-Smyth disease.

DR. SILVERMAN: Early on it was sometimes called Caffey-Silverman Disease, but everyone thought this referred to Fred Silverman, a radiologist. In a German book on pediatricians in the world I'm listed as "William

Silverman, American radiologist" the result of this infantile cortical hyperostosis mix up.

DR. GARTNER: But that experience didn't change your career away from pediatrics.

DR. SILVERMAN: Or premature infants. There was very little opportunity to satisfy my preoccupation with premature infants early on. In the 1940s Babies had a primitive 4-bed nursery for out-born premature infants. The intramural premature nursery was 2 blocks away, in the huge Columbia-Presbyterian Medical Center obstetric unit [The Sloane Hospital for Women]. It was a long walk. As a result it was physically divorced from Babies Hospital and was an unexciting place. In those days it was run by authoritarian nurses, who provided expert but unimaginative care; there was very little pediatric input. The obstetricians were in charge in those days and they were not really interested in the day to day activities. So there was very little going on. In 1949, things changed dramatically.

DR. GARTNER: What happened in 1949?

DR. SILVERMAN: One of the most important things that happened in 1949 was the addition of "weight at birth" and "duration of pregnancy in weeks" to the standard birth certificate. Suddenly premature infants became visible. For years Ethel Dunham had been beating the drum for this move. Also, it all came together in 1949 when the Hill-Burton Act was passed and federal funds became available for building new hospitals, made necessary at the end of the war after the long period of inaction since the 1930s. Hill-Burton also provided funds for infant stations where these high-risk neonates and premature infants could be transported from smaller hospitals to centers for specialized care. Dick Day, who had now come back to Babies Hospital planned the first premature infant station at the Babies Hospital. Dick knew I was quite interested in this and invited me to help him run this new facility. This began our close association. Dick went to Cornell just before the war, to do some studies on thermal regulation of the newborn. There he carried out his classical studies on heat exchange, using a new device, a gradient calorimeter, invented specifically for this study. The physicist who worked with Dick was a man by the name of James [D.] Hardy [1904-1985; New York and New Haven], who later became the world's leading authority on the topic of thermal physiology. Hardy came to Cornell to help with metabolic studies of adults. Dick Day went to Cornell because of Hardy. Day's interests in newborn and premature infants date from that study in thermoregulation.

In 1949, Dick had Hill-Burton funds in hand, he had the interest, and he put together a plan. The new premature infant station was, for its time, very large (24 cribs), and the timing coincided with the introduction of the Air

Shields Isolette Incubator. Babies Hospital was the first of the premature infant stations equipped entirely with Isolette incubators. The design called for the intake of New York City air into a plenum; the air was washed, warmed, passed through ultraviolet light to kill microorganisms, and then piped under pressure to outlets at each of the Isolettes. Air entered each Isolette at pressure above that of the room so there was a nice outflow, and a gradient from the incubator to the room to the hall. The idea was to have a sweep of air as a barrier to air-borne infection. Dick Day went to great lengths not only to develop the plan but to also demonstrate its effectiveness. The opening of the nursery was delayed because Dick carried out experiments; he sprayed microorganisms into the rooms and timed the rate of their clearance. I can't remember the name of the organism he used, but it was said to be a nonpathogenic … in those days. [laughs]

DR. GARTNER: I hope so.

DR. SILVERMAN: I wonder if there are micro-organisms that are truly nonpathogenic for premature infants. In any case, those studies were done and the station was opened in, I think, either October or November of 1949. I remember it was late 1949 because of a very dramatic incident that took place shortly after we opened. A premature infant, my private patient, developed early vascular signs of retrolental fibroplasia [RLF]. We had never seen an example of acute RLF prior to 1949 The disease was first described in 1942, and was called the "Boston Disease" because Theodore Terry [1899-1946; Boston] and Stew [Stewart] Clifford [1901-1997; Boston] first described it, and most of the early cases appeared there. Prior to 1947, we saw RLF in older infants or young toddlers when they were referred to Algernon Reese [1896-1981; New York] at Columbia, America's premier ophthalmologic pathologist. When the premature infant station opened, Al Reese arranged to have his fellow, Fred [Frederick C.] Blodi [1917 – 1996; Iowa City, Iowa], later a famous figure in American ophthalmology, examine the eyes of premature infants at weekly intervals. That had never been done before in New York. When Blodi began to examine the infant's eyes, the first example of early vascular RLF turned up in my patient, the child of a very prominent member of the biochemistry department, whose wife had a horrendous history of recurrent miscarriages. After 6 miscarriages, this premature infant arrived weighing 1.1 kg, very small in those days, but the baby did remarkably well. I find it hard to say retinopathy of prematurity; RLF was such a big part of my life. When Blodi reported the early abnormalities of the retinal vessels in December 1949, the drama in this nursery began. In those days Columbia-Presbyterian Medical Center was like a small town. When the professor's child developed early changes of RLF, everyone at Columbia knew about it within 24 or 48 hours, and the entire institution felt involved.

We were decimated because the child had been doing quite well, minimum

respiratory difficulty, feeding well, and gaining weight. When the first ocular changes appeared we panicked. Fred Blodi suggested we try the newly-available "miracle drug" ACTH [Adrenocorticotropic hormone] for its anti-inflammatory effect to inhibit the retinal vessel proliferation. Well, you can imagine the whole medical center was sort of in on this, this very dramatic disease and never before used medication. ACTH had never been used in children, young infants, much less a newborn or a premature infant. I couldn't imagine what the dose should be. We quickly looked at some animal work to extrapolate a dose. Unbelievably, within days after beginning ACTH wild retinal vessel proliferation subsided! The whole process improved. Applause everybody; it was very theatrical. We promptly reduced the dose because the side-effects were horrendous. The infant became ravenously hungry, extremely irritable and weight gain ceased. But, when the dose was reduced, the retinal changes flared up. We increased the dose, and the vascular changes again subsided. The infant was now in pathetic condition; crying constantly and looking horrible with all the signs of adrenocortical hyperactivity. We tried again to reduce the dose of ACTH and this time there was no retinal flare-up. We stopped the ACTH and the eye changes returned to virtually normal in about two and a half weeks. The changes were closely monitored by Fred Blodi. This was a very dramatic experience; looking at the pathology directly with an ophthalmoscope and seeing it change under your eyes. This seemed an incontrovertible cause and effect. The whole medical center applauded our daring exploit. We then began to see early vascular changes of retrolental fibroplasia in spades. It was very common in our brand new facility. We treated it with ACTH; 31 infants with early RLF were treated. The effects on the infants were encouraging. But, we had a nursery full of screaming infants whose appetites we could not satisfy. Growth was inhibited and we documented this with x-rays. Dick Day and I were very worried about this effect of ACTH and wrote an article about the growth inhibition. Here were these dramatic results. Among the 31 ACTH treated babies, there were 4 failures and only 2 with cicatricial RLF, the severest form.

Well this, as you can imagine, was a very difficult dilemma. The threat of blindness was horrendous, and we seemed to have a dramatically effective treatment. The word got out and before long there were reports from all over the U.S. and even Britain, about our miraculous treatment and cure for RLF. But, there were a number of things that bothered us. One, we had some failures here. But more importantly, Fred Blodi, who was monitoring the eyes of premature at premature infants in Lincoln Hospital, in the Bronx observed an infant whose vascular changes subsided spontaneously. He was called in consultation to another hospital where he also saw spontaneous resolution of RLF without ACTH. This put us in a very difficult spot which was made even worse because Dick Day and I got religion about 2 years before this time; we became devotees of medical statistics. [laughs] [Austin] Bradford Hill [1897 – 1991; London, England] wrote a classic book on

medical statistics in 1937; a small volume which just reads beautifully. Dick Day found a copy, read it in 1947 and gave a talk on it at Babies. He made a believer out of me. The 2 of us began to criticize everyone's work because they were making observational studies and no experimental studies, making ourselves a nuisance about our preoccupation with medical statistics. And now here we were with an observational study with no concurrent controls! This was particularly worrisome because of the horrendous side-effects of ACTH. What should we do now? We found ourselves hoist on our own petard!

This was the end of 1950. We went to see the chairman of the pediatric department, Rusty McIntosh. We laid out this dilemma in front of him. We told him we were frightened about the side-effects of ACTH, and we had no concurrent controls. What we would like to do, we told him, is to carry out a randomized clinical trial, a method that had never before been used in studies of human infants. It grew extremely emotional, the idea of withholding a cure for infants simply to test it. All of the issues that we now understand are obvious, but this was the very first experience. In the half hour we were with him, Rusty McIntosh listened to our arguments. Remember, this was years before ethical review committees. Then the chairman of the department decided everything that was done or not done in his department. In those days Rusty smoked a pipe; he was a man of very few words, quite reticent. He puffed away silently as he listened to our presentation. I'll never forget his reply as long I live: "You must do it." Not, you can do it, you MUST do it; he emphasized the must.

Since we had never done this before, we turned to the classic method of randomization used in textbooks of statistics. We filled a bowl with white marbles and blue marbles, told the nurse to shake the bowl vigorously and to turn her head away and pull out one marble, which designated ACTH or control. One morning I came in, when a new infant was about to be assigned. Our head nurse, a wonderful nurse, went through the procedure exactly as we told her. She pulled a marble out. It wasn't the right color, so she put it back and pulled out one that suited her. [laughs] Obviously, the ritual needed to be tightened up. It was a dramatic period, you know. We quickly accumulated enough cases, but, the trial had many shortcomings. There was no masking of the observers and randomization was hardly masked. Much to our amazement, we demonstrated very, very quickly, that there was no significant difference between the ACTH treated group and the concurrent controls in retinal changes. And, there were more deaths in the ACTH group. What we had not appreciated early on was, in addition to the metabolic effects and growth stopping, the ACTH group were having more fatal infections.

Well this, this 2 year period of seeing a favorable experience with an exciting new treatment and then having it properly evaluated and dashed, was an

incredible learning experience for all of us. As you can imagine, I became a randomized control nut, drove everybody crazy about the need for doing clinical studies in a scientific way with rigor. And one had to bite the bullet and do this. The backing which we got from Rusty Macintosh was a very, very important part of this. And Dick Day deserves a tremendous amount of credit, again, for taking the lead; after all he was in charge, I was his assistant. But it was quite an experience. And I think it was this experience which made Dick Day very discouraged about our knowledge of infant care. His interest in the premature infant began to wane following this.

By the 1950s we were all very disheartened when we recognized that RLF was the leading cause of pre-school blindness in the US, and, increasingly so, in other developed countries. Following our ACTH trial, we carried out another very small and discouraging trial on the effect of limiting light exposure for premature babies. Theodore Terry, who had described this disease in Boston, wondered whether premature exposure to light might be the cause of retrolental fibroplasia. No one had ever examined this in any rigorous way. This trial took place when Jack [John C.] Locke [1920-2004; Montreal, Canada] took over as the new ophthalmology monitor in the nursery. Jack Locke was very tall and very proper. I'll never forget this; he stood up when Dick Day and I met with him, and he said, "As sure as I'm standing here, it's light. It has to be light." After our experience with ACTH you can imagine what our response was. We said, "Prove it." And he did a trial with light, again, which was very disappointing. And that pretty much brings us up to about 1951.

DR. GARTNER: I was just going to ask, what was your oxygen practice? This all began, the RLF experience began when you had the new incubators.

DR. SILVERMAN: Exactly. When our new premature center was opened, it was equipped with newly-available, expensive Isolette incubators. The reason why they were expensive is that they were very carefully designed to provide high oxygen concentrations quickly and to maintain these concentrations without variation. Tight gaskets were used to prevent leaks. An engineer at Air Shields invented an ingenious device. On the side of the Air Shields incubator there was a fitting for oxygen and another fitting for room air, or in our case, air which came in air under pressure. As the oxygen came in, the float valve cut off room air and the oxygen concentration rose quickly to fulfill the standard practice in the 1940s of rearing infants in high oxygen to promote normal rhythmic breathing instead of periodic breathing of prematures in room air. The reason why this was standard practice at the time is because of an observation that had been made by Jim [James L.] Wilson [Ann Arbor, Michigan] that periodic breathing in premature infants could be brought to a regular rhythm by increasing oxygen concentrations; the smaller the infant, the higher the concentration required to produce this rhythmic breathing. The reasoning was that the

periodic breathing was probably a sign of anoxia and might be related to the well-known high incidence of brain damage in these babies. So this was the rationale, and this had been accepted everywhere. All of these infants were receiving high concentrations of oxygen. By high, I mean probably 60-70%. The reason I say probably is because, at the time, we had no easy way to measure oxygen concentration. That capability arrived in 1953. Pediatricians and nurses interested in the care of premature infants were absolutely convinced that high concentrations of oxygen was what was important to these marginally viable babies in the 1940s and 1950s.

As a sidebar on those hectic early days of the premature infant station, I should mention an incident involving Fred Blodi. Fred Blodi had been examining the eyes of every premature infant in this nursery for 3 years, with close contact during ophthalmoscope examinations. He was then found to have laryngeal tuberculosis. Hundreds of infants had been exposed. The reason I'm now bald is due to incidents like that. Unbelievable; we, of course, had to bring all the infants in and do skin testing for tuberculosis. Miraculously, not a single case was found. The Gods were with us that time. These dramatic events at the beginning of my involvement with the premature infant were very discouraging. Here we're putting in all of this effort to keep infants alive while an unprecedented epidemic of blindness was taking place, even in the most advanced hospitals, those who had the [Isolette] incubators. There is another point to make about the incubator effect, but let me save that until I tell you about the controlled trial of supplemental oxygenation which took place. Some hospitals in our country were said to have no retrolental fibroplasia at all. They didn't even know what we were talking about when we reported retrolental fibroplasia. The one in which this was most notable was Tulane [University]. Ralph Plateau of New Orleans, showed up at every meeting of those interested in the retrolental fibroplasia epidemic and told everyone they [at Tulane] followed their infants very carefully, and had never seen a case of RLF or blindness at Tulane. In Boston, where RLF was first described, [V.] Everett Kinsey [1909 – 1978; Boston and Detroit], a research biochemist at the Massachusetts Eye and Ear Infirmary, was intrigued by RLF and Leona Zacharias, the wife of a famous physicist in Boston, joined forces and carried out the first survey looking for suggestive associations of cause and effect. Kinsey and Zacharias compared treatments of 50 infants with RLF with 250 premature infants who did not have RLF. They found a few interesting associations. The disease was unknown in Boston until 1938, when it suddenly appeared and became epidemic, coinciding with the increased use of water-miscible vitamins. Increased use of medicinal iron, and increased use of oxygen, also tracked beautifully with the increase in RLF; more closely with vitamins and iron than with oxygen.

There was now a clamoring from everywhere, something had to be done about RLF. The director of the National Association for the Prevention of

Blindness, Franklin Foote, a former public health officer demanded that we take some kind of concerted action. All this clamor led to a meeting in 1953 at the National Institutes of Health in Bethesda, a very small place in those days, with everyone in the US interested in RLF. Other countries were not represented, incidentally. It was occurring in other countries, but was much more common here. Canada and these other countries had RLF; it suddenly appeared, but not in the numbers that it occurred here. Everyone assembled said, "We have to do something."

Dick Day and I lobbied for a controlled clinical trial of supplemental oxygen practices. Some felt the association with liberal use of oxygen was so well established that a trial was not necessary. Others argued that limiting oxygen would increase mortality and brain damage and that a trial would be immoral. And it was very hot. Very hot. Finally, to everyone's credit, a randomized clinical trial design was accepted. Just before this national trial was proposed, there had been an attempt to do a controlled clinical trial of oxygen in Gallinger Municipal Hospital [now the District of Columbia General Hospital] in Washington, DC. Arnall Patz [1920 – 2010; Baltimore, Maryland], who was a young house officer in ophthalmology, was told by Leroy Hoeck [1911 – 2009; Clinton, Maryland], a pediatrician, "All this oxygen we're giving to these babies must be doing something." And Patz replied, "No, it can't be oxygen. The kind of proliferation that was being shown here is the result of hypoxia, of proliferating vessels attempting to vascularize a low oxygen area." Patz read more about the topic and then decided it might make sense. He and Hoeck tried to carry out a controlled clinical trial to test the suspicion about high oxygen treatment just before this meeting. The reason it's important is because Patz was at the meeting at Bethesda. Patz and Hoeck's trial clearly demonstrated that the infants who'd been exposed to liberal oxygen had a higher risk of RLF. The problems with the Gallinger trial were serious; not all eligible infants were enrolled, and the nurses were so convinced that liberal oxygen was life-saving that they turned the oxygen up at night in the restricted oxygen group and then turned the valves down in the morning. This contaminated the two groups. Patz, to his credit, not only knew these defects in the trial; but he joined those calling for a large a multi-center, rigidly controlled trial of the oxygen question.

A plan was devised; it was unfortunately a compromise, and the weak design led to problems that plague the field to the present day. It was decided that there were two competing risks: retrolental fibroplasia on the one hand, and mortality on the other. It was decided that fears about an increase in mortality had to be addressed first. As a result, during the first 3 months of the trial, 2 infants were allotted restricted oxygen for every one assigned to liberal supplementation. The reason that was chosen is that if restriction of oxygen increased mortality, one could see it very quickly. Then the rest of the trial would continue to alternate or go only to the restricted oxygen if

mortality was not affected, and that's how it turned out. In these first 3 months, mortality at these 18 institutions was not higher under limited oxygen. For the remaining 9 months, all enrolled infants received restricted oxygen. The trial was designed to end after one year, and when 3-month follow-up eye exams were complete, the results would be announced.

The unusual design of the 1953-54 national study was suggested by Bradford Hill, the British statistician who invented the format of the randomized clinical trial. In later years, I went to see Bradford Hill to ask him about the trial design; he said "I don't remember." [laughs] The principal investigator was Everett Kinsey, who moved from Boston to Detroit, Michigan. The trial, involving 18 hospitals, all east of the Mississippi, was run out of his office in the biochemical laboratory of the ophthalmology department. When you had an infant who was eligible under 1500 grams, and age 48 hours, I would send a telegram to Detroit, and the assignment came back by return telegram, the infant was put either into routine, which was over 50%, for 28 days, or restricted, which oxygen was below 50% and only as necessary for cyanosis and stopped as quickly as possible. This was the contrast. Why were they enrolled in 48 hours, I questioned for 40 years or more. This has been driving us crazy. Was it that mortality in those days was very high, and most of the burden of mortality was in the first 2 days? It was decided that they should be enrolled at age 48 hours. Well, this came back to plague us, as you can imagine. The other thing about that trial which was very interesting is this was 1953, 1954. July 1, 1953 to June 30, 1954 were the dates of the trial. This was the time of the McCarthy era, and believe it or not I got a call from the FBI about mysterious coded messages that I was sending to Detroit to enroll these infants. [laughs]

The other thing I remember about that trial is that this was a missed opportunity. Since early mortality rates were quite high in those years, this was an opportunity to get a better handle on the pathology of the early stages of RLF, and so we all agreed that when infants died we would send the eyes to Detroit, and this would be an opportunity to get a better handle on the earliest changes and their development. So hundreds, literally hundreds of eyes in 18 institutions were all sent to Detroit. Nothing was ever done, they disappeared. No one has the foggiest idea of what happened to them. Another one of these crazy things.

The other thing was a dramatic event in March of 1954. There was an article published from Bellevue Hospital, pointing out a controlled clinical trial in which the results clearly indicted liberal oxygen. More importantly, they claimed restriction of FIO2 under 40% was safe; mortality was a little higher in the restricted group but not significant itself. Bellevue urged that routine high oxygen should be stopped immediately and, thereby claimed [retrolental fibroplasia] could be completely eliminated. That idea, that under 40% oxygen was safe, was planted for the first time in that article, and that

became a real issue in the years that [went by]. When I say we were startled, it's because Bellevue was a member of this 18 hospital consortium of a collaborative controlled trial that could not be reported until September 1954, when the last enrollee had a 3-month follow-up. Had this trial been started before the collaborative trial? Was this the Bellevue portion of the trial? We could not find out at the time. No one has been able to find out since that time what the true facts are. There should be a simple answer to that; they have never been answered. When the under '40% is safe' claim surfaced, it was picked up by the New York Health Department, New York City Health Department, and a memorandum was sent to all the nurseries, by this time there were a number of centers in New York City, that oxygen should be restricted. The prescription was a very straightforward, no ifs, ands or buts: oxygen should never be used unless the infant was cyanosed, and when it is used it should never exceed 40%. I mean, this was a clear directive. And here the collaborative controlled trial, the cooperative, was continuing with intake until June the 30th. As you can imagine, there was tremendous confusion.

DR. GARTNER: How was that resolved?

DR. SILVERMAN: It was never resolved. The Bellevue group refused to explain.

DR. GARTNER: The Bellevue trial went on in violation of the protocol?

DR. SILVERMAN: No, no, in the trial, after 3 months, all of the infants were being restricted. So in essence, this was being done. The thing that made the Bellevue trial quite distinctive is that oxygen was mixed, premixed, so that the concentration of oxygen was 38%, and one could not make any mistakes, this is all that was available. Not many hospitals resorted to that, because by 1953 the oxygen analyzers had arrived. And as a matter of fact, the oxygen analyzer for ambient oxygen, measuring FIO2, quickly came on board with this trial. All of the institutions were given, for the first time now, paramagnetic analyzers, and you could monitor the concentration that the infant was exposed to.

DR. GARTNER: Were those Beckman instruments?

DR. SILVERMAN: Those were made by Beckman at the time, yes, the paramagnetic principal was used, based on Linus Pauling's invention. The other interesting thing about that is that Tulane, which joined the cooperative trial, for the first time saw retrolental fibroplasia. And there was a lot of snickering about that and so forth, but as one looks back on it, the concentration for the first time had to be documented. And at Tulane they did not have these expensive Isolettes. They had the old fashioned Gordon Armstrong incubators with no gasketing; it leaked like a sieve. It was

impossible to get the concentration much above 35%, and when Tulane had to meet the conditions of high oxygen in this cooperative trial with an oxygen analyzer to document it, they had to tape all the slots in the incubators to make them gas proof. The minute that occurred, it was a very dramatic thing as one looks at it in retrospect; when the oxygen analyzers documented high oxygen concentrations, the eye disease appeared.

One of the other dramatic events during that trial, as people were biting their fingernails, getting more and more anxious, particularly after this article from Bellevue about the role of oxygen. Harry Gordon [1907-1988; New York], who was a highly respected pediatrician, had refused to enroll infants in this trial when he was in Denver. By that time he had gone to Sinai Hospital in Baltimore, but an article of his came out reporting the Denver experience, demonstrating that they had no retrolental fibroplasia after they reduced oxygen use. This was the reason, of course, he didn't want these infants enrolled.

Another trial that was reported came from Philadelphia between 1953 and 1954, with everyone biting on their fingernails, purporting to show that rapid weaning from oxygen increased the risk of RLF. This association had been made previously by an ophthalmologist in East St. Louis by the name of [Thaddeus] Szewczyk [1916-2002; Belleville, IL], who claimed the abnormal changes could be reversed by placing infants back into oxygen. He was a very good observer, looking at the eyes, and he said RLF happens when they're removed too quickly. And again, everyone said, "Prove it." An ophthalmologist in Philadelphia, whose name escapes me at the moment, reported during this interval, that indeed there was a rapid removal/slow removal contrast, and that one could radically reduce the risk by putting the infant back in oxygen when the early changes occur. Well as you can imagine, again, it was a controlled clinical trial, but those who were in the rapid removal period had been put back in oxygen, so again it was contaminated. One didn't know how to interpret those findings. Needless to say, these confusing claims and counterclaims had the effect of heightening interest in the cooperative study results.

Well anyway, all of the drama peaked in September of 1954, which was the first time that one could report the results of the cooperative trial which ended on June 30. It was necessary to look at the eyes for two and a half months to demonstrate whether RLF did or did not occur, whether it was progressive and whatnot. The announcement was made at a meeting of the American Academy of Ophthalmology and Otolaryngology in New York City, on September the 19th. The announcement made a tremendous splash as you can imagine, because the study clearly demonstrated that oxygen exposure, above FIO2 of 50%, increased the risk of RLF cicatricial damage threefold. Also, it is important to remember that infants in restricted oxygen had a lower risk but it was not zero. And that was the difference between

this national trial and the Bellevue trial. The claim by Bellevue said flat out that RLF-blindness could be completely prevented. These discrepant claims became a matter of controversy for years.

DR. GARTNER: During this time of all these exciting studies in the late 1940s and early 1950s, were you in practice?

DR. SILVERMAN: Yes, at Columbia I was what was called "geographic full time." In those days, pediatric departments were not only small, but the salaries were very small; much too low to raise a family. I had an office at Babies Hospital where I saw private patients, so I earned my own salary. But I was geographic full time and that's what allowed me to participate in these activities. It was sort of a compromise; it went on for a number of years. I was satisfied with the arrangement even though I earned much less than full time practitioners.

DR. GARTNER: And you were doing general pediatrics.

DR. SILVERMAN: Yes, general pediatrics, but, increasingly, as my name was associated with newborn infants, I was asked more and more to see newborns or to deal with problems about the newborn, and particularly about RLF. We were intensely interested in the late effects, the consequences of RLF. A number of associations were made in that trial that I think have plagued us since that time, and some that had not been predicted. For example, the national study indicated that RLF risk was 3 times higher in multiple birth, but this was not confirmed in other studies. We became aware of the perils of "data dredging." One other interesting observation in this very large cohort that was very provocative was that the risk went up with each day in oxygen. There were 700-odd enrollees. Each day in oxygen increased risk until it reached a plateau after 7 to 10 days when there was no further change in risk. Interestingly, no association was found between risk and oxygen concentration. So the lesson one learned from this was to remove them as quickly as possible. The large national trial failed to confirm the Bellevue claim that under 40% was safe, but it was so seductive it caught on and was quickly adopted as the conventional wisdom. I mean it sort of made sense, but nobody really looked at this as carefully as Kinsey, who pointed out that if you looked at the results there was no concentration of oxygen at which risk disappeared. He felt very strongly that a doctor should understand that there is no perfectly safe concentration. But, Kinsey was a biochemist and I think people tended to minimize his role. Harry Gordon played a very important role following the announcement by pointing out the defect in the trial with respect to mortality. He pointed out that infants were not enrolled until they were 48 hours old. Thus, nothing could be said about the influence of oxygen curtailment on mortality in the first 2 days of life, the age-interval when most deaths occurred in this pre-ventilator period. And it took 5 years until Hopkins reported that hyaline-membrane disease

mortality increased in the 5 year period following restriction of oxygen.

Kenneth Cross later pointed out that oxygen restriction both in England and in upper New York State [after 1955] was accompanied by a halt in the previous downward trend in mortality on the first day of life. So there was, in fact, a mortality cost, but only in the first day of life interestingly enough. And that gave everyone pause. Cross argued that there were 16 deaths to prevent each instance of RLF blindness. This was a sobering observation.

After the oxygen trial in 1953-54 and the polio vaccine trial in 1954, Congress began to pour huge amounts of money into research that would wipe out major human diseases. It made a tremendous impact. The *Saturday Evening Post* did an article which had wide, wide circulation broadcasting the Bellevue message that "oxygen under 40% is safe." And that became, well, as you can see, increasingly an issue. Most of these things were being argued in court, not in medical meetings, because malpractice lawsuits exploded.

DR. GARTNER: Back to something you mentioned, which I don't want to lose sight of because it was an interesting and important point. You mentioned that the creation of the premature units, as new hospitals were being built, was part of the legal mandate of the Hill-Burton Act. How did that happen to get built into the Hill-Burton act?

DR. SILVERMAN: As a result of lobbying by the Children's Bureau. The Children's Bureau had a long interest in infant mortality, sparked by Ethel Dunham [1883-1969; Washington, DC], who was in the Children's Bureau. She carried out a national survey and showed very clearly how few medical schools were teaching anything about newborn or premature infants and how few specialized units there were in the U.S. Dunham's data were used in writing the Hill-Burton legislation. It wasn't a mandated act, but money was available. In New York City, 16 premature infant nurseries used Hill-Burton money. None of the other units in New York City were quite as elaborate as the one we had at Babies, and that was a reflection of Dick Day's interest in planning the unit. As it turned out, an unfortunate consequence of the elaborate design didn't surface for almost 15 years. The design included an ultraviolet lamp in the ventilation system which generated dangerous ozone levels for thousands of infants. The pulmonary effects of this exposure were never evaluated.

DR. GARTNER: Do you want to continue with the story of retrolental fibroplasia research?

DR. SILVERMAN: Yes, as I've said, Tulane experienced RLF in the national trial. Prior to this, RLF was unknown in this huge premature unit. Monitoring of oxygen concentrations during the trial produced conditions associated with an increased risk. When the trial was completed analysis of

the association between oxygen and incubator type were examined and none were found. Of course there was no association between risk and type of incubator because the concentration was now being monitored. Another thing is the role of the float valve. This device made it possible to sustain high concentrations of oxygen in the Isolette®. The day that the results of the national trial were announced in September 1954, that there was an association between prolonged high concentrations of oxygen and RLF, Sam [Samuel Y.] Gibbon, the president of Air Shields, manufacturers of the Isolette®, came to our hospital [Babies], and he and I monitored the concentrations of oxygen in two Air Shields incubators with and without the float valve. He wanted it to be done in the field, not at the factory. This took hours, so we had an opportunity to see, during this period of time, the role of the float valve. And I must say to his credit that the following day he sent a telegram to every hospital in the world that bought Air Shields Isolettes, saying "discard the float valve." And since that day I have been looking for one and can't find it. [laughs] They're all gone. I regret to this day I didn't save a valve for historical purposes. You know, the total number of infants who were blinded in the 1942-1954 epidemic of RLF has never been tallied. Ten thousand is the closest number I have been able to find as a rough guess; 7,000 of these were in the US, more than in any other country.

DR. GARTNER: I remember in subsequent years, the Isolettes had a valve which limited the concentration to 40%, which was presumably the Air Shields' response to this.

DR. SILVERMAN: Yes, there was no question that the "under 40% is safe" dictum became the rule about oxygen in the 1955-1965 era. Surprisingly, there was virtually no dissent and no systematic look at the consequences of the policy change. Only in retrospect did we find that the increase in early mortality accounted for the virtual disappearance of RLF. The most susceptible infants died very early. Looking back, it seems incredible that we failed to see what was happening right in front of our eyes.

DR. GARTNER: Perhaps you can turn back to some more personal issues relating to your career. It's clear that Dick Day was a role model.

DR. SILVERMAN: Yes, no question, Dick was my hero.

DR. GARTNER: In many ways. And you talked about him. Were there some other people who you would classify in the same way as role models?

DR. SILVERMAN: Donovan McCune [1902-1976; New York] was a brilliant pediatrician at Babies Hospital. He had many personal problems, but he had a very incisive mind. I admired his skepticism and the way he looked at evidence. There was no question that he was a role model. Jack Caffey, at Babies, was a real curmudgeon. We used to call him Black Jack,

and Cactus Jack. He was very gruff. When Dick Day and I were driving everyone crazy with our emphasis on statistics, clinical epidemiology and numbers, Jack Caffey, at one point got so exasperated, he said, "Bill, I wouldn't believe it even if you proved it to me." And [laughs] I, at the time, so patently illogical, but, as the years went by I realized he was absolutely right; there are no complete proofs here in medicine. We're always dealing with probability; there are no absolute proofs. So Jack Caffey was in many ways a role model. Hattie Alexander was another stellar member of the Babies Hospital staff. I identified with these teachers; not one was a team player. Rusty McIntosh, our chief, assumed complete responsibility in ways that are unimaginable. At the time of the ACTH trial, I'll never forget his words: "You *must* do it." I admired his role. He was also a fantastic editor.

Every paper that left our institution had to go through his hands, and those of his wife, Millicent, who you know, was the president of Barnard College and an expert in English. So most of the English was prettied up. After Rusty went over every paper, the syntax had to pass the eagle eye of Millicent McIntosh [Millicent C. McIntosh; 1898 – 2001; New York]. His correction of the prose was really wonderful. Rusty McIntosh certainly played a very big role in my life. Dick Day was a relentless critic and a breath of fresh air when I was a junior member of the staff at Babies. I became a critic when I came to Babies Hospital exposed to these other skeptics. The one thing I've said over and over is not one of these people that I admire so was a team player. None of them were team players. They were individualists, you know, and I think that probably explains my life-long problem with team-think. [laughs]

DR. GARTNER: Perhaps. [laughs] You mentioned Hattie Alexander and you mentioned some other women.

DR. SILVERMAN: Yes, Beryl Paige. Beryl Paige and Dorothy Andersen were pediatric pathologists who were wonderful, wonderful observers.

DR. GARTNER: There were a number of women in pediatrics.

DR. SILVERMAN: Yes, oh yes, at Columbia, which is interesting because many people have said to me that Rusty McIntosh didn't hire many women. But many stars in the department were women.

DR. GARTNER: Were there women trainees with you and the residents?

DR. SILVERMAN: Yes, when I was a resident we had 5, as a matter of fact, out of a total of 11 or 12 [residents].

DR. GARTNER: You were in general pediatric practice for some years.

DR. SILVERMAN: 17 years.

DR. GARTNER: How would you describe the quality of general pediatric practice at that time?

DR. SILVERMAN: Well, I'm glad you said that because during this period of time, when I was in general practice in the 1940s and 1950s, I had an impression that American pediatrics was going off in a different direction compared with other countries. In other countries, Britain particularly, and even Canada to some extent, pediatricians were specialists who saw sick children. They did not see well babies. Well babies were seen by general practitioners. In other words, there was a strong general practice base in these other countries, and pediatricians were specialists in sick children. In the US, more and more, pediatricians were seeing well babies. That was not the case when I first entered pediatrics. There were relatively few pediatricians if one compares it to present, and there were a lot of family practitioners. But general practitioners were clearly second class citizens; they were really sort of drummed out of existence in this country. Pediatricians became the general practitioners for children. I felt that that trend was going to dull pediatrics. You may remember that during those times there were many letters and articles in *Pediatrics* about pediatricians who were dissatisfied with what they were doing, because seeing well children was not very intellectually stimulating. They had to see a lot of children every day because the fees were so low. Assembly-line quick check-ups became the American norm. I deplored this trend and spoke out about it. Needless to say, I was not very popular with main-line pediatrics. Pediatrics went off in a different direction and became general medicine for children. And I think that dulled the edge.

DR. GARTNER: What long term effect do you think that has had on pediatrics in the present day? Has that altered pediatrics; would pediatrics have been different today if that had not been the case?

DR. SILVERMAN: I think that if that argument had resulted in some change early on, we would have fewer pediatricians than we have at the present time. It's the number which is so much larger than other developed countries as a result of this decision by pediatricians to see well children. And, I don't think our children are healthier. Our leaders in pediatrics wanted to get rid of the notion that family practitioners could care for normal children and they pushed for increasing the number of pediatricians, who, they argued, understand growth and development, and should manage immunizations and emphasize feeding. Our glut of pediatricians, many more than other countries continues to be a problem.

DR. GARTNER: Was that one of the reasons that you left general practice and moved into full time neonatology?

DR. SILVERMAN: I grumbled about this for a long time, and with the passage of time I found myself fascinated by the newly recognized problems of the newborn.

DR. GARTNER: What do you see as the biggest changes in pediatric practice in general? Not neonatology, but in general, over the past 40 years or so?

DR. SILVERMAN: Well, my impression, and, as you know I've been away from the front lines for years, is the trend of medicalizing [laughs] child care. I think parents have been rendered relatively uncertain of their competence. They turn to the pediatrician for the answer to every question. I see this as a problem. Parents should be made to feel confident about making common sense decisions about child care. I think one of the problems of having too many pediatricians doing general practice is the effect it has had on disempowering parents. Parenting could be made much stronger if pediatricians spent their time saying, "You should be able to decide that; it doesn't make all that much difference, you decide."

DR. GARTNER: Do you see a trend in major conceptual [pediatrics], aside from the actual practice settings, and the numbers and the qualities of practice? Are there major concepts in pediatrics that have changed in the past 40 years or so?

DR. SILVERMAN: The character of pediatric pathology has changed very dramatically. When I was a young pediatrician our hospitals were filled with children who had acute illness. Relatively well children had severe acute infections. These were conquered by antibiotics, and the cured children were sent home, often, intact. The hospital population changed dramatically over the years; more and more chronically ill children, children with malformations, many of whom died early in the past, were now filling hospital beds and their abnormalities were being vigorously attacked. This changed the character of pediatrics completely. Many pediatricians in those years said: "I went into pediatrics because it is such a cheerful specialty, you know, you have young children and parents and kids get well and they're gone." They deplored this change as pediatrics began to resemble gerontology. Pediatrics is completely different from when I began. And the trend began during the time that I was doing the pediatric practice.

DR. GARTNER: Are there any other reasons that you made the decision to leave general practice?

DR. SILVERMAN: I think I felt it was unfair to my pediatric patients since most of my attention was focused on the premature infant, and this was becoming of course much more exciting and more demanding. The care of the premature infant was changing dramatically. So I thought it was very

unfair to be distracted; at least that's how I rationalized it to myself. I felt that I had to go where my head was.

DR. GARTNER: Was the economic situation for a full-time academic practice changing?

DR. SILVERMAN: Of course, no question, that improved as well. I could now support my family on an academic salary. Trying to raise 3 children on a full time salary in the 1940s and 1950s was impossible.

DR. GARTNER: But increasingly became possible?

DR. SILVERMAN: Became possible, and yes, that played a role in my decision.

DR. GARTNER: What about the major scientific advances in pediatrics in general, outside of neonatology, over the past 40, 50 years? What do you see as the big changes that occurred?

DR. SILVERMAN: Well, our ability to combat infections changed everything. I gave the first dose of penicillin to 8 neonates with congenital syphilis when I was a resident at Babies Hospital. This was a completely unprecedented miracle in pediatrics. To develop a very strong response to these acute illnesses, I mean it just changed the character of pediatrics; no question about that. The post war emphasis on nutrition was impressive, and of course that work continued. We like to think that our children are now being fed better than anywhere on earth. I think the other big change that has occurred is one of attitude about disability. Children with disabling conditions, I think, are now being treated very differently than they were when I was a young pediatrician. I'm particularly aware of this, because I've been interested in blind children, those children who were blinded with RLF, became toddlers and children and now school age and young adults. I have been following this now for more than 25 years. And it's the change in the attitude about "the disabled", about a blind person, that has changed. And I think pediatrics was in the forefront of that as well, to begin to pay more attention to children with all disabilities and their problems. I've been on the board of directors of the Blind Babies Foundation of San Francisco. We've changed the status of these children and adults from "disabled" to self-sufficient persons participating fully in every-day life.

DR. GARTNER: Perhaps we can just go back a bit to your being in general practice. Did you make house calls? House calls were part of the scene at that time.

DR. SILVERMAN: Interestingly enough, it was not only that we made house calls, but I made house calls in New York City, if you can imagine!

(laughs) I could park my car anywhere day or night. New York City was very different than it is now. I felt that house calls were a very, very important part of understanding a child and the family. And I found people were so different in their behavior at home as compared to my office or in the hospital. I always felt that house calls were a very, very important part of general practice. But it became increasingly impractical. New York City became crowded, and pediatricians, by and large, stopped making house calls. Mothers wrapped up their feverish kids, with 105° temperatures, in blankets and brought them in the office. That was unheard of when I first began but the culture changed. I've become even more convinced that you don't really understand people until you see them in their own setting, not in ours.

I've learned more about the blind as friends, hiking with them, visiting in their homes. You then understand the issues very differently than you do in the hospital. I've become convinced we simply don't understand their lives when we see them only in our offices or in the hospital.

DR. GARTNER: Tell me more about your involvement with the blind community.

DR. SILVERMAN: Well, when I came back to California in 1968, first I wanted to get back to my home state, and, second, I learned that there were more ex-RLF blind young adults in California than anywhere else because the educational opportunities for the blind were greater here. You see there's a school for the blind right next to the University of California. Early on the university was re-enrolling blind students and making it possible for them to go on to higher education. The law school was the first to enroll blind students. So these opportunities for higher education brought many families to northern California. I contacted families of RLF-blind kids, and that's how I was appointed to the board of the Blind Babies Foundation, which was set up in the late 50's to provide parents with advice about how to rear a blind infant. That was a dramatic and important development. I've also served on the professional advisory committee of the Blind Babies Foundation and also on the LightHouse for the Blind. As a result of these activities, I've seen the long-term consequences of the RLF epidemic. These people, many of them in their 40s, face an unemployment rate of almost 80%. Their parents are my age, in their late 70s, and are saying to me now, "What is going to happen to my children when I die?" And so these are the echoes of the 1942 to 1954 epidemic. The effects are still with us.

DR. GARTNER: Have any gone to medical school?

DR. SILVERMAN: Yes, as a matter of fact, one of my patients who was a surviving twin, who weighed 1,000 grams, or maybe even a little less, a surprisingly small infant for the 1950s, not only grew up to go to college and

to travel the world independently, but to go to medical school and then to go into pediatrics. Her retrolental fibroplasia left her with fairly serviceable vision, but there's a late problem. Some of these ex-premies with RLF develop partial retinal detachments and other complications with age. But this woman's deafness was much more limiting. We had a terrible time trying to get her into medical school. Medical schools don't want deaf students. [University of] Rochester finally took her and she became a very good student.

DR. GARTNER: She was not totally blind.

DR. SILVERMAN: No, no.

DR. GARTNER: Are there any completely blind people who entered medical school?

DR. SILVERMAN: None that I know of, that are completely blind. But, I'm convinced they should be given a chance. The ability of some blind people is just incredible. I should mention that the survivors of the 1942 to 1954 epidemic are different from the blind whose parents in later years were given advice by organizations like the Blind Babies Foundation. When parents are taught to provide early sensory stimuli, auditory stimuli, tactile stimuli, talk to the infant, to make up for the loss of vision, that advice given very early has produced blind children that differed completely from that first epidemic. All of the blind "isms" that we used to see, the rocking and the gouging of the eyes, the autistic symptoms, you don't see that anymore. It's just incredible that this early attention has had a very sharp effect on these behaviorisms. I suspect the new approach has had other effects, as well, but nobody's been looking at that systematically. It's been a very interesting experience to see how these new blind are different in other ways. In the original RLF cohort, blindness was usually the sole disability. Now, of course, neurological disorders are almost the rule. Isolated RLF-associated blindness is rare. There are usually other neurological and cognitive problems and they overshadow the visual impairment.

DR. GARTNER: I remember some years ago you did interviews with RLF survivors, asking them about their blindness, their own personal attitude toward being blind in relation to their previous care. Do you want to talk a little bit about that?

DR. SILVERMAN: Yes, there is a skill center for the blind in the [San Francisco] Bay area in which blind young adults are taught how to live independently. I wanted to speak with this group because many of them were blind as a result of RLF. This was about 20 years ago. We had long conversations, and the interesting thing about these conversations is that no one had talked to them about the cause of their blindness. They were told

that they were premature infants, but their parents did not want to talk about it. Their doctors didn't want to say anything. There was an embarrassment, it seemed. But I interpret it as part of a lot of guilt; that this was the result of medical error. So I said, "Look I'll be very happy to talk to you about the history of RLF if, in exchange, you tell me what your experience is, what has it been like to grow up blind." So that was a very interesting exchange. I related the whole RLF story, with no holds barred about how wrong we had been and the mistakes we had made, and they told me with no holds barred what it is like to be blind in our sighted society.

One man told me that God was punishing his family. His family was told by their preacher that they had been sinning; the blindness was retribution on high. That's what his preacher told him. Incredible experiences they've gone through. Others spoke of themselves as super "crips." They made it and there is nothing that they can't do, skiing, going to school, etc. The only thing they couldn't do was learning to drive a car. One of these young adults told me that not only was everybody avoiding the topic of prematurity, but they can't even imagine what a premature infant or a premature nursery was like. So I said, "You mean you would like to see a premature nursery?" She said yes, and a few others said yes. So I arranged a visit in which these blind young adults went to a premature nursery here in San Francisco. I told the nurses they were coming. The nurses had some conversations with the blind visitors, and then I invited them all to come here at my home for pizza. The blind young adults and the nurses came and talked to one another here. We made sure they had plenty of beer with the pizza, so they were quite uninhibited. There were some very, very moving exchanges as you can imagine, with the nurses particularly. One nurse said: "When I'm finished with my duty as an intensive care nurse, and I come home, I can't go to sleep. I say, who am I doing this for? Am I doing it for you or for me?" The culture of the blind is very interesting, and also very disturbing. They haven't been able to become employed and live independently. Some have wonderful jobs, but the majority are completely dependent financially on parents or on SSI [Supplemental Security Income].

DR. GARTNER: I didn't realize their unemployment was that high. I want to ask you about another career move that you made; that was your move into bioethics. How did that come about? What were the major influences that led you in that direction?

DR. SILVERMAN: I think that the most important thing that led me to speak out about these issues, was this experience with the young blind adults. And the nurse's question, "Who am I rescuing babies for?" resonated. And I'd become interested. I had become more outspoken because I think that the effort which is put in to keep marginally viable infants and severely malformed infants alive and the amount of time and money expended and number of personnel and the expertise committed, is not balanced by a

similar effort to help the families when they go back out in the community. Many of these families are ill prepared to deal with normal children; they're so economically deprived, there's so much social chaos. The disconnect between what's done in the NICU and what is done after they go home has bothered me. Increasingly I have been writing, speaking and expressing myself about it. So my interest in bioethics is: what are the long term social consequences of the activities of the present intensive care unit and the premature unit of my day? I see now how short-sighted I was as an eager young resident rescuing 400 or 620 gram premies. I was focused on their immediate survival. The parents were looking to the future. As I grew older I realized the parents were absolutely right and this led me to question my short-sightedness. We have to figure out some way to face these issues; otherwise it's obscene. I really think it's obscene. I was going to say immoral, but certainly obscene, probably immoral.

DR. GARTNER: What are your feelings about academic medicine, academic centers and the whole academic enterprise? How do you view them, past and present?

DR. SILVERMAN: When I was at Columbia in the middle 1960s, it was a time when the amount of money available for research increased dramatically. The polio vaccine, the oxygen trial and whatnot, influenced the legislature to pour money in. The NIH increasingly had extramural funds for studies. It had a dramatic impact on academic institutions like Columbia. I was on a committee of the medical school in those early years of temptation. We asked, "How big does Columbia want to grow? How large will the medical school be in ten years?" So we canvassed every head of a department in the medical school. Not one single head of the department was willing to make an estimate of that size. And you know what happened, all medical schools expanded explosively. Additionally, academic activity became a team sport. The individualists I so admired at Babies, were succeeded by managers with hordes of trainees. Individual provocative thought was replaced by group-think. I see that distinction as a very sharp one, that one change which has occurred. And as you can see, I think I prefer the other. I think that's one of the problems with academic medicine. In the mid 1960s suggestions were made that neonatology should become a separate academic discipline with certification by boards and whatnot. Suggestions of this were made at the time of the spring meetings in Atlantic City. I can't remember the year, but again it would be about the mid-1960s. I was very much against that move. Obviously I lost. I objected because I felt that it would separate the activities in the nursery from what happened afterward. Early on, when rounds were made, for example, at Babies Hospital, we went through the whole hospital, floor by floor, and looked at all patients. Consultants came from cardiology, other specialties and whatnot. Increasingly that changed as the departments grew, and what were vertical rounds, vertical rounds meaning you start at the top of the hospital

and go down, became horizontal rounds, in which the cardiology group would make rounds on the cardiology patients. Specialization gave a more restricted view of what pediatrics is all about. That was why I was against specialization for neonatology. In other countries, pediatricians interested in neonatal medicine retained their activities in general pediatrics and they asked more questions about outcome. It's the matter of the early events, early activities, and late outcomes, that connection I think is threatened by having the increased specialization, the neonatologist who never leaves the unit. That's why I was against it; obviously I lost. And the specialty has grown. Needless to say, my views about specialization were never popular.

DR. GARTNER: I don't know that you lost. [laughs] Were you involved with the American Academy of Pediatrics?

DR. SILVERMAN: Yes, I was the chairman of the Committee on Fetus and Newborn, and I served a term as chairman of the editorial board of *Pediatrics*. Clem [Clement A.] Smith was the editor of *Pediatrics* at that time. Charlie [Charles] May was the first editor, and then Clem Smith took over. What I remember most is that during Clem Smith's tenure Clem developed rheumatoid arthritis, acute, very disabling kind of acute rheumatoid arthritis. The question arose at the Academy of Pediatrics whether he was fit to carry on as editor. Since I was the chairman of the editorial board, you know, this was all discussed. And our feeling was that his thinking wasn't impaired. He was carrying out the work; he just needed a little extra help. Steroid treatment was available and improvement could be expected. Our feeling was that he should not be let go, because it meant an awful lot to him. And I thought Clem was doing a very good job. So I went to the Academy meeting in Atlanta. I made a plea to keep him on, and I'm very glad they did. As it turned out, his symptoms responded quickly. I think things worked out very well.

When I was Chairman of the Committee on Fetus and Newborn, a number of issues came up. Standard terminology for newborn infants and prematurely born infants, standard definition of gestational age, etc. were formalized. We made recommendations that were used thereafter.

Another event when I was the chairman of the Committee on Fetus and Newborn was an incident in upper New York State, which you may remember, of salt poisoning. In the days before infant formula was purchased commercially, it was made in each hospital. And a nurse accidentally put in salt instead of sugar, and there were a number of deaths from acute hypernatremia. As you can imagine, this made the national news, and I was asked, as the chairman of the Committee on Fetus and Newborn, to comment on this disaster on a national radio program called Monitor. And I was interviewed by Frank Reynolds, a very sharp reporter asking me what do you think and so forth. Then he said, "Dr. Silverman, when the

nurses make up formula, don't they taste what they feed to the babies?" [laughs] And I said, weakly: "I'm afraid that isn't routine." But you'll notice in the next recommendations by the Fetus and Newborn Committee, it advises that nurses taste the formula.

DR. GARTNER: Have you continued your involvement with the Academy?

DR. SILVERMAN: No, I've had no formal association except my interest in history and contributions to the Academy's historical archive.

DR. GARTNER: How about other organizations? What roles have you played in other national or international organizations?

DR. SILVERMAN: Yes, I continue to be involved in the evidence-based medicine movement that promotes controlled clinical trials. This became a very important part of my life and I had become very involved with others in this move for evidence based medicine. The centers for evidence-based medicine is at McMaster University in Canada, led by Dave [David L.] Sackett; [1934 - ; Hamilton, Ontario, Canada], and in England at Oxford, led by Iain [D.] Chalmers [1940-; Strathclyde, England]. I had an opportunity to be in [University of] Oxford as a Christensen Fellow at St. Catherine's College, and that firmed up my attachment to the Cochrane Collaboration. Recently I was appointed a Cochrane Fellow, so I've kept up with the growth of the evidence-based medicine movement which I've been involved in from the very beginning. I met Iain Chalmers, the man who established the Cochrane Collaboration, just as he finished his training in epidemiology with Archie [Archibald L.] Cochrane [1909 – 1988; Cardiff, Wales] in Wales. We became very close and we've been seeing each other over the years. So I feel that that's a group in which I've not only participated but encouraged, and I'm very pleased to see what's happened with that development.

I've had lectureships but no other organizations. I served on the advisory committee for the World Health Organization for a number of years, but it was a dummy appointment. I was never called upon to advise about anything.

DR. GARTNER: You used the name "Fumer" for your email address. Would you care to comment on that?

DR. SILVERMAN: Well, for the last ten years I've been writing a column for *Paediatric and Perinatal Epidemiology*, since that journal began. Jean Golding, the editor, wanted to have a section called, "From Our Correspondents." She asked if I would be willing to be a correspondent. I thought about it, and asked whether she would allow me to write the column anonymously and if I could call this column, "Fumes from the Spleen." She was very gracious and said I could do that. So, I've been writing that column

for about 10 years, and that column is signed, "Malcontent." So when I discovered email I thought I would use "fumer" as my screen name. I've now written about 45 of these essays for *Paediatric and Perinatal Epidemiology* and I'm now assembling them for publication by Oxford University Press. I have a thing about anonymity, feeling, with [W. H.] Auden, that a pen name forces the reader to focus on what's said instead of who said it. But, Oxford University Press doesn't agree, so the essays will come out under my name and the title of the book will be, *Where's The Evidence?*

DR. GARTNER: Have you published under other anonymous names?

DR. SILVERMAN: Well, it's not a very well kept secret that I've used the name "Student" for contributions to *Pediatrics*, over the years. The pieces are usually white-space fillers; but, I've written a couple of articles under the name "Student" as a tribute to Dick Day who said, "A student is someone who thinks otherwise." Dick encouraged students to disagree with their teachers, and that is really the essence of the reference to the term. Dick Day and I talked about this issue for a very long time and when I wrote my book, *Human Experimentation*, I dedicated it to Dick and I used his aphorism. I think it's very, very important that students should be disrespectful, that they should be skeptics. Petr Skrabanek [1940 – 1994]; Dublin, Ireland] from Ireland, who died recently, was another leading skeptic. I've been in touch with him over the years. He encouraged medical schools to have clubs dedicated to medical ignorance. Students should be encouraged to get together and look at what is known. I'm encouraged by the news that the University of Arizona College of Medicine has established a course on ignorance; but it's the only one, and I'd love to see it.

DR. GARTNER: Interesting. Let's go back a little bit to the formula issue and feeding, what we feed preemies particularly, and sick newborns in terms of formula, breast milk, and where we've gone with all of that.

DR. SILVERMAN: Yes, I think we've gone, of course, a very long way from the original recommendations of the French to feed breast milk, and to arrange wet nurses or any way one can get breast milk for newborn infants. Yes, I think that the big move, the first big move was the Cornell group's advice to reduce the fat content of milk for premature infants. And I think what bothered me about that advice was the narrow view: how can we get the premature infant to gain more quickly so he can leave the hospital? In the early days we were not permitting parents to come in [the premature nurseries] or to touch their infants because we were so fearful about infection. We were trying to get them out of the hospital into the parents' arms more quickly. You know, that was very mixed up; the concept was very mixed up. And I think that one again says, feeding for what? What are you attempting? What body composition are you attempting to attain? I'd

love to get back to breast feeding and breast milk, and breast milk [banks]. The low-fat high-protein feedings went on in this country for 12 or so years before there was concern about high tyrosine levels and follow up about the cognitive status of those infants that triggered concern about its harmful effects. The practice of early fasting and early thirsting [of newborns] was another strictly American practice that was never evaluated despite great suspicions about it. Yes, the thesis was that the newborn, especially the very small premature infants, had a surfeit of water and electrolytes, and that one had to wait until this surfeit was eliminated before [starting] feeding. That practice, you know, based on this thesis went on in this country for years. It was the oxygen trial which awakened me to how important it was to take all of these practices which had never been evaluated and to try to look at them systematically, and to say at the outset we don't know the benefits and, God knows, many times cannot predict the harms. That led, as you know, to my maniacal preoccupation with controlled clinical trials. That preoccupation began when the practice of using Alevaire detergent mist was debunked by our randomized trial.

DR. GARTNER: Years ago you returned to California from New York and you changed your career and made a lot of changes in your life. Can you tell us a little bit about that, how that came about?

DR. SILVERMAN: Yes, that was a kind of a rough time [late 1960s]. I was beginning to have many second thoughts about neonatal intensive care, which was becoming very intensive. I had a lot of doubts about how far down [in birth weight] we should extend the effort and I quite frankly was beginning to feel homesick for California after 28 years in New York. So we came back to northern California ostensibly to open a neonatal intensive care unit at the Children's Hospital of San Francisco. My feeling was that I wanted this intensive care unit to be a little less intensive and to have a lot of consideration about what happens after the infant is discharged. Unfortunately, that really didn't work out at all. The promised cooperation of the obstetricians wasn't forthcoming. But another reason I came back [to California] was a burning desire to contact the blind, and this worked out extremely well. So much so that the California Department of Rehabilitation hired me as a medical consultant and this put me in touch with blind young adults who were attempting to become employed and live independently. So I used this as an opportunity, and it was a very fruitful opportunity, to interview the blind and their families to learn what their lives have been like. That's been very, very rewarding. Most of my activity following that was that. I also felt a burning need to write the story of the retrolental fibroplasia epidemic, So I spent quite a few, I was going to say months, but several years is what it amounted to, to write *Retrolental Fibroplasia: A Modern Parable* [published by Grune and Stratton]. It's now out of print, but the book is available on-line. [http://www.neonatology.org/classics/parable/default.html] I was pleased to see that it was well received. For me it was a wonderful

catharsis to be able to say what I really thought about that incident.

Increasingly, I became involved in Ian Chalmers' evidence based medicine movement. That led to the book *Human Experimentation: A Guided Step Into The Unknown* [Oxford University Press 1985], I went to Oxford on a Christensen Fellowship at St. Catherine's College to write that book. Oxford University Press was a wonderful, wonderful publisher. My first book was the third edition of Dunham's *Premature Infants*, published by Hoeber. That was a very different experience.

DR. GARTNER: Do you have another book in the making now?

DR. SILVERMAN: Yes, I am co-editing the book *Bioethics in Perinatology* and writing "*Where's the Evidence*?" also by Oxford University Press. I have 45 essays to put in.

DR. GARTNER: I look forward to that.

DR. SILVERMAN: I've not told you about the adventures following the national oxygen trial. This turned out to be a very intense 7 year period. The lesson of oxygen and retrolental fibroplasia led to questions about other ticking bombs in the nursery. There was a certain urgency to this because, for example, the policy of initial thirsting and fasting was extended to 24, 48 and even 96 hours.

DR. GARTNER: Yes, I remember that.

DR. SILVERMAN: Sid [Sydney S.] Gellis [1914-2002) of Boston advised that incubators be kept at high humidity, and even later, filled with water mist as treatment for hyaline membrane disease so these infants would not dry out too quickly. These interventions had never been evaluated. Interest in hyaline-membrane disease or respiratory distress syndrome was sparked by the fact that infants raised in Isolette incubators were naked and their chest retractions were more visible than ever before. The Isolette incubator was higher than the old-fashioned incubators, and you could see the infant at room's length. Now nurses stared at these babies as if they'd never seen them before. The retractions and the grunting were striking and this new awareness was behind the proposals for treatment with water vapor. The propellant for the water vapor was oxygen. So here comes the prohibition on prolonged high concentrations of oxygen, but water vapor had to be propelled. The lesson of the oxygen RLF study was: what do we do? Has it ever been documented that this in any way improves respiratory performance? Anecdotal evidence was no longer good enough. And then as if that wasn't bad enough, there was a very spectacular claim made by a man in North Carolina, that a detergent called Alevaire was a cure for respiratory distress, if it was nebulized and inhaled by infants. This was written as an

article in the *Journal of the American Medical Association [JAMA]*, was widely publicized. There were newspaper articles about airplanes flying to remote nurseries where they had an infant with respiratory difficulty to deliver the life saving Alevaire.

When this practice began, the Alevaire seeped into the motors of the incubators, fouling up the motors, so they burned out. We soon asked, "Why are we using Alevaire, when it was perfectly obvious that we needed to evaluate all new treatments rigorously?" So, it was most urgent to find out if Alevaire and water mist really worked. Use of these interventions exposed our babies to more oxygen than we were now comfortable using. Over the next 7 years we did a series of controlled trials which turned out to be very surprising; different than I ever expected. The first trial compared Alevaire with water mist; this was a fixed sample-size one year trial. The nurses were by this time also quite convinced it was necessary to do controlled trials and their cooperation was marvelous. At the end of one year we found there was no difference in outcome. We tried to publish this in *JAMA*. *JAMA* delayed publishing it for almost 8 months. I wrote letters asking about the delay and learned the company that was making Alevaire was exerting strong pressure to block publication of our paper. It led to quite a brouhaha. It finally was published. Within days after it was published, the company salesman came by grinning from ear to ear. I said, "Why are you so happy, after this adverse report on Alevaire? He said, "Don't worry. Your paper will have no influence on our sales." And he was absolutely right. Doctors continued to use the Alevaire mist. Negative trials, I have discovered, have really little impact on practice.

Following the Alevaire experience, I asked, "Why are we using water mist; it's never been tested adequately." In the 1920s [Kenneth D.] Blackfan and [Constantin P.] Yaglou did a 7 year observational study looking at the relationship between body temperature, air temperature, humidity, and outcome. They recommended that infants be kept in moderate, 60-70% humidity, and this became standard practice. When their observations were published in 1933, we decided to get back to those conditions step by step; so, the next trial compared water vapor with high humidity. Once more the results were exactly the same – no difference. I invented a retraction score so the nurses could standardize their observations of respiratory activity. This crude approach was surprisingly reproducible. It was adopted for everyday use in premature units. The respiratory scores, the mortality rate, and the findings at autopsy were exactly the same. Following this negative result, we said: "Let's get back to Blackfan and Yaglou's conclusion. We compared high, 80 to 90% relative humidity with 30 to 60%. The trial took a year. Now to our complete astonishment, there was a significant difference in mortality! Infants in high humidity, had a lower five-day mortality. I simply could not figure out why that was so. We looked at the post-mortem, findings and found no differences. Infection was the same; we could find no

obvious differences in these two groups. This was a real puzzler.

As I looked more carefully, I did find a small difference in body temperature. Infants in high humidity, where vapor loss was less, had higher body temperatures, but the difference was very small. It seemed incredible that a crude outcome like mortality would be influenced by such small differences in body temperature. So we decided we must now examine the unpredicted outcome by comparing the two air temperatures at the same high humidity. We used a new method of sequential analysis to evaluate mortality differences continuously. Now, to our intense satisfaction, infants in the warmer incubators survived in greater numbers. In 1958, we overturned the Blackfan thesis that low body temperature in premature infants was "normal"; a claim that lasted 25 years without challenge. Finally, we compared 2 humidities at the same warm body temperature, using a servo-controlled loop control to maintain the same body temperatures in the two humidities. This device was used to carry out the trial; it was later adopted for everyday care under a radiant heater. The radiant heater was also devised for our temperature/humidity trials. As these trials were going on, there were also questions about how to manage the premature infants' high risk for infections. The Swedes began using prophylactic antibiotics and the reasoning seemed sound because it was very difficult to make the early diagnosis of infection in the smallest infants. The only question seemed to be what is the best agent. For a period of time we were using penicillin and sulfisoxazole (Gantrisin) as the prophylactic combination.

A new antibiotic, oxytetracycline, was introduced, and this was easier to administer. So I said, "Ah-hah, this is an opportunity finally to do something." We devised a factorial design for this trial in which half of the infants were either on the old antibiotic regime, penicillin and Gantrisin or oxytetracycline. These were interdigitated in the temperature trials so we carried out 2 trials in the same time and tested interactions. As you know, we came up with an incredible outcome! We demonstrated very clearly that the infants who received the old accepted drugs had a much higher mortality rate. The second to fifth day mortality rate was considerably higher, and kernicterus, a completely unexpected association, was 9 times more frequent. This was a spectacular end to this trial. The trial was considered to be so mundane. I wanted the medical students and the house officers at Babies to get more experience with randomized trials, so I proposed that they conduct this antibiotic trial. They all refused, "Too dull." They said it isn't interesting enough.

DR. GARTNER: [laughs]

DR. SILVERMAN: It turned out that this antibiotic trial was the most spectacular project that one could imagine and convinced me even more that we had to test absolutely everything, every intervention used in the care of

premature infants. Also, as a result of the Gantrisin trial, it was very clear that we could not continue to do fixed sample-sized trials in which we postulate the differences expected, compute the number required to test the question, begin the trial and at the end look at the results. The Gantrisin trial could have been stopped very much earlier if we had a monitoring plan. And it was this experience that led us to sequential analysis. As we talked about how to get around the strictures of fixed-sample size design, John [W.] Fertig [New York] remembered that the mathematics department at the Columbia University main campus had developed a scheme for evaluating the duds in the production of bombs for the Navy. They worked out a plan to look at the dud rate without blowing up all the bombs in a batch. They developed a sequential scheme, so the minimum number of bombs would have to be exploded to estimate the true dud rate. Well it turned out that was just the principle we were looking for. We wanted to expose the minimum number of infants to compare conditions that would allow us to confidently conclude there was a significant difference in outcome. So that period of 7 years in which we were doing these trials, was very, very educational. We had disastrous experiences; we were forced as a result of that to look at more sophisticated designs for randomized trials. I was, at the end of that 7 years, needless to say, a confirmed randomized trial addict. it was that experience more than any other which sort of continued my interest in encouraging randomized trials and why I tried so hard to convince my coevals to adopt this powerful methodology. It couldn't prevent all disasters, but it could reduce the number injured. It's taken a long time. I mean, it's taken many, many years to convince everyone that their hunches, their ideas, their hopes, have to be tested by formal and rigorous methods.

John Fertig, the statistician at the Columbia School of Public Health, was a wonderful mentor during all of this. Dick Day had originally made contact with him, when Dick got interested in statistics. I would go to see Fertig with Dick until Dick left to go to Downstate Medical Center in Brooklyn and then to The University of Pittsburgh Medical School. I then took up with John Fertig. He used my trials for his students. It was a wonderful experience and a very successful way to demonstrate to his students in statistics the importance of clinical investigations. Whenever I developed a protocol, I would take it over to John Fertig and he would present it to his students as a class problem. I would sit in on the discussions. It just was a wonderful relationship. The difficulty was I couldn't get anybody to go to these sessions with me. [laughs] I wanted the younger staff to get involved but there was no interest. That 7 year series of trials was such a convincing lesson of the power of the format to detect important effects of seemingly minor changes in clinical management. For example, that small changes in heat loss have a measurable effect on mortality. I've always regretted that we didn't examine the thermal effects further. We didn't examine, for example, the effects of a warm torso and cool head, whether or not you could achieve the same protective effect of warmth while driving respiration with a

cool face. There were a lot of unanswered questions. And also unanswered questions about hypothermia. There had been some very provocative studies in small experimental animals about inducing hypothermia and prolonging resistance to asphyxia for a much longer period of time. If you rapidly cool the animal, they were able to tolerate lack of oxygen for a much longer period of time. These animal observations were translated into action. Virginia Apgar [Professor of Anesthesiology at Columbia University] began treating asphyxiated newborn infants by plunging them into ice water. But, she was never willing to carry out a formal trial. This was particularly distressing at the time because we were looking at effects of minute changes in heat loss on survival while in the delivery rooms, 2 blocks away at the Sloane Hospital for Women, the anesthesiologists were putting infants into ice water! Although these were term infants, none the less I was just horrified by what I saw as irresponsible trial and error – the results were uninterpretable. The next chapter in neonatal pediatrics began in pediatric units, not in the delivery room. The delivery room was the province of the obstetrician and the obstetric anesthesiologist and we pediatricians were clearly persona non grata. So all of these things were happening in the delivery room, and we were sitting there horrified. It was a lack of communication.

DR. GARTNER: What years was that?

DR. SILVERMAN: This was in 1962, 1963, roughly. It was when Virginia [Apgar] had transferred from her post in the department of surgery, where she was in charge of training nurse anesthetists, to the delivery room where she promoted more active resuscitation of asphyxiated infants and marginally viable neonates who, in the past, were allowed to die quietly.

DR. GARTNER: Was that just at Columbia, or do you think that was universal?

DR. SILVERMAN: Communication between pediatrics, obstetrics and obstetric anesthesiology was particularly bad at Columbia because of the physical separation, but the separatist attitude was pretty general. For example, when neonatal resuscitation and intubation was taught at Saint Vincent's Hospital in New York by Dr. Paluel Flagg, an anesthesiologist who developed a special laryngoscope for the newborn, the obstetric residents were sent for formal training, but the pediatricians were not invited. So there was a lag before the pediatricians got involved at Columbia. Although it was exaggerated at our place, the divide was pretty general in American medicine. It required neonatal intensive care to make this connection, and that was later, about 1966, 1967.

DR. GARTNER: Do you have any major unanswered questions in newborn care? There are many more controlled trials under way now, but do you feel that

there are some important questions that we haven't looked at?

DR. SILVERMAN: Well, many of the measures that are used in neonatal rescue have never been subjected to formal tests. When Jon [E.] Tyson in Texas wanted to do a controlled clinical trial of bicarbonate infusions in asphyxiated infants, he was unable to get it done because it was impossible to obtain informed consent for this emergency measure. Many other commonly used measures haven't been tested. And, as new therapies are introduced in neonatal medicine, I see history repeating itself. A new technique is introduced, pilot observations are recorded, results are deemed so dramatic that the innovation is accepted as standard procedure. The controlled clinical trial, if it ever gets done, is performed years later. ECMO [extracorporeal membrane oxygenation] is a good example of that. The long delayed ECMO trial was performed by the British. The technique was shown to be quite effective, but it was years before the trial was carried out and the long-term consequences are still unknown. These hard lessons we learned have been ignored as new generations came along. They keep making the same dangerous mistakes over and over again. All innovations need to be seen as double edged swords. You have to look at both edges of the blade.

DR. GARTNER: Do you have any thoughts about some of the more unusual procedures that are being done in neonatal intensive care, like kangaroo care? What do you think?

DR. SILVERMAN: I thought kangaroo care was interesting, and I still think it's quite interesting. And I think, as a matter of fact, that the attempts to look at it in formal trials should be encouraged. Claims made about "bonding" seem very reasonable to me, and I would love to see it pan out. And I'm pleased to see that nurses are the ones who are looking at these innovations. Cryotherapy for Stage III retinopathy of prematurity (ROP) reduces the risk of blindness, but not to zero. So, ROP remains a very fascinating challenge. The current laser trial is testing a procedure which has been used very widely. The trial of light exposure is underway to see whether there is an effect on visual outcome. The current light trial is more elegant than the crude studies conducted years ago. The ophthalmologists are now able to look at the retina much more completely than was possible with the direct ophthalmoscope. Some of the young pediatric ophthalmologists are becoming interested in retinopathy of prematurity because it is still the second most frequent cause of blindness of preschool children in Northern California. Cortical blindness is the leading cause, but ROP is still a major problem. The suggestion was made by Szewczyk in 1952 when he put infants back in moderate oxygen, that the vascular abnormalities improved. There was a controlled clinical trial which seemed to confirm the maneuver. The result was not accepted because of contamination. The controls that showed progression of lesions were treated

with the oxygen intervention. No one has taken that any further, but now it is being looked at by Dale Phelps in Rochester. She is doing a so-called Stop ROP trial because she found in her kitten model that she was, indeed, able to ameliorate the neovascularization by using moderate oxygen. And so it's very, very brave to do this, needless to say, given our litigious society. More than 30 years too late, but it's being done well. I'm also encouraged that the ophthalmologists are involved. That's another thing I'd like to talk about for a moment.

The National Eye Institute and the National Cancer Institute, have led the way in doing on-going clinical trials. They've led the way by going to the cancer meetings and giving courses to the oncologists about clinical trials. The National Eye Institute has also done that and has conducted very extensive trials on diabetic retinopathy. They have taught practicing ophthalmologists the essentials of the experimental method used in randomized trials. I'm very unhappy that the NH, National…

DR. GARTNER: NICHD [National Institute of Child Health and Human Development].

DR. SILVERMAN: NICHD, I always forget the initials. That they did not lift a finger to promote randomized clinical trials on critically important questions in pediatrics. On the contrary, they discouraged this methodology. And I know the reason. It was very clear that the leaders in the NICHD simply did not regard clinical trials as worthwhile. And so I'm very unhappy about the fact that they haven't gotten behind this movement. For example, the role of vitamin E in RLF arose when [William] Owens and [Ella] Owens at Hopkins many, many years ago started a trial of tocopherol to prevent eye damage and used concurrent controls. They began to see signs of positive effect. The chairman of the department of ophthalmology said, "It is immoral to continue," so the trial was stopped. Everyone began to use vitamin E, but they could not reproduce the results at Johns Hopkins. Interest in this therapy disappeared until it was revived in recent years. A number of trials demonstrated an effect, others did not. But there has never been a proper large scale, multicenter trial. When the NICHD director was approached about it, he said, "Clinical trials never proved anything." He then said, "I know the chemical formula of tocopherol. If you want to learn about the biological effects of vitamin E go to the laboratory, not to the bedside." Is it any mystery why NICHD failed to encourage experimental methodology at the bedside?

DR. GARTNER: Do you think the NICHD was burned perhaps by the national cerebral palsy study which cost so much and turned up so little?

DR. SILVERMAN: I agree. I agree with you completely. But, the extremely expensive cerebral palsy study used very weak observational

methods; hardly an argument against concurrent controls. The CP study was a scandal; 121 million dollars down the drain.

DR. GARTNER: Huge amount of money.

DR. SILVERMAN: In that strictly observational trial the participants could not agree on the variables to be examined, so they included them all. They argued that that, "The questions will emerge after the study is completed."

DR. GARTNER: The NICHD has recently established networks of for both maternity and for newborn clinical studies. Do you think those are a good way to go?

DR. SILVERMAN: A long time coming, but I applaud the fact that they've seen the light. I have a problem; a chronic complainer, you know. The NICHD trials should be much larger than they are. In small scale trials the studies go on for years. They're not only inefficient, but the difficulties multiply. People get discouraged. Large trials can be completed quickly and results are more generalizable. Richard Peto and his group at Oxford have been arguing for large scale trials, enrolling thousands, not just hundreds of participants. When I was on the Data Safety Monitoring Committee of the NICHD I made myself thoroughly disagreeable by bringing this argument up constantly, saying, "Why aren't the trials larger?"

DR. GARTNER: What do you think about the Academy of Pediatrics' efforts with the PROS [Pediatric Research in Office Settings] network, the Pediatric Research in Office Settings program, the attempt to use office based populations.

DR. SILVERMAN: I applaud any effort looking at interventions systematically. I think this is a way of educating physicians. Physicians need to be discouraged from saying, "What do you think about a treatment?" but to ask "What is the evidence?" Office-based research will increase awareness and focus. Seek that evidence wherever you can. It's wonderful to encourage office based research.

DR. GARTNER: Now I would like to ask you to gaze into your crystal ball and try to see where you think pediatrics in general, not just neonatology, will go in the next ten years. What do you see in the offing?

DR. SILVERMAN: I'm no longer on the front line, but as I read what's happening I see that our field is now driven by economics. The market model is used to direct pediatrics and all of medicine. That bothers me; market driven changes as opposed to evidence based changes. I'm not optimistic about how one can change this trend. We are spending more of our gross national product on health care than any other country on earth and we're beginning to run into a dead end. As you know, I've been very

critical about our failing to set out limits. The social consequences of this failure are incalculable.

DR. GARTNER: You don't see the economists in medicine as data gatherers, as a means of collecting data in a formal scientific way. Their end points or their reasons for doing it may be economic; you don't see them as useful to the enterprise of collecting data?

DR. SILVERMAN: Well I think they are useful. In essence they put these complaints into quantitative terms so that one can look at them more objectively. Yes, I think that the economic analyses spell out what the problem is. Do we have too many physicians? The answer is yes. Do we have too many neonatologists? I think so, certainly more than other countries. And we're spending more money and not having any better results.

DR. GARTNER: What do you think medicine will be like 50 years from now? Will it look anything like what we have now?

DR. SILVERMAN: [laughs] I graduated from medical school 55 years ago, and medicine now does not resemble the medicine that I saw 55 years ago in any way, shape or form. Virtually everything that I was taught, except for anatomy, turned out to be wrong. So I think the future will be dramatically and unpredictably different. In what way it's going to be different, I don't know. My own feeling is that we're going to be reined in by sharp limits. I see two forces that are on a collision course. On the one hand, medicine is becoming much more effective, and much more efficient but more monolithic. We're looking for the best treatment, one treatment. On the other hand, society is becoming more diverse. Multiple cultures are demanding to be heard. The homogeneous societies that we knew in the past are all becoming extremely heterogeneous. If I'm correct the two forces are on a collision course and medicine is going to have to yield; you're not going to change cultures. Medicine is also going to have to be much more responsive to different requests for treatment, or to withholding treatment. Pulling out all the stops to rescue a 400 gram, 500 gram, premature infant is unacceptable to some segments of our society; it's very acceptable to others. And since we're running into this collision, medicine is going to have to be responsive to tailor their methodology. The principal thing I see at the moment is this collision course. We want the best medicine, we want the best evidence for the best medicine, but that doesn't mean we must apply that evidence uniformly. We're going to have to be much more malleable.

DR. GARTNER: Now before we leave the general pediatric area and go more into the neonatology, looking back at your career, how do you feel now about your career in pediatrics, in general?

DR. SILVERMAN: Would I have done the same thing?

DR. GARTNER: Would you do it again?

DR. SILVERMAN: No. Definitely not. I'm very disappointed. I'm very disappointed that I didn't speak up earlier about where we are going. I'm very unhappy that as neonatal medicine began to grow, and it was very exciting, we, the leaders did not stop earlier and say, "Where are we going?" I was in a leadership position and I should have insisted that we decide about the goals of this exciting new field of pediatrics. The message of the Hill-Burton Act, which led to the development of premature infant stations, and to intensive care, was to reduce mortality, and, if possible, morbidity. But these crude outcomes were extremely shortsighted and, I think, quite insufficient. They continue to be insufficient. What are the social consequences of unlimited rescue? This is a much more difficult question to answer, but it's a question that has to be asked. Over and over, as I compare what I did, and now examine these blind young adults, I say to myself, why wasn't I at a younger age more tuned in to the fact that it's the long term consequences which are important?

Yes, I wish earlier in my career I had been much more critical about the social goals of neonatology. You hardly have to be very smart to realize that all of this has social consequences. Even the biological consequences of this activity must be taken into account. We are changing the survival of newborn human infants in ways that has never been done in the million year history of our species. And with the genetic revolution coming along, it's obvious that we're going to be seeing even more radical change. What are the long term social consequences of these unprecedented activities? We know, for example, that the sex ratio of neonatal survival has already been changed. This crude marker of altered biological outcome suggests that we're altering the gene pool of our species. I think we should become much more curious about this and try to document what the biological consequences of all of these activities are. And to ask hard questions about frequency of the cystic fibrosis gene or others, how much has that changed as a result of all of these activities? I have seen very little interest in this and I wish there was more. So I find myself at this stage of the game, looking back on my career with this feeling that there's still a lot to complain about. I still feel that it's necessary to hold the feet of people who are now in this field to the fire, to continue to put pressure on them to ask difficult questions, to keep saying how do we know what we're doing. I've quoted Captain Ahab more than once about this issue, "All my methods you know are sane, it's my goal that [laughs] is mad."

DR. GARTNER: So you would still go into pediatrics.

DR. SILVERMAN: Yes, I have no regrets.

DR. GARTNER: But you would do it differently?

DR. SILVERMAN: I regret not being more critical. When Dick Day, my idol, was awarded the Howland Medal in 1986, I called him the "Quintessential Skeptical Inquirer." He made a nuisance of himself to a lot of people who could not stand that carping. But I see even more that this is so important in neonatal medicine, a new field, only 30 years old at the very most. Certainly we should be asking much more difficult questions.

DR. GARTNER: Although there's so much still to be done, what are your thoughts about the status of children today in our society, particularly in the United States, compared with say 40 years ago? Are we better, are the children better off, are they not better off?

DR. SILVERMAN: Well, I'm distressed by statistics which say that the number of children living in poverty is going up, and that it's higher than most other countries. I am very distressed about the status of children. The safety net is being unraveled. I can't agree that there has been improvement. I think as a matter of fact there has been a worsening as you see what's happening in the inner cities; it just breaks your heart.

There was one incident that I have to tell you about because it had a very dramatic effect on my thinking. I've written about this before, but I want to say it again. It was all epitomized in one incident early on, before respirators were being used as extensively, before blood sampling and monitoring were used. We had an 800 gram premature infant at Babies [Hospital], quite immature. This infant was being cared for with everything that we could possibly apply. The cost was not hundreds of thousands of dollars as it would be now, but it certainly was in the tens of thousands. This child was sent home to a cold water walkup in upper Manhattan, and within a week the child had its nose eaten off by a rat and subsequently died. That horrible image says everything. We must put as much effort into what happens after babies leave our temples of healing as we do when they're under treatment with the latest machinery for rescue.

Perhaps I should tell you also about the change that occurred when the premature infant station was transformed into a neonatal intensive care unit.

DR. GARTNER: Good. I was going to ask you about that, but, you go right ahead. [laughs]

DR. SILVERMAN: I feel a need to talk about that. The year 1965 stands out in memory, because in 1965 we had an International Congress of Pediatrics in Tokyo. Did you go to that Congress by any chance?

DR. GARTNER: No.

DR. SILVERMAN: It was a typical international meeting, a lot of jolly fun but not much of substance. Jack [John] Sinclair, who was my fellow at that time, went with me. Jack and I go to Tokyo; our wives, left behind, have not forgiven us to this day. I convinced our funders that it would be just as cheap to have us fly back to New York by continuing eastward [through Tokyo] after going to Copenhagen to recruit technicians who had developed techniques of microchemistry. We were beginning to use the respirators and needed a practical method to monitor these respirators and we did not have microchemical methods. The Astrup method was developed in Denmark at the time positive pressure ventilation for polio victims replaced Drinker respirators. It was the fact that they didn't have enough Drinker respirators that forced them to use positive pressure ventilation. The application of this micro technique to premature infants was a natural. So we recruited Knud Engel to be director of a microchemistry laboratory at Babies [Hospital] and he brought along Danish technicians. This new capability at Babies Hospital made intensive care methods practical. The shift from premature infant station to neonatal intensive care took place in a highly visible manner. It was a dramatic shift. I'm putting it in cause and effect terms because one followed the other.

Now, the transformation was not done easily. Particularly because we had a cadre of nurses with a lot of experience in premature infant care whose cardinal theme was "hands off." The nurses were sure the marginally viable neonates should be handled as little as possible, keep them quiet, not have any fussing. Suddenly we move from that to the exact antithesis. In-dwelling catheters were inserted, blood was drawn frequently to set the respirators. The change could not have been more dramatic. And as it turned out in most units, certainly at [Babies Hospital] Columbia, it was not possible to do this with the same nurses. We had to recruit an entire cadre of young nurses who had no fixed ideas, and to train them from scratch. Now we had a neonatal intensive care unit with a special staff of nurses, microchemistry laboratory, and a flurry of activity. The contrast with the quiet of the old set up could not have been greater. That dramatized this difference. I find it interesting to see that attempts are now being made to provide very small infants with quiet surroundings and to disturb them as little as possible. In addition to microchemistry and new nurses, the temptations were just enormous to build monitoring devices. This change was done precipitously, with no evaluation at all. The other dramatic change was the matter of allowing parents to come in and to touch and see their infants. In the past in the premature infant stations parents had to look at their infants through glass windows. I remember a poignant sight when a mother used binoculars to get a close look at her child as tears ran down her cheeks. It was heartbreaking. We did a controlled trial of gowning and demonstrated that there was no difference in infections. That broke the ice. The whole

character of this area which used to be so quiet became the most hectic and noisiest part of the hospital, and the most brightly lit part of the hospital.

DR. GARTNER: Yes, I remember those changes; it was not easy at all. What do you recall as your earliest recollection of thinking of yourself as a neonatalogist, as a doctor of newborn medicine rather than a generalist? Can you mark that moment?

DR. SILVERMAN: Yes, I have struggled about that for most of my pediatric life, and I have not yet overcome it yet. I still don't see myself as a neonatologist. And the reason I don't is, again, I'm so preoccupied with the post neonatal. Yes, I can remember very clearly when at the Spring Meetings in Atlantic City, it very soon became a custom for a group of people with similar interests to get together and have dinner. Little by little this became known as the newborn dinner. And it was very striking, I could see the handwriting on the wall. Each year the newborn dinner would get larger and larger. And I think it was that meeting in Atlantic City which led to the acceptance of Buck [Alexander] Schaffer's [Baltimore, MD] new label as "neonatologists." And I would say that the years that I'm talking about are the early 1960s, 1960, 1961, when little by little the newborn dinner became a larger and larger activity.

DR. GARTNER: Did you ever notice the response of people when you said that you were going to the newborn dinner? People who were not there?

DR. SILVERMAN: Yes, exactly right, it became, it became *the* place to go and *the* place to be seen. And I would look at other people and say, "Well I thought he was a nephrologist, but here he is." After one of these dinners, Bob [Robert] Usher, brought up the idea of forming a specialty with all the trimmings of certification, etc. I was dead set against it, but the tide in favor of it was unstoppable.

DR. GARTNER: What support did you get in your neonatology career? Academic support, financial support, personal support. What were the encouragements to become a "neonatologist"?

DR. SILVERMAN: Early on the stipends for academic positions were very low. I solved this by being geographic full time, earning my own living. But when I began to do these studies I needed some money to carry them out. Not a lot of money, but I needed some money. It always shocks people when I remind them how these early studies that we were doing with retrolental fibroplasia, the ACTH study, and the other trials were funded. I would get on an "A" train in Manhattan, go down to 42nd Street, walk several blocks to the east side, take an elevator and go upstairs and speak to a private fund, The Milbank Memorial Fund, that was very friendly to Columbia Presbyterian Medical Center, and Babies Hospital. I would say, "We need

$3,000 to carry out this study about blindness and the premature infant," and the check was written out while I stood there. I would put it in my pocket and go back to the hospital. This was before the explosive increase in the extramural program of the NIH. I was very fortunate because Columbia had a lot of very wealthy patrons and funding was very informal; if you're doing the work *there* it must be all right. Of course that changed. I did not apply for huge grants from the NIH until we set up the microchemistry laboratory and the expenses began to mount. They were funded by the National Institutes.

The hospital gave me no help at all during this early time. For the first time in the history of our hospital the president of the hospital was an accountant [laughs]. Prior to that, every president was a physician. Babies Hospital was an independent corporate entity in the medical center [Columbia Presbyterian Medical Center]. We had a separate board. We even had our own dining room. When the accountants took charge, they decided this made no sense to have your own chemistry laboratory for example. That's when everything changed. The market drove all decisions. Needless to say, I was very frustrated. With the development of the neonatal intensive care unit, I felt it was very important to be as close as possible to the delivery room. When I proposed the move, the administration refused to consider it. That was one of the reasons I left Columbia and New York. The hospital would not go along with a rather expensive move, which was eventually made, as a matter of fact. But the real reason I left was because I was having grave doubts about neonatology and what I was doing. And I felt the tug of California. Very little support came from the hospital. Support of the neonatal movement came principally from federal government grants and also from the March of Dimes. Virginia Apgar used to be at Columbia and her role in these developments is also quite interesting. She left Columbia to become the medical director of the March of Dimes and she moved the March of Dimes in the direction of perinatal and neonatal activities. The March of Dimes provided a little support, but then I left. The problem with funding was that we were dealing with patients who came from the lowest economic strata of the city. We didn't have wealthy donors. But every once in a while we did. And I'll never forget, we had a newborn infant of a father who was the head of the largest company in the United States making electrical switches. He was a blustery executive type, with a very young wife, and they had this very small premature infant. I told them that apnea was a prominent problem of these infants and they have to be carefully watched. The father said, "You mean you're doing that by eye; you don't have an electronic monitor?" [laughs] This was before companies were making these instruments. They did not look on neonatal medicine as a place to make money. They would not do it because they said the market was so small. I told him about this and he said, " I'll send my engineer around tomorrow, you'll have a monitor in no time." He was right. He provided us with a crude apnea monitor in a matter of days.

DR. GARTNER: What company was this?

DR. SILVERMAN: ACE Switches or something like that, I've forgotten. His engineer came, looked at the problem, took a silastic tube, filled it with carbon granules, put the tube around the infant's chest and we could monitor respiration, just like that. The engineer said it was a very simple problem, but where is the market for this? Of course the market changed as the intensity of care increased. This is now very big business. This is an interesting part of the history of neonatal medicine. You're hearing all of my war stories, Larry.

DR. GARTNER: I love them. What would you consider your single most important contribution to neonatology? If you could single out one thing.

DR. SILVERMAN: Yes, yes. Shall I say, proudest, I feel best about the demonstration that small differences in heat exchange produce measurable effects in mortality of premature infants. I'm proud of the way we did it with a series of randomized trials. That 7 year period ended with this insight about temperature. That is most satisfying to me and I feel best about this. I also feel best about it for another reason. When Dick Day was doing his pre-war studies at Cornell with Jim Hardy using exquisite techniques to measure heat balance in premature infants, he concluded that these infants were homeothermic like any other mammal. Newborn infants have low body temperature because their losses are too great and they are unable to generate and conserve heat. He wrote that paper up and took it to Boston where Blackfan and Yaglou purported to show that premature infants were poikilothermic and that low body temperature was normal in these small babies. Dick's results indicated that excessive heat loss prevented the premature infant from achieving the homeothermic set point of 37 degrees centigrade. When he presented this argument to the people in Boston, they said; "That's very interesting, but your findings are of no practical importance." They showed Dick Day chart after chart in which premature infants with non-fluctuating low body temperature were doing fine, gaining weight and thriving. Dick was very downhearted after all of this work, to be told it is all for naught. He writes the paper up, and tries to get it published, and it's rejected over and over. Then he adds a caveat in the paper: "These studies were done on infants who are older than two weeks of age and larger than most premature infants. Thus, these results should not be extrapolated to those [smaller premature infants]." The paper was finally published and it sank like a stone. There was no appreciation of what he had done, how elegantly it was done. It was quickly forgotten. When I was faced with the problem of caring for the 620 gram premature infant in 1945, I looked to the authoritative recommendations about body temperature, and it read, "Keep body temperature stable, don't worry about the level." I didn't know about Dick's paper. Fifteen years later I was able to demonstrate the practical

importance of Dick's thesis. This was the most satisfying event in my career. Even though I stumbled on it by accident, I was able to demonstrate the relevance of his elegant work. And that had the kind of closure that was very important to me. I regret that I didn't take the work further. There are still so many other unanswered questions about thermal influences on growth and well being of prematures. I wish I had taken it further. But that series of events, Dick Day's work, forgetting it, pooh-poohing it, and then suddenly to come out and say, "Wait a minute, this is relevant." No question about it, that's it.

Incidentally, Dick Day's difficulty in getting his paper published without the caveat was paralleled by my trouble getting the SPR [Society for Pediatric Research] to accept my paper [laughs]. They were tired of controlled trials. I had done a series of trials over the years and presented them.

DR. GARTNER: But it did get on the program?

DR. SILVERMAN: It did not.

DR. GARTNER: Oh, it did not get on the program.

DR. SILVERMAN: It wasn't accepted. [laughs] I loved that. And I look back with amazement at their snobbery about any work not done in the laboratory.

DR. GARTNER: Who have you trained in neonatology? Who were your fellows or trainees? Jack Sinclair, obviously, but…

DR. SILVERMAN: You should say who trained me. I got more out of my fellows than I was able to give them. Yes, Jack Sinclair was the first person who came specifically for a neonatal fellowship. You must understand the business of having trainees, of having fellows, was just beginning in the 1960s. It was not the institution that it is at the present time. But Jack came to me and said that he would love to work with me, and I said, "Great, I'll see if I can find you a salary." And I found him a salary. A number of other people came. Lou [Louis] Gluck, for example, spent some time with me while he was a house officer. And I encouraged him to do some work he wanted to do on white cells of premature infants. But this was not a formal fellowship. I certainly regard Lou as one of the persons who at least heard my message.

DR. GARTNER: He did. He heard your message.

DR. SILVERMAN: I was driving everyone crazy at Babies with my preoccupation with methodology. And so Lou came, and who else came. Jeff [Jeffrey Pomerance], and a few other people spent some time with me, but I didn't have a formal training program for fellows. There were a lot of

people who came and spent a couple of weeks. I've had such mixed feelings about asking people to undertake neonatology as a career, that one would train and aspire for. I dragged my feet about recruitment. I thought it was an interest that one would develop as part of being a pediatrician, seeing the whole thing. I was never very enthusiastic about increasing the number of neonatologists.

[Ruth Silverman, RN, Bill's wife, adds the following names of those who had some "fellowship" training with Bill. "Jon Scopes of London was a fellow. I know he was there (at Babies Hospital) during 1965. Gabriel Duc was a fellow in 1967 and returned to Switzerland and, ultimately, Zurich, to become a well-known European neonatologist. Eugene W. Adcock was also a fellow with Bill at Babies Hospital. He had a neonatology unit first in Houston, Texas and later in Winston-Salem, North Carolina. In San Francisco, while Bill as still at Children's Hospital, Gerald Merenstein was sent by the U.S. Army to do a Fellowship in Neonatology with Bill. Also, Harry Dweck did a fellowship with Bill at San Francisco Children's Hospital."]

Jack Sinclair was different; he was so bright and so inquisitive, I felt my job was clearing the way for him. It was a very exciting experience for me. It was more than a year actually, because he spent time after it was over. I got more out of it than he did; it was a great time for me.

DR. GARTNER: I do remember having a conversation with you at Babies Hospital somewhere in the 1960s. We were talking about what this was that we were doing, what it should be called, and you very clearly expressed the same thought that it should not become a discipline, a specialty or something like that.

DR. SILVERMAN: Isn't it discouraging that I've made no progress in all of these years? Yes. As a matter of fact, when the word neonatology was invented by Buck Schaffer at Hopkins, I avoided using the label. It quickly caught on with me kicking and screaming, digging my heels in. Yes, Buck invented the term neonatology.

DR. GARTNER: What are you doing now? What's your current activity in addition to putting together the book of your essays?

DR. SILVERMAN: I always like to have a writing project. If I'm not writing, I'm very unhappy. As E.M. Forster said, "How do I know what I think until I read what I have written?" That strikes home with me. I find myself constantly struggling with my ideas, but, when I sit down and write them down, I begin to make some headway. To me that's the most satisfying exercise. Some of the stuff gets printed, others do not. So I'm writing all the time, sometimes snatches, but I need to have a writing project, and that has made, you know, the recent years very enjoyable to me because I'm writing on anything that I want to; anything that comes to mind. The last piece I

wrote came out two weeks ago; it is called *Crap Trapping*. You can see where my mind is.

DR. GARTNER: [laughs] I love getting your emails, your articles by email, I really love that.

DR. SILVERMAN: So that's my principal outlet. The other is my work with the blind. I don't find that satisfying but I think it's important. Many people have said to me, "You must feel guilty about all these blind babies and feel driven by that guilt." I think that's unfair. No one could have anticipated what happened. But I think I do have a responsibility to find out the dimensions of this tragedy, to involve myself with what is going on in their lives. These young adults are in need of a lot of understanding. I'm now accepted in the blind community. They understand, they don't ask what I am doing in their meetings. I enjoy that very much. I'm on the professional advisory committee of the Blind Babies Foundation in San Francisco. At the moment the professional advisory committee is trying to do something about educating parents, teachers and physicians in other specialties about ROP [Retinopathy of Prematurity] blindness and other forms of preschool blindness. These are not high incidence disorders, so each teacher sees very little of that. The Blind Babies Foundation is developing fact sheets on ROP and on cortical blindness, which is now the greatest single cause of blindness in Northern California. I'm very, very proud and delighted that the Blind Babies Foundation of San Francisco was invited to the White House Convention on Zero to Three [White House Conference on Early Childhood Development and Learning] that Hillary Clinton convened on early education to talk about the importance of early education of the parents of a blind child. And I was very pleased about that, because the Blind Babies Foundation led the way in the revolution in the way that parents rear their blind kids. Recently, the parent of a blind child came on as the director of the Blind Babies Foundation – that's progress. That pleases me, and so I like to spend as much time as I can on that. Ruth and I travel as much as possible and we walk as much as possible. [laughs]

DR. GARTNER: Great. Sounds lovely. Now, I want to broaden our discussion. Up to now we've been talking about you and your career and the things that touched you directly. Now I'd like to get your insight into the field of neonatology generally, and see what your views are on these issues. One question that often comes up is, when did newborn medicine first develop? What are its origins?

DR. SILVERMAN: I would say, Larry, that it was the French. The organized movement began in France after the Franco-Prussian War (1870-71), to improve survival of marginally viable infants. That's really when it began. And the goal was very clear; they wanted to increase infant survival at a time when the birth rate was dropping. They foresaw another war with

Germany, whose birth rate was on the increase. So I think the object was clear. The intervention was also clear; improve the physical environment of the infant, expert nursing and so forth. From the very beginning, Pierre Budin, one of the French pioneers, stressed the fact of having outlying stations to instruct parents in the care of the babies after they left the hospital and to monitor their weight gain. He saw the big picture right from the start and I always like to remind people of that. When the 100th anniversary of the Port Royale Station [Maternité de Paris, Port-Royal] in Paris was celebrated 2 years ago I went to Paris and emphasized, in the talk I gave, that Budin provided a model that we, in the US, should have acted on.

DR. GARTNER: We haven't talked much about obstetrics. What about the relationship between pediatrics and obstetrics and gynecology, in the development of perinatology?

DR. SILVERMAN: Budin and [Stéphane] Tarnier were both obstetricians. When I was a house officer, obstetricians were the ones who were principally involved with the newborn. Obstetricians were in charge of the newborn nurseries. This was not considered to be a pediatric interest. Pediatricians were called as consultants and infrequently at that. Whenever the obstetricians wanted an opinion, we were permitted to come into the delivery room or nursery. At Columbia, the nursery was in the Sloane Hospital for Women, a separate building from Babies Hospital. The obstetricians regarded the newborn as their primary responsibility, and at Columbia they certainly acted that way. When I was an intern at the University of California in San Francisco, the care of the newborn was clearly a part of obstetrics. That did retard the development of pediatrics. When pediatricians began to take over at Columbia in 1952 or 1953, I began to make rounds on the newborn nursery in Sloane Hospital and I was looked on askance, "What are you doing here?" People couldn't understand. And we were not welcome in the delivery room. The first moments of life belonged to the obstetricians. Virginia Apgar changed the culture of the delivery room. She is the one who broke that taboo. It happened at Columbia and I remember exactly how it happened.

For years Virginia Apgar was in the department of surgery where she ran a program for training nurse anesthetists. When it was decided that there would be a separate department of anesthesia at Columbia, they recruited Manny [Emanuel M.] Papper, a highly respected research-oriented anesthesiologist. Virginia Apgar's program was closed down. It was a slap in the face for someone who had done a terrific job. You knew her personality, very bubbly, effervescent. She felt badly used. It was that putdown that led her to reinvent herself. Ginny Apgar [laughs], went into the delivery room, said, "My God what's going on here, you know, you're in the dark ages." It was common practice to take marginally viable infants, very small, and put them aside and allow them to die with no attempt at

rescue. They were recorded as stillborn. Virginia Apgar changed all of that, dramatically. She ensured that it would remain changed by inventing a scoring system so you had to look at the baby. The scoring system recorded the vital status of the infant at one-minute of age. This did away with the stillborn fiction. It was a brilliant maneuver which led to the active rescue of infants previously abandoned. Virginia is the one who changed that. And she then made the connection to pediatrics when Stan James, a pediatrician, trained by Dick Day at Downstate [Medical Center in Brooklyn] came to Columbia. Dick advised him to apply for a position in pediatrics at Columbia. There was no position open at Babies Hospital, but Virginia Apgar thought she might have a position for him in the department of obstetrics. She was in the department of obstetrics; she's was still not in the department of anesthesiology. Virginia and Stan began their activities of describing neo-natal asphyxia in physiologic terms, and quickly demonstrated that the biochemical changes in neonatal asphyxia were no different than in adult asphyxia. Virginia was an enthusiast. When Dick Day and I were driving everybody crazy about statistics, Virginia is the one I think who resented this as much as anybody. We kept talking about numbers and study design. I like to think that it was our making ourselves unpopular, that made her go to Hopkins [Johns Hopkins University School of Medicine] and take their famous course in statistics at the School of Public Health. When she came back, and I'll never forget to this day, she looked at Dick and me and said "Now I know what you guys are talking about but I still don't believe it." [laughs] But there's no question that her semi-quantitative scoring system, soon adopted over the whole world, forced people to look at the newborn infant with new eyes and it sparked the rescue philosophy in obstetrics and neonatal pediatrics. So the relationship between obstetrics and pediatrics had that kind of history. It was the activities of Virginia and others that brought the two disciplines together. I wanted to physically bring them closer together at Columbia, to have one next to the other.

DR. GARTNER: What about today, in the modern period, the relationship between obstetrics and pediatrics or neonatology? How do you feel about that?

DR. SILVERMAN: I get the impression, and it has to be an impression because I'm not on the scene, that relationships are very much more harmonious than they were in the past. They seem to be talking to one another in a way which was certainly not true of my day. And even in Virginia Apgar's day I can remember she brought it together, but it didn't flow, it wasn't, "This is our patient." One of the real achievements of the perinatal/neonatal movement is improved communication. I'm also encouraged by signs that parents are consulted more than in the past – although there's a long way to go.

DR. GARTNER: I was going to ask you about that. How did that come

about? There was a period when we kept parents out of the units, isolated them from the decision making; now we're involving them to a much greater extent. How did that transition come about?

DR. SILVERMAN: Well, strangely enough, this business of allowing them to come in and touch their infants at a time when the infants were desperately ill broke the barrier. I think Marshall Klaus had a major influence in humanizing the atmosphere of birth, delivery and neonatal care when he pointed to animal behavior and the importance of encouraging early attachment of mother and infant. Marshall deserves a lot of credit for beating the drum about these issues. I've criticized the design of some of his trials, but I can't deny that he changed attitudes and behaviors for the better.

DR. GARTNER: Was Marshall at Columbia at some point?

DR. SILVERMAN: No, Marshall was never at Columbia. He was here at UC [University of California at San Francisco] with Julius [H.] Comroe [Jr.].

DR. GARTNER: Oh, he was out here the whole time.

DR. SILVERMAN: Well, he was, that's right; he was at UC. He began as a respiratory physiologist.

DR. GARTNER: Looking broadly at neonatology over the past 30 to 40 years, what do you think have been the major clinical advances?

DR. SILVERMAN: I think undeniably, the recognition and gradual development of strategies to manage hyaline-membrane disease/respiratory distress syndrome, was certainly a major accomplishment. So I think that would be a single thing that I can think of with respect to that.

DR. GARTNER: To which technologies are you attributing the improvement?

DR. SILVERMAN: First the use of respirators adapted for minute infants was technologically fantastic. And then the development of the surfactant story as Mel [Mary Ellen Avery, 1927--2011, Boston] worked on this assiduously. Mel Avery deserves all the kudos she's received for her part in working this out. I think that's major. As far as bilirubin metabolism, you know better than I how well, or how poorly, that was done. I haven't even talked about the conflicts about bilirubin between Boston and New York. I think the thermo-regulation beginning with Dick Day and followed by our trials was a notable accomplishment. Feeding questions are still a work-in-progress. I think the mother/newborn attachment work deserves to be ranked high on the list. The disasters with Gantrisin, chloromycetin, epsom salts, one after another, all shouted for the need for a neo-natal

pharmacology. I'm disappointed that it hasn't been worked out. This was one of Lou Gluck's early dreams, to develop a neonatal pharmacology, but he never took it up seriously.

DR. GARTNER: Presumably, the clinical advances were built on research developments. We talked a lot about research that you've been involved in. Are there some other research areas that were particularly major achievements in neonatology?

DR. SILVERMAN: Well the conquest of Rh disease, erythroblastosis fetalis, was one of the first accomplishments of this field, but it's interesting how that happened. When the Rh antigen was identified, the disease defined, and finally treated with exchange transfusion, these activities all transpired, interestingly, out of the context of a newborn nursery or premature nursery. It was dramatic as I think about it. When an affected infant was taken from the newborn nursery or from the premature nursery and taken to the operating room for the exchange transfusion, he was now considered to be contaminated and couldn't come back to the newborn or premature nursery. The infant went to a special side ward on the sick infant floor of Babies Hospital. The nurseries, premature and full term, remained quiet backwaters. Here was this dramatic achievement of exchange transfusion but no ripples in the nurseries because the infant was gone. Management of pathologies took place among other sick infants under general pediatric supervision and by nurses versed in the care of the sick. He was isolated, of course. It was a very interesting thing, yet it sort of slipped by, if you see what I mean, that the post exchange transfusion care of this infant was outside of the newborn nursery. The newborn nursery remained calm, peaceful. It is hard for me to tell you how much the nursery nurses resented having doctors come in to do hands-on procedures and even for complete examinations. [laughs]. Amazing as you remember what happened thereafter.

DR. GARTNER: Are there any other research areas that you think of that were major?

DR. SILVERMAN: Dick Day's demonstration that brain tissue respiration was inhibited by bilirubin, whether that's the mechanism or not, at least pointed to the fact that it has something to do with causation of kernicterus. I think Dick's work changed the thinking about jaundiced infants very dramatically, and this was the beginning of the on-going debates about how to estimate risk, the 20 milligram limit arguments that continue to the present day. You know better than I about the bilirubin concentration as an estimator of risk.

DR. GARTNER: We're still fighting that.

DR. SILVERMAN: Yeah, it's amazing how the bilirubin debate has gone on for so many years. I'm trying to think of others. Hypoglycemia comes to mind. Marv [Marvin] Cornblath was the principal protagonist. The arguments were influential. It is important but I don't think it's turned out to be as important in caring for these infants once we did away with prolonged thirsting and [delayed] feeding of the smallest infants.

DR. GARTNER: That's right.

DR. SILVERMAN: The feeding. There was so much preoccupation with the feeding of the premature infant and of course that can't be dismissed. I remember when the importance of taurine was first recognized and was considered a major insight to improve feeding. I guess I find that hard to know. Recognition that high protein feeds were dangerous was an important milestone. I can't think of any other notable breakthroughs. You must remember I'm almost 80 years old.

DR. GARTNER: [laughs] Oh but you have 80 years of memories. [laughs] How about education in the field of neonatology? What do you think have been the major advances or changes?

DR. SILVERMAN: Well of course, the dramatic thing is hands-on learning, having fellows come in and being educated by doing was the approach, and I suspect continues to be the approach. I wish that had been developed more seriously. Even from the very beginning, the neonatologists got so excited about technological machinery. That has been disturbing to me. I wish we had paid more attention to formal instruction about values and to question where are we going and what are the goals of neonatology. That should be considered an important part of the education of doctors who are making incredible decisions with life-long implications in the lives of so many people. An observer in a neonatal intensive care unit said to the neonatologist, "I'm so impressed with how you were able to take these extremely frail babies who were virtually nothing and restore them to life, gain weight and whatnot." The response of the young rescuer was, "We could keep a Big Mac alive." Now that shallow attitude demonstrates a serious problem. There should be more thought to what incredible things you are doing. That's the part of the education that I would stress. I think that it's needed, and I hope it's being done now; I don't really know.

DR. GARTNER: I'm sure not enough.

DR. SILVERMAN: The pathophysiology of the marginally-viable is exciting. These infants are like a new species. That insight came at the time of the therapeutic disasters. We simply cannot extrapolate from other patients to this new species. That realization was very important, and I think educators must take up this challenge; extremely premature infants are

unlike any infants who have lived in the past. What are the implications of this fact? More thought, much more thought should be given to this awesome problem.

DR. GARTNER: Let's talk a little bit about fellowship training and what it ought to consist of. Do you have any other thoughts about the training of neonatology fellows? Neonatology is now the largest subspecialty of all of pediatrics, and they are training huge numbers of fellows. Do you think they're training too many?

DR. SILVERMAN: Well, that's what I said in the piece that I wrote about this. When I looked at the number of neonatologists per 1,000 newborn infants, we certainly have, by far, more than any other country. No one knows what the correct number is, but I think we ought to ask ourselves just exactly that; how many do we need? Until decisions are made about limits, it seems to me that we've painted ourselves into a corner by having a large cadre of workers. Now, I sound like a worn record, but my feeling is that in the training a good deal of attention should be paid to what happens, what are the consequences, what are the social consequences. This should be part of the formal training. Neonatologists should spend much more time looking at blind infants, other handicapped infants, the broken families, etc., etc. Exciting things are being done to try to improve outcomes. I think neonatologists should be aware of it, get interested and even participate.

DR. GARTNER: You talked about the impact of the new medical economics on pediatrics and the direction of pediatrics. What is the new economics of medicine doing to neonatology and neonatologists?

DR. SILVERMAN: I wish I could tell you that I understand what it's doing, but I have the impression as I speak to neonatologists that they are very concerned about cost cutting because they are in a very lucrative field of medicine. Can our health care system afford to keep very minute, very damaged babies alive? I think we're coming to that crunch, and I would say that neonatologists are threatened, and with good reason. We are now spending about 4 billion dollars per annum.

DR. GARTNER: Just on premature infant care.

DR. SILVERMAN: On neonatal intensive care. My guess from the curbstone is that economics are going to play an increasing role in further development of neonatal rescue.

DR. GARTNER: You talked about a number of individuals who have contributed significantly to neonatology. Were there other individuals who you haven't mentioned who ought to be mentioned as having made sentinel contributions?

DR. SILVERMAN: Jim Wilson in Detroit made a major impact even though it turned out that his contribution led to overuse of oxygen. I know he was very unhappy about what happened. He felt that the suggestion about using high oxygen to treat periodic respirations should have been evaluated before it was adopted as standard treatment. Virginia Apgar's contribution to the resuscitation practices in the delivery room was enormous. There's just no question about that. And Stan James, who worked out much of the early physiology about recovery from asphyxia certainly made a major contribution. Marshall Klaus, as I said, deserves a lot of credit in changing practices.

Many "proto", I call them "proto" neonatologists who set the scene for the later developments, like Harry Gordon, Sam [Samuel] Levine, like Dick [Richard] Day, like Julius [H.] Hess in Chicago. They should not be lost sight of, because in a sense they were the ones who kept up some interest so it wasn't completely ignored. Of course Budin and Tarnier in Paris and Herman Bundesen, the public health officer in Chicago, played important roles. Bundesen began beating the drum for rescue of frail infants. The history is colorful, but until it became a formal occupation the impact was relatively small. These early actors would be flabbergasted at what has happened.

DR. GARTNER: Well, there are people in Chicago who say that Hess, despite the fact that he was chairman of the department at the University of Illinois, in fact did nothing except premature infant care his whole life.

DR. SILVERMAN: Really, that's interesting.

DR. GARTNER: All he ever cared about was care of the premature.

DR. SILVERMAN: Incidentally, I once met Hess.

DR. GARTNER: Did you?

DR. SILVERMAN: Did I ever tell you about my encounter with Hess?

DR. GARTNER: No.

DR. SILVERMAN: When the post-mortem diagnosis of hyaline-membrane disease was being changed to the clinical recognition of respiratory distress syndrome, 2 meetings were convened, one in Chicago and one in Toronto. At the Toronto meeting the name respiratory distress syndrome was adopted. The meeting in Chicago was a preliminary session on respiratory problems of the newborn premature infant. I think everybody left that meeting feeling that we've got to do something about making this disorder more visible. The

Toronto naming followed that. At the end of this meeting in Chicago, time would be late 1950s, I received a note that Julius Hess wanted to talk to me. I was thrilled at this opportunity. "I'd love to meet Julius Hess." I go to meet him, and he said, "When does your car leave for the airport?" [laughs] I told him and he said, "I'll drive you there." So we get into his chauffeur-driven automobile, and Julius Hess has me at his mercy until we get to the airport. He spent the entire time complaining, "What are you guys doing? We never had blindness." In essence he said, " You're destroying my edifice." Of course, he was right. One has to point out in the history of this that Julius Hess invented an incubator, called the "Hess Bassinet for Oxygen." So, the notion of routine oxygen administration began with him. But, in his incubator the oxygen concentrations never got high enough [to cause retrolental fibroplasia]. [laughs]

DR. GARTNER: Yes.

DR. SILVERMAN: Unlike the Air Shield's Isolette, Hess's unit was too inefficient. But I'll never forget my meeting with Julius Hess. It wasn't a pleasant exchange at all. He virtually accused me of blinding all of these babies.

People have often asked why I was spending so much of my time with the blind. Stan James told some of my friends, "Bill is feeling guilty." Yes, I feel guilty. I feel that I have responsibility having been involved; I think that's the part of my guilt. I feel I should have been more critical.

DR. GARTNER: Among the people who contributed to neonatology, you didn't mention our favorite person, Martin Couney. Should we list Couney as a major contributor to the field?

DR. SILVERMAN: Couney [(1870-1954) Brooklyn, New York] was a popularizer. That should not be lost sight of. Alexander Lion [in France], was the first to exhibit premature infants, but it was Couney who took it all over the world. So Couney deserves to be acknowledged as a pioneer. Couney said "I made propaganda for the preemie." He did. You're right. Now [Arvo Henrik] Ylppö [1887 –1992; Finnish pediatrician] interestingly enough, never gets mentioned on many lists. But, in 1917, he was performing autopsies in Berlin and he was the one who proposed the 2.5 kilogram dividing line for the classification of prematurity. As far as I am concerned, one of his most important modern contributions is that he took Clem Smith [1901–1988, Boston] on about the issue of thirsting and starving premature infants in the first few days of life. A festschrift was published to celebrate Ylppö's 70th birthday and a number of papers were written for it. Rusty McIntosh and I submitted a rewrite [laughs] of our high humidity versus low humidity paper. In the festschrift were two papers on the topic of when newborn infants should be fed, one by Clem Smith, and the other by Arvo

Ylppö. This was the first time that somebody challenged Smith's recommendations to delay feeding of premature infants. I would like to think that it had an influence. There was only one clinical trial done of early feeding versus late feeding. That was done in Germany by a man named [J.] Gleiss. When I was writing the third edition of Dunham I looked up this literature. I found Gleiss's trial and communicated with him. There's no question, survival can be influenced by early feeding. I think it was Arvo Ylppö who challenged it for the first time. I never met Ylppö. Lou Gluck met him and I really envy him that. I would have liked to have met the old man.

There are other famous figures I guess we should mention. One is Dr. [Victoria] Mary Crosse [1900–1972; Birmingham, England]. Mary Crosse in Birmingham wrote a little book on the newborn infant that was very influential. She was very short and very feisty. She was the one who noticed that they never had a case of retrolental fibroplasia in Birmingham until the National Health Service made it possible for them to buy those expensive American incubators. She was the first one to make the connection between oxygen use and the risk of RLF-blindness.

DR. GARTNER: Really.

DR. SILVERMAN: She presented her statistics about how RLF followed this change. Someone from Australia heard about this observation and took the message back to Melbourne, where Katherine Campbell heard about it and examined the outcomes in nurseries in which oxygen was given quite liberally, and others in which, for economic reasons, it was given as little as possible. Campbell found a difference in retrolental fibroplasia. Kate Campbell's article was published first. So Campbell is usually given the credit for establishing this association, but Mary Crosse is the one who mentioned it first. Others found no association. There was a fellow by the name of [Marcel] LeLong in Paris, who found that those who got oxygen most liberally had the lowest risk of RLF. In Oxford [England], there was an increase in RLF as oxygen use was liberalized, but RLF then decreased as liberal oxygen use continued. There were all of these contrary observations. Everyone forgets about the heated meeting in Bethesda in 1953 when these issues were being debated. There was a lot of conflicting evidence. The quality of the evidence was not good and it pointed in both directions. Beryl Corner [1910 – 2007] was another figure in neonatal pediatrics in Bristol, England. She was a friend of Dorothy Andersen [*1901-1963, Pediatric Pathologist, Babies Hospital, Columbia University, New York]*. Whenever Dorothy Andersen went to Bristol, she would say, "I've got to corner Beryl." Apparently they argued all the time. Beryl Corner heard about our early favorable experience with ACTH, and she began to treat the early changes of retrolental fibroplasia with that hormone. Even after our negative trial was reported, she continued to use ACTH. I understand she continued it for

years thereafter. There were a number of these odd little things. Beryl Corner was a leader in the care of newborn and premature infants in that part of Britain. Her other claim to fame was her skill in raising newborn apes, great apes, in her premature nursery! [laughs] She was a very colorful figure. When Mary Crosse, and Kate Campbell visited me in New York, they made quite a sight. Mary Crosse was very short and Kate Campbell was a giant of a woman. It was like Mutt and Jeff.

Stewart Clifford [1901-1997; Boston] in this country doesn't ever get mentioned. Stewart Clifford is the man who saw the first example of retrolental fibroplasia. It's interesting, he made a house call, and in those days you made house calls to follow up a premature infant, and he sees this child with nystagmus and white pupils, and he told the parents, "I'm afraid your child can't see." He arranges to have the child seen by an ophthalmologist [Paul A. Chandler]. That was the first case. Within a month, Stew saw a second case, and the second case, interestingly enough, was in the famous, very wealthy Sun Oil Company family. This child was now seven months of age. Stew couldn't find the first ophthalmologist, Paul Chandler, because he was out of town, but Theodore Terry [1899-1946; Boston], was in town and he was able to see this child on a Sunday morning. Theodore Terry says to the parents, "I'm afraid your child has congenital cataracts." He admitted the child to the Massachusetts Eye and Ear Infirmary and was about to start the cataract surgery, when Paul Chandler just happened to come by and said, "I'd like to see this baby. I saw something just like that; it's not congenital." He convinced Terry it wasn't a congenital cataract. Terry then accumulated 5 cases, and then 112 cases, and soon he became the acknowledged RLF expert. Terry died as a relatively young man.

DR. GARTNER: Had RLF been seen and recognized in Europe before this?

DR. SILVERMAN: Algernon Reese [1896-1981] at Columbia had a worldwide reputation as an ophthalmologic pathologist, and he looked at old collections of pathological specimens in newborn infants with various kinds of blindness. He was convinced that RLF did occur much earlier. He saw examples in Berlin, for example. But it was very rare. In other words, everybody was quite sure that it must have happened, but it was quite unusual. It was agreed that the increase that began in the 1940s was unique and alarming.

DR. GARTNER: But it hadn't been reported prior to this.

DR. SILVERMAN: Not as an entity related to prematurity. Terry's report was the one who made the connection with prematurity and he is given the credit for this discovery.

DR. GARTNER: That's an important contribution. You talked about the concern that you have about saving ever smaller and immature preemies. How should we be dealing with that issue?

DR. SILVERMAN: I would like to think that we would develop a newborn medicine which was responsive to parents' wishes within reasonable limits. Common sense. If there is a very marginal infant, or even a marginal infant, and the parents want only comfort care; I would argue that we should support that. Now it's true that errors are going to be made, needless to say, but it's an imperfect world. Many infants who were abandoned in my day and given nothing but comfort care survived. My first experience with a 620 gram infant when I was a resident was an example of such. It doesn't happen often, but we need to recognize that we don't have complete omnipotence. Moreover, as our society is becoming increasingly pluralistic we cannot impose a one-size-fits-all solution to marginal situations in medicine. I think medicine, in general, and neonatal medicine in particular, should become more responsive and less proactive. Medicine's aim, in my view, is to reduce pain and suffering, not to postpone death, nor to increase the number of individuals living on this planet.

DR. GARTNER: We see from time to time parents who want a child saved at all costs, even when we, the neonatologists, feel very differently about it.

DR. SILVERMAN: Yes. I've written about that; I call it reverse consent. In other words, should physicians consent to unreasonable demands which will subject that child to unnecessary pain and suffering? Physicians have no obligation to respond to unreasonable demands. And I feel that parents have the right to refuse, within broad limits, the care or intervention offered for their children. But they do not have the right to demand that I be a party to creating unnecessary pain and suffering. I realize this is a pat answer, but I've thought about the dilemma for a long time. And I also know it's easier to say than do, but I think we need to draw lines of behavior. Parents have very broad rights to make decisions for their children, but they are not endless. And physicians also have rights; they are not obliged to torture infants. Balancing the two limits should allow us to set a sane course for the future as medical action becomes increasingly powerful.

When I was young, I was asked over and over again by parents, "Please don't try too hard, doctor." In recent years, I'm told, you don't hear that plea anymore. Quite the reverse; it's now, "Do everything you can." That's an interesting change in attitude. I suspect it's the result of popular propaganda in the media. Medical prowess has been so overblown you hear parents say they're not worried about blindness, "You can transplant a new eye." These unreasonable expectations are driven by the media.

DR. GARTNER: In neonatology we've recognized many errors in

management. You've touched on a couple of these. What additional ones have you not yet touched on?

DR. SILVERMAN: The Thalidomide disaster certainly has to be mentioned because it had not only such a huge impact, but because it changed the rules with the Kefauver-Harris Amendment. Although Thalidomide was not released in the US, it was a very close thing. So that incident I see as a real watershed. And this was the first time federal law specified the requirement for controlled clinical trials. It demonstrates this whole matter of evidence-based medicine. A theme keeps recurring: negative trials have very little impact on practice. Everyone says that the streptomycin trial for tuberculosis, run by Austin Bradford Hill, in 1946, was the first randomized control trial. That's not strictly so; there were a number of earlier trials. But they were negative trials; they did not demonstrate an effect. The studies were promptly forgotten. Moreover, when doctors are told that studies demonstrate a treatment they're using is ineffective, they say, "Well, I have nothing else to do and it isn't going to hurt. I have to do something." The "I-have-to-do-something" drive, and "since-you- demonstrated-no-effect,-I'm-not-going-to-do-any-harm" arguments are pervasive. For example, the Bellevue report of oxygen and retrolental fibroplasia, noted, "There's no difference in mortality." But, there was a small difference in mortality. The sample-size was too small to detect the significance of the observed increase in mortality with oxygen restriction. Negative trials lead to what's called the file drawer effect. People don't even want to publish negative trials, and that contaminates the literature, because you simply don't have negative examples. Evidence-based religion, which I belong to, argues very strongly that all trials should be registered in advance, before they're done, to guarantee that the outcomes will be known, no matter what the results. I think they're making some progress. The Cochrane Collaboration is getting behind this. The *British Medical Journal* is getting behind this movement. Even the staid *New England Journal of Medicine* is talking about the need to register trials. There's also a strong movement for submission of protocols for trials before they're done, and to have these preapproved for publication. If this trial is done with these details, we will publish it. Pre-trial approval is an idea which makes sense.

DR. GARTNER: Yes.

DR. SILVERMAN: The file drawer effect is a very real problem. You can see my Oxford experience has really influenced my thinking.

DR. GARTNER: Any other major errors in our history of neonatology? There's chloramphenicol. What others?

DR. SILVERMAN: Chloramphenicol was a very big one. It was shot down by a controlled trial in Los Angeles. Chloramphenicol, DES, Thalidomide

and Gantrisin are only the tip of the iceberg. Many interventions have never been evaluated. Who knows how much harm has been done? Testosterone was once used to make premature infants grow more rapidly. Ditto for thyroid hormone. No one ever followed these infants to determine long-term outcomes.

DR. GARTNER: Yes, that's come back. Thyroid is not gone.

DR. SILVERMAN: Yes, to influence the course of hyaline-membrane disease, right. And, the positive pressure device which infants were put into to mimic uterine contractions on the fetus.

DR. GARTNER: Oh, and the little tank respirator.

DR. SILVERMAN: This device, invented in Texas, exposed a lot of infants to hyperbaric oxygen. No one ever looked at the retrolental fibroplasia risk.

DR. GARTNER: Oh, the Bloxum Airlock

DR. SILVERMAN: The Bloxum Airlock administered 60-70% at above atmospheric pressures, so these infants were exposed to a good jolt of oxygen, and some of the premature infants were left in the Bloxum Airlock for as long as 7 to 14 days. Term infants were in for several hours or one day at most, but the premature infants were in it for some time. That was never looked at. Many of these practices died a natural death as doctors moved on. "You can't just stand there and do nothing; you've got to do something," they say. Gastric oxygen was used for years, and even by Ylppö in Europe. Oxygen was instilled by tube into the stomach of premature infants - a very common practice that was never formally evaluated; it simply disappeared. Even subcutaneous oxygen was proposed by Hess at one point, but he dismissed it. At one time it was tried in Europe. There had been so many outlandish interventions that came and went. The extent of damage was never assessed.

DR. GARTNER: So your answer to preventing future errors of this kind would be to test every new therapy?

DR. SILVERMAN: Yes.

DR. GARTNER: In a formal, controlled clinical trial?

DR. SILVERMAN: Yes, that's the message. I came to this with great difficulty. My feeling is that we're dealing in an area of medicine where the frontier is very, very fuzzy; where many interventions that are being done have not been evaluated, and you have to have a continuous program in which you're looking at everything. Physicians hate to freeze what they're

doing and wait for an answer. When something new comes along they're chomping at the bit to use it.

DR. GARTNER: The cancer people, at least the pediatric cancer people, do that for all of their treatments. Every single treatment. No one gets treated any longer in pediatric cancer without a controlled clinical trial.

DR. SILVERMAN: Exactly. They've had very able leadership. And the National Eye Institute is following in their footsteps. I hope the NICHD will see the light.

DR. GARTNER: You talked about the participation of parents in decision-making, particularly for the small baby and about life and death. Are there more ways that parents could be involved in neonatal intensive care?

DR. SILVERMAN: I would like to see parents involved in active comfort care. It's more than simply stroking and talking to their babies. I would like them to have competencies. One of the lessons from parents of blind children is that the feeling of helplessness when the child is put first into their care can be dispelled with instruction. Parents need to be actively engaged in caring for their kids while in intensive care. Nurses understand this more and more, and try to get parents involved as soon as possible.

DR. GARTNER: You talked about your involvement with ethical decision-making in the nurseries. What other ethical issues do you think are important that we haven't dealt with?

DR. SILVERMAN: Well, Jon Tyson [University of Texas, Houston] has written about an "ethics of evidence." One has an ethical obligation to confront our ignorance honestly. Valerie Miké, a statistician at Cornell University, has written about this as well. There is an ethics of evidence, and it's everybody's job to understand that. Guessing in medicine went on for thousands of years, but it's a dangerous game. Everybody gets upset when I stress the negative aspects of intervention, the unexpected damage that is always possible. I stress the negative because we tend to overlook it so often, and I think this gives an "ethics of evidence" its basis in reality. We're not dealing with theoretical possibilities of damage; they are real and physicians must take them into account.

DR. GARTNER: You were the one who introduced me to the whole area of history of neonatology.

DR. SILVERMAN: I introduced you? [laughs]

DR. GARTNER: You introduced me to it. And I just wonder if you have any thoughts about what we, who are involved in pediatric history, should be doing?

DR. SILVERMAN: I hope there will be more formally-trained historians like Jeffrey Baker [Duke University, Durham, NC]. He's a member of the department of pediatrics and practices general pediatrics, but his academic specialty is history. One should encourage that, to have people who want to do it seriously. Now I did it, and still do it, as a lark. I'm not a trained historian. I'd like to see people like Jeffrey, a trained historian, look at some of these questions which I find fascinating but have never been approached in the way in which they should be approached as a pro. It's amusing and interesting, and I think gives one insight as well.

DR. GARTNER: You didn't talk about your experience at Bellagio. Tell us about Bellagio.

DR. SILVERMAN: It was an amazing experience. When I was writing the chapter for the book on retinopathy of prematurity, which John [T.] Flynn and I co-edited, I had to put together all of these other contributions and mine. I applied to the Rockefeller Foundation for a one-month stay at the study center in Bellagio, Italy. It was an absolutely perfect place for this task. And it was an exciting month. The applicants are advised that you go there when the project is going to be finished rather than started. You can go either way but there is no reference library. Fortunately we got an appointment, and the appointment was for December. A few months later we were called and asked could we change our December appointment to mid-summer, to July because the scholar scheduled for July was pregnant. I think they went down the list to find the couple least likely to get pregnant. We were a safe substitute. So just by chance we went there at the most perfect time of the year, in July. It's an unbelievable place; the Rockefeller Foundation got the Villa Serbelloni as a gift from the heiress of the Hiram Walker liquor foundation. She married an Italian count, and a year or two after they were married he died, leaving her with the title of Contessa and this enormous multi-roomed villa that used to be a castle. The Contessa entertained on a grand scale, once bringing the Berlin Philharmonic Orchestra to entertain her guests. When she was in her 80s and feeling she was about to die, she called Dean Rusk, President of the Rockefeller Foundation, to say she wanted to give the Villa Serbelloni to the Rockefeller Foundation and wanted it to be used to improve international goodwill. And she gave the Foundation a million dollars a year to keep it up. Within a week after transfer of title she was dead. As somebody pointed out, the Rockefellers don't kid around. Rusk didn't know what to do with it, so they decided to establish the visiting scholars program, which is really an amazingly thoughtful, very effective program. Scholars come for a month, and their comings and goings are staggered so that you keep meeting new people. Each day you are seated at dinner next to someone else. It was an opportunity to meet people from widely varied fields. Fortunately, when we were there, there were no other physicians. There were musicians, artists,

chemists, authors. The setting was just idyllic. At first when you arrive you say, "How can I possibly get any work done in this beautiful setting," but within 24 hours guilt sets in [laughs] and you go to work. The Foundation provides you with a typewriter and paper; you have to bring your own computer if you're using that. But it is a perfect place and the experiences we had, meeting many people who we've kept as friends, was just incomparable. So the book got assembled and my chapters written and it was a wonderful experience. I urge you to apply. Jack Sinclair and the statistician who works with him, went there when they were finishing their book on the newborn.

DR. GARTNER: Sounds great. Is there anything that we've left out that you particularly want to include?

DR. SILVERMAN: Let me look at this. I think that's it.

DR. GARTNER: Well, I have a few things on the future of neonatology, and we've covered some of these already, but it's always fun to think about where things are going. Given that there are going to be limited resources, both for clinical care for premature infants and sick newborns and for training and research, how would you allocate those limited resources in the future?

DR. SILVERMAN: I would certainly give a large hunk of the resources to try to investigate basic mechanisms. I would like to think that some of the funds would be used for clinical evaluations. Obviously, this is my prejudice. How that should be divided, you know, 50-50, is hard to say, but I think those are the two places to try to establish a firmer base for our knowledge so we guess less and less and have solid footing, solid steps to put our feet on. I think so much of what one does in clinical medicine is by guess and by golly. You know, you've got to somehow narrow that, and the only hope is to fill the gaps in our knowledge. I think the impending genetics revolution is going to have an impact here as well, a very strong impact, and will probably change everything beyond present comprehension.

DR. GARTNER: So you'd keep a balance of both basic and clinical research?

DR. SILVERMAN: Yes.

DR. GARTNER: Do you have any inklings in your own head about what is likely to be discovered in the next 10 or 20 years? What do you think that is going to lead to in the next neonatology?

DR. SILVERMAN: Well, one of the things I'm worried about is cloning and genetics and our ability to change and to use these dramatic changes in our patients. I'm worried how one draws the limit. What are we doing that will

change human existence so drastically? Correcting metabolic defects; now where do we go after this child is grown and becomes a parent? Those temptations for immediate improvement of this child's existence have to be tempered by what one sees as long-term biological effects. We're going to have to exercise restraint, and even though it becomes more and more exciting, there has to be restraint. I gave the Windermere Lecture to the British Paediatric Association, now the Royal College of Paediatrics and Child Health, a few years ago, and the title was, "*The Line Between Knowing and Doing in Medicine, A Challenge for the New Millenium,*" a very flowery title. That's really what I have in mind. How do we draw that line between knowing and doing? I think we have gone from knowing to doing without pausing and asking what that has done to our values. I want that line drawn, that introspective line that takes into account what one does to separate knowing from doing. That is the message that I delivered to the British, and I would like to broadcast that as widely as possible. The line between knowing and doing.

DR. GARTNER: You don't believe that those who say because we can do it, we are going to do it?

DR. SILVERMAN: Unfortunately, that's been true in the past, as people point out, no technology has been limited. It hasn't been possible to restrain anything, atomic bomb, and everything since. We will never be able to restrain this. We sure as hell better try, because I think the need for this kind of restraint is different than it was in the past for the reasons of pluralism. When you're dealing with populations which are increasingly heterogeneous, medicine has to be responsive, not proactive, but responsive to need. We need more humility in medicine in general, and especially in neonatal medicine.

DR. GARTNER: Women in particular, but minorities in general, are entering into medicine in larger numbers. What do you think the implications of that are, particularly for neonatology, and particularly I emphasize the women? What do you think that's going to do?

DR. SILVERMAN: I hope it will humanize medicine. I really hope and expect that it will humanize it. I think women may be more thoughtful in making many of the decisions in neonatal medicine. Let's face it, hormones do influence behavior. After all, I've had very long experience with nurses, very skilled nurses, and I found them to be thoughtful. Minorities will also play a larger role than in the past, another welcome development. Prematurity is related to social class; social class is related to ethnicity. I'd like to see the same kind of humanization from those who can understand. Someone who knows the culture of a Mexican neonate has a different view on how to inform and how to ask culturally. Otherwise you're talking past one another all the time. And certainly in the Black culture as well. You have to

strive, it seems to me, to have a pairing between the actor and the actee. The one who's going to change things so dramatically and those whose whole family lives are going to change, there has to be a better fit from the point of view of the value system and culture. We don't pay a lot of attention to the gap between the social class of the doctor and the families. It is often immense. We have to somehow take that into consideration. I would like to see a better matching, and I see the arrival of women, and minorities as providing better matches.

I grew up in southern California, close to a very large Mexican population, so I developed a lot of empathy for this warm culture. Although I don't understand it completely, I'm more sympathetic than others who've not seen it up close. When I went from Los Angeles to San Francisco, and then from San Francisco to New York, the cultural differences were strikingly different. When I came back to California, I realized that I identified more with the culture I knew best. I understood what they were saying in a way I didn't understand Black New Yorkers. That is an issue when we're in a position to change people's lives so drastically.

DR. GARTNER: What do you think of the future needs in terms of people power in neonatology? Would you change the job description, we had this evolve in the last 30 years or so in neonatology?

DR. SILVERMAN: Technicians and nurses.

DR. GARTNER: Nurses, technicians, fellows, faculty; would you like to see those changed in some way? And if so, how?

DR. SILVERMAN: Yes, I was amazed to see how quickly technical developments shifted emphasis from the patient to the machine. Before the apnea monitor, nurses' observations were much more detailed. I can also see the advantage of skilled technicians when the house officers change every month. One of the things that bothers me very, very much is a remark that I heard not once, but a number of times, "We don't expect this infant to live, but it will give the house officers some experience in the techniques." That has to be examined head on; that is a real problem for me. If one can use the expertise of the technician and be content to have medical trainees as observers who don't all have to learn these techniques, it would make for a humane scene. Neonatal intensive care units have metastasized so there are more and more small institutions with neonatal intensive care and many relatively unskilled people are carrying out procedures beyond their expertise, driven by the large amount of money to be earned in this industry

DR. GARTNER: What about future relationships between neonatology and other disciplines, either inside or outside of pediatrics? Subspecialties, general pediatrics, obstetrics, anesthesiology, philosophy, music? [laughs]

DR. SILVERMAN: Bioethics developed on my watch, so to speak. There was no such thing as a bioethics person when I began. Now, every hospital is virtually required to have an expert in bioethics. I cannot see how one shifts the responsibility for decision-making to a bioethics person or bioethics committee. It's diffusing responsibility for the decision. I like the way the bioethics committee in Holland is used. The bioethics committees in Holland and maybe in other European countries examine these ethical dilemmas after the fact. They don't participate in the heat of the decision-making, they attempt to instruct. They use concrete examples from the immediate past to help doctors make future decisions. They elucidate bioethical principles, but leave decisions to the physicians, who must take many other things into consideration. Now, that makes sense to me. I see the advantage of the post-hoc examination.

DR. GARTNER: The autopsy.

DR. SILVERMAN: Exactly. The autopsy of the ethical principal.

DR. GARTNER: What advice would you give to the next generation of neonatologists? In one sentence [laughs].

DR. SILVERMAN: [laughs] In one sentence: Be careful!

DR. GARTNER: That's good advice.

DR. SILVERMAN: I would like to inculcate statistical methodology and logical thought, that is, evidence-based medicine.

DR. GARTNER: And if you were in residency now, would you pick neonatology for a fellowship?

DR. SILVERMAN: I really don't know, Larry. I really don't know whether I would or not as a matter of fact. I think I would find it very hard to spend all of my time in the neonatal intensive care unit. No, I don't think I would. I don't think I would choose a neonatal fellowship.

DR. GARTNER: Well, as my assistant, Carol Gartner, would you like to ask any questions? Anything we've left out?

DR. C. GARTNER: No I think you've covered things very well.

DR. GARTNER: I want to thank you very much, Bill, this has been really a wonderful, wonderful interview, and you have a lot of very, very wise things to say. As always, you've been my teacher and my guru, as I always tell people, and a wise one. I thank you very much on behalf of the entire Academy.

DR. SILVERMAN: Larry, thank you, thank you, you're very kind and I really appreciate what you've done. Both of you.

DR. GARTNER: Our pleasure.

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CURRICULUM VITAE

William A. Silverman, M.D.
90 La Cuesta Drive
Greenbrae, California 94904
Phone (415) 461-2030

Birthdate: 23 October 1917, Cleveland, Ohio

Married: Ruth; Children, Daniel, Jen, David

Education: B.A. University of California, 1939
M.D. University of California Medical School, 1942

University Appointments

College of Physicians and Surgeons, Columbia University
- Assistant in Pediatrics, 1946-48
- Instructor in Pediatrics, 1948-51
- Associate in Pediatrics, 1951-55
- Assistant Professor of Clinical Pediatrics, 1955-58
- Associate Professor of Clinical Pediatrics, 1958-60
- Associate Professor of Pediatrics, 1960-67
- Professor of Pediatrics, 1967-68

University of California Medical School, San Francisco
- Adjunct Professor of Pediatrics, 1970-73

Hospital Appointments

University of California Hospital
- Intern (Pediatrics), 1942-43
- Resident (Pediatrics), 1943-44

Babies Hospital, Columbia-Presbyterian Medical Center, N.Y.C.
- Resident (Pediatrics), 1944-45
- Assistant Pediatrician, 1946-50
- Assistant Attending Pediatrician, 1950-58
- Associate Attending Pediatrician, 1958-65
- Attending Pediatrician, 1965-68

Children's Hospital, San Francisco
- Chief, Perinatology Section, 1968-70

Other Appointments

Department of Rehabilitation, State of California
Medical Consultant, 1974-1986

San Francisco Lighthouse for the Blind
Board of Directors 1978-83, 1984-88

Larkspur Library, Larkspur, California
Board of Directors, 1979-

Blind Babies Foundation, San Francisco
Board of Directors 1981-1990
Professional Advisory Committee 1990-

License

State of California, 1942-

New York State, 1945-

Certification

American Board of Pediatrics, 1947

Professional Societies:

American Pediatric Society

Society for Pediatric Research

Perinatal Research Society

American Academy of Pediatrics

American Medical Association

The Harvey Society

The Society for Clinical Trials

Special Appointments

Study Section, Human Embryology and Development, National Institute of Health, 1968-71

Chairman, Committee on Fetus and Newborn, American Academy of Pediatrics, 1961-67

Editorial Board PEDIATRICS(Chairman) 1962-68

Editorial Counsellor, BIOLOGY OF THE NEONATE, 1965-

WHO Expert Advisory Panel on Maternal and Child Health, 1967-

Research Advisory Committee, United Cerebral Palsy Foundation, 1967-69

Consultant MCH Pan American Sanitary Bureau, 1967-69

Subcommittee on Causes of Neonatal Death, Nation Office of Vital Statistics, 1954-60

Pediatric Advisory Committee, New York City Health Department, 1958-68

Medical Committee:Planned Parent-World Population,1967-68

Subcommittee on Hospital Emergency Services. National Research Council, 1968-71

National Advisory Committee on the Early Years, American Foundation for the Blind, 1985-1988

Controlled Clinical Trials
Suspended Judgment column editor 1989-1994

Paediatric and Perinatal Epidemiology
Editorial Board 1991-

Special Honors

E. Mead Johnson Award for Research in Pediatrics, American Academy of Pediatrics, 1958

Career Scientist, Health Research Council of the City of New York, 1962-68

Walter B. Seelye Lecture, University of Washington School of Medicine, 1960

Constantin P. Yaglou Memorial Lecture, Harvard School of Public Health, 1960

Clifford D. Sweet Memorial Lecture, East Bay Children's Hospital, Oakland, California, 1964

James Marvin Baty Lecture, Boston Floating Hospital, Boston, 1964

MacKid Lecture, Calgary General Hospital, Calgary, Alberta, 1968

Louisville Pediatric Society Lecture, Louisville, Kentucky, 1969

Edwin Schorer Memorial Lecture, Kansas City, Missouri, 1969

Day Lectures, Columbia University, New York, 1975

Apgar Award of American Academy of Pediatrics, 1979

Daniel Y.E. Perey Research Lecture, McMaster University, 1982

Christensen Visiting Fellow, Oxford University, 1983

C. Warren Bledsoe Award, American Association of Workers for the Blind, 1983

Scholar in Residence, Rockefeller Study Foundation, Bellagio, Italy, July 1985

California Perinatal Association Annual Award, Oct 1985

Centennial Medalist, Babies Hospital, May 1987

National Perinatal Association Award, November 1987

L. J. Filer Lecture, University of Iowa, May 1988

Ray A. Kroc Visiting Professor, Bowman Gray School of Medicine September, 1991

Keynote Address at 125th Anniversary of Sinai Hospital of Baltimore, October 11, 1991

Keynote Address at "Doing More Good Than Harm Conference NY Academy of Sciences March 22-25, 1993

Third Annual Silbert Neonatology/Perinatology Lecture Cedars-Sinai Hospital, Los Angeles Jan 28, 1993

The Archie Cochrane "Effectiveness and Efficiency Anniversary Lecture
Radcliffe Infirmary, Oxford March 17, 1994

Visiting Fellow, The UK Cochrane Centre, Oxford March 1994

The Line Betweeen "Knowing" and "Doing": Medicine's Dilemma at the End of the Twentieth Century. The 1994 Windermere Lecture to the Annual Meeting of the British Paediatric Association April 1994

Honorary Member of the British Paediatric Association. Elected on April 13,1994.

The 1994 F. Stanley Porter Lecture, "The Future of Clinical Experimentation in Neonatal Medicine" Eastern Virginia Medical School, Norfolk Virginia, June 2, 1994

Distinguished Alumnus Award of The Babies Hospital October 23, 1994

Thomas Cone Jr. Perinatal History Lecture "Proto-neonatology: Children's Bureau and Ethel Dunham." American Academy of Pediatrics, October 15, 1995

Elected as a Founder Fellow of the Royal College of Paediatrics and Child Health.
London, October 31, 1996

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