Computing, mathematics, and the nephrologist

Sick people with major fluid and electrolyte disturbances often only need simple treatment based on mathematical reasoning for their problems to be solved. Describing the methods, and then educating others in these methods, was probably the major clinical contribution of those who created nephrology as a defined branch of medicine. Decisions based on this integration of several items of numerical information in the management of electrolyte disorders, planning dialysis treatment, and other aspects of nephrological practice are important components of the daily routine in any clinical renal service. Renal physicians as a group are probably more numerate than many of their colleagues, perhaps because those who are not comfortable with numbers do not acquire the specialty. The ability to comprehend a problem expressed mathematically might be the reason that the specialty became better organized than most. The specialty has collected facts and figures concerning the size of the problem we face in the community and the results of the treatment provided. Some such numerical “facts” have been essential to negotiate for the expensive facilities that are needed to treat endstage renal failure. These and other facts collected by the specialty, in the central registries that evolved, have been useful when considering different modes of treatment and the contribution to the outcome of different aspects of management. It is clear from two of the articles in this symposium that there is further progress to be made using these large computerized centralized collections of data, but more sophistication in how this is done is needed if full use is to be made of these huge stores of data.

The main reason for this issue is identifying the potential for smaller local computers to help patients. This issue was conceived in 1980 following a successful symposium on the topic held in Nottingham, England, when many British nephrologists observed for the first time how a computer makes the creation of graphs easy and quick, and saw demonstrations of other actual and potential uses of this new technology. There has been no attempt to make this a proceedings of that meeting, but many who spoke contributed to this issue and have made significant progress since that time. The stimulus to that symposium was the introduction to Nottingham of a clinical computer system that began at the Charing Cross Hospital, London; it is described in this issue by Gordon and colleagues and is a system which had outstanding graphics and other useful features even at that time. Since that symposium many renal units both in the United Kingdom and abroad have had further experience of the improved quality of care that is possible when physicians have better control over collected information as a result of computerization. They have also felt the excitement when the understanding of information increases at a very rapid rate. Other experiences of using computer-stored data in nephrology are described in this issue by co-editor Dr. William Stead and his Duke University colleagues and by Dr. Victor Pollack and his group. Many decades of computer programming time were needed to get these systems to their present state of development. The Duke University goal was, and is, concerned with the replacement of the nephrology record (that is, the medical written notes), while de Wardener’s and Gordon’s aim was to supplement this by getting the computer to do things that would otherwise be impossible or are usually poorly done with noncomputerized record keeping. The Cincinnatti contribution draws attention to the computer’s potential to store and sort and classify large quantities of diagnostic information, and their article should help remind nephrologists that much of current classification is arbitrary and that with an increased ability to acquire and sort information some classifications will not survive. Classification can, without a constant review, stifle progressive thought. Throughout the world, other systems are in routine clinical use, no doubt with a range of strengths and weaknesses. The majority of these systems are functioning in the departments where they evolved and were dependent on the efforts of one or more enthusiasts; progress will be faster now that these groups of individuals are learning how to communicate, as are their computers. Other articles in this issue concern themselves with how to use computer-stored information and, in particular, with methods to use the numeric information. The calculating power of modern equipment makes many more mathematical tasks feasible. Small renal unit based equipment facilitates tasks that would have been impossible with even the most sophisticated equipment available anywhere two decades ago. This creates exciting possibilities and techniques discussed in articles in this issue by Gore, and by Wing and his colleagues, which thus far have mostly been used on large central computer registers may now also be relevant to those developing computing systems within their own hospital or unit. It has been encouraging to observe that overinterpretation of information, due to an unsophisticated approach to heterogeneous data [1], has become less common as programs and presentations have improved, and with increasing numbers of statisticians collaborating in developing methodology. It will be important that these lessons are not relearned as physicians obtain access to facilities making analysis easy as interpretation will still need skill and common sense.

Mathematical techniques needing the calculating power or the manipulative facilities of a computer can now also be used in the management of individuals. Data collected from patients at intervals have been traditionally recorded on flow sheets and sometimes as graphs. Mathematical transforms, for example, logarithms or reciprocals, are increasingly used to present curvilinear trends as a series of points that can be analyzed as linear trends [2-7] and mathematical modeling to assist in monitoring such trends to predict future events and to help make decisions; they are becoming a routine part of care in a few units. The papers by Farrell and his colleagues, by Morgan

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and Will, and by our group are all concerned with different aspects of the increasing use of mathematics, which is usually very simple in application, if sometimes complex to be fully understood.

The observation that mathematical rules do work, even in sick people, establishes that many of the events in the human body take place in a predictable way, otherwise they could not be easily described mathematically. In patients the measurements used as a monitor of progress alter as a result of changes in one or more of the control systems which influence them, and also as a result of other factors that can influence or modify the measurements. Some physicians were surprised when a complex summated series of events, such as those associated with the development of renal failure in glomerulonephritis, could be associated with mathematically predictable changes in plasma creatinine and could be mathematically described and modeled. The multiple events proceeding are, however, at a basic level of physical and chemical processes and so, if this is remembered, it is less surprising that biological events, even in disease, can be described mathematically. We can anticipate more disease states that are capable of being mathematically described as methods of measurement improve and as new methods are introduced to analyze and identify the systematic and random noise which has so often limited interpretation [6, 7].

In experimental physics progress was made in steps, with physics and mathematics varying as to which achieved the next step forward in knowledge. Clinical nephrology could be approaching a similar relationship with mathematics with the outlook for collaborations between those whose skills are mathematical and those that are biological. An example of this integration of the biological and the mathematical is the evolution of thought about the pathophysiology of renal failure. Nephrological thinking has had to incorporate observations showing that the majority of patients progress into renal failure in a predictable way, usually either as a hyperbole or as an exponential, when renal function is considered against time. This observation contributed in a major way to the current interest in whether a metabolic or physical process, common to many or even all patients with chronic progressive renal failure, is responsible for much of the deterioration in function preceding and resulting in endstage renal failure. A mechanism common to all might account for the mathematically organized progression seen in such patients despite diverse initial pathologies. In some such examples one of the mathematical transforms found to describe the progression, that to the reciprocal, was chosen on the basis of known physiology [C = UV/P, and therefore C \(\alpha\) 1/P, leading to the plotting of 1/P when using plasma creatinine to study the behavior of clearance over a period of time]. The linear progression, when the reciprocal was plotted against time, suggesting that nephron loss is at a fixed rate, could not have been anticipated from known facts, but it was an unexpected bonus of using the physiologically correct transform when considering data. Much thought is now being given to explain the observation, and new therapeutic approaches may result. Similar methods of studying sequential changes in plasma creatinine after renal transplantation [8], and in acute renal failure, lead us to suggest that some pathophysiological aspects of the events merit more study than they often get, and that some theories about mechanisms are probably incorrect. In particular the very sudden transitions from deterioration to improvement seen with allograft rejection, when creatinine is plotted using an appropriate transform, suggest a much more cataclysmic event than conventional methods of presenting data had suggested. It seems likely from these observations that there could be a large vascular component to the functional changes. Prognosis after renal allograft rejection may, as in the renal damage associated with eclampsia, be related to the severity of this vascular component as much or more than to the severity of the immunological assault. Perhaps progressive renal impairment after rejections should be compared to the progressive renal impairment seen after partial bilateral cortical necrosis in eclampsia, with progression and further glomerular sclerosis long after the cataclysmic event which marked the onset of renal failure.

Another example of when current pathophysiological thinking about a process, such as renal osteodystrophy, does not explain mathematical observations is provided by plots of alkaline phosphate results against time in patients on therapy. There are hyperbolic or exponential curves of improvement in many patients during the treatment of osteodystrophy. This observation, made by physicians using simple mathematics to observe day-to-day change in patients under their care, could not have been anticipated from known physiology [8]. An obligation now exists for those concerned with bone pathophysiology to explain the observations and also to explain why it is some and not all patients whose blood levels of bone enzymes change in such an orderly manner.

There are other patterns of change that can be described mathematically, some of which should be obvious, such as the rhythmic oscillations in most physiological states. The most obvious of these oscillations are the short ultradian rhythms of heart rate and brain activity; the possible relevance to the nephrologist of analyses of electroencephalographic waves is considered in this symposium by Bourne and his colleagues. Circadian and other rhythms, both longer and shorter, have been topics of interest for a few individuals for years, but the general availability of computers and the development of established methodologies for analysis should make it easier for doctors to consider these more when studying clinical problems whether of a diagnostic or treatment nature; the clinical relevance of these interesting phenomena will be increasingly recognized.

It was clear at the Nottingham symposium that the computer had established itself in several renal units as a new and useful tool that was resolving old problems but also finding new questions. Similar conclusions were reached by those attending meetings in the United States and elsewhere. A beginning has been made to answer some of these questions. Answers may arrive by the use of computer techniques, the more traditional methods, or by using other methodology yet to be described. The nephrologist who should be a numerate technologist as well as a physiologist and physician may well be the person to coordinate the elucidation of old and new problems using both established and newer technologies.

The renal patient will always need care, but now care includes an increasing role for the computer. The doctor's own personal computer, his neurological system, will still correctly compute a useful proportion of the problems, while many other problems will be better considered with the help of an appropriate computer system and with or without some of the
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Summary. The potential of computing and mathematics to make major contributions to nephrology by making information retrieval and presentation more accurate, more complete, and more rapid and by providing immediate access to computational and graphic facilities is emphasized in this symposium issue. The realization that disordered physiology due to disease may not prevent the course of an illness being described in mathematical terms should encourage physicians, and others interested in pathophysiology, to integrate mathematics and statistics into their thinking and their practice.

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