Diagnosis in Renal Disease—II*

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Advances in Clinical Taxonomy

Physicians entrusted with the care of patients have many reasons for being conservative, and our attitude to major innovations may at times have been overly cautious. I am not aware of any unseemly haste among nephrologists to grasp the opportunities which, as I believe, are becoming available to us through developments in data-processing and in computation. If this is a correct assessment we are lagging behind our colleagues in epidemiology and in social medicine, and also in the clinical laboratory. Certainly, epidemiological and other numerical data lend themselves more obviously to storage and analysis, and clinical interest in data-processing has been very largely limited to the codification and storage of past records. I would not wish to undervalue this activity, but in most clinical situations I confess to finding the oral history and present state of the patient more useful in diagnosis than are the records of past illness, as seen through the diagnostic spectacles of an earlier day. Things will become better as the codification of clinical data progresses and also as we develop better access terminals to stored data—the second being very important, lest we find ourselves with the rhetorical question, “For the purpose of making records inaccessible do we really need computers when we already have microfilm?”

The idea that computers can “replace doctors” in diagnosis seems to me a Luddite bogey. If other technical innovations in medicine are any guide, more doctors and other trained staff will be needed, the dividend being seen in greater accuracy rather than in any saving of manpower; and I would be the first to deprecate the idea that a patient's first encounter in the outpatient clinic should be with a complicated questionnaire. This for two reasons. Firstly, criticism of “impersonality in hospitals” will not be dissipated by form-filling, and the patient coming to hospital expects to see a doctor and not a machine. Secondly, though it is foolish to deny almost any future possibility, I cannot for a long time ahead envisage the emergence of a practical computer-based *general* diagnostic programme. A prerequisite for this would be an analysis of the entire diagnostic process in mathematically operational terms. At present we cannot be certain of the structure of the diagnostic process, ideally perhaps a branching system of logical elimination of possibilities, but more often in practice an apparently intuitive exercise in pattern recognition, in which—Jourdain-like—we apply the “new mathematics” of sets without being aware of it. Nor is it certain that the mathematical techniques yet exist for handling the range of discriminants required for a general diagnostic approach.

Once the nature of the clinical problem has been defined, however, we enter what McGirr (1969) has called a “sheltered situation,” in which computer-diagnosis is feasible. When our general inquiry has made us confident that the patient's main trouble stems from the kidneys, we are in one type of defined situation, though what remains is still far from simple. The task which remains is, in essence, to elaborate a picture of the patient's illness, to review the current stereotypes of renal diseases, and to allocate the patient to the most appropriate available class, or “disease.”

It is my belief that the collection of data, the stereotypes of disease and the allocation process can all be improved by present and future techniques of data-processing and computation.

Collection of Data

It is difficult, perhaps impossible, to take a history without at the same time trying to interpret it; under pressure of time a short-cut interpretation may make us omit essential facts whose relevance is not at the time apparent. A structured interview or a form for general diagnosis is a manifest impossibility; but within a defined area a form is a valuable safeguard against sins of omission. It is significant that on the one hand well-designed clinical research generally includes a form, and on the other hand the retrospective survey of ordinary clinical notes reveals so many gaps. The design of a good form takes a lot of time, but this is nothing to the frustration and error which can arise from the lack of a system in recording. The form should be filled in by the doctor, and not by the patient. If digital analysis is ultimately to be undertaken, symptoms and signs should be scored at the time, when the patient can be referred to, and not in retrospect from a verbal description. Systematic note-taking is of course no new thing, but perhaps we now have the additional responsibility of recording our observations in such a way as to make later quantitation easier, and not preclude it. (As an aside, why cannot quantitation be brought into some of the anatomical distinctions which we believe important? Could the description “membranous” not be enriched by a measure of thickness, allowance having been made for tangential cutting? Or the description “proliferative” by a cell-count?)

Stereotypes of Disease

Textbook descriptions of diseases are no doubt based on observed brute facts, but they also contain a large element of subjective construct, both in the recall of experience and in its presentation. Without opening the large general question of the sense in which “diseases” exist at all, we can perhaps assert that even for the pragmatic purposes of operational medicine our patterns of disease are biased by selection, whether conscious or unconscious—for example, the contrast between clinical diabetes and hyperglycaemia as revealed by surveys—by undue emphasis on the unusual striking clinical experience, and by secular modifications in diseases themselves, so that an obsolete pattern may become set in an authoritarian description. Our concepts of diseases and syndromes should be constantly open to renewed appraisal in the light of new observations. This process can be facilitated only by ongoing analysis of new data by the most developed methods, so that, for example, our notion of the incidence of various organisms in urinary infections may indicate local and contemporary experience rather than reflect an authoritative analysis made far off and long ago. This simple example is clearly well within the scope of manual data-processing, but computerized data open the possibility of multiple correlations some possibly unsuspected.

In addition to refining established stereotypes, and maintaining their relevance to current diseases, I believe that computerized data could assist the recognition of new syn-

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dromes. Since computers cannot yet explain themselves, perhaps I may again be allowed to use a simple example, illustrated in Fig. 1. In the universe of acute illnesses some will be due to streptococcal infection. A large number of these will show none of the conventional features of acute glomerulonephritis—haematuria, hypertension, and oedema; but some will show one or more of these features, and some will show all three. This last group shows the syndrome of post-streptococcal acute glomerulonephritis. It was, however, noted that some patients with the cardinal features of acute glomerulonephritis had no evidence, clinical or serological, of preceding streptococcal infection of throat or skin. This is in essence a group which possesses the four indicants†—*acute illness*, *haematuria*, *hypertension*, and *oedema*—but lacks the fifth indicant—*recent streptococcal infection*. Mental comparison of five indicants is simple; but a computer allows a similar operation to be carried out with 20 indicants or more. There is perhaps no more here in principle than a search of Hollerith cards, but the speed of the operation, when computerized, raises it to a new dimension of practicality.

FIG. 1.—For explanation, see text.

In what way could this establish new syndromes? Clearly, the recognition that some patients lack one of a group of 20 indicants does not itself establish a syndrome; but the recognition of exceptions is the first prerequisite of a more intensive scrutiny, which might then reveal further indicants. To return to the example, some patients with non-streptococcal “nephritis” are found to show the additional features of haemoptysis and very low serum iron, defining the syndrome known to nephrologists as lung purpura with nephritis (Rusby and Wilson, 1961), to chest physicians as one variety of idiopathic pulmonary haemosiderosis, and to those who have not read the original description as Goodpasture’s (1919) syndrome.

Allocation Process

A good deal of attention has justifiably been paid both to the recording of clinical data and to the evolution of disease patterns; a somewhat extended review is given by Feinstein (1967). Somewhat less attention has been paid to the operation of comparing these two categories of information, perhaps because the daunting effort of analysing the diagnostic process has been evaded or discouraged by labelling it “intuitive.” My own interest in the problem was first aroused by Card

†An indicant may be any symptom, sign, or other character of a patient in an episode of illness, but is distinguished from “ordinary” characters by its diagnostic relevance (which may, of course, be manifest only in retrospect). Card and Good (1970) define an indicant as “any piece of evidence that might be relevant to the probability that a disease is present.”

(1967)—careful though he is to stress the magnitude of what has yet to be learnt both about the operations of diagnosis and the mathematical techniques which might make them susceptible to computation, with its mechanical advantages of accuracy, speed, and tirelessness.

The operation of making a diagnosis may not be too different from what we have just outlined as the mode of search for a new syndrome; we are again concerned with significant intersection of “sets”—that is, individuals who share a particular character. Boolean algebra is concerned with the manipulation of sets, and when the number of sets is large the simplicity of the basic principles becomes overlaid by the complexity of the necessary mathematical operations. The path through a Boolean lattice (Fig. 2) becomes harder as the number of subsets increases, and the speed and accuracy of a computer become necessary. One current controversy in the discriminant analysis of disease is the attention which should be paid to “prior probability”—that is, such information as is available on the relative incidence of the conditions being considered. In the Bayesian approach more weight is given to prior probability, whereas in the method of “relative likelihood” (Boyle *et al.*, 1966) weighting is based on the observed frequency of indicants in the diseases under study, and not on the reputed frequency of the diseases themselves. In the work on thyroid the method which neglected prior probability gave more accurate results. When one takes into account the fallacies inherent in estimates of incidence, and the different populations served by the family doctor, the general physician, and the nephrologist, the apparent inferiority of the Bayesian method seems understandable.

FIG. 2.—Representation of (part of) a Boolean lattice, made up of subsets containing the elements A, B, C and D, and arranged in such a way that each row of subsets contains one element more than that below it. The lowest row, whose members each contain only one element, could represent alternative presenting symptoms of the complex “ABCD.” The thicker lines indicate alternative paths through the lattice, one starting from “A” and two from “D.” The starting point could, of course, be a combination of two symptoms—for example, “AB” in the left-hand path. That this lattice is only part of a larger one is indicated by the dotted portion of the diagram, which introduces a further element “E.” A complete lattice incorporating E as well as ABCD would of course be more complex than the ABCD lattice displayed here in full. Stored information on the relative frequencies of ABC, ABD, ACD, and BCD could facilitate search for the next step in the lattice, once one of the combinations of two elements had been reached.

Card and Good (1970) distinguish a number of steps in the diagnostic process. Given some knowledge of what diseases are prevalent, the steps become (a) singling out the next facet (facet is defined as “a set of mutually exclusive indicants which might be either atomic or compound—e.g., the tem-

perature or the type of sputum"); (b) estimation of the initial probabilities; (c) evaluation of the likelihoods; (d) calculation of the intermediate probabilities, during movement through the search tree; (e) deciding on whether to elicit further indicants; and (f) choice of final diagnosis.

It may be noted that this scheme *does* include an assessment of initial probability (step b), but it is not given the weighting of the Bayesian approach. The number of steps may seem large, and even incongruous with an introspective survey of "making a diagnosis." But the breakdown is the consequence of a search for operations which are mathematically possible. As Card (1967) pointed out, a successful calculus of medicine could give information on prognosis and on management just as much as on diagnosis. It would also be possible to incorporate a bias towards treatments which were practicable as well as effective.

Consultative Programmes

There are limited areas of medicine—for example, acid-base problems—in which quantitative information is obtainable, but in which errors of interpretation can readily arise, it may even be from overlooking one of a number of possibilities. In such areas computer programmes prepared by experts in the field can take the place of textbooks, and possibly improve on them, in that a good programme responds to questioning, whereas in a textbook the required information often seems to bury itself unseen in a closely printed page. Bleich (1969) described the computer evaluation of acid-base disorders; and through the kindness of Dr. Roy Maffly I have recently had the opportunity of access in Stanford to a programme prepared by Dr. W. B. Schwartz in Boston. An excerpt from our "conversation" (see Appendix) perhaps displays the ability of a good programme to detect mistakes, and to bring up possibilities which might not leap to every mind. I do not, of course, know how much effort went into the compilation of this programme, but I am sure it was considerable; and to cover larger, and less quantitative, areas of medicine in this way would not be possible.

Having claimed a place, at least in the future, for the computer in practical diagnosis, I should perhaps end by recapitulating what I see as limitations, but others may see as safeguards. Firstly, the techniques of the questionnaire and computer cannot themselves constitute the initial approach to the patient; only when his medical situation has been defined in general terms may limited programmes of data-recording and data-processing come into operation. Then "on-line" dialogues with computer programmes prepared by experts may be undertaken in defined areas, but the generality of such programmes is clearly limited by the narrowness of expertise itself. Finally, just as with radiological and biochemical apparatus, what the computer largely offers is manipulative skill of a new order; it cannot replace pattern recognition by our private intracranial assortative devices. Perhaps it never will; but to explore its potentialities is not to abdicate our responsibilities as doctors, but to seek to strengthen our skills, in the cause of more accurate, consistent, and detailed diagnosis and treatment.

I am indebted to Professor W. I. Card for discussion and comment on the section relating to clinical taxonomy.

Appendix. Excerpt from "Conversation" with a Programme on Acid-Base

TO ACTIVATE THIS PROGRAM A CO₂ CONTENT OF LESS THAN 25 M.MOLES L MUST BE ENTERED.
TOTAL CO₂ (OR CO₂ CONTENT) M.MOLES L 19
PH, PLEASE 8.0
THIS IS OUTSIDE THE RANGE USUALLY ENCOUNTERED CLINICALLY AND MAY REPRESENT A LABORATORY ERROR IF THE VALUE IS CONFIRMED THE PROGRAM WILL CONTINUE IF IT IS NOT CONFIRMED IT WILL RETURN TO THE FIRST STEP.
PH 8.0 TOTAL CO₂ PCO₂
(M.MOLES L) (MM.HG)
8.00 15.0
THIS PCO₂ IS LOWER THAN THAT OBTAINABLE WITH MAXIMAL HYPERVENTILATION. THEREFORE, A MISTAKE MUST HAVE BEEN MADE IN THE PH OR TOTAL CO₂ DETERMINATION. THE PROGRAM WILL RETURN TO THE FIRST STEP.
TOTAL CO₂ (OR CO₂ CONTENT) M.MOLES L 19
PH, PLEASE 7.3
PH 7.3 TOTAL CO₂ PCO₂
(M.MOLES L) (MM.HG)
7.30 12.0
THE PCO₂ IS HIGHER THAN ONE WOULD EXPECT FOR THIS DEGREE OF METABOLIC ACIDOSIS (AS DETERMINED BY THE FALL IN TOTAL CO₂) AND RAISES THE POSSIBILITY OF A SUPERIMPOSED PULMONARY PROBLEM INTERFERING WITH THE PATIENT'S ABILITY TO VENTILATE PROPERLY. APPROPRIATE PULMONARY EVALUATION SHOULD BE UNDERTAKEN.
SERUM SODIUM, MEQ L (NORMAL 138-142) N 140. CHLORIDE, MEQ L (NORMAL 100-110) C 100.
ANION GAP (NORMAL 7 to 12) IS 21
METABOLIC ACIDOSIS WITH AN INCREASED ANION GAP IS SEEN IN:
1-DIAZETIC KETOACIDOSIS
2-SALICYLATE POISONING
3-ETHYLENE GLYCOL POISONING
4-METHYL ALCOHOL POISONING
5-PARALDEHYDE (RARELY)
6-LACTIC ACIDOSIS
7-RENAL FAILURE
IT IS NOT UNCOMMON TO FIND MORE THAN ONE SOURCE FOR A METABOLIC ACIDOSIS WITH A WIDENED ANION GAP IN THE SAME PATIENT.
TYPE THE APPROPRIATE NUMBER IF YOU WISH:
0-NO LOGIC STATEMENT
1-LOGIC STATEMENT ALONE
2-LOGIC STATEMENT AND REFERENCES
3-REFERENCES ALONE L 3
REFERENCES
1. REIMAN, A. S. RENAL ACIDOSIS AND RENAL EXCRETION OF ACID IN HEALTH AND DISEASE. IN DOCK AND SHAPIRO (EDS): ADVANCES IN INTERNAL MEDICINE CHICAGO, YEARBOOK PUBLISHERS, INC., 1964, P295.
2. SCHWARTZ, W. B. IN BEESON AND MCDERMOTT (EDS): TEXTBOOK OF MEDICINE 12TH EDITION, P764.
BLOOD SUGAR, MGS% (NORMAL 80-120) B 100
SERUM KETONES, TITER (INVERSE OF DILUTION) (NORMAL 0) K 0
SALICYLATE LEVEL, MGS% (NORMAL 0) S 0
CREATININE, MGS% (NORMAL 0.4-1.2) G 4
MG% 100% ARE NORMAL OR BELOW THE LEVELS ASSOCIATED WITH ACIDOSIS. ALTHOUGH THERE IS RENAL INSUFFICIENCY, IT IS NOT OF THE MAGNITUDE ASSOCIATED WITH THIS DEGREE OF METABOLIC ACIDOSIS. OTHER SOURCES THEREFORE, SHOULD BE SOUGHT.
SINCE KETONES (0), SALICYLATE LEVEL (0.0 MGS 100ML), AND CREATININE (4.0 MGS 100ML) ARE NORMAL OR BELOW THE LEVELS ASSOCIATED WITH ACIDOSIS, LACTIC ACIDOSIS OR TOXIN INGESTION (METHYL ALCOHOL, ETHYLENE GLYCOL, PARALDEHYDE) MUST BE RULED OUT. BLOOD LACTATE LEVELS AND REVIEW OF HISTORY ARE STRONGLY ADVISED.
IF YOU NOW DESIRE THE LOGIC DISCUSSION ENTER: 4-FOR LOGIC STATEMENT, 5-FOR LOGIC STATEMENT & REFS. 6-REFS. ALONE. 7-NO FURTHER INFORMATION L-7.

REFERENCES

- Bates, R. C., Jennings, R. B., and Earle, D. P. (1957). *American Journal of Medicine*, **23**, 510.
Black, D. A. K. (1960). *British Medical Journal*, **1**, 667.
Black, D. A. K. (1970). *Scientific Basis of Medicine. Annual Reviews*. In press.
Bleich, H. L. (1969). *Journal of Clinical Investigation*, **48**, 1689.
Boyle, J. A., et al. (1966). *Quarterly Journal of Medicine*, **35**, 565.
Burch, G. E., Chu, K. C., Colcolough, H. L., and Sohal, R. S. (1969). *American Journal of Medicine*, **47**, 36.
Burch, G. E., and Colcolough, H. L. (1969). *Annals of Internal Medicine*, **71**, 963.
Burkholder, P. M. (1968). In *Structural Basis of Renal Disease*, edited by E. L. Becker, p. 197. New York, Hoeber.
Caravano, R. (editor) (1968). *Symposium on the Present State of Research on Group A Streptococcus*. Amsterdam, Excerpta Medica.
Card, W. I. (1967). *Medical Annual*, p. 9.
Card, W. I., and Good, I. J. (1970). A mathematical theory of the diagnostic process. In preparation.
Ellis, A. (1942). *Lancet*, **1**, 34, 72.
Feinstein, A. R. (1967). *Clinical Judgement*. Baltimore, Williams and Wilkins.
Glynn, L. E. (1969). In *Clinical Aspects of Immunology*, edited by P. G. H. Gell, and R. R. A. Coombs. Oxford, Blackwell Scientific Publications.
Goodpasture, E. W. (1919). *American Journal of the Medical Sciences*, **158**, 863.
Hodson, C. J. (1968). In *Renal Disease*, edited by D. A. K. Black, p. 136. Oxford, Blackwell Scientific Publications.
Lewis, A. A. G. and Wolstenholme, G. E. W. (editors). (1954). *CIBA Foundation Symposium The Kidney*. London, Churchill.
McCarty, M. (editor) (1954). In *Streptococcal Infections*, p. 130. New York, Columbia University Press.
McGirr, E. M. (1969). In *Computers in Medicine*, edited by J. Rose, p. 19. London, Churchill.
Muehrcke, R., and Pirani, C. L. (1968). In *Renal Disease*, edited by D. A. K. Black, p. 170. Oxford, Blackwell Scientific Publications.
O'Grady, F., and Brumfitt, W. (1968). *Urinary Tract Infection*. London, Oxford University Press.
Platt, R. (1959). *Lancet*, **1**, 159.
Rusby, N. L., and Wilson, C. (1961). *Quarterly Journal of Medicine*, **29**, 501.
White, P. D. (1944). *Heart Disease*, 3rd ed., p. 259. New York, Macmillan.
Wolstenholme, G. E. W., and Cameron, M. P. (1961). *CIBA Symposium Renal Biopsy: Clinical and Pathological Significance*. London, Churchill.
Wrong, O., and Davies, H. E. F. (1959). *Quarterly Journal of Medicine*, **28**, 259.