The Bad Old Days

by
Eleanor Taylor

Since thirty years in one institution represents a milestone of sorts in one's life, it seems an appropriate time to reflect and examine some of the changes that have occurred in the clinical chemistry laboratory during those years.

Some of the information is from memory, but because I am a "saver," the technical details are directly from old procedure manuals. The dates of changes noted were obtained from records carefully kept by Florence White who was the chief tech of the lab from its vague beginnings until 1969 and continued by Elinor Douty since then. Perhaps somewhere "under the dome" official records exist; I don't know where to begin to retrieve them.

Hopkins, or rather all of East Baltimore, was a very different place in 1950. The neat row houses of the area were kept spotless (just as they look in the pictures in the National Geographic). Women were seen out scrubbing the white marble steps in the morning; there were screens at the windows with scenes painted on them which permitted one to look out of, but not into, the house. Parking on the street was the order of the day for there were no parking lots, and the streets were safe to walk, especially if one wore the traditional white coat which identified him as belonging to "The Hopkins."

It is hard to condense so many years of changes into a short talk; since clinical chemistry is such a dynamic field with change occurring constantly and rapidly (perhaps this is one of its many aspects that have maintained my interest for so many years), I have decided to look at these changes from three aspects:

1. Environmental
2. Staff
3. Patient Service/Technique

The first entry in the old ledger is dated 1943. I know some laboratory work was done previous to this time by Mrs. White; in the 1930s, she was the entire staff of the lab. Several other entries occur during the 1940s, the most notable being the introduction of the Coleman Electric Spectrophotometer; previous to its introduction, an instrument was used to visually

compare the color developed in a patient's sample to that developed in a primary standard solution treated similarly. By 1950 the list of tests offered by the laboratory was very similar to that offered in routine chemistry today, with the notable exception of some enzymes such as CK, LDH, ALAT, ASAT. The main laboratory was located in the room which now serves as the office, data storage and snack area, room 552. The area just east of that (now G.S's office) opened into the larger room and served as Mrs. White's office and special chemistry and development lab. The machine repair shop area was a large wall full of hoods, Kjeldahl burners, and distilling assemblies. The large room was not air conditioned and temperatures in the "Kjeldahl corner" were recorded as high as 114°F. The staff usually changed into "lab clothes" after arriving at work – and changed back to more respectable ones before leaving. In the summer, temperature-dependent reaction tubes were immersed in water baths containing ice cubes to bring the temperature to 30° for reading at the spectrophotometer. The smaller special room had a window air conditioner which worked only intermittently, occupied the only window; the doors were always kept closed, so the atmosphere in there was often extremely unpleasant. I'll have more to say about this "bad air" later.

In 1957, the lab moved into its present location and has undergone one major renovation of that area in 1970 which necessitated moving into the pathology building and operating under great obstacles, such as very poor quality deionized water, lack of adequate lighting, compressed air, and other necessities for about eight months.

There has never been a time when we have felt that we had enough space – or enough staff. There have always been too many stats and a generally heavy workload. The census figures I've located indicate a total of 131,392 tests were performed in 1950 (by a staff of 15), increasing to 580,101 in 1967, the last year the census was counted <u>manually</u>. Since then the computer has kept track of the number of tests performed; in FY1978 about 600,000 tests were done.

<u>Staff</u>

Hiring practices were very different. There was no internal bidding system and new employees were often hired because they knew a current employee or came from a school well-

known to the director. There were no restrictions on information to be sought at a selection interview so questions concerning pregnancy, children and their care, and even husband's occupation were asked.

The lab staff was composed entirely of women until 1968, probably accounted for by the extremely poor pay provided by the hospital. Most of the staff were local residents and when I first came here, all but three of the staff of fifteen chemists were from Goucher College. There was only one Med. Tech. among the staff, the rest all having degrees in Chemistry or Biology. In addition to the chemists there were four lab helpers who cleaned our glassware. None of this was disposable and there was not sufficient quantity for a whole day, so it was washed, placed in a drying oven and reused many times over each day. These items included pipettes, flasks, bottles, test tubes, funnels, volumetric flasks, and specialized pieces such as Kjeldahl flasks and separatory funnels. There were no clerks – all clerical duties such as answering the phone, writing a lab log and writing reports were done by the technical staff. STAT requests were phoned back by the last person to enter a stat result on the requisition. In the mid fifties Mary Brockmeyer was hired to take care of the telephone, and in the '60s the clerical staff was increased to two. There was a definite sense of belonging to the Hopkins family and although the Hospital was large, the staff became acquainted with many employees of other areas. This was due, at least in part, to the fact that there was no messenger and delivery service; the house staff often carried specimens (especially stats) to the lab; supplies were obtained by trundling the lab cart down to the basement (and sub-basement) and picking them up. I was fortunate to accompany Elinor Douty on many of these trips and learned much from her contacts. She has carried this "supply" duty in addition to her laboratory assignments all these years and has made an immeasurable contribution to the smooth and continuous operation of the lab.

The lab was open from approximately 8:30-5:00, Monday- Friday, 8:30-1:00 on Saturday, and closed Sunday. All staff worked these 5-1/2 days/week. Somewhere in the mid-fifties the staff was signed alternate Saturdays, coming in 1/2 hour earlier each morning during the week with a Saturday off. It was not until the late 1960s that the regular staff covered weekends, evenings, and overnites. That is not to say stat lab services were unavailable during those times. Prior to 1953, EVE-ON coverage was provided by the Osler resident staff; after that time, there were usually throughout any one year 15-20 medical students who were assigned coverage of the off shifts and provided schedules of their assigned times six months in advance.

If he (no women were allowed to work at all) could not work at the time assigned, it was the responsibility of the student to find a replacement and notify the laboratory chief. These students were required to run each test in duplicate and the system worked reasonably well but required an enormous amount of training time. (Initially these students were paid on a per test basis and really fared extremely well for an evening's work; this system was soon replaced by payment for hours worked).

During all the years prior to 1968 the laboratory was under the Department of Medicine and directed by physicians, some of whom were chemists, some of whom were not. In 1968 the Department of Laboratory Medicine was formed and Dr. Rex Conn came as Director of the Department. Dr. Rock was the first Director of Clinical Chemistry, coming here in 1971; he hired our first Clinical Chemist and from that time on the laboratory has been constantly expanded and developed to its present state.

Patient Service/Technique

Patient services provided are so dependent on technical development that I cannot separate the growth of the two. To consider all tests would provide enough material for a week-long symposium so I have chosen a few striking examples.

Beginning with blood drawing – This task was performed on in-patients by house staff and medical students; there was no blood drawing team. Outpatients were drawn by the hematology lab staff. Blood was drawn in a glass syringe, usually a very large one and transferred into heavy glass ignition tubes into which we had laboriously fired with silver nitrate the words "Chem Lab". It was not until 1969 that Vacutainers came on the scene at Hopkins. In addition to the many tubes of blood drawn on a patient, 5 ml. were drawn and placed in a bottle containing an anticoagulant for preparations of a protein-free filtrate used for measuring non-protein nitrogen and sugar levels. Samples drawn for electrolytes were often "under oil"; this meant there was a layer of oil on top of the blood often overflowing down the sides of the tube, making it very messy to handle.

Specimens were brought to the lab by the orderlies, one from each service. This was convenient for it meant that all medical patients were accessioned and processed as a group, all surgical, etc. This made result retrieval easier than it might be otherwise in a non-alphabetized handwritten log.

While some of the staff processed the specimens via centrifugation, as today, others were busy working "on the line" preparing filtrates and measuring off aliquots of these filtrates for analysis. Space and time have always been in short supply so there was always a sense of urgency to process the samples as quickly as possible and get them stored out of the way so the next batch could be handled. As soon as "the line" was finished, hopefully by eleven o'clock, each person moved to her assigned bench and started the day's analysis. (Some tests, such as sugar and NPN, total protein/albumin were begun early in the morning and continued in batches all day.) In addition to doing the analysis, each person was responsible for preparation of reagents and working standards for the particular test she was running. Since all of the work was done by hand, the greater portion of the day was spent standing working at the bench. Broken veins and varicose veins were just another occupational hazard as a result of so much standing.

With the introduction of the first AutoAnalyzer in 1957 and the addition of air conditioning in 1958, life began to improve. That first AutoAnalyzer had no platter beneath the manifold tubes to hold it together and required some time and skill to assemble, but once plattered manifolds appeared, it meant a person could with great ease, switch from one test to another and utilize one AutoAnalyzer for several batched tests during a day.

Probably "the bad old days" vs. "the better today" is best exemplified from the standpoint of the patient. Let's take as example today's SMA 12. From one Vacutainer holding 7 ml, 12 tests can be run on less than 2 ml of serum by one technologist in less than one hour.

In 1950 this would have required approximately 10 ml of serum (4 tubes of blood) and 5 ml of oxalated blood. It would have required six technologists and would have taken a minimum of four hours before analysis of all components was completed. The equivalent of an SMA 6/60 analysis would have required 5 technologists working simultaneously for approximately 30 minutes.

Some tests are basically unchanged other than decreases in sample and reagent volumes as better pipettes and spectrometers became available. Examples are bilirubin, creatinine, amylase. Other methodologies changed so drastically it seems miraculous or revolutionary; for example, cholesterol from extraction in hot alcohol/ether, evaporation of solvent, washing with chloroform, and then finally redissolving in chloroform before undergoing the Liebermann-

Burchard reaction which produced a color required about 4 hours. Today minutes from CentrifiChem pipettor to printed tape via the magic of enzyme reagents yields a result.

Two striking examples of the evolutionary process are represented by total protein and albumin, and Na/K. Total protein and albumin were first done in this laboratory employing the Kjeldahl nitrogen determination. This involved a harsh, but slow digestion with sulfuric acid, then releasing the nitrogen as NH_3 by distillation, trapping it in a bottle containing a boric acid solution to which an indicator had been added. This was then titrated with acid of known concentration; hence the nitrogen content of the sample could be calculated, and the amount of protein present calculated from this nitrogen content. Albumin was measured in the same way after first separating the albumins and globulins by salting out the globulins with sodium sulfate and centrifugation under pressure created by the addition of ether. Usually the person doing this test wore her very oldest clothes, did not go to lunch, and left the lab feeling exhausted but really efficient if she had put thru 30 samples for TP and Alb. all in the one day. It was in this particular area that the temperature frequently reached 100 F. Recall too, we made our own reagents; this test required large quantities of conc. NaOH which was prepared in a 20-gallon enameled can and stirred into solution using a wooden stick – truly a witch's brew.

The volume of work increased so that we had to find a way to put thru more tests/day. The solution to that was "miniaturization" of our Kjeldahl procedure. All volumes were decreased, the digestion took place in a Lindbergh heater holding 100 tubes at a time and the final nitrogen content was measured by Nesslerization. This was some improvement, but not much, and the biuret-reaction was finally introduced into the lab as a routine procedure. Not too long after that step, both TP and ALB were run on a single-channel AutoAnalyzer.

Filter paper electrophoresis of serum proteins was first introduced here in 1953 utilizing a homemade set-up consisting of glass rods held by rubber stoppers mounted in a vegetable crisper from a refrigerator; the buffer was contained in small cake pans and the paper was suspended into it from the glass rods. It worked – but as always in this lab it had to be first compared against a reference method. There was a Tiselius moving boundary electrophoresis system available in the School of Hygiene. It occupied the entire room and I could run one sample per day. Fortunately, it did not take too many samples to satisfy the director that the correlation between the two procedures was satisfactory. Our paper runs took overnight for electrophoresis; they were then interpreted visually the next day much as CK isoenzymes can be today.

Na and K were initially done in another laboratory once or twice a week by an ashing procedure. When introduced here, they were run on a Beckman D-U Spectrophotometer with a flame attachment. This had a very temperamental atomizer/burner which burned oxygen/acetylene. To insure a stable current, it was run off two storage batteries which were charged every night. The temperamental flame could tolerate no protein so TCA filtrates of the serum sample were prepared, then further diluted before being introduced into the flame. There was no internal standard and only Na or K could be read at one time. The procedure of course then involved reading all the Na's, drawing a curve and interpreting patient samples, then reading K's doing the same. It did not lend itself to STAT work! There was a period of time when several people became rather sick each time they ran Na/K: pounding headache, watery eyes, flushed face. After weeks of investigation it was found we were introducing nascent Cl^- into the poorly ventilated room and nearly doing ourselves in as we bent over that instrument. Our first small hood was installed over the flame after that, and the lab has remained "hood happy" ever since. In 1957 this wretched instrument was replaced by a very simple flame photometer utilizing natural gas and air and requiring only dilution of the sample with a lithium solution before reading. This, however, was a reading from a single galvanometer and still required interpolation of patient results from a standard curve. And still only Na or K could be read at any one time. In 1968, our first IL 143 arrived and is probably the one in the lab now – what an improvement to have direct readout of Na and K simultaneously and quickly.

As you would expect, the greatest change of all occurred with the introduction of the SMA 12/30's. In 1965 we received instruments #2 and 9 from Technicon. These were so-called "hospital" models and had a flame component. They really handled the bulk of the workload. They were so archaic, however, within a year and a half they were traded in on two new 12/30 models.

The other big change that occurred about the same time was the introduction of a laboratory computer. The 12/30's were on-line by 1967 and the technologist running the "non-stat" 12/30 was also the computer operator (there was no EDP division). The computer also generated patient reports beginning in 1967. However, it reported only the SMA tests; all other results were logged and reported by hand.

Very few tests were run truly "micro"; however, those that were, were always run in duplicate. Instrumentation was not developed for handling small volumes and we had some specialized equipment made by the Surgery Department machine shop.

Special Chemistry/Data Reduction

Special Chemistry in some fashion has always been a component of this lab. Reference labs were just coming into being in the 50s so exotic tests were generally performed here or in the university labs. We had one director who believed we should attempt to provide any test requested if he reviewed the request for the test and felt it necessary for the care of the patient. This often involved searching the literature, ordering supplies, setting up the test – for a single shot. Other tests were run infrequently, but on a continuing basis – such as magnesium, phospholipids, total lipids, urinary amino acids by paper chromatography, lipase, Vitamin A, catecholamines and porphyrins. There likewise has been some TDM ongoing thru the years. In the 1950s sulfa levels were routinely run every day; bromide, thiocyanate, and salicylate volumes seemed about the same as today.

The hospital had its own milk processing plant and the laboratory, as part of its "special" services, measured the fat content of the milk and checked the pasteurization process by running an alkaline phosphatase level on each day's batch of milk.

There were, of course, neither calculators nor computers available for many years and any statistical studies were sheer torture to perform. Slide rules helped but not much with addition. Most correlation studies were actually done by simply plotting on regular graph paper, and eyeballing the result.

Overall, life for the technologist or technician has improved in several ways. The environment is cleaner and better, modern instrumentation allows the analyst to be seated at least part of the day, and is generally "fun" to use. Much of the drudgery of repetitious pipetting and handling of test tubes has been eliminated in most routine testing areas. One facet of a technologist's position is immeasurably better than in years past; his (or her) name is now included among the authors of a paper for which he has often done a great deal of work. Thirty years ago there would have been an acknowledgement for "technical assistance" at the end of the paper.

In summary the lab has grown both in volume of tests, assortment of tests offered, and certainly in staff size. The hospital has grown and changed; health care has changed into an industry or business and has lost some of its polish in my estimation – employees used to refer to the hospital or "The Hopkins"; now they refer to it as the John. However, I still think they were the bad old days; the patient had to give up much more blood for testing, the methodology was in some instances not as specific, certainly not as fast; the work was harder physically, there was no pension or life insurance plan, Blue Cross was voluntary and paid by the employee, and starting salary for a technologist was about $2500/year.

I wonder what the lab of 2010 will be like – will there be a lab at all or just a sensor implanted in each human at birth which feeds all his biochemical parameters into a computer somewhere underground in Washington, D.C.?

TO THE CHEMICAL DIVISION OF THE MEDICAL CLINIC

Name in full _____ _____

Date _____ Ward _____ Time Taken _____

Diagnosis _____

Examination desired _____

_____

FORM 3046 _____ Asst. Resident

REQUISITION (SINGLE COPY)

Form 2027 CHEMICAL DIVISION MEDICAL CLINIC

NAME _____ Dr. _____

Ward _____ Date _____ History No. _____

BLOOD ANALYSIS

NPN _____ Mgm. % Chloride _____ Meq. per L.

Sugar _____ Mgm. % CO2 comb. Power _____ Meq. per L.

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REPORT (SINGLE COPY, GUMMED BACK) CIRCA 1950

JHH Clinical Chemistry Lab - Significant Events

1946 - Consolidation of multiple univ. labs into Clin. Chem Lab under Dept. of Medicine
"Photoelectric" spectrophometer (visible only)

1951 - flame photometer for Na/K (prior analysis for Na/K = 2 days!)

1953 - paper electrophoresis for serum proteins (prior, only room-sized Tiselius apparatus was used)

1955 - 2 students hired to cover lab eves, ON (paid per test!)

* 1957 - Single channel AA

1958 Lab was air-conditioned!

1959 - Commercial "control" serum available

1963 - 3 AA in use (SUN, gluc, CO_2, Ca, P, chol, TP, Alb, Creat)

1965 - 2 12/30 SMA

* 1967 - 2 SMA 12/30 + computer (IBM 1140, I think)

1968 - First reports generated by computer (SMA tests only)
cost = $ 12.60 computer counts test/mo.

* 1969 - SMA 12/60 ; blood gas analyzers
many new instruments available: Vis/UV spectro, fluorometer, atomic absorption spectro., osmometer
purified enzymes as reagents - ∴ kinetic enzyme measurement begins.
[illegible] - staff, 24 hr, 7 day operation

1971 - ~~color~~ increase in prof. staff - residents' program began (RCR, GI, HS)

* 1972 - Special Chemistry lab established - great proliferation of tests & equipment - RIA, TDM
QLC, centrifugal analyzers, γ-counters, HPLC, various automated analyzers such as Astra, Abbott, etc.

1984 move to Meyer basement
increase in endo, TDM ; add. TOX
SMAC, GC/MS, prolif. of immuno-analysis

Directors

1930 - 1945 - Dr. Mary Buell (M.D.)
1946 - 1957 - Dr. Fred Baines (M.D., Ph.D.)
interim - Dr. C. L. Conley (M.D.)
1958 - 1968 - Dr. Ken Zierler (M.D.)
} Dept. Medicine

Established Dept. Lab Med.
1968 - 1978 (?) - Dr. Rex Conn - (part of) Lab. Med + Clin Chem until RCR came
1971 - Dr. Robert Rock
1979 (?) - Dr. Daniel Chan

for "chart form" display the following might be interesting:

1- workload increase
2- variety of tests offered (about 25 in 1946!)
3- number of employees (8 technical, 2 helpers in 1946)
4- hours of operation
5- emergency vs. routine tests
6- turn-around time
7- instrumentation - e.g. formerly universal for many tests vs. dedicated instr. popular today
8- beginning tech salaries! ($1500/yr. + lunch!)