Biological and social systems are inherently complex, so it is hardly surprising that few if any human illnesses can be said to have a single "cause" or "cure." This article applies the principles introduced in the introductory article in this series to three specific clinical areas: the control of blood glucose levels in diabetes, the management of diagnostic uncertainty, and health promotion.

A complex adaptive system is a collection of individual agents with freedom to act in ways that are not always totally predictable, and whose actions are interconnected so that the action of one part changes the context for other agents. In relation to human health and illness there are several levels of such systems.

- The human body is composed of multiple interacting and self regulating physiological systems including biochemical and neuroendocrine feedback loops
- The behaviour of any individual is determined partly by an internal set of rules based on past experience and partly by unique and adaptive responses to new stimuli from the environment
- The web of relationships in which individuals exist contains many varied and powerful determinants of their beliefs, expectations, and behaviour
- Individuals and their immediate social relationships are further embedded within wider social, political, and cultural systems which can influence outcomes in entirely novel and unpredictable ways
- All these interacting systems are dynamic and fluid
- A small change in one part of this web of interacting systems may lead to a much larger change in another part through amplification effects.

For all these reasons neither illness nor human behaviour is predictable and neither can safely be "modelled" in a simple cause and effect system. The human body is not a machine and its malfunctioning cannot be adequately analysed by breaking the system down into its component parts and considering each in isolation. Despite this fact, cause and effect modelling underpins
much of the problem solving we attempt in clinical encounters; this perhaps explains why we so often fail.

### Summary points

| Human beings can be viewed as composed of and operating within multiple interacting and self adjusting systems (including biochemical, cellular, physiological, psychological, and social systems) |
| Illness arises from dynamic interaction within and between these systems, not from failure of a single component |
| Health can only be maintained (or re-established) through a holistic approach that accepts unpredictability and builds on subtle emergent forces within the overall system |
| Three examples of complex situations (glycaemic control in diabetes, uncertainty in clinical diagnosis, and health promotion) illustrate that these principles can provide the key to practical solutions in clinical care |

### Glycaemic control in diabetes

Figure 1 shows a page from the diary of a man with type 1 diabetes. It includes biomedical details (blood glucose concentrations, insulin doses given), physiological inputs (meals and snacks) and outputs (exercise), social events (a party), pathological states (vomiting), and clinical encounters with health professionals (an appointment with his general practitioner and a phone call to the nurse). It gives a flavour of the complex interplay between physiology and behaviour and of the huge distance between the health professional in the clinic and the patient's experience of day to day control of his blood glucose. Even though this record is more detailed than most, it is still a woefully incomplete source of data from which to attempt to predict the course of the patient's blood glucose level and to advise on insulin dosage or dietary modification.

The physiological variation of blood glucose levels has been generally assumed to be linear, but in fact there is a chaotic non-linear and unpredictable component in the profiles of both diabetic and non-diabetic individuals. Such chaotic dynamics is common in other physiological systems. One researcher used a neural network (adaptive software system) to study the detailed profile of a patient closely monitored for two years. An attempt to predict glucose values on the basis of past patterns was successful for the first 15 days but thereafter failed, and the model needed reconstructing. Predictability could not be maintained without continual feedback of the most recent
data to retrain the neural network on a weekly basis because the statistical properties of the profile were highly variable. Complexity is a fact of life for many patients with diabetes, who are aware that their profiles may be unpredictable over a matter of hours and can become frankly chaotic at times of intercurrent illness. Standard advice often erroneously assumes that key factors in the equation (for example, the amount of injected insulin needed to bring the glucose concentration down by a given amount) are constants (a common conjecture in linear models; actually they are variables6), and that the adjustment of a single variable (usually insulin) is the best way to "fix" the glucose concentration.8

### Key points in applying complexity theory to diabetes

- The blood glucose profile discussed in the clinic is at best a small slice of historical data through multiple interacting systems whose predictive properties tend to change over a period of about two weeks

- Complex systems frequently produce fluctuations that are often explicable only at the level of the whole system. It may therefore be better to work within broad boundaries of "good enough control" rather than adjusting insulin doses impulsively from day to day in response to serial blood glucose measurements

- Patients whose diabetes shows a chaotic tendency in whom similar starting conditions produce widely varying outcomes will find simplistic cause and effect explanations of their profiles particularly unhelpful; "chasing the tail" approaches to insulin adjustments may increase rather than decrease glycaemic instability

- In the future, tight glycaemic control may be achieved by adjusting several variables in orchestrated fashion using a neural network software system. Such systems will require frequent feedback of emerging results, to allow them to respond adaptively to changes in the system's overall properties in a way which mimics the intuitive decision making skills of a patient with tightly controlled diabetes.

Such approximations lead to superficially plausible explanations and predictions of the general format "I see that your morning glucose level was X the day after you did Y the night before," but the model underpinning these statements may be a poor reflection of the real world of everyday glucose variation. The use of linear "sliding scale" insulin regimens beloved of inexperienced junior doctors generally leads not to improved glycaemic control but, in hospital inpatients, to a threefold increase in hyperglycaemic oscillations.9 Similarly, advice to outpatients based on a set of linear assumptions is particularly likely to fail in those whose diabetes is prone to chaotic behaviour, in whom similar starting conditions may lead to widely differing glucose profiles.

A complex adaptive system is often characterised by the presence of an "attractor," which defines the context of its behaviour within broad limits.2 For instance, the body contains a number of mechanisms that interact to allow the core temperature to remain within a specific range. The actual
temperature may vary in a fairly regular but non-linear pattern for a number of reasons sleep, exercise, drinking iced water but if the temperature control mechanisms are working they will keep the body within a narrow "normal" range. However, there are conditions, such as swimming the Channel or when pyrogens are released in infection, when the thermostatic mechanisms cannot maintain body temperature within the range set. These states, described as "far from equilibrium," allow an alternative attractor to define a new context for the system in this example a new temperature range and potentially a new pattern for temperature fluctuation.10

| Some principles to assist decision making in the complex zone (adapted from Zimmerman et al15) |
| Use intuition and muddle through Doctors frequently make what would be the best but not definitively the "right" decision on the basis of experience, evidence, and knowledge of the patient's story16 |
| Experiment Try different management options with patients, using an empirical trial of treatment13 or a plan-do-study-act cycle17 |
| Minimum specification Offer patients general goals, suggestions, and examples but do not attempt to work everything out for them your tidy solution is unlikely to be compatible with all aspects of their lifestyle and values |
| Chunking Instead of trying to sort out every problem, try solving one or two (using problem solving techniques, for instance18); other solutions may follow naturally once a new pattern has emerged |
| Use metaphors Communication can be difficult when issues are complex. Using metaphors can often create a shared understanding for example, "you seem like a tree bowed over by the wind" or "what does that last hypo remind you of?" |
| Provocative questions Ask questions that might throw light on basic assumptions, especially when the patient is "stuck" for example, "if you got better, might this cause some problems for you?" |

In the real world, patients must rely on recent blood glucose results and knowledge of the broad attractor properties of their own glycaemic profile combined with experience and intuition. Helping
patients to reflect on and refine their own intuitive judgments may be more beneficial than specific advice on today's or tomorrow's dosage schedule, since the principles on which this advice is based are likely no longer to apply within days. The DAFNE (dose adjustment for normal eating) randomised controlled trial compared traditional clinical care with a patient centred approach; this was introduced in an intensive residential course in which patients were encouraged to develop and draw on an intimate knowledge of their own profiles and body rhythms and to experiment with practical methods to respond to these variations. The residential group achieved, and sustained, levels of glycaemic control similar to the "tight control" group in the trial but without the risk of disabling hypoglycaemia.11

Managing uncertainty in the clinical encounter

Diagnostic uncertainty is common, particularly in primary care,12 and diagnostic agreement between clinicians is surprisingly poor, even over "hard" observable criteria.13 In the clinical encounter, and also in wider aspects of decision making in health care, we are often expected to produce a definitive answer in conditions of high uncertainty and low agreement. The certainty-agreement diagram (fig 2) can be used to estimate whether the issue is simple (high certainty, high agreement), chaotic (low certainty, low agreement), or complex (intermediate levels of one or both).

![Certainty-agreement diagram after Stacey14 and Zimmerman15](image)

In a patient with a problem, the levels of agreement and certainty can be mapped for the clinical findings, the relevant scientific knowledge base, and the patient's values and priorities. If these all fall into the simple zone for example, in an otherwise fit elderly patient with a fractured neck of femur who is keen to have surgery it is reasonable to use mechanistic management techniques (and, if they exist, evidence based guidelines). However, the relevant facts and values usually fall outside this zone for example, the child with eczema unresponsive to emollients whose estranged parents have conflicting views on the use of topical steroids and homoeopathy, or the patient with symptoms suggestive of early meningitis but without any definite signs.

Clinical judgment in these circumstances involves an irreducible element of factual uncertainty and relies to a greater or lesser extent on intuition and the interpretation of the wider history of the illness.16 In such cases uncritical adherence to rules, guidelines, or protocols may do more harm than good, and tools for dealing with complexity (originally developed in a management context) may be helpful (box). 2 14
Promoting health  the wider context

Individuals operate within networks of relationships and information sources that have a profound effect on their health choices, some of which are easily identifiable and fairly stable (for example, family, friends, colleagues) while others are more ambiguous or ephemeral (a newspaper health column, a trip to an alternative practitioner, the internet). The activities and influences of these networks are often hidden from the clinician—in other words, they serve as a "shadow system."^2

There is often a strong temptation to try to override or discredit the shadow system, but this approach ignores how tenacious and powerful its influence can be, and the fact that the patient cannot simply walk away from it. A more productive approach is to explore and map the shadow system and work alongside it. For example, it is now widely agreed that we should seek concordance with, not compliance from, patients in relation to taking their medication.^19

The growing literature on changing patients' behaviour in relation to lifestyle focuses on those who are "resistant to change." Complexity science suggests that "readiness to change" occurs when a system is in a state far from equilibrium; there is then sufficient tension to change.\(^20\)\(^21\) In such circumstances a small influence can have a large effect on behaviour—for example, brief advice apparently leads 2% of smokers to quit, while more intensive advice and discussion in the consultation has little additional impact.\(^22\)

Aiming for concordance in smoking cessation means working with system attractors that define the context for a patient (such as, does their partner smoke? do they smoke at home or at work? what is their daily intake? and so on). The attractor keeping them in the smoking context will be unique for any particular patient, as will be the new attractor that is most likely to change their system. Change literature emphasises the importance of providing alternatives that are compatible with the system to be changed.\(^23\) If the patient is already in a state far from equilibrium (for instance, a first pregnancy), offering a new attractor is likely to have a synergistic and powerful effect.

The effectiveness of interventions is highly dependent on the context in which health care is delivered.\(^2\) In relation to medication, for example, Balint felt that what mattered was "not only the medicine . . . or the pills . . . but the way the doctor gave them to the patient . . . in fact the whole atmosphere in which the drug was given."^24\) The placebo effect might be thought of as the patient's own complex system self adjusting from the old attractor (disease state), through the effect of a new attractor ("remembered wellness"), to the context of the body being fit.\(^25\) Using this analogy, the doctor or, more usually in health promotion these days, the nurse who negotiates lifestyle change is helping the patient discover the far from equilibrium conditions that encourage the system to change attractors and hence find a new context.

Conclusion

We all know from experience that the management of clinical problems is rarely simple. Yet most of us were taught about and tend to adopt a mental model of the human body as a machine and
illness as due to malfunction of its parts. Such linear models drive us to break down clinical care into ever smaller divisions and to express with great accuracy and precision the intervention to be undertaken for each malfunction.

Complexity science suggests an alternative model that illness (and health) result from complex, dynamic, and unique interactions between different components of the overall system. Effective clinical decision making requires a holistic approach that accepts unpredictability and builds on subtle emergent forces within the overall system. As the examples in this article have shown, complexity theory saves both clinician and patient from a futile quest for certainty and upholds the use of intuition and personal experience when general scientific rules are to be applied to the individual in context.

The next article in this series will apply the principles of complexity science to the organisation of health services, and the final article will explore its implications for education, research, and continuing professional development.

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References


5. Kroll MH. Biological variation of glucose and insulin includes a deterministic chaotic component. *Biosystems* 1999; 50: 189-201.[Medline]


12. Rosser WW. Approach to diagnosis by primary care clinicians and specialists: is there a difference? *J Fam Pract* 1996; 42: 139-144.[Medline]


