

Persistence . . . and Prayer: From the Artificial Kidney to the AutoAnalyzer

LEONARD T. SKEGGS, JR.

I am a relic of the last century, born in 1918, the last year of the first World War. At that time, there was no radio, no television, no commercial air travel. There was no welfare, no social security, no Medicare, and only the rich paid income taxes. Influenza, strep throat, pneumonia, tuberculosis, polio, and high blood pressure were deadly diseases.

I was 11 when the stock market crashed and the Great Depression began. Unemployment reached 25%. The most precious thing a person could have was a job. In 1940, I entered graduate school studying biochemistry at what is now Case Western Reserve University. Victor Myers was head of the department. He was near the end of his career and was prone to talk about his old friends Otto Folin and Stanley Benedict and others and their struggle to learn how to analyze blood. They were the first clinical chemists. They had no pH meter, no spectrophotometer. Optical densities were estimated by visual comparison of standard and unknown. They had to calibrate their own pipettes. It could not have been easy.

When I entered the department, most everyone used DuBosc visual colorimeters. We had one Evelyn photoelectric colorimeter with glass filters and one newly invented Beckman pH meter. There was no good way to determine the quantitative amino acid composition of proteins. No one understood what the purine and pyrimidine bases and nucleic acids were good for. The *Journal of Biochemistry* published one modest volume a year.

I do not think any of us understood that we were caught up in a wave of scientific and technological progress that would grow and gather speed at an exponential rate. I am glad to have lived during this period and to have been a very, very small part of it all.

By 1941, I had my Master's degree and was working

for my PhD. My sweetheart, Jean Hossel, was in her third year of nursing training at nearby St. Luke's Hospital. We planned to get married the next year. Then suddenly, without warning, the Japanese struck at Pearl Harbor. It was on a Sunday in the early afternoon. I was in the Rat Room at the Cleveland Clinic doing vaginal smears on rats. That evening, while sitting in my 1936 Ford V8 coupe outside of St. Luke's Hospital, Jean and I decided to marry without delay. We were married 5 days later, as soon as the license permitted, and Jean moved into my rented room with me because the rent had been paid.

Not long after that we were both at Ben Venue Laboratories, which had a contract to lyophilize blood plasma for the army. Jean was in charge of a group of nurses who made up pools of plasma and distributed them in transfusion bottles. The bottles were shell-frozen. I was given the responsibility of drying them from the frozen state. This was a new and little-known process. It was a very difficult time and a heavy responsibility until we finally learned the process.

By the spring of 1943, drying plasma had become a routine process. I persuaded my draft board to reclassify me from 2b to 1a and enlisted in the Navy. I was given orders to report to Officers' Training School at Cornell in August.

In the intervening 3 months, I worked at the SMA Corporation on the purification of penicillin from culture medium, which consisted of corn steep liquor; a thick dark brown gooey liquid. All I remember now is that we extracted the penicillin into amyl acetate and back into water. I remember very clearly Dr. Paul Gyory storming into our laboratory one Saturday morning demanding penicillin. I gave him the dark brown solution I had just made. He took it to the hospital, gave it to his patient, and saved his life. This was a thrilling moment for me that I will never forget. The discovery of penicillin was perhaps the greatest discovery of the 20th century.

After Officers' Training, I was ordered to the USS Hovey, DMS11, a World War I destroyer converted to minesweeper duty. I served as Gunnery Officer until we were torpedoed and lost our ship in the Lingayen Gulf in the Philippines.

Department of Biochemistry, School of Medicine, Case Western Reserve University, Cleveland, OH 44094. Fax 440-256-3280; e-mail doc@arcwebserv.com.

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The war over, I went back to school on the GI bill and with my mother's help. Victor Myers died, and Jack Leonards was appointed acting chairman of the department. Jack came in the laboratory one day in an excited state. He had a monograph written by Willem Kolff, a Dutch physician who had invented an artificial kidney (Fig. 1) that actually kept uremic patients alive by dialysis. It consisted of a rotating drum partially immersed in a big tub of a salt solution around which cellophane sausage tubing had been wrapped. Blood was taken from the brachial artery and propelled through the tubing, using the principle of Archimedes' screw, and then returned to the vein, largely cleared of urea and unknown toxic substances.

I thought we could do better. Jack liked my idea, took departmental funds committed to other projects, and had our first kidney made by Sieberling Latex Products. It consisted of several units, usually 12, each consisting of a pair of molded rubber pads with two sheets of cellophane between them (Fig. 2). The patient's blood was propelled by a pump between the cellophane sheets while dialyzing solution ran on both sides between the cellophane and the

rubber pads. The urea clearance varied between 60 and 80 mL of blood cleared per minute; we could return the blood of uremic patients back to near normal within 6 to 8 h. I remember one comatose patient that we treated who after treatment demanded steak for breakfast. Our kidney was the first flat-plate kidney (1) and was an important step in the development of today's artificial kidneys.

After obtaining my PhD, I took a job as head of the Clinical Chemistry Laboratory at the Veterans Administration Hospital associated with the Case Western Reserve University Medical School. My boss was Joseph Kahn, pathologist and chief of the clinical laboratories. Joe had worked with Harry Goldblatt, who had shown that hypertension could be produced in animals by reduction of the blood flow to the kidney (2). He also showed that the increase in blood pressure was attributable to the liberation of an unknown pressor substance into the bloodstream (3). This was a discovery of the first order, being the starting point in the development of our present understanding of high blood pressure. It should be understood that at that time there was no good way to control the blood pressure of hypertensives, and as a consequence, many died of stroke or kidney and/or heart failure. Many young men and women in their 20s and 30s contracted malignant hypertension with very high, uncontrollable blood pressure and died. Harry Goldblatt should have received the Nobel Prize but did not.

The most important question among those who were interested in or working in hypertension at that time was the identity of the pressor substance from the ischemic kidney. It was known that extracts of kidney did contain a pressor substance called renin, but many thought that renin could not be the causative agent in hypertension because it was tachyphylactic. That is, after several doses were given to animals, it no longer raised blood pressure.

Irvine Page and Oscar Helmer (4) in this country and Eduardo Braun-Menendez and his group (5) from Argentina simultaneously discovered that kidney extracts containing renin when incubated with blood plasma produced a heat stable, dialyzable, pressor substance, now called angiotensin.

Joe Kahn and I, with no research funds, borrowed time from our other duties and equipment and material from everyone we could and decided to look for angiotensin in the dialysates of the blood of hypertensive dogs (Fig. 3). Using the artificial kidney, we equilibrated the dogs' blood against large volumes of dialyzing solution for 90-min periods. We worked out a method of purifying the dialysate, reducing its volume from 300 mL to 1 mL. This small volume was assayed in rats (Fig. 4). The results are tabulated in Table 1 and show significant amounts of angiotensin in the dialysate of hypertensive dogs and almost none in normotensive dogs (6, 7).

This was the beginning of our work in experimental hypertension, which continued until my retirement in 1988. Joe and I were soon joined by Walter Marsh who left us and was replaced by Kenneth Lentz. Still later, Harry



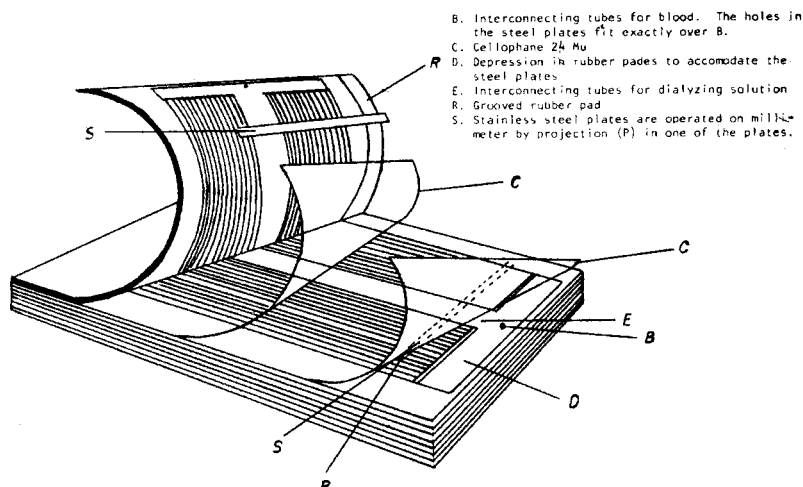
Fig. 1. The first successful artificial kidney.

The inventor, Dr. Willem Kolff, is at the right. A drum is in the foreground with cellophane sausage casing wound around it immersed in a tub of salt solution. When in use the drum rotated, thus propelling the blood through the tubing.

Skeggs Leonard

Fig. 2. The Skeggs-Leonard kidney.

The top rubber pad is shown folded back to reveal two sheets of cellophane. Blood flowed between the sheets with dialyzing solution flowing on both sides in many parallel grooves in the pads.



Hochstrasser and Frederick Dorer became members of our group. Ann Gould and Melvin Levine were also with us for a time. My good friend Joe Kahn worked with me until he retired shortly before I did. The accomplishments of our group can be understood by reference to a simplified diagram of the renin angiotensin system shown in Fig. 5.

We set out to purify angiotensin. We soon learned that there were actually two forms of the peptide, angiotensin I and II (8). We isolated angiotensin I in pure form and determined its amino acid concentration (9, 10). We purified angiotensin II and determined its amino acid composition and sequence (11, 12). We discovered that angio-

tensin I is converted to angiotensin II by the angiotensin-converting enzyme (13), which we partially purified and found that it was activated by chloride ions (14).

We also found that angiotensin I has no effect on blood pressure, whereas angiotensin II molecule-for-molecule is perhaps the most powerful pressor agent known (14).

We purified renin substrate from hog plasma and found that it had several different forms (15). Subsequently, we degraded the substrate molecule with trypsin and obtained a peptide substrate. The peptide was isolated from the digest, and its structure was determined and found to be that of a tetradecapeptide (16). The structure was confirmed by synthesis, yielding a fully

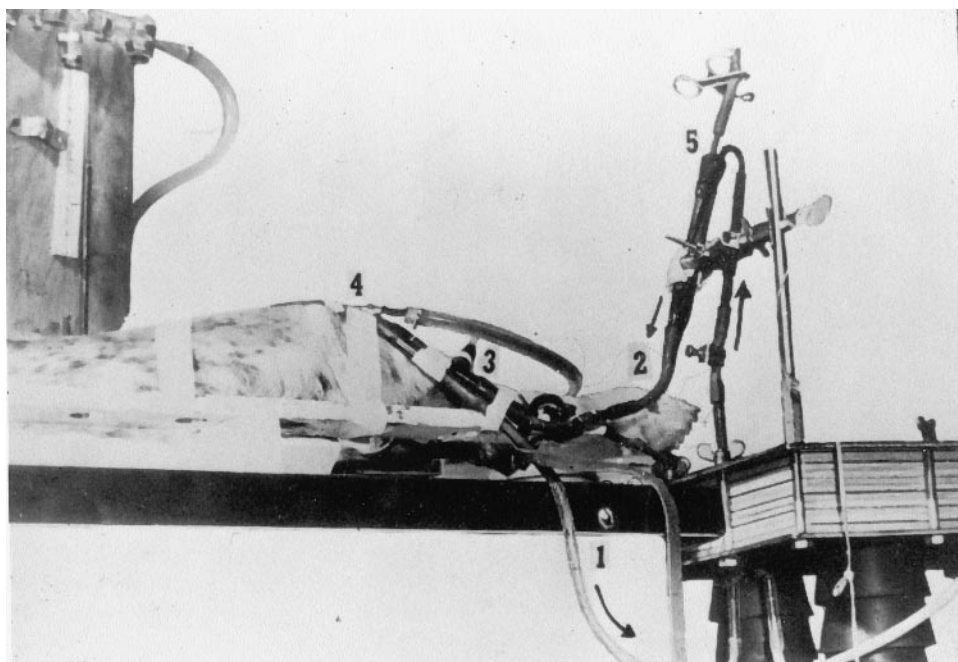
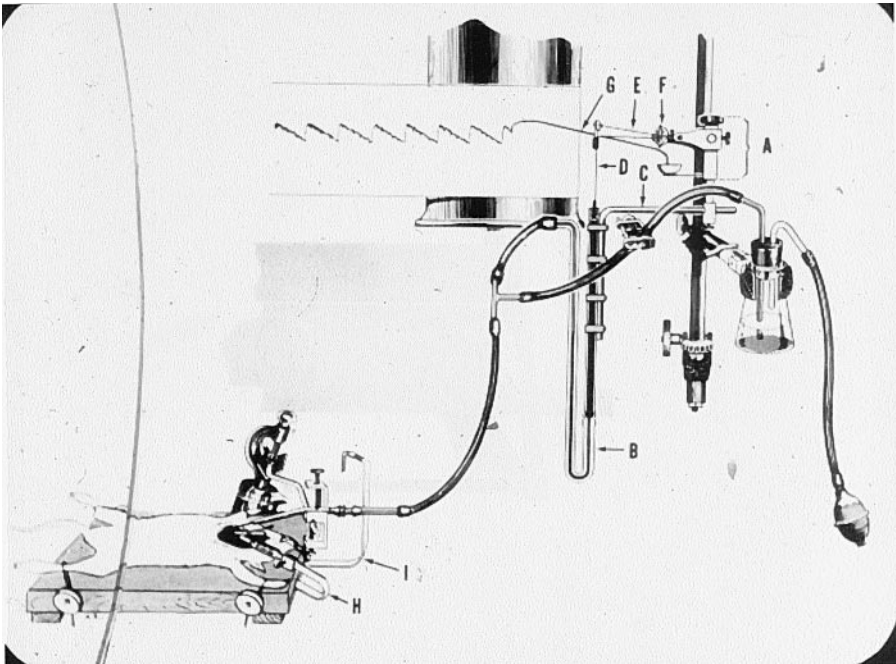


Fig. 3. Dialysis of the blood of an anesthetized dog.

Blood flowed from the femoral artery through four units of the dialyzer (tubing 1), returned to the femoral vein (tubing 2) through an air trap (5). A home-made mercury manometer showing mean arterial pressure is at the upper left.

Fig. 4. Assay of extracts of dialysate in anesthetized rats.

Tubing leads from carotid artery to a home made manometer equipped to record on a kymograph. Small samples of extracts (0.05–0.25 mL) were injected into the jugular vein. The rise in mean blood pressure was compared with the response to injections of a standard angiotensin solution.



active molecule (17). Finally, nine different peptides were synthesized that represented portions of the peptide molecule, and the kinetics of their reaction with renin were determined (18).

Since then, inhibitors of the converting enzyme have been developed that effectively block the renin-angiotensin system in vivo and are widely used to control high blood pressure and to decrease the after load on the heart in congestive heart failure.

While I was deep into research on hypertension, I was also being paid to run the Chemistry Laboratory for a 1000-bed hospital. I had three, sometimes four, technicians who also collected all the blood samples, washed and sterilized their glass syringes, sharpened and sterilized their own needles, and washed their own glassware. We did have glass filter colorimeters, which were just then replacing the old visual DuBosque colorimeter. Car-

bon dioxide combining power was done with Van Slyke’s manometric apparatus, with frequent mercury spills that ended up in the cracks of a wooden floor. Each day, my technicians had hundreds of manual operations to perform while talking to each other about last night’s date, the baseball game, or just polishing their white shoes. I had one very good male technician, Al Nagy. He was the only one I ever knew who could smoke a pipe and pipette at the same time.

I was worried about the quality of the results. I put unknowns into every batch of analyses and found frequent, very bad errors. There were just too many manual operations. I dreamed of a machine that would do analyses without error.

One day, it suddenly occurred to me that analyses could be done in a continuously flowing stream rather than batchwise or discreetly. I told Joe Kahn what I was

Table 1. Demonstration of angiotensin in dialysate of the blood of hypertensive dogs.

Normotensive dogs			Hypertensive dogs			
Dog number	Sample 1, units/L	Sample 2, units/L	Dog number	Mean blood pressure, mmHg	Sample 1, units/L	Sample 2, units/L
34	Trace	0.04	42	140	0.20	0.33
37	Trace	0.03	43	150	0.21	0.20
38	0.08	0	32	200	0.33	0.33
38	0.04	0.04	28	165	0.20	0.32
39	0.04	0.04	29	175	0.08	0.10
43	0.06	0.03	16	165	0.08	0.11
44	0.05	0.06	16	155	0.08	0.22
45	Trace	Trace	31	205	0.42	0.33
42	Trace	0	30	150	0.08	
32	Trace	Trace	27	155	0.05	0.02
			27	155	0.07	

Renin Substrate**Asp Arg Val Tyr Ile His Pro Phe His Leu Leu Val Tyr Ser R ----****Angiotensin I****Asp Arg Val Tyr Ile His Pro Phe His Leu + Leu Val Tyr Ser R ----****Converting Enzyme →****Angiotensin II****Asp Arg Val Tyr Ile His Pro Phe + His Leu**

Fig. 5. Outline of the renin-angiotensin system.

thinking. He urged me to build such a machine and loaned me the money that was needed to get started. I could not resist his offer. And that was just the beginning. In all, Joe loaned me about \$5000, of which \$3500 went for lawyers' bills. Without Joe's financial and moral support, I would not have made the AutoAnalyzer. I bought what was necessary and built model I, working in my basement at home on nights and weekends. The result was the prototype shown in Fig. 6. The small bottles at the right are urea calibrators; the large bottles contain reagents. A peristaltic finger pump is just to the left. Polyethylene tubing runs from the pump to mixing coils, a dialyzer, and Coleman colorimeter fitted with a flow cell made from a bent pipette. I fed samples by hand into the machine and read and recorded the colorimeter every 15 s. After graphing the colorimeter readings, I knew my idea would work. I had the proof of concept.

Model II is shown in Fig. 7. The method, calibrators, reagents, and pump and dialyzer were the same as in Model I. The tubing was 0.030-inch diameter polyethylene. The grooves in the dialyzer were square, 0.030 × 0.030 inches. The colorimeter was my own design with a 6 V incandescent light source powered by a constant voltage transformer with a glass filter. The flow cell was 0.020 inches in diameter × 2 cm long. The detector was a photomultiplier tube. The output was fed into a 10 mV industrial potentiometric recorder.

At the outset I made every effort to prevent air from getting into the flowing stream. When changing samples I was careful to pinch the aspirating tube to prevent air from being introduced. Occasionally I did not get the tubing pinched and an air bubble would get in between samples. Of course, I noticed that the separation of samples was much better with the air bubble than with-

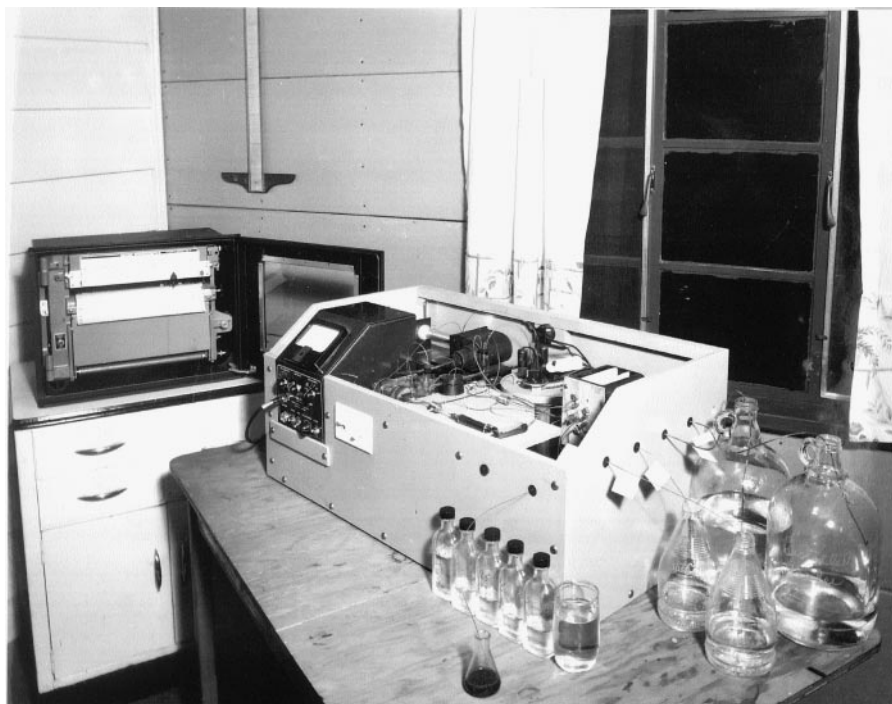


Fig. 6. The first continuous flow analyzer in the author's home.

Big bottles at the *right* contain reagents, small bottles contain urea calibrators. From *right to left*, the peristaltic finger pump propelled solutions through polyethylene tubing to mixing coils (polyethylene tubing coiled around test tubes) to a Plexiglas dialyzer to a Coleman colorimeter fitted with a flow cell fashioned from a pipette.

Fig. 7. Model II of the AutoAnalyzer.

Urea calibrators are in the small bottles in the foreground. From right to left, the pump, incubating bath, dialyzer, colorimeter, and photomultiplier control unit are visible.



out. Thereafter I always introduced air between samples and soon was adding air during sampling and in the dialysate stream as well.

The flow diagram of Fig. 8 contains my adaptation of a well-known urea method in which I substituted a dialysate for a protein-free filtrate. The sample stream was incubated with urease; the liberated ammonia entered the

stream of dialysate, which was nesslerized and passed through the colorimeter.

A typical recording (Fig. 9) shows 90-s samples of four urea calibrators with increasing and decreasing concentrations, together with their optical densities. Although a steady state was attained quickly, the record is noisy. I simply drew a line through the peaks to estimate an average peak value.

Typical results are shown in Table 2 and are satisfactory when compared with those obtained with manual urease-aeration-titration method, which was the best method available for urea in those days. The closeness of the higher values is striking.

At this point I licensed my machine to a small but reputable manufacturer of laboratory equipment. I sent him model II, together with my sketches and notes. Unfortunately, he thought I would furnish him with drawings for a finished marketable product, whereas I thought his company would engineer the final product. After several months we parted company. I got back a beautiful but empty stainless steel cabinet and a box full of my parts.

At this point I was very discouraged and was going to quit and put the box of parts up in the attic. Jean said, "No". She would not let me give up. So I built model III (Fig. 10). Many of the parts were the same. There was a new automatic sampler, a new dialyzer, and a colorimeter and heating bath. Model III was capable of determining urea and also glucose, using ferricyanide and inverse colorimetry.

I then built model IV in an attempt to further improve the machine. The result is shown in Fig. 11. It featured still

FLOW DIAGRAM OF UREASE METHOD FOR UREA

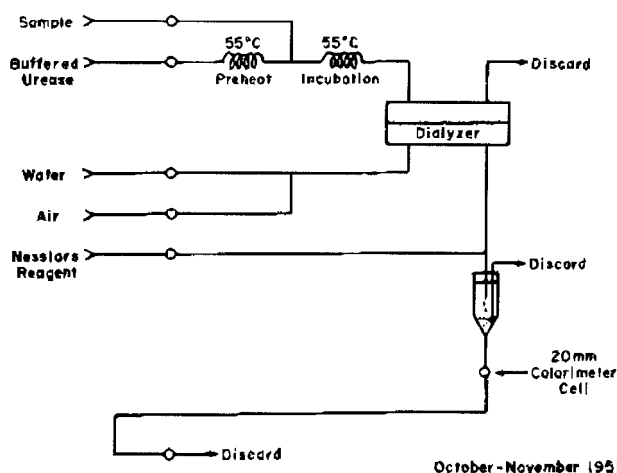


Fig. 8. Flow diagram of the method for urea.

Sample and urease solution were pumped (○) through mixing coils in an incubating bath where ammonium hydroxide was produced from urea. The mixture was passed through the dialyzer and discarded. Ammonium hydroxide dialyzed into the stream of air-segmented water, was mixed with Nessler's reagent, debubbled, and passed through the colorimeter flow cell, producing a recording as shown in Fig. 9.

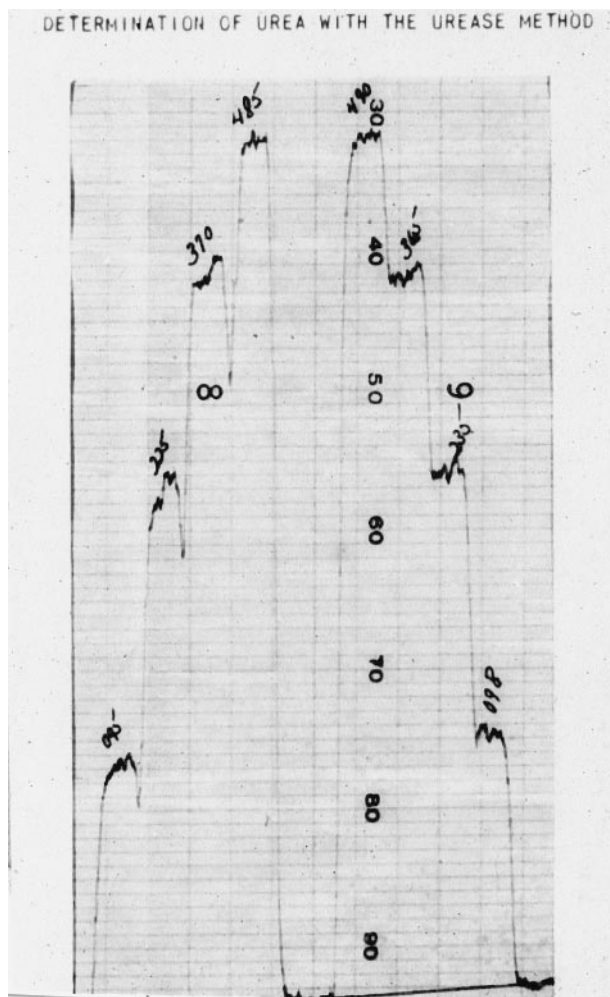


Fig. 9. Recording of four urea calibrators with increasing and decreasing concentrations.

Optical densities are written above the peaks.

another colorimeter of my design. The colorimeter cover is shown at the left. The sampler from model III was used but is not shown. Model IV is now in the Smithsonian Institute.

It was during this time that I tried very hard to find a company to further develop, manufacture, and market my analyzer. Several companies turned me down. It seemed that no one wanted it. I told Jean that if I had a gold brick, I could not sell it because no one would believe it was gold. It was very discouraging. Finally, there was one person who had a very small company with few resources who offered me a contract. Jean and I talked it over and decided that I had better sign the contract. That was on a Friday morning. I put the contract in my pocket, ready to mail, and went to work. Later that day, a salesman from Technicon, Ray Roesh by name, came into the laboratory. He had heard of the machine and wanted me to bring it to New York on Monday. He insisted; I could not get rid of him. He even followed me into the

Table 2. Comparison of analyses for blood urea nitrogen.^a

Sample	Urease-aeration-titration	AutoAnalyzer
1	7.7	8.2
2	8.6	9.6
3	15.3	14.0
4	31.2	32.4
5	10.8	10.6
6	5.9	6.2
7	10.9	9.8
8	12.8	12.5
9	18.2	17.9
10	12.1	11.6
11	8.8	9.2
12	3.2	4.4
13	19.7	20.3
14	17.8	18.0
15	13.2	13.1

^a Performed on November 7, 1951.

men's room. So I finally agreed. The contract in my pocket was forgotten.

Jean and I loaded the analyzer into our 1949 Ford, dropped our young daughter Laura off with her grandparents, and headed for New York. They put us up at the Waldorf. Monday morning we drove to the Bronx. We took a freight elevator to the sixth floor of a warehouse where Technicon was located. Jean and I set up the machine, drew blood from each other, and put it in the sampler. I did not tell them anything. As the peaks appeared on the recorder, Andy Ferrari and the others started to tell me how to build it. I signed a contract with Technicon several months later.

At that time Technicon was owned by Edwin C. Weiskopf, whose family came from Germany where they made thermometers. Mr. Weiskopf died in 1968, and his son Jack Whitehead inherited the company. Their principal product when I first met them was an automatic tissue staining device invented by Harry Goldblatt. They were good people who strove to make a product they could be proud of. I never had an argument with them. It is much to Jack's credit that he founded the Whitehead Biomedical Institute with a large part of his estate.

Technicon spent 3 years engineering and developing the first single-channel AutoAnalyzer, I described the method and Technicon's first AutoAnalyzer in 1957 (19). The first 10 analyzers sold for \$3200 each and went to 10 selected laboratories across the country. I thought it was so expensive no one would buy it; I was wrong. Technicon soon had many orders to fill. It was an instant success.

Within a year the Coleman Company brought out an analyzer that was a clear infringement of my patents. Technicon sued Coleman. The trial was in Federal court in Chicago. I was on the witness stand for 3 days. It was very difficult. I went to the sanctuary in the Downtown Temple at the top of one of Chicago's skyscrapers every morning to ask for strength for the coming day. Technicon won on all four counts of infringement.

Fig. 10. Model III AutoAnalyzer for either urea or glucose, with cover raised.

Strip chart recorder at the *right*, sampler at the *left*.



Technicon's sales mounted, and soon many laboratories across the country had one or more AutoAnalyzers, including my own laboratory.

I soon realized that although one might have several single-channel AutoAnalyzers, there were many manual operations to do and many opportunities for error, particularly in calculation of results and the handling of data (Table 3). What was needed was a machine that would do all of the commonly ordered analyses on one sample, calculate the results, and record them on one piece of paper.

I built the first model of such a machine in my basement in the evenings and weekends with the help of

Harry Hochstrasser. Harry also worked with me in our Veterans Administration hypertension laboratory. Fig. 12 shows the sampler: four pumps, a dialyzer, a 95 °C bath, flame photometer, and multiple colorimeter as viewed from above. Recorders are not shown. Another view (Fig. 13) shows the primary recorder, calibration equipment, and a second recorder that presented the analytical results.

The flow diagram is shown in Fig. 14. Albumin was determined directly on diluted serum using HABA dye. The rest of the sample went through a dialyzer, and the nondialyzable stream was used to determine total protein and CO₂. The dialysate was used to measure glucose and

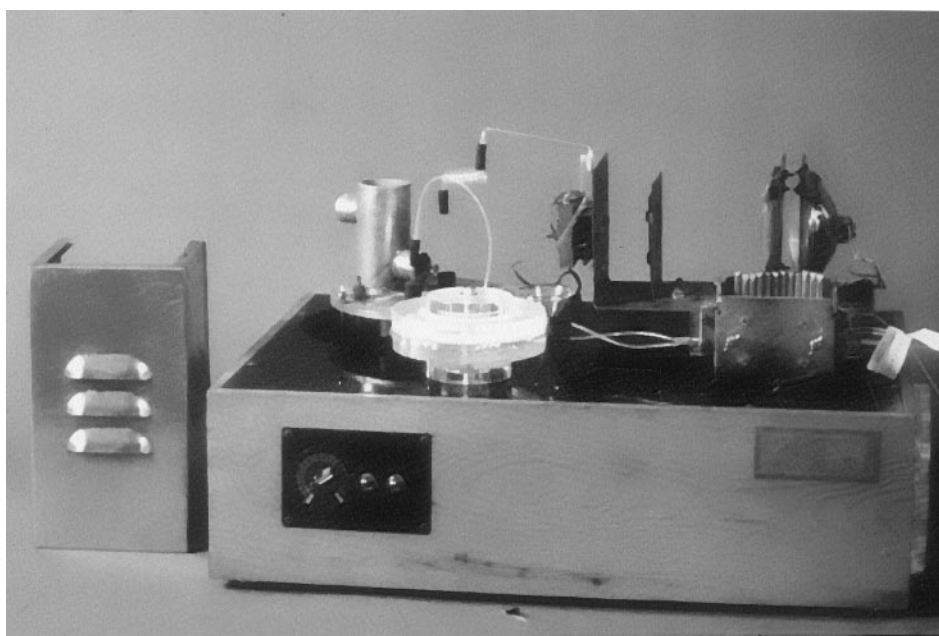


Fig. 11. Model IV AutoAnalyzer.

Finger pump shown at the *right* in front of the colorimeter with cover (at far *left*) removed. Condenser of 95 °C heating bath at *left rear*. Flat, spiral Plexiglas dialyzer at *left*. Model IV is in the Smithsonian.

Table 3. Daily laboratory routine.

1. Clotted bloods and requisition slips arrive in laboratory.
2. Prepare sera.
3. Examine requisition slips and from them make identifying lists of sera that are to be analyzed by each method. One list for each method.
4. Divide each serum sample into several sample cups. One cup for each test that has been ordered.
5. Place cups into sampler tray using sequence given on identifying list. A separate tray for each method.
6. Perform analyses automatically.
7. Calculate all records.
8. Record results on identifying lists.
9. Copy results from identifying lists onto requisition.
10. Send requisition to the physician.

urea as well as chloride, sodium, and potassium by flame photometer. The colored streams were hydraulically phased with delay coils so that peaks from a given sample arrived at the colorimeter in sequence and were recorded in sequence as shown in graphically calibrated form in Fig. 15.

This first multiple analyzer was described in *Clinical Chemistry* in 1964 (20). It yielded excellent analytical results but ran only 20 samples per hour. It did prove the concept and led to the very successful SMA 12/60 (Fig. 16). It was a workhorse. In my own laboratory, serving a 1000-bed hospital, the 12/60 with one operator handled most of the work of the laboratory in 4–6 h. A typical SMA 12/60 record is shown in Fig. 17.

The 12/60 was the first analyzer to use controlled, regular bubble introduction, which reduced noise and permitted a 60-sample per hour rate. This was the work of Bill Smythe at Technicon and was a great improvement. It did not use an integrated flow diagram. Analytical

streams were independent from each other but were hydraulically phased.

The culmination of the series was the SMAC, Sequential Multiple Analyzer Computer, which performed 20 analyses on every sample every 20 s (Fig. 18). The computer made hydraulic phasing unnecessary and simplified calculation and printing of results.

The SMAC was a very expensive machine, costing over \$200 000. However, in a laboratory with a large number of samples per day the cost per sample could drop as low as \$2 or \$3 per sample, or 10 to 15 cents per analysis. In the 1940s, the cost of a single blood sugar was in the order of \$5 or \$6.

The SMAC was very successful and was sold all over the world. Eventually, it was criticized for its lack of selectivity. Critics said that it was wasteful and used too many reagents to do analyses for anything more than the physician really needed. My own view was that it was much less expensive to do 20 different analyses on every sample, which nearly always included all of the tests physicians needed, than to sort out all of the samples and perform only those analyses that physicians actually ordered. Moreover, early work by Ralph Thiers and his group had shown that a multiple analysis often gave the physician unexpected and valuable information (21).

Technicon, however, was sensitive to the wishes of the marketplace and modified the SMAC so that the operator could enter only the analyses that were requested and only these results would be printed. All of the results from the other analytical channels were there, of course, but were not printed and were discarded! This ensured that the requesting physician was not troubled by any unexpected but important abnormality in the whole 20-channel analysis.

Technicon attempted to modify the SMAC so that it

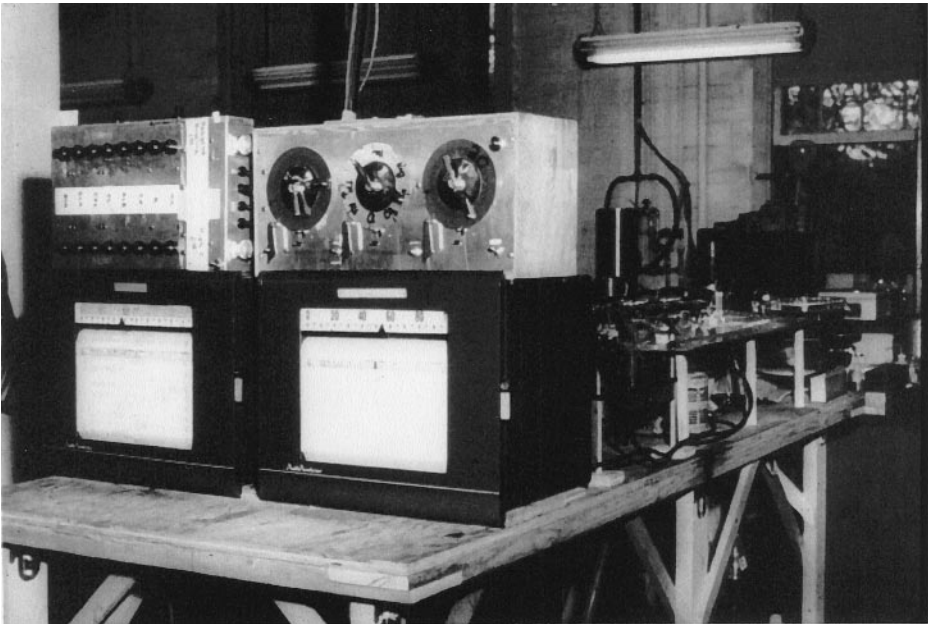


Fig. 12. The first Sequential Multiple Analyzer as viewed from above.

Sampler is at the lower right. Dialyzer is at the upper right; 95 °C heating bath at the upper left. Four pumps with flame photometer are partially shown at extreme upper left; multiple colorimeter at the lower left. Recorders are not shown.

Fig. 13. Sequential Multiple Analyzer showing primary recorder at lower right with timing controls on top.

Calibrated recorder at left with calibrating controls on top.



would actually only perform those analyses on an individual sample that were requested by the operator. Although they made a major effort, spending a great deal of money, the project failed. This would have been the ultimate machine. Perhaps they gave up too soon.

It was not long after this that Jack Whitehead sold Technicon to Revlon and I no longer visited Technicon.

My own contribution to continuous flow analysis, other than as a consultant, ended with my development of the first SMA in 1964. Most all of the major findings of my laboratory in the VA hospital in the field of hypertension, listed above, were also made before this time.

By the mid 1970s, it had been well established that the blood pressure of most hypertensive patients was attributable to the enzyme renin, which could be assayed in their blood (see Fig. 5). However, there was and still is a smaller but very significant group of hypertensive patients who have little or no renin in their blood. I thought it was important to discover the mechanism that raised their blood pressure. I worked on this problem with Joe Kahn, Ken Lentz, and Rick Dorer at the VA laboratory until my retirement in 1982 and then went to work with my good assistant Roseann Eadie (Fig. 16) in the Biochemistry Department at the Medical School.

FLOW DIAGRAM OF EIGHT-CHANNEL SEQUENTIAL ANALYZER

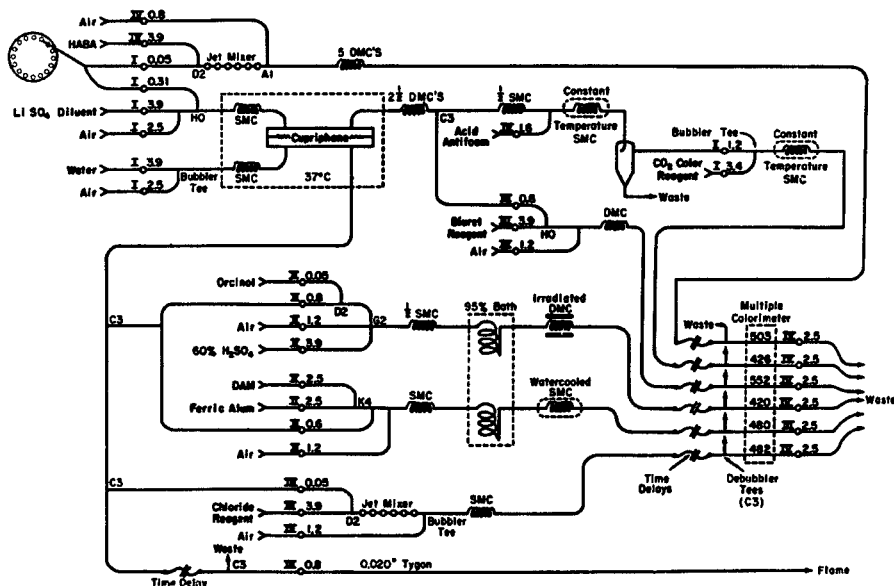


Fig. 14. Flow diagram of the eight-channel sequential analyzer.

Samples were diluted, segmented with air, and passed through the dialyzer. The non-dialyzable stream was divided and used for carbon dioxide combining power, albumin, and total protein. The dialyzable stream was divided and used for glucose, urea, and chloride, and sodium and potassium by flame photometer. Delay coils were used to cause the colored streams from each channel to arrive at the colorimeter in sequence. There was one light source and photoelectric detector that shuttled between stationary flow cells.

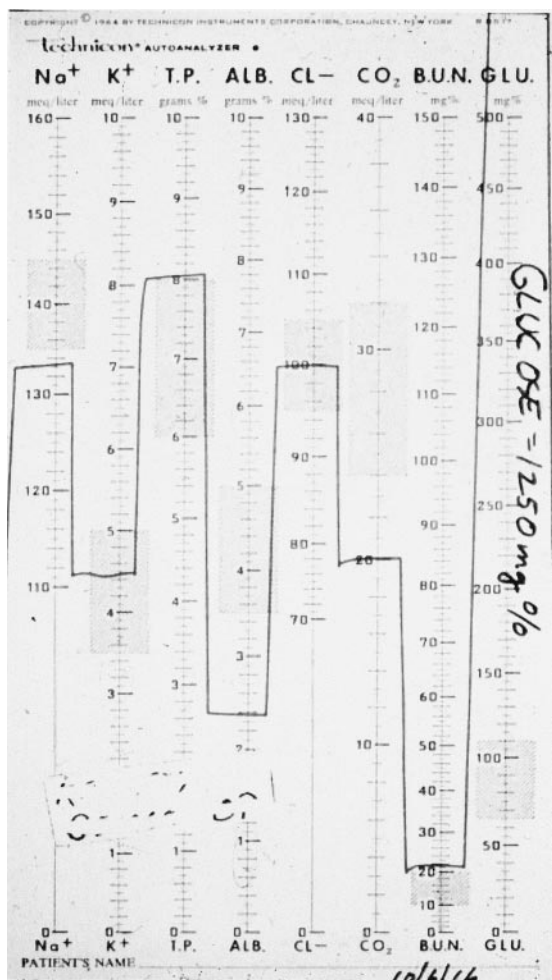


Fig. 15. Record from the first Sequential Multiple Analyzer.

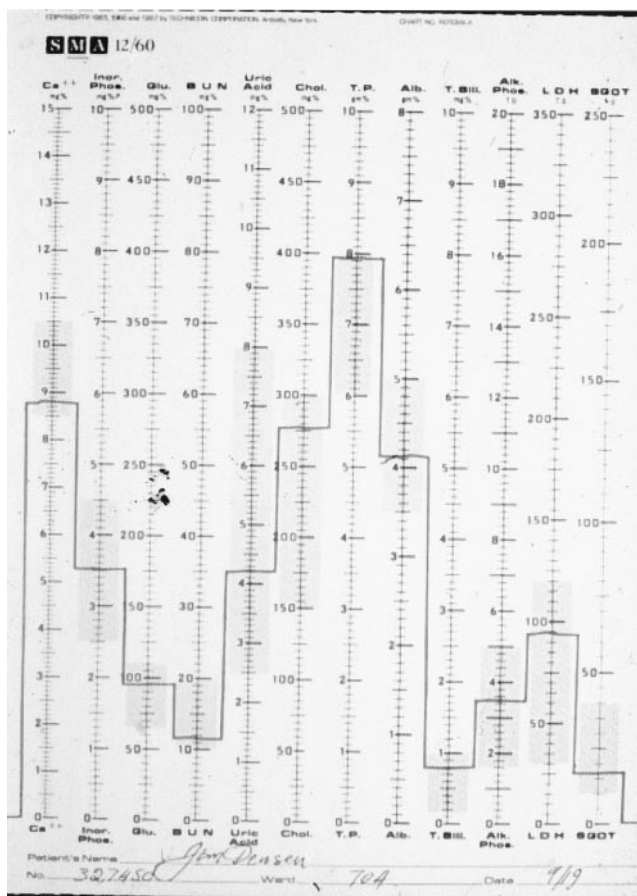


Fig. 17. Record from the SMA 12/60 with all values falling in the shaded "normal" range.

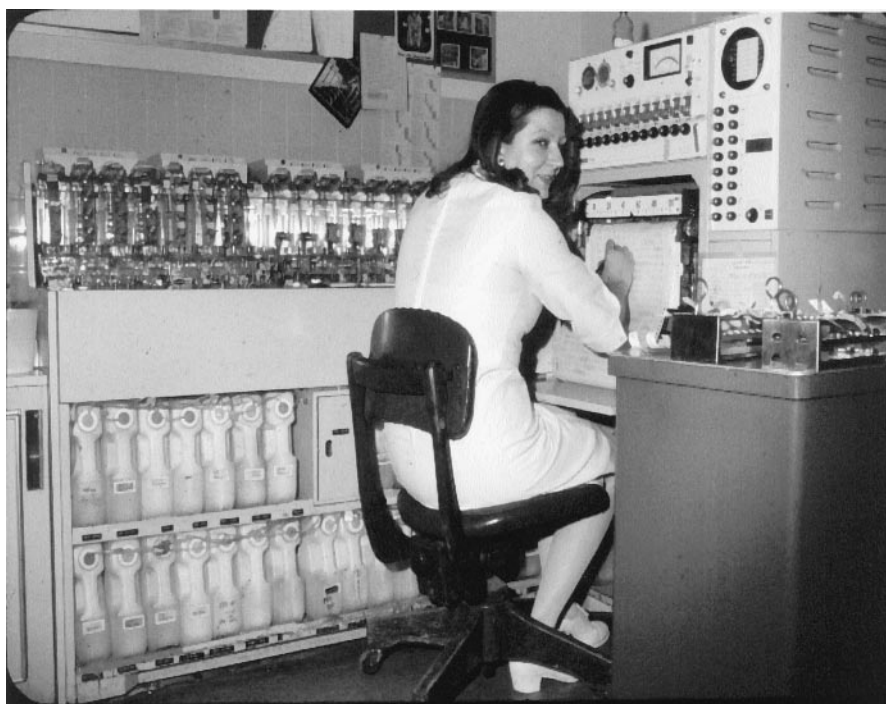


Fig. 16. SMA 12/60 in use in the author's laboratory at the Veterans Administration Hospital.

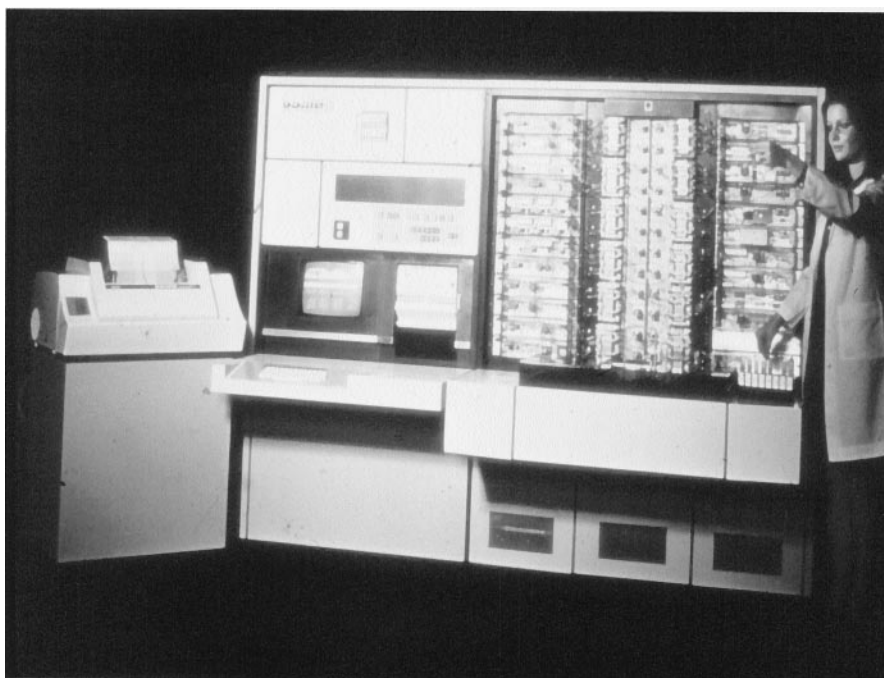


Fig. 18. SMAC, Sequential Multiple Analyzer Computer.

After 6 more years, I finally reached the conclusion that low renin hypertension is caused in some mysterious way by renin or an altered form of renin without there being any significant amount of renin in the blood (22). I decided further that I would need a whole new lifetime to solve the problem and retired for the second time in 1988.

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