SOME APPLICATIONS OF PHYSICS TO CLINICAL MEDICINE

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INTRODUCTION

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Recently Dr. Alex Comfort (1963) has referred in a particular context to the 'irruption of the physicist' into the medical field. Although his entry has been generally less dramatic than this would suggest, the physicist is increasingly to be found in the membership of clinical departments and research teams. Most teaching hospitals and many other large hospitals have physics departments and the sphere of application of physics to medicine has widened greatly beyond the field of radiotherapy, in which quantitative physical work was originally done. This has come about partly because the clinician has employed physical agents such as X-rays and radioactive substances, which require physical measurement of a highly sophisticated order for their use and control, and partly because new physical methods, particularly electronic techniques, have extended the range and type of measurement which can have diagnostic significance. Not least among the characteristics usually found in the physicist is his inclination towards quantitative and mathematical expression; this, if realistically applied, can be an asset of great importance. As Mayneord (1942) once pointed out, some words of Richard Mead, who was physician to Newton, make interesting comment today; '... that Mathematical Learning will be the Distinguishing Mark of a Physician from a Quack; and that He who wants this necessary qualification will be as Ridiculous as One without Greek or Latin!' It is hoped that this article will indicate some of the ways in which, in this department, physical and mathematical methods aid clinical research. We know that today these examples are paralleled by similar work in many other medical centres here and abroad. Rather than contribute one long paper, going deeply into a particular subject, we have presented five comparatively short sections which give sufficient detail to put each topic before the reader and show its relation to some aspect of clinical medicine.

REFERENCES


THE SPECTROCHEMICAL ANALYSIS OF BIOLOGICAL MATERIAL

J. B. Dawson

Spectrochemical analysis uses the emission or absorption spectrum of an atom excited in either a flame or electrical discharge to detect the presence of and, if standard conditions of excitation are used, measure the concentration of an element in a sample.

This method of analysis as a means for the identification of an element has been known from the time of the work of Herschel and Talbot in the 1820's. However, not until the 1930's did its use become widespread, delayed largely by technological difficulties and an insufficient demand.
for an analytical method offering the particular advantages of spectrochemical methods. These advantages are:

1. Specificity; each spectral line is characteristic of the element emitting it.
2. Sensitivity; elements in concentrations of the order of 1 part in $10^4$ of solution may be estimated.
3. Accuracy; a reproducibility of ±2% and an absolute accuracy of ±2 to ±3% can be achieved.
4. Small samples; in some cases only a few µg of material may be required for an analysis.
5. Speed; in a routine spectrographic laboratory up to 50 analyses per hour can be performed on one instrument.

The advantages of spectrochemical analysis make it an attractive method for the estimation of elements in biological material. Not until a simple and inexpensive flame-photometer became available in the late 1940's, however, did the method become widely used as an analytical method in chemical pathology laboratories. The full potential of the method has not yet been exploited neither in the investigation of the biological role of trace elements nor in the automation of the estimation of, say, Na, K, Ca. Two aspects of spectrochemical analysis have been studied in some detail in this department, firstly, atomic absorption spectroscopy, with particular reference to the estimation of magnesium, and secondly the development of a high speed scanning spectrophotometer for the simultaneous estimation of several elements.

**Atomic Absorption Spectrophotometry**

In its application to the analysis of biological material this technique may be best described as absorption flame-photometry. The sample, in solution form, is sprayed into a flame, the heat of the flame breaks up the sample into an atomic vapour. The optical density of the flame containing the atomic vapour to light of a wavelength corresponding to a resonance transition of the element to be estimated is then measured. The absorption obeys the Beer-Lambert law and therefore, as the concentration of atoms in the flame is proportional to the concentration of the element in solution, the optical density of the flame is proportional to the concentration of element in solution; by calibration of the instrument with solutions of known composition unknown concentrations may be determined. Compared with emission flame-photometry, absorption has two advantages:

**Greater sensitivity.** The absorption signal is dependent on the number of atoms in the ground state, not the excited state as in emission. At the temperature of flames, up to 2,500°K, say, the former is at least $10^4$ times greater than the latter.

**Freedom from radiation interference.** As the effective bandwidth of the system is that of the natural width of the spectral line, 0.05Å approximately, high selectivity is possible.

The atomic absorption spectrophotometer has four basic components:

1. A source of resonance radiation. This is usually a hollow cathode discharge lamp in which the cathode is made of the metal to be estimated.
2. A means of producing an atomic vapour. Commonly this is an air-acetylene flame using an elongated burner to give an absorption path of about 10 cm.
3. As a wavelength selector a diffraction grating or prism monochromator is used.
4. A photomultiplier is used for the detection and measurement of the resonance radiation.

Magnesium is one of the most convenient and sensitive of elements to be estimated by atomic absorption. The element is also of considerable interest to the clinical biochemist as its metabolism is not yet fully understood. To further a study of magnesium metabolism it was therefore appropriate to set up an atomic absorption spectrophotometer and evaluate the instrument for the estimation of magnesium in biological material. It has been found that the method is extremely suitable for the estimation of magnesium in biological materials, giving an absolute accuracy of ±2 to ±3% at levels of 0.5 part per million (Dawson and Heaton, 1961). At the present time a more versatile instrument than that in routine use is under construction. A review article by Willis (1963) may be consulted for a comprehensive account of the application of atomic absorption spectroscopy to the analysis of biological material.

**High-speed Scanning Spectrophotometer**

This instrument is designed for the simultaneous estimation of sodium, potassium, calcium and magnesium in biological samples. The sample is excited under standard conditions in either a flame or electrical discharge. The intensity of the emission or absorption spectra of the element is then measured by the spectrophotometer. The spectral region 3,000 A.U. to 6,000 A.U. (approximately) is scanned at 5 c.p.s. The signals arising from the spectral lines of interest are selected by means of an electrical wavelength scale generated by an auxiliary optical system and are then fed into a number of integrating circuits. The charge accumulated in these integrators is measured and is proportional to the amount of light of the selected wavelength emitted by the sample.

Preliminary trials of this instrument using flame excitation of the sample show that a resolution of 5Å can be achieved. This resolution is certainly
adequate for the measurement of the elements of common biological interest and, although the trials are not yet complete, an overall accuracy of 1 to 2% is anticipated. The completed instrument will be fully automated with automatic dilution of the sample and print-out of the analytical results.

REFERENCES


X-RAY IMAGE DETECTION BY ELECTRONIC METHODS

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In diagnostic radiology, the excellence of the conventional radiographic screen-film combination as a means of detecting and displaying the X-ray pattern (the radiation image) is qualified by its inability to show movement. The technique of fluoroscopy, in which the light image on the fluorescent screen is viewed by the dark-adapted but otherwise unaided eye, has long been employed in an attempt to overcome this disadvantage. Unfortunately, because of restricted optical aperture and low retinal efficiency, the eye responds to only a very small fraction of the light emitted by the screen, and only about one-fifth of the information inherent in the screen image is transmitted to the brain. This inefficiency of information transfer also renders it necessary in clinical work to use dose-rates which are higher than appear at present to be desirable. These fundamental deficiencies, together with the inconvenience of the darkened room which can be a great handicap in complex techniques such as cardiac catheterization, seriously limit the clinical applications of fluoroscopy.

Many attempts have therefore been made to improve the collection of light and therefore of information from the fluoroscopic screen. The first successful device, called the X-ray image intensifier tube (Colman, 1948), had a high efficiency of light collection, but also a number of disadvantages. The field size was restricted to about 4½ inches in diameter, and the quality of the image was greatly affected by contrast loss due to various internal factors. Because it was necessary to view the image through a microscope, the radiologist's movements were seriously restricted.

In 1957, after considerable theoretical study, work on a new type of X-ray image detector (first described by Morgan and Sturm, 1951) was undertaken in this laboratory, assisted by a generous grant from the Nuffield Foundation. In this image detector the fluoroscopic screen is viewed by a television camera incorporating a large aperture lens and a very sensitive television camera tube, the image orthicon. After amplification in the electronic circuits the output image is displayed on the screen of a conventional television receiver. Initial experiments were first carried out with standard television equipment, and subjective assessments were made of the information-gathering properties of the system (Hay, 1958; 1960). In the present experimental system, a 12¾ in. diameter fluoroscopic screen is used in conjunction with an f/0.68 mirror optical system (Bouwers, 1950) and a special 4½ in. image orthicon tube (Banks, 1958). In this system, although considerable light is lost between screen and photocathode, the light transfer is about one hundred times that of the eye and little information should in principle be lost. Subjective measurements of information transfer (Hay, 1962) show that at conventional dose-rates the improvement over fluoroscopy is about five times; conversely for image quality approximating to conventional fluoroscopy the dose-rate may be reduced generally to about one-twentieth that of fluoroscopic levels.

This image detector has been used in a variety of clinical procedures, and as might be expected it displays all the advantages generally associated with television techniques. The radiologist and his collaborators can work in subdued artificial light and complex techniques such as cardiac catheterization are greatly facilitated, and are often so accelerated that a substantial dose reduction to the patient results from reduced operating time as well as from the lower dose-rate. The facilities available for the electronic control of contrast and other image parameters are useful; for example, the inequalities of X-ray transmission seen in the region of the diaphragm can be compensated so that an image of even overall illumination is obtained. Radiological demonstrations are possible to large audiences (the technique is being used in this University in the teaching of human physiology to medical students) and the moving image may be recorded either on cine-film via the television screen or on magnetic tape.

Television systems of various types are now in widespread use in radiology. There is a commercial version of the system described above, and the
The Spectrochemical Analysis of Biological Material

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