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A History of Bio-Science Laboratories

Bio-Science Laboratories (BSL) was started in February 1948. In 1985, it was acquired by SmithKline Beckman, becoming part of its laboratory network that was renamed "SmithKline Bio-Science Laboratories." In 1989, following the acquisition of SmithKline Beckman by the Beecham organization, the network was again renamed, "SmithKline Beecham Clinical Laboratories" (SKBCL), and the name "Bio-Science" disappeared from public view except for scattered references in the SKBCL Directory of Services. In 1948, the BSL staff consisted of its four founding partners, who had only a few thousand dollars for initial capital. When the last of the founders retired in 1981, BSL had >20 major US locations and three foreign branches and affiliates; conducted several hundred different tests, with sales in excess of $85 000 000; and employed >1500 people in the US alone. Change, sometimes quite severe, characterized its life; the one constant that penetrated all aspects of the organization, however, was the dedication of its founders to professionalism, quality, and research. The following personal and reflective narrative is intended to present both a history of BSL and an account of its contributions to the profession of clinical chemistry and to the AACC.

In 1948 the practice of medicine in general, and of laboratory medicine in particular, was far removed in scope and sophistication from what we see today. For example, the principal antibacterials were a few sulfonamides and penicillin; psychopharmacology was virtually nonexistent; adrenal and thyroid hypofunction were treated with endocrine organ extracts; and plasma cholesterol had just appeared on the scene as being somehow related to atherosclerosis and coronary artery disease. In the clinical laboratory, chemistry's contribution to the assessment of health and disease was minor in comparison with the roles of bacteriology, hematology, and urinalysis. Thyroid status was assessed through determination of the basal metabolic rate. The few protein hormones that could be measured were bioassayed by using frogs, rabbits, and mice. Enzyme assays did not appear until 1954. Analytical precision was encompassed in the concept of assaying duplicates. The independent clinical laboratory was definitely held in low regard, a grudgingly accepted adjunct to the hospital laboratory, because of what was perceived to be "poor" quality of performance and a "commercial" taint. To round out the context, Medicare and the Clinical Laboratory Improvement Act of 1967 were 20 years in the future. Few states had any legislation pertaining to the clinical laboratory. Not until December 1948 would 11 scientists get together in New York City to form the American Association of Clinical Chemists.

The Start-Up

It was with this situation in mind that three Army officers and one Navy officer decided they were ready to take up the challenges of postwar civilian life. They had served during World War II in their professional capacities: one was a physician who had decided while in medical school that he didn't want to practice medicine on patients; the other three had doctorates in bacteriology. The four had met after the war at Camp Detrick, MD, and were doing research in biological warfare. Duty at Camp Detrick was fine, but it was still just part of the transition process in returning to civilian life. As civilians they wanted to continue with research and planned to fund this ambition with a laboratory business doing mainly industrial analyses backed up by a medical clinical laboratory. Southern California seemed to be the right place; opportunities in the region were expected to grow and the climate was benevolent. The four men were Sam Berkman, PhD; Orville Golub, PhD; Richard Henry, MD; and Milton Segalove, PhD (Fig. 1). The business was to be named Bio-Science Laboratories.

The quartet moved to Los Angeles with financial help from friends and family that, when added to their personal savings, amounted to $55 000. This was to support the four families and launch the enterprise. Each drew a salary of $5000 annually; the rest of the nest egg was used to rent space, buy equipment and supplies, and provide working capital.

In February 1948, BSL opened for business. Henry and Berkman manned the clinical laboratory in a small office building in Beverly Hills, and Golub and Segalove worked in a larger laboratory about five miles (~30 km) away, near Culver City. Duties included everything from cleaning animal cages to venipuncture of patients and doing tests to the usual battery of clerical tasks. Then there was constant selling; Henry visited physicians and Golub called on industrial firms. Sometimes the skies were sunny as exemplified by the numerous specimens that appeared on opening day. Sometimes the skies were dark, such as the next 6 weeks, when hardly a specimen arrived.

Growth was not remarkable, working capital sometimes got perilously low, and disaster often seemed close. Acceptance by the local medical community was slow and sometimes resisted. For example, Henry had joined the laboratory director subsection of the county medical society. A pathologist who owned and directed an independent laboratory objected to Henry's presence

Fig. 1. The founders of Bio-Science Laboratories.
Left to right: Richard Henry, MD; Orville Golub, PhD; Milton Segalove, PhD; and Sam Berkman, PhD, in February, 1969, at the time of Dr. Segalove's retirement.

and invoked a bylaw that prohibited laboratory directors from being in business with "lay persons," including doctoral scientists. He was given the alternatives of dissociation from his partners or withdrawing from the Association; he chose the latter.

The encouragement of the original supporters, however, kept the scales tipped in the direction of staying open. Despite the slow growth, fiscal policy remained clear: the "business" came first and spare cash was plowed back into it. An employee was hired to free the four from some nontechnical duties, such as washing animal cages and tending animals. When possible, newer and better equipment was bought. But business growth was not comforting.

The Breakthrough

In 1949, an event occurred that had important lasting consequences, the result of a staff contact at the Los Angeles County Hospital, a huge acute-care public institution and the teaching hospital for the University of Southern California (USC) School of Medicine. Dick Henry had been accepted to the USC teaching staff at its county facility. There he was introduced to Paul Starr, a physician with a national reputation as a clinical and research thyroidologist. In 1951, physicians interested in assessing thyroid status had to rely largely on measurement of the basal metabolic rate, a measurement that was highly variable and nonspecific. Starr convinced Henry that thyroid status could be assessed reasonably well at the Hospital because Al Chaney, its Chief Clinical Chemist, had developed a reproducible method for chemically measuring the protein-bound iodine of serum (PBI), and inferentially the serum thyroxine concentration. The method was complex, quite laborious, and required the use of intricate customized glassware—yet it worked. Because Chaney had a small private laboratory business in Pasadena in addition to his appointment at the Hospital, the benefits of this measurement were available to only a few practitioners in the community and to the patients of the Hospital.

With Chaney's generous loan of the special glassware needed, Henry and Golub went to work at BSL setting up the PBI method. The method involved serum protein precipitation and washing, wet digestion of the protein pellet, distillation of released iodine into a receptacle, and measurement of that iodine by its catalysis of the reduction of ceric ion by arsenite. The digestion was an art; iodine in the air and on the premises was a contamination disaster; and little was known about specimen stability. It was a miserably difficult, one-specimen-at-a-time procedure but it could be made to perform. Since the four partners had to work all day to keep the business going, method development had to be done at night and on weekends. It took Golub and Henry about 6 weeks to learn how to control the test, assess its accuracy and precision, and establish the conditions for specimen stability. The method remained tedious and laborious, but its improvement allowed the PBI to be measured reliably over a wide range of conditions and values. Once the improved test became available to the Los Angeles medical community, business growth at BSL accelerated markedly.

Repercussions of this development came to light when Lawson Wilkins, at the Johns Hopkins Medical Center in Baltimore and a pioneer in pediatric endocrinology, became aware of BSL's ability to do the PBI. Apparently his awareness came from one of his students, a Beverly Hills internist and a client of BSL. At Wilkins's instigation, the Medical Center laboratory sent specimens to BSL for analysis: "splits," repeat splits, resubmissions, and "spikes"—all blind. The results were so good that daily shipments from Hopkins soon became routine.

When the dry ash method of Barker, Humphrey, and Soley was published in 1951, BSL quickly adapted it to mass production. I remember in 1966 that we were analyzing well >1000 specimens a day, coming from all over the country and abroad, with exquisite precision and a routine turnaround time of 24 h. Today I doubt that the PBI is being done in the US at all.

The Learning Curve

The lessons from these experiences were fundamental. First, recognition by the independent laboratorian of the present and future needs of the medical community for new diagnostic aids could lead to significant growth. This was supported when the Johns Hopkins Center soon began making requests for other tests, the kind that in the early 1950s were called "reference" or "specialized." Accordingly, BSL's attitude on new test development became increasingly aggressive, favoring significant risk taking. Indeed, BSL led the way in making specialty tests available to the national medical community. A few of these are shown in Table 1. Other laboratories, for various reasons, considered these tests to be only of research importance, but at BSL they represented opportunity for growth. Today, many of those are "old hat," done routinely by using kits and automated instrumentation.

Secondly, the basic commitment to quality became strongly reinforced. Henry, as director, was morally and

Table. 1. Specialized tests and year first offered to the medical community.

Test	Year
Protein-bound iodine in serum	1950
Direct determination of epinephrine and norepinephrine in urine and tissue	1956
Assay of 17-hydroxycorticosteriods in urine	1957
Chemical assay of aldosterone in urine	1959
Paper chromatographic identification of amino acids in urine	1959
Radiometric assay of uranium and plutonium in urine	1961
Electrophoretic measurement of thyroxine-binding globulin in serum	1961
Ultracentrifugal confirmation of hyperlipoproteinemias	1965
Long-acting stimulator of Graves disease in serum	1962
Chromosome analysis	1968
Direct measurement of free thyroxine in serum	1970
Lecithin/sphingomyelin ratio in amniotic fluid	1973
Estradiol receptor assay in tissue	1974
Parathyroid hormone in serum	1974
Angiotensin-converting enzyme in serum	1976
HPLC measurement of propanolol in serum	1978
Hemoglobin A_{1c} measurement by isoelectric focusing	1982

professionally committed to patient care, as were his partners. This attitude was concretely transferred to the first-level supervisors, giving them the authority to cancel an analytical run if, *in their opinion,* the results were suspect. Similarly, managers were *required* to request discontinuance of testing if the procedure was not functioning properly. That such decisions sometimes entailed costs and reductions in revenue in the five and six figures range was irrelevant.

I remember in 1964 requesting suspension of our double-isotope derivative assay for urinary aldosterone because of spurious counts in the quality-control assays. At that time, we were the only independent laboratory offering this assay and the volume was enormous, but the department was shut down. Charles Sobel (he was Chief Chemist of BSL from 1950 until his retirement in 1968) and I and the "aldo" staff formed a research team that worked 12-h days continually for several weeks to solve the problem. Although we notified our clients of this state of affairs, the specimens continued to pour in, and we had to commandeer refrigerators and buy additional units to store the specimens until the assay could be resumed. The problem was solved when we found that one of the radioactive reagents had an odd contaminant. The cost of correcting this problem was considerable, but the loss of revenue was probably minuscule because, throughout this episode, our clientele did not slow down their submission of specimens.

Those were the days before modern automation was even a concept. Automation then really meant mechanization. Nevertheless, business growth increasingly required specimen processing in large batches. Specimens used exclusively for quality control constituted at least 10% of those run in a batch, and they covered the full range of clinically expected values. In addition, several layers of quality assurance schemes were put in place, ranging from on-site visual inspection of quality control records through several in-house systems (such as mailing assayed specimens to ourselves) to services obtained from governmental and professional agencies.

The PBI story had a third outcome. Service to Johns Hopkins showed that the East Coast medical community was only 24 h and a 6¢ postage stamp away. This market potential was immediately appreciated and Orv Golub was soon arranging to send announcements about the PBI to physicians and laboratories all over the country. BSL became known, perhaps pejoratively, as " that mail order lab out West." The fact of the matter was that tests of the quality that Johns Hopkins could get were also made available to practitioners in such places as International Falls, MN, and to a 99-bed hospital in the Florida panhandle.

A final significance of the PBI story remains to be told. The availability of this measurement nationally excited a great deal of interest. Many phone calls and letters came requesting information about interpretation, interferences by drugs and diagnostic materials, and what were then called "normal" ranges, and the like. This prompted the production in 1951 of a leaflet entitled "The PBI and Other Tests of Endocrine Dysfunction." It was a purely informational publication, detailed and referenced, and dedicated to better understanding of the interpretation of such specialized tests. The leaflet has since disappeared; no copies exist that I know of. Its effects, however, were long lasting: It was followed by a much larger booklet addressing a wide range of specialized tests in chemistry, toxicology, microbiology, and immunology. This booklet became known as "The Bio-Science Handbook" and was revised whenever a new group of tests had been put into operation or when a need for updating was perceived. This occurred almost annually: The laboratory scientists in charge of the various specialties were its authors. The Handbook was used not only by the client laboratories but also by hospital and academic programs because its original orientation was maintained: to provide information important to the medical understanding and interpretation of specialized laboratory tests.

The Growth Curve: Getting Bigger

The full effect of these events accelerated a change in the nature of BSL. The volume of work in the clinical part grew sharply and steadily, while the industrial end languished. It became increasingly apparent that large manufacturers of biological products referred their testing needs to in-house services, and there was a dearth of smaller organizations that could use the BSL analytical capabilities. The industrial laboratory of BSL did have one solid client: the clinical part of BSL. With the start of the PBI assay, specimen processing was increasingly referred to the larger capacity of the Culver City branch. By 1952, the clinical operations so dominated the industrial operations that the partners had to recognize that their business really consisted of specialized laboratory testing for the national medical community.

In the early years, through 1979, the owners made other attempts to diversify, ranging from returning to

industrial analytical chemistry, making science-based educational toys, breeding research animals, and manufacturing laboratory instrumentation, to selling clinical chemistry test kits. Success with these ventures was at best modest and, in spite of the efforts and resources devoted, the outcomes were unimpressive.

Growth of BSL rushed forward. The original site near Culver City was about 2000 sq. ft. In 1953 BSL moved to a facility of ~6000 sq. ft. in an industrial area in West Los Angeles. This open space between two preexisting buildings was soon enclosed with a floor, a roof, and two ends put in place, and the interior became the laboratory. By 1955, it was obvious this facility would be soon outgrown. Land was bought on a main thoroughfare nearby and a first-class 16 000 sq. ft. building was constructed and, occupied in 1957. By 1960, this area was doubled and, in 1964, land was again sought for a larger facility. In 1966, BSL moved into its permanent home, a 70 000 sq. ft. laboratory located on 17 acres of land in the San Fernando Valley. By 1970, this was increased to 100 000 sq. ft. and to 125 000 sq. ft. in 1975. When several outbuildings were added, the physical size of the laboratory stopped being of interest to anyone other than the plant engineer and the accountants.

The story of BSL, however, is not about the growth of facilities but of its professional staff. In 1950, Charles Sobel, who had been Chief Chemist for the Health Department of the City of Chicago, joined BSL. He was broadly experienced in analytical chemistry, very inventive, and practical. He had learned clinical chemistry during World War II as a field hospital laboratory officer in New Guinea. At BSL, his forte was devising new and better ways to do old jobs and to improve accuracy and precision while maintaining efficiency. As a troubleshooter, he was rarely led astray by superficialities. In 1955, S. L. Jacobs, an organic chemist, joined the group; in 1956, Neil Chiamori, also an organic chemist, was recruited.

As volume and capabilities grew, it became obvious that the laboratory was tied to quality, and new tests and the issue of doctoral-level support became important. The question now became, how fast and in what direction? Jacobs and Chiamori were the first steps, but by 1959 the partners felt that more specialists were needed. In 1959, B. N. Horwitt (endocrinology), V. J. Pileggi (chemistry), and I (radioisotopes) were recruited. We were followed in 1960 by I. Olitzky (microbiology), in 1961 by G. Stevenson (toxicology), and in 1965 by G. Kessler (automation) and H. Goldenberg (research).

These were not the only doctoral recruits. A common corporate practice was to reorganize operations as conditions changed and challenges were perceived. As a result, technical departments were subdivided into sections, each having one or more doctoral scientists responsible for its operation, and more doctoral managers were recruited. Fig. 2 shows the rate at which the doctoral staff grew. At its staffing peak in 1981, BSL had >49 doctoral personnel, covering the entire range of medically related scientists and including biostatisticians and computer specialists.

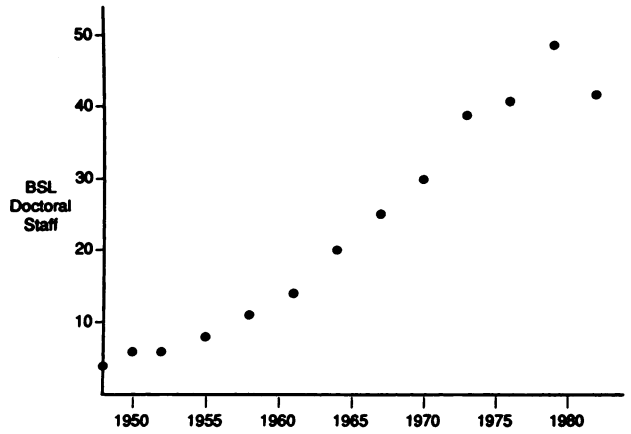

Fig. 2. Growth of doctoral staff at Bio-Science Laboratories, 1949–1982.

Although BSL philosophy had focused strongly on professionalism, growth meant formalizing a variety of policies to accommodate the changing character of its scientific staff. From the beginning, attendance at scientific meetings was encouraged and fully supported; giving a research presentation was not a necessary precondition. Participation in the affairs of professional organizations was also encouraged and supported. Many staff members held significant elective and appointed offices in the AACC as well as serving on a variety of its committees. Richard Henry was President of the AACC in 1963, and Ralph Thiers in 1973. Frank Ibbott was a Director-at-Large from 1972 through 1974; Larry Jacobs served as Treasurer during 1982–1985. In addition, many of us headed and worked on committees at the national and local section level and took on leadership responsibilities for putting together at least three national meetings sponsored by the Southern California section: the Los Angeles meeting in 1962, the Las Vegas meeting in 1974, and the Anaheim meeting in 1982. Furthermore, BSL support of staff participation was not narrowly limited to scientific organizations but reached into public and civic affairs. Dick Henry was heavily involved in drafting the original regulations implementing the Clinical Laboratory Improvement Act of 1967, and others of us were involved in local civic functions, with the blessing and support of the laboratory.

Research

At the outset of the enterprise, research was a raison d'etre. The four founders, being quick learners, realized that research was not a reward but a necessity, albeit a pleasant one, if the future was to be grasped. Accordingly, once the PBI story had been digested, research began to be regarded in a different and evolving manner. Research was seen as the way to maintain and improve quality as well as the way to increase efficiency and productivity and to discover and exploit new opportunities. Research was the way *all* methods and procedures were brought into the repertoire offered to the medical community. New methods could come only from two sources: from re-researching the scientific literature or from the concepts and efforts of the BSL staff. Accord-

ingly, the newly recruited doctoral scientists were expected to participate actively in the research life of the laboratory. The following is an example.

Early in 1959, the founders recognized that no one then at BSL was capable of exploiting the potential of radioactive materials for clinical chemistry; that was the reason I was hired. When I arrived toward the end of 1959, space was again tight; expansion of the West Los Angeles facility was in the planning phase. I was given a chair in the library as my office, a laboratory the size of a walk-in closet, and one technologist. I was to do research with radioactive materials. The charge given to me was literally that broad, and it characterized the corporate attitude: research was important and necessary, from new methods, method improvement, and adaptation of methods used in research to routine service. It was up to me to discover useful avenues and to choose the projects after consulting with others on staff. Short-term payoff was not decisive, and maintaining the laboratory's reputation for innovation was a powerful motivator in selecting a project. What pertained to me applied to all the other doctoral scientists on the staff.

From the start of Bio-Science through most of 1965, research was done in an unstructured atmosphere: Each of us did his own thing with no compelling central organization. With the compartmentalization and growth of the laboratory, however, a difficult management problem emerged. The department heads, such as the chiefs of Chemistry or Endocrinology, began to use their research technicians in production whenever crunches occurred. Various approaches, from admonitions to the assignment of a group of "floaters," were tried to avoid such personnel diversions; none was satisfactory. Accordingly, a formal research department was established in mid-1965, staffed with three doctoral-level scientists and several technical assistants. Policy encouraged department chiefs to continue with research, but support would last only so long as their research staff was used for that purpose.

This organizational form, in contrast to the previous "laissez faire" form, persisted through the mid-1970s. During that time, the Research Department grew in size and capabilities. For example, toward the end of 1969, the Department had several doctoral researchers, including a biostatistician, each supported with technical assistants; at its peak in 1982, there were seven full-time Ph.D. scientists in the Department, and its personnel budget alone was >$800 000 annually.

By 1969, however, the direct role of the department chiefs began to diminish, until it was uncommon for one to be doing "hands on" research. This came not from corporate policy nor from the knuckle-rapping of the loss of research technicians but from the evolving challenge of the increasing complexity of production. The role of the chiefs became consultative, operating through involvement in specific projects of the Research Department and through participation in the progress report seminars of that Department.

At some point in the mid-1970s, research took another step in the direction of structure. A Research Committee was formed, charged with the selection of research projects to be undertaken. The Committee included a corporate executive, the Medical Director of the Van Nuys facility, the head of the Marketing Department, the corporate coordinator of research, the head of the Research Department, and, I think, one or two others. Except for the marketing head, all were scientific personnel. Marketing's function was to give us an insight into the outside world's interests but the preponderant determinant in selecting projects continued to be the professional judgment of the scientific people. This structure continued through 1982; I am unaware of what happened after that.

Table 2 helps provide an overview of research and research publications at BSL; the actual number of methods researched and the number of papers published are significantly larger (present in-house records are not complete). Many were quite simply new tests, sometimes for newly reported constituents of clinical interest. The areas covered every specialty of the clinical laboratory, from the most routine clinical chemistry through toxicology, immunology, and endocrinology to cytogenetics and receptor assays. A large proportion of the publications, >10% involving various laboratory specialties, were methodological, ranging from quality-control procedures and statistical criteria through reference range refinements.

Publishable research was certainly encouraged, but the mission of the Research Department went well beyond this. Studies on specimen stability, improvements

Table 2. BSL research publications, 1951–1982.

Subject area	Number
Chemistry	
Enzymes	20
Proteins and amino acids	13
Lipids and lipoproteins	11
Drugs and drugs of abuse	9
Liver function	9
Inorganic materials	8
Misc. (vitamins, porphyrins, etc.)	18
Endocrinology	
Thyroid status	20
Protein hormones	7
Adrenocortical function	7
Adrenomedullary function	6
Androgens and estrogens	4
Misc. (cyclic AMP, prostaglandins, receptors, etc.)	5
Biostatistics	
Accuracy and precision	6
Normal values and reference ranges	4
Quality control and control charts	3
Misc. (stability, method comparisons, etc.)	8
Microbiology and immunology	14
Technology	
Instruments	10
Continuous-flow analysis	5
Misc. (kit evaluations, etc.)	7
Public policy and education	7
Chromosome studies	5

in accuracy and precision, method simplification, process computerization, phasing new tests into routine operations, adaptation of research procedures for routine use, and troubleshooting method breakdowns: These activities were also on our plate. On several occasions, teams from the Research Department were dispatched to various of the affiliates, both in the US and abroad, to assist in introducing the methods developed and in operation at the Central Laboratory. It was commonplace to have healthcare institutions of all stripes engage BSL in the design and execution of research programs of variable duration and complexity, in which the specimen analysis would be done by BSL. Several of these arrangements involved developing and installing new methods. For example, the National Institute of Arthritis and Metabolic Diseases instituted a broad lipid research project concerning the role of cholesterol in coronary artery disease. This program, which lasted from 1973 through 1984, involved the repeated periodic analyses for several blood constituents in >3800 subjects. This was an international project, and BSL was involved from the early planning stages throughout the entire execution of the study. Similar projects were engaged with various individual investigators and several pharmaceutical organizations. Hence, Bio-Science's activity in research was much broader than apparent from its armamentarium of exotic tests and its publications list. Research was a basic element in the corporate culture, reflecting itself in staffing, budgeting, and all aspects of planning, making BSL an exciting workplace.

Research and the Niche

Bio-Science's contribution to the practice of laboratory medicine was the creation/discovery of a niche in the economy: a national market characterized by an appetite for new, specialized tests. This was particularly envisioned as applying to methods devised for particular research interests and usually coming from some academic institution, then modified for use in the specialty laboratory, far removed in time and space from the patient.

Throughout its life, BSL was committed to research and its fruits. After institution of the Chaney PBI method in 1951, there was a continual string of publications on that method and its refinements. Following these papers came reports on methods of other markers of thyroid function: the "T_3" uptake (1960), measurement of the thyroxine-binding globulin in serum (1961), a column chromatographic method for thyroxine (1962), the detection of the Long-Acting Thyroid Stimulator of Graves Disease (LATS) (1962), the direct measurement of "free" thyroxine in serum (1971), and the measurement of thyroxine by competitive protein-binding (1972). These lines of research development are just examples of numerous similar programs, mainly in endocrinology, in which methods were adapted from the research laboratory to application in a high-volume service laboratory. An example was a series of refinements of the analysis for aldosterone in urine, ranging from Nowacznski's chemical method (1958) through the Kliman and Peterson double-isotope derivative assay (1962) to a radioimmunoassay (1976).

A dramatic example of jumping on the research bandwagon was the estradiol receptor assay. The Research Committee had kept the need for such an assay on its short list for some time but lacked a suitable opportunity. Early in 1974 a group of European research workers published an assay for estrogen and androgen receptors in the *British Medical Journal*. We promptly arranged with J. P. Persijn, one of the coauthors, to set up the method at BSL. The assay used surgically removed breast tumor tissue and was valuable in the therapeutic strategy for metastatic breast cancer. Persijn brought several hundred patients' specimens with him, and a BSL research crew was quickly assembled. Within weeks, the method, including a number of significant improvements, was in place and, by the end of 1974, was running routinely. Although this was early in the understanding of the applicability of the assay, it was quickly seized upon and increasingly used.

Another assay is an example of the bizarre. In 1958, J. M. McKenzie published an assay for the bioassay on thyrotropin (TSH) in serum. It was not very good at low levels but did demonstrate the presence of a humoral factor that showed a long-acting stimulator effect on the thyroid (LATS), unlike TSH. No one really understood the LATS part of the assay and it more reflected an academic interest than a medical concern, at least at that time. Nevertheless, we felt that we had to set it up because of our commitment to leadership in specialty testing. It was an unbelievably complex procedure, requiring dozens of mice and loads of ^{131}I, and was frightfully expensive. With the assistance of W. Vanderlan of the Scripps Research Foundation and D. Solomon of the UCLA Medical School, assay development was started in early 1962 and in operation by mid-1962. At first, we would get about one specimen a month, a vexing situation. I think it was at least 5 years before the volume of samples allowed us to break even on costs. It was a triumph of principle over business sense that turned out favorably. By the time the assay was supplanted by a simpler methodology, the medical community was using it heavily and we were showing profits.

Finally, the ultracentrifuge story. Around 1948, Gofman and coworkers showed a link between serum cholesterol concentrations, atherosclerosis, and coronary artery disease. Bear in mind that this was in the pre-Fredrickson era, which began in 1969. Again, the commitment to leadership was evident. Around 1964–65, we bought two ultracentrifuges, a Beckman Model L preparatory and a Model E analytical, for the determination of low-density and very-low-density lipoproteins. The medical community, academic and otherwise, was aware of this capability but used it sparingly. This was another example of principle triumphing over business sense; I doubt whether we recovered even the electricity costs for running the assays.

Many other examples, both successful and foolish, could be provided. Nevertheless, adventures such as the above secured the preeminence of Bio-Science, and for

about 20 years BSL occupied this niche almost exclusively. Our preeminence and exclusivity was challenged first by the Nichol Laboratory and then later when the laboratory business began to consolidate into large chains, where specialization was felt to be affordable in terms of assets and staff.

Management

The developments of the first decade of its life propelled changes in the future organization and operating philosophy of BSL. The business had gotten too big to have a loosely structured organization and still afford direct control of operations; a more formal and sophisticated system was required. Beginning in 1959, the early staffing strategy of generalists was changed to one of specialists, and the four partners began to move out of technical operations, becoming managers of those who managed. By 1965, the necessities of the future had become clear: the four had become managers of those who managed research and the earlier dream of personally doing research was gone.

Accordingly, two patterns of activity emerged. First, starting about 1965, the four partners, and later the next level of managers, undertook various formal and structured educational programs in management principles and technics. This impulse was maintained throughout the rest of Bio-Science's life and was extended to all levels of management and supervision. Second, changes in business and technical organization became commonplace. These ranged from dividing technical operations into 4 broadly defined units to more than 10 narrowly defined units, from single departmental leadership to shared leadership—and back again.

Various factors underlay these changes, such as the need to increase efficiency, to sharpen technical control, to respond to the emergence of new specialties and technology and so forth. Throughout these fluctuations was the growth of the clinical scientists from managers of technology to operations managers, whose duties increasingly embraced production, research, finance, staffing, and corporate planning.

I believe that this state of affairs and its philosophical implications had a unique though subtle and indirect effect on our profession and Association. What had evolved was an increasing broadening and independence of the clinical chemist from that of a manager of specialized technology to the operation of independent profit centers and participant in the overall management and development of the Company. To give this some perspective, remember that in those days, the late 1960s through the early 1970s, the clinical chemist was largely regarded as a scientific resource person and an adjunct to the pathologist; real professional independence and control were uncommon. By the mid-1970s, the AACC was just beginning to think of educational programs in technical management. So Bio-Science had an impact on our profession by providing a model of the clinical scientist as an independent leader of a technical enterprise, with broad capabilities and responsibilities.

The Growth Curve: Getting Different

In 1966, an event that determined the nature of Bio-Science's future took place: a minority interest in the ownership of the laboratory was purchased by the Dow Chemical Co. This action was the first step in a process that resulted in complete ownership by Dow by 1973. The consequences of the Dow association were many but, for the purposes of this story, their main importance lay in two areas. First, the Dow relationship provided a sense of financial stability that stimulated BSL to embark on a broadly conceived program of growth by acquisition, association, and branch development. Second, the professionalizing of the clinical scientist as business managers achieved greater importance now that Dow offered a model and advancement opportunities that had not previously existed. As far as Dow was concerned, the BSL acquisition was a step in the penetration of the medical and biological sciences fields, which Dow perceived as areas of rapid growth and opportunity.

In the 14 years of my acquaintance with Dow, it in no way inserted itself into the professional operations of BSL. We continued with what we had always been doing, and with the same constraints and hopes. The concerns for quality and research exactly suited Dow's philosophy, and laboratory safety was greatly stimulated at BSL by Dow's highly developed safety programs. What was necessary was the assurance of the continuity of technical leadership. In 1967, James Winkelman, MD, was brought in as Assistant Director. Winkelman was a well-trained clinical pathologist, bright, energetic, and aggressive, with a natural bent for the borderland world where technology and business meet. He pursued technical and professional interests at the corporate level. This was the first step in changing the corporate organization to prepare for growth.

Throughout the 1960s, BSL dominated the national market for specialty testing, with the majority of the larger hospitals, clinics, and healthcare institutions in the US as clients. However, the profits and growth possibilities of the clinical laboratory business were attracting the attention of large companies such as W. R. Grace, Abbott Laboratories, Revlon, and Bristol-Meyers, who, like Dow, began to acquire or build chains of medical laboratories. For Bio-Science a 6¢ stamp and 24-h service could no longer be enough: A local presence distributed throughout the marketplace was required. The first step in implementing this concept was the acquisition of the Samson Laboratories in 1968.

BSL was strongly managed and its leaders recognized that growth by accretion would be a new experience; hence, a testing of that challenge was necessary. Samson was a modest laboratory with a good reputation but not much in the way of specialty testing. Its value lay in giving BSL the chance to learn how to manage a laboratory from a distance, where central management could not be so strongly applied. This turned out to be a real learning experience.

Samson Laboratories presented a multitude of prob-

lems, ranging from top-level interpersonal relationships through communications to technical operations. BSL's system and attitudes in planning, control, and systems orientation increasingly came into conflict with the highly personal and informal style of a smaller business. It was difficult for the manager of a small organization to accept the idea that the concerns of the parent entities, such as Dow and BSL, could sometimes be at stake. The mix of a past owner and his staff staying in place and management from afar was fraught with difficulty and could, on occasion, be dangerous. The lesson learned was that future branches would have to be mini-BSLs, built from the ground up, using official BSL methods, BSL systems, and BSL-tested equipment and led by BSL people.

Accordingly, in 1970 a Directors Training Program was established at the Van Nuys facility, its purpose being to train doctoral personnel for directorship of branch laboratories. Because the Branch Directors would have little of the support available at Van Nuys, the programs covered all facets of the laboratory business: technical operations, office operations, personnel administration, government regulation, finance, and so forth. This program produced a stream of Directors for about the 10 years the branch movement was under way.

At the same time as branches were being established, other forms of expansion were under way. BSL had contracted for the total management of the laboratories of several small hospitals. The clash with the hospital culture was an alien experience; this form of expansionism stayed small and lasted only a few years. More successful were the "total equity" acquisitions with the original ownership and management being kept in place, as in the Dow–BSL model. One was in Canada, another in Brazil, a third in Hawaii, a fourth in Boston, and several in southern California. There were also two joint start-up ventures involving foreign chemical companies: C. H. Boehringer in Germany (1971) and Teijin in Japan (1977). With BSL providing technology and training, laboratories were set up in these countries, and the successful businesses established are still operating to this day.

Thus, the growth phase that started in 1968 with the acquisition of the Samson Laboratories resulted 14 years later in a network of >25 branches and affiliates, with the main laboratory in Van Nuys at its center. During those 14 years, sales quadrupled, profits doubled, the staff grew to >1500, and the "system" continued to constantly reorganize itself. A systemwide specimen pickup service was instituted in early 1974, and a national network of sales representatives was in place by early 1976. By 1978, almost all locations were computer-linked with each other and the main laboratory, with the linkup serving not only technical and analytical operations but also administrative and financial functions. The branches used the same analytical methods and quality-control and assurance systems so that, except for the local service, clients everywhere were receiving the product of a single laboratory: BSL. That had been the main professional principle governing the growth movement and it had been achieved.

The Beginning of the End

In 1982, after the founders had all retired, Dow sold BSL to the American Hospital Supply Corp. Because, to all appearances, the relationship had been nothing but mutually beneficial, I can only provide personal speculations as to Dow's motive in this action. The chemical industry as a whole is cyclical in nature; its peaks and valleys in profits arise from a variety of causes in the world marketplace. Dow has prided itself, and still does, in never having missed or reduced a dividend payment to its stockholders. The late 1970s were not good years and threatened this commitment. Because operations were not sufficiently profitable, liquidation of assets was the route taken: ergo, the sale of BSL. For AHS, Bio-Science was very tempting: It was expected to meld beautifully into the AHS hospital supply and communications networks. The purchase was accomplished in record time, a matter of a few months.

AHS, however, did not keep BSL very long. The venture went the way of many in the late 1960s. The clinical laboratory business looked promising, but learning to deal with its particular nature required a goodly amount of stamina and expertise. Also, in my opinion, there was an inadequate understanding of the difference between a case of test tubes and a clinical laboratory report. It took only two annual business cycles for AHS to learn that it didn't want to pay the price. During those 2 years, many of the doctoral-level managers left BSL and the Research Department was reduced significantly. BSL was again sold, this time to the then SmithKline Beckman, an organization that knew the business and was willing and able to allocate the resources necessary for growth.

The Ties that Bind

In a sense, Bio-Science, as I knew it, was a unique enterprise. The four partners were distinct personalities, varying greatly in their drive, self-assurance, sociability, political bent, intellectual interests, and other attributes. They were alike, however, in their competitiveness, ranging from "very" to "totally." One would think that it was a situation ripe for conflict. Onlookers often wondered how the association could have lasted and how this four-headed organism could produce such a successful enterprise. What helped smooth the interrelationships among the four founders, particularly after the first 10 years, when the size and complexity of the developing enterprise began to emerge, was the gradual separation of some of their main responsibilities within the organization. This process was an evolution based on exclusively pragmatic considerations that respected individual strengths and tolerated individual weaknesses. Berkman was the business manager; he later became busy with acquisitions and was the principal contact with Dow. Henry maintained his interest in research and general laboratory management. Golub became the marketing specialist and set up the branch

expansion and the sales force. Segalove took over the day-to-day administration and personnel management until he retired in 1969.

I believe that two things were, paradoxically, the glue and the lubricant that kept the organism intact and functioning smoothly. One was their early recognition that they had a successful enterprise under way and it needed to be cared for. The business was not looked upon as a "cash cow" to be milked for immediate gain. The opposite was the case; capital was plowed back to improve instrumentation, an uncommonly large proportion of professionals was employed, better and more secure quarters were obtained, risks were supported financially, and preparation for the future was foremost. For example, when they understood in 1951 that the PBI would make the business more secure, they rewarded themselves with a raise of $500 annually. Knowing the four, this kind of decision could only have come from business judgment, not lack of enthusiasm for the future.

The second tie was their philosophical unanimity. The partners thought as one in matters of professionalism, goals, ethics, and principles. This unanimity determined safety practices, quality control and research productivity, service to public and professional organizations, public image, and service to the patient. Although the philosophical character of BSL arose from the personalities of the four, it was also firmly grounded in the belief that if you build a better mousetrap, the world will beat a golden path to your door—which, of course, it did.

Don't think this is entirely an encomium. The founders were not easy taskmasters, nor did they conduct their interrelationship in Olympian harmony. High standards of professionalism and quality meant high standards of performance. Executive frustration was easily aroused, and patience was not to be taken for granted. The four argued often on matters of procedure and overlapping areas of authority. They could be critical of each other's performance as well as that of the rest of the staff. Mutual respect, professionalism, and a dedication to the common interest, however, took the edge off, made the working environment productive, and kept the staff morale high.

It is said that human organizations, be they university departments, governmental agencies, or industrial enterprises, are reflections of the personalities of their leaders. From the perspective of the clinical chemist, the irreplaceable personality molding Bio-Science Laboratories was that of Dick Henry. He was the legal and actual director of the laboratory, and his influence was largely confined to technical operations. I believe Dick fully believed that nobody could do anything as well as he. And he was often right. He was fast thinking and impatient, and had great energy. If he couldn't do something very much better than most, he wouldn't do it at all. His mind was truly an organ of pleasure. He was continuously competitive and could be so outspoken as to make compromise impossible. He could tell you flat out when you were wrong and be astonished that you would be disturbed by his statement; for him, right was right and wrong was wrong. He had a gene for fairness and another for integrity; his dedication to quality of performance and to the welfare of the patient was evident to all. He commanded great respect because of his intellectual prowess and his honesty. Because of these traits, his abrasiveness was usually accepted and commonly thought of as understandable if not justifiable.

The following anecdote may provide some flavor and insight. In 1965, I became Dick's assistant and "enforcer." On those occasions when I would come to him for guidance, invariably his impatient reaction would be, "Well, do the right thing!" He meant it quite literally and without qualification but was not unaware or insensitive to the repercussions of that kind of answer. This attitude could have severe consequences. For example, his contract with Harper and Row to publish *Clinical Chemistry: Principles and Technics* required periodic updates. The first edition, which he had written entirely by himself, had been an extremely arduous task; hence, he turned the 1974 edition into a collaborative effort involving the entire doctoral staff of the laboratory. Another similar effort was slated for the late 1970s, and all the manuscripts were completed on schedule except one, the chapter on statistics. Dick felt that without this chapter the book would be second-rate and therefore unacceptable: Thus, the third edition was cancelled. He understood the cost of this action in all regards, both to those who contributed as well as to the laboratory and the profession; indeed, his dedication to the second edition had been, "To the families of men who write books." As severe as this decision was, however, all of us as well as Dick's partners accepted and supported it. I think the publishers may have a third edition underway, entitled *Henry's Clinical Chemistry*. I am sure that it will be received with nostalgia by many besides me.

Endpiece

I close with another nostalgic indulgence. *Clinical Chemistry News* in 1992 reported the induction of AACC's 10 000th member. Quite properly, this event was recognized and celebrated as symbolic of the growth and development of our Association and our profession. Bio-Science was born at the same time as our Association, and its growth and development paralleled and influenced that of the AACC. However, BSL has now virtually disappeared except for such personal and reflective accounts as this.

I thank the management of the Van Nuys, CA, facility of the SmithKline Beecham Clinical Laboratories for making their files and records available to me. My special thanks go to Caroline Elman, Information Specialist/Librarian of that organization, for her gracious and generous help. My thanks go also to Orville J. Golub, one of the four founders, for keeping me from making errors of fact. Lastly, I thank the Executive Committee of the AACC History Division for stimulating me to write this article and for their invaluable efforts in pre-editing it.

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