

TECHNICAL EVOLUTION IN THE CLINICAL LABORATORY

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*Neither the naked hand nor the understanding
left to itself can effect much. It is by
instruments and helps that the work is done -
Francis Bacon, Novum Organum (1620) (see Note a)*

Abstract - An historical account of the introduction and application of instruments in the clinical laboratory is presented.

An Utopian report was published some 365 years ago under the title *Nova Atlantis* about the scientific and engineering state of the future. Describing 'laboratories', the report says: 'We also have glasses and means to see small and minute bodies, perfectly and distinctly; as ... the constituents of blood and urine, which are not otherwise visible' (Note a). The author was Francis Bacon, once Lord Chancellor under James I and the originator of the term 'experimental natural sciences'.

It took about 200 years for that vision to start to be turned into reality, when laboratories first emerged where blood and urine were studied systematically, for purposes of medical diagnostics.

That period of time is characterized by the efforts of scientists and engineers to resolve two fundamental contradictions which are inherent to clinical chemistry:

- the contradiction between speed and precision of analyses;
- the contradiction between the limited amount of available material for investigation and the limit of detection.

THE DEVELOPMENT BETWEEN 1840 AND 1957

Clinical laboratories evolved in Central Europe in the days of 'Vormärz' (before 1848), when things had started to move in all fields of medicine. Independent clinical-chemical laboratories were first set up in Berlin, Würzburg, and Vienna (Refs. 1-3). The technological evolution in these laboratories, the latest outcome of which is the kind of equipment we are going to discuss at this congress, will be the subject of the following study.

Clinical chemical laboratories around 1840 were not very expensively equipped. Various glass utensils, water and sand baths, platinum dish and spoon, blow pipe, and thermometer were used. In terms of precision instruments, there were balance and microscope. Johann Florian Heller of Vienna made out the following account (Ref. 4): 30 guilders for the required minimum of chemical utensils, 40 guilders for an analytical balance, and 90 guilders for a medium microscope, magnifying up to 250 times. A total, in order to make a comparison, which amounted to about 13% of a full professor's annual salary. If one was also interested in science, there would be a combustion apparatus for elementary analysis after Liebig.

Some 50 years later, by around 1890, the outfit of clinical chemical laboratories had changed. Above all, the clinicians themselves had discovered the laboratory (Refs. 5, 6). Clinical chemical and patho-biochemical research was flourishing at university clinics, with a corresponding growth in equipment. Physical measuring devices made their appearance in the clinical laboratory: the polarimeter, the visual colorimeter after Duboscq, and - following Kirchhoff's and Bunsen's discoveries in 1860 (Ref. 7) - the spectroscope. Kirchhoff and Bunsen, in 1862, described a 'small spectral apparatus for use in laboratories' (Ref. 8). Only a short time afterwards, it was being marketed by instrument dealers at about £5 or about 1% of a laboratory director's annual salary (Ref. 9). For the history of photometry see Ref. 10. Through

Note a. Francis Bacon, *Nova Atlantis* (1627), quoted from Francis Bacon, *Sylva Sylvarum sive Hist. naturalis, et Nova Atlantis*, Amsterdam, Elsevier, 1663: 'Habemus etiam artificia, et perspicilla, quibus corpora minuta et pusilla, distincte et perfecte cernimus, ... plurima in urinis, et sanguine, alias item non visibilia'. The motto is quoted from F. Bacon, works (F. Spedding *et al.*, ed.), vol. 4, 47 (1857-1874).

efficient accessories, quantitative spectrophotometry, too, was made possible although it was only used for research (Ref. 10). The same is true of the blood gas pump (Ref. 11) designed by physiologist Carl Ludwig (see Note a). Around that time, the use of a centrifuge for the separation of serum and urine sediment found its way rather hesitatingly into laboratories, although a manually operated laboratory centrifuge had been known as early as 1852 (Refs. 13-16). Outside Germany, developments were not so fast. From 1890 on, simple 'ward laboratories' were set up, especially in the USA, which served all-diagnostic purposes and - according to contemporary reports - could be fully equipped at about US-\$300, covering a 10 sq.ft. area (Refs. 17-19).

In our study, let us now take another leap forward by about 50 years to the thirties of the 20th century. In 1931, clinical chemistry had been given its name and a well-defined concept appeared in the epochal work of J.P. Peters and D.D. van Slyke (Ref. 20). Apart from the devices for gas analysis which van Slyke himself had designed (Ref. 21), few new instruments were used at the time. What strikes one in particular is that electric (let alone electronic) equipment was still hardly ever used in the laboratory although the triumphant advance of electricity in general technology and in the home was well under way by then. Otto Folin's methods (Ref. 22) had given a boost to visual photometry. As well, Ivar Bang (Ref. 23) had been the first to introduce workable micro-methods for clinical applications (see Note b).

The years of the second world war stopped the progress of technological evolution, at least in Europe's clinical laboratories. In the meantime, however, various physical techniques had matured and in the 1950's, these were introduced more or less at the same time in clinical laboratories (Ref. 24). A major breakthrough came with the photoelectric photometers. Although the photoelectric effect had been known to physicists since the end of the 19th century, it was only in the 1930's that the first photometers with photoelectric cells came onto the market (Ref. 25). For a long time, chemists both in the clinic and outside felt they were less reliable than the long-known visual devices (Ref. 26).

Flame photometers, atomic absorption spectrometers, pH measuring instruments with glass electrodes, and separation methods such as electrophoresis are further examples of physical methods introduced after the second world war.

Through the use of physical methods and brilliant miniaturization of instruments, it became possible to resolve the afore-mentioned contradiction between the quantity of samples and the limit of detection, at least to a very large extent.

If those technological innovations of the 1950's alone had brought substantial changes to the appearance of clinical laboratories, the invention of the first fully mechanized analytical device, the 'Autoanalyzer', by Leonard Skeggs in 1957 initiated a technological revolution with far-reaching consequences on the structure and organization of clinical laboratories (Ref. 27).

The development of mechanized analytical devices has also more or less resolved the second contradiction in clinical chemistry - that between speed and precision.

At this point I should like to break off our brief overview of technological evolution in the clinical laboratory and leave discussion of the most recent decades with their second and third generations of fully mechanized equipment and the arrival of the computer - a phase most of us should still remember quite well.

Rather, I wish to attempt a more generalized definition of the technological evolution we have reviewed so far, and finally give a little more prominence to the background of the picture thus obtained.

EVOLUTION FROM THE TOOL TO THE MACHINE

Technological development in the clinical laboratory, as described above, is very much like the development of technology generally, albeit strongly out of phase. The pattern of evolution (tool - machine - automation) has been described by H. Schmidt (Ref. 28) and in the more recent *Contributions to a Philosophy of Technology* by L. Tondl (Ref. 29).

The first utensils were simple tools to extend the natural capabilities of the human hand.

Note a. In 1858 Carl Ludwig designed a mercury blood gas pump, the design of which was published by his pupil, J. Setschenow (Ref. 12).

Note b. Ivar Bang used about 100-150 mg of blood, which was absorbed in the form of a drop into a piece of filter paper and weighed out immediately by torsion balance. The substances to be determined were extracted quantitatively from the filter paper and determined gravimetrically or titrimetrically. Bang's method reduced the sample material by more than 2 orders of magnitude. The method was first published in 1913 and described in a monograph (Ref. 23).

Michael Faraday, in 1827, summarized chemical laboratory technology as 'chemical manipulation' (Ref. 30). Around 1840, at a time when the industrial revolution, by the introduction of machines, was creating social problems and frightening and threatening many people - one might think of the weavers' rebellion in Silesia in 1844 - the clinical laboratory saw the transition from the tool to the instrument. The capabilities of man's senses are extended by the instrument, e.g. by amplification (such as by microscope) or by transformation of physical phenomena which are not by nature accessible to the senses (such as by polarimeter) (Ref. 31). It was only around the turn to the 20th century that a machine was used for the first time - the centrifuge, which might be classified as an 'engine'. A real 'machine', i.e. one relieving man of work, did not emerge until after the second world war, with the Autoanalyzer (Ref. 27). Therefore, while machines had long established themselves in general engineering and in everyday life, clinical laboratories were still largely using instruments, although very refined ones.

In the history of engineering, machines were followed by automation, i.e. the use of machines whose control loops provide them with self-monitoring and self-adjusting capabilities. Automated production processes - such as in car manufacturing - came into use after the first world war with the aid of the photoelectric cell, which was not to be used in the laboratory until 30 years later. Finally, automation found its way into the clinical laboratory also, but only following the arrival of the microprocessor, which was invented in 1971 (see Note a).

This brief account shows that the technological evolution in the clinical laboratory has more or less followed the course of general engineering. However, after starting with a considerable time-lag over engineering, advancement has gained considerably and, as a result, a few years has been enough for the clinical laboratories to catch up with 200 years of industrial engineering development (Ref. 32).

SCIENTIFIC AND SOCIAL BACKGROUND

It would be a gross simplification to omit the scientific and social background from a description of technological evolution in the clinical laboratory. At this point, we can only outline some aspects of that background.

Scientific instruments are the work of the hand of man; but who were the men who made these utensils? Except for a few exceptions, they were not the users of the instruments (scientists) but craftsmen with special skills in metal-working, later also in glass-working. The few works on the social history of instrument-making are widely scattered but the reader is referred particularly to Refs. 33-38. In the 16th century, we find the watch- and clock-making crafts in full bloom in Germany and France. In the 17th century, specialists for thermometers, barometers, optical instruments, etc. emerge, mainly in Italy and England. The choice and working of suitable materials became more and more the responsibility of the instrument-maker who initiated many improvements. In the 19th century, we observe another social shift, which becomes evident when we study the making of instruments for the clinical laboratory as our obvious field of interest. The university mechanic, till then directly working for a scientist at a university institute, set up for himself and opened a business of his own. A famous example is Jena university mechanic Carl Zeiss, who opened his own workshop in 1846. The industrialization of instrument-making had begun. The demand for scientific instruments grew extraordinarily fast in the second half of the 19th century. More and more instruments were needed, not only in science but also in industrial production and everyday life - indeed, the manufacturing of instruments almost becomes an index of industrialization (Ref. 39). This, in turn, reacts on instrument-making itself: manufacturing by craftsmen was replaced with industrial production. At the same time, endeavours were made to place instrument-making on a reliable scientific basis, turning the craftsman more and more into an engineer. Carl Zeiss himself, who pleaded for an 'orderly cooperation of science and technical art' (Ref. 40), set an outstanding example in his association with physicist Ernst Abbe. Then, in the 20th century, it can be seen that research, development, and manufacturing have all been taken over by industrial apparatus engineering companies.

Before we turn to the human being who uses the instruments of a clinical laboratory - physician, clinical pathologist, clinical chemist - it will be helpful to take a look at the underlying scientific concept (Refs. 41-44).

In France, in the early 19th century, a new, strictly empirical school of medicine had prevailed. From it originated, starting around 1840, in France and England but particularly in Austria and Germany, the so-called 'Physiological' or 'Scientific Medicine'. Especially young Robert Virchow, the French and German physiologists, as well as Justus Liebig stood up, with a great deal of dedication and optimism, for the use of the 'methods of natural sciences' in medicine. As Virchow pronounced so characteristically: 'Medicine wants to be not only a

Note a. The microprocessor chip Intel 4004 of the Intel Corporation was the first one to be marketed.

united science, it wants to be a natural science - indeed, the most beautiful and supreme of all natural sciences' (Ref. 45).

Under stimulus from the successes in physics and chemistry, the general endeavour was to reduce all processes of life, without any exception, to physical and chemical processes, to interpret 'pathology and therapy as mechanical sciences' (Ref. 46).

Although this concept has undergone manifold modifications in the course of time, medicine as a natural science is still the declared objective today.

The reception by practitioners of the new diagnostic capabilities of the clinical laboratory was rather hesitating at first. Many felt that pathological chemistry was just idle boast, as Virchow reported (Ref. 45). There would have been several reasons for this attitude: the scientific edifice of pathological physiology was still unfinished and was only partly able to explain the pathologico-chemical signs observed, and the use of complicated apparatus was unfamiliar and had a deterrent effect. Paul Ehrlich warned in 1883 that diagnostic tests had to be 'simple to interpret and execute' - in other words, requiring 'neither a lot of time nor complicated apparatus nor particular chemical skills or education' (Ref. 47).

Quantitative methods were particularly slow in being adopted into medical practice (Refs. 48, 49). Perhaps this was owing to the fact that in the middle of the 19th century, the predominance of pathological anatomy placed the morphological approach into the foreground. On the other hand, the quantitation of objective factors was something new to the physician. For example, the thermometer was considered 'unsuitable for assessing the qualities ... of pathological body heat', 'the best instrument', it was said, 'which the physician can possibly use remains his hand' (Ref. 50).

The situation changed gradually after the last decades of the 19th century when clinicians themselves started taking an interest in clinico-experimental research (Ref. 5). This is particularly true of the universities of the German-speaking countries. Clinical laboratories were established and clinical chemical examinations were made the object of intensive studies. As a result, subsequent generations of medical students were more and more instructed in the bedside application of clinical chemical examination methods.

Then, in the 20th century, practitioners can be seen to withdraw increasingly from the clinical laboratory. Firstly, the work was delegated to ancillary staff with the medical technologists emerging as a specialized profession; then after the second world war, the methods of the clinical laboratory had become so complicated that a new class of academic specialist - clinical chemists or clinical pathologists - took over research and routine work in the clinical laboratories.

TECHNICAL THINKING AND ACTING IN THE CLINICAL LABORATORY

The clinical laboratory is closely related to scientific medicine, a relationship which has brought it immense advancement but also problems. The historical picture of the technological evolution which I have tried to outline to you must account for these problems, but what are they? It can be shown that with the beginning of medicine as a natural science, the ways physicians used to think and act changed fundamentally (Ref. 51) - they started to think and act 'technically', by employing natural sciences for the achievement of practical medical goals. Let me explain this in a little more detail. 'Acting technically' means an attempt being made on the basis of known laws of nature, which are interpreted as laws of causality, to achieve practical medical goals in a planned, specific, efficient, and controllable manner. For example, this may be a therapy using a medicament whose effect is known at the molecular level; or it may be the identification of physical and chemical facts as causes ('causae') of a disease. As well, technical actions may consist of the determination of physical or chemical quantities from which a diagnosis is derived. This last example is particularly indicative of technical action in that it uses instruments, machinery, and automation in the clinical laboratory.

This 'technization' of medicine has come under a good deal of criticism. Suffice it here to recall the vehement attack by Ivan Illich in his book *Medical Nemesis* (Ref. 52), whose title refers to Nemesis, a Greek goddess who punishes human arrogance.

In fact, several dangers are threatening modern medicine with its technical approach. In view of our particular approach here, I would like to stress two areas of danger which are especially important to the clinical laboratory: technocracy and dehumanization.

The philosophy of technology speaks of technocracy if man's actions become dependent on technical constraints alone (Ref. 53). This also means that man is no longer in command of a machine. For example, that was what Norbert Wiener, the father of cybernetics, feared from the computers since they operate much faster than does man, so that under adverse circumstances man may have no time to intervene (Ref. 54).

Dehumanization, the second area of danger in modern medicine I would like to cite is a particular threat to the work of the clinical laboratory, in that the laboratory staff, both physically and in their thinking, move away from the patient.

'First we digitised them' - as F.L. Mitchell (Ref. 55) put it - 'then we punched them into cards, and now we have reduced them to a few spots of magnetism on a strip of tape'. Or, according to a clinician (Ref. 56), 'Laboratory methods tend to make one forget the patient altogether in the nicety of the scientific'.

What are the consequences of all this? The answer must be the same in medicine as in technology at large: the use of technology requires regulation (Ref. 57), the prevention of abuse, and perhaps also self-imposed limits (Ref. 58).

Applied to the clinical laboratory, I would like to list four points which I feel are important.

1. Turning to the patient again, improvement - or resumption - of the dialogue between the clinic and the laboratory. The clinical chemist or pathologist must once again be a clinical scientist rather than an engineer.
2. Avoidance of any dependency on analytical devices, by thorough knowledge of those devices. A 'black box' or 'pushbutton' philosophy towards equipment is dangerous.
3. Observance of the medical principle, 'primum non nocere'. This means, among other things, the avoidance of abundant production and allowing for the economic situation of the health system. When new equipment and methods are developed, the consequences must be appraised ('technology assessment').
4. The methods of a clinical laboratory must also be available to the population in 'remote areas'. In other words: equipment must be developed which is suitable for use in such areas (Ref. 59).

Our starting point was Francis Bacon's Utopian idea of the scientific and engineering state of the future. Bacon's vision is full of optimism that natural sciences and engineering, in *New Atlantis*, will unite in harmony to the benefit of mankind.

We have long made reality of the technical facts that Bacon anticipated but the harmony between engineering and medical action, in medicine as well as in the clinical laboratory, remains to be found.

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