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APPLIED EVIDENCE

New research findings that are changing clinical practice

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Is your practice really that predictable? Nonlinearity principles in family medicine

These patient cases show "nonlinear" thinking better grasps complexities and handles the unexpected

Practice recommendations

- Heighten your awareness of nonlinear patient behaviors including sensitivity to minor changes, resistance to change, sudden dramatic change in behavior, and intermittent catastrophes.
- Nonlinearity means we should expect the unexpected but limit unpredictability through in-depth knowledge of patients and context.
- Reinforce positive attractors, use small well-timed interventions, and encourage healthy variability and nonlinearity.

Had Sir Isaac Newton attempted family medicine, he likely would have been uncomfortable with its nonlinear aspect typified by unpredictable disease courses and treatment responses.

Linearity forms the basis of our knowledge… Life in a Newtonian world is ordered and predictable, where causes are directly linked to effects and behavior is linear or cyclic (periodic). In this world, stability and predictability define a healthy system. Furthermore, by understanding the parts of a system, we understand the system. As physicians, we are trained to expect this linear, predictable, reductionistic view of health.

…but it does not reflect the human system. However, humans are complex adaptive systems, characterized by multiple interconnected and interdependent parts at levels from the microscopic to the community. Interactions change over time, producing synergistic nonlinear behavior as components periodically self-organize into functional groups.

TABLE 1 compares the Newtonian world view with that of complexity science. Although all of the characteristics of complexity science are relevant to family physicians, this article will focus on the nonlinear behavior of patients as the visible, unpredictable, and often frustrating manifestation of the complexity characteristics. **TABLE 2** defines specific characteristics of nonlinearity.

In understanding nonlinearity—as depicted in 4 patient cases presented here—family physicians can learn to

- expect the unexpected
- reduce unpredictability by learning about patients and their context
- attack patient resistance by seeking epiphanies or using positive attractors
- recognize the sensitivity of our patients' trajectories and use or anticipate it
- promote the healthy benefits of nonlinearity.

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TABLE 1

Basic tenets of Newtonian and complexity world views

CHARACTERISTIC	NEWTONIAN	COMPLEXITY
Cause-and-effect	Every effect has a clear cause	Events not always linked to a cause
Predictability	Predictable	Not predictable
Dynamics	Linear	Nonlinear
Whole vs parts	Whole equals sum of parts	Whole is not the sum of its parts
Adaptation to stress	Predictable, logical stress-reducing behaviors	Unpredictable, sometimes detrimental responses
Leveraging change	Predictable response to intervention	Multiple, well-timed interventions may be necessary

Nonlinearity as a truer model of health

Although our basic medical knowledge is built on a reductionistic approach that assumes linear dynamics, our models rarely account for more than 30% of whatever outcome we are investigating. Clinical providers are often faced with the unexpected.

Although linearity suggests that illness should respond in predictable ways regardless of the environment, family physicians know that context is critical. In addition, the human condition is often nonlinear; nonlinear dynamics (chaotic or random dynamics) have been documented in physiology,[1] psychology,[2,3] sociology,[4] business,[5–7] and economics.[8]

In fact, nonlinear dynamics are often a sign of health. For example, mood may vary in linear patterns among patients with affective disorders; therapy for mood disorders may work by changing the pathological linear dynamics in mood into more healthy nonlinear dynamics.[9] Linear (or periodic) dynamics often indicate a pathological condition.[10,11]

As science and medicine begin to embrace the nonlinearity of complexity science, we must anticipate, recognize, and apply nonlinearity to the care of our patients. This is particularly important for family physicians.

Applying nonlinearity to patient cases

The following cases demonstrate characteristics of nonlinear dynamics (**TABLE 2**).

Case 1: Sensitivity to initial conditions

I.C. is a 25-year-old teacher who is 6 weeks postpartum. Recently, while at a local shopping mall, she experienced a sudden onset of chest discomfort, palpitations, dizziness, trembling, and a sense of impending doom. The episode peaked in intensity within 3 minutes and lasted 20 minutes after leaving the mall. Although she has not experienced another attack, she has progressively limited her activities since, until now, she has not been able to bring herself to re-enter the mall for fear of another attack. In fact, she reports intense anxiety in anticipation of possibly visiting the mall and has begun limiting her driving in general.

Agoraphobia is linked to the location and interpretation of the first panic attack.[12] This demonstrates the concept of *sensitivity to initial conditions* whereby small differences in starting values result in very different behaviors later. In other words, apparently minor differences in a patient's initial physical and emotional state can translate into drastically different outcomes over time.

This emphasizes the need for physi-

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Nonlinear dynamics are often a sign of health; linear dynamics may indicate a pathological condition

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TABLE 2

Nonlinear characteristics relevant to family practice

CHARACTERISTIC	DEFINITION	CLINICAL EXAMPLE
Sensitivity to initial conditions	The phenomenon wherein a small change initially can send the system on a new trajectory, drastically changing the system's subsequent performance	Panic attack experienced without a perceived reason can lead to agoraphobia, whereas a similar but "explainable" attack may be perceived by the patient as merely annoying
Attractor	Set of values to which a system migrates over time. An attractor limits the range of possible behaviors of a system and prevents random activity, but does not dictate the specific path the system follows	Self-destructive behavior—eg, alcoholism—is governed partly by a learned set of beliefs and expectations (negative attractor) that limit a person's ability to make healthy choices. Treatment may be aided by substitution of a positive attractor—eg, well-being of family
Bifurcation	Sudden qualitative change in the behavior of a system as the system reaches a "tipping point"	Epiphanies, such as those realized in the decline of a relative who shares a disease, can provide leverage for change in behavior
Self-organized systems	System of tenuously linked parts at the edge of stability. Complex interrelationships among components produce a system in which a single event can result in a cascading effect due to the coupling of components	Detrimental self-organized behavior may manifest in a person's over-reaction to a minor stressor. Using multiple stress reducing techniques and encouraging connectedness with others can introduce healthy, chaotic variability

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Understand the details around stressors by asking patients about their perceptions of the events

cians to pay attention to detail during stressful events that patients experience. For example, if a patient experiences the first panic attack in a self-perceived "safe" environment or interprets the attack as a normal response, she may avoid the disabling consequence of agoraphobia and remain functional. There are other examples of this sensitivity to small changes, such as siblings of similar genetic make-up and environment who exhibit markedly different health as adults may do so because of "minor" life events each experienced.

Similarly, patients with chronic stable disease who, after a minor event, suddenly change their disease trajectory may be demonstrating sensitivity to initial conditions. This sensitivity has been proposed as an explanation for sudden infant death syndrome[13] (SIDS) and "brittle" diabetes.[14] Treatment response may depend on sensitivity to initial conditions; cases documenting placebo effects or unpredictable potassium excretion on readministration of potassium-sparing diuretics are examples.[15]

Implications for management. Sensitivity to initial conditions has several implications for patient management.

First, we need to recognize the impact it has on patients. Minor life changes can alter the trajectories of patients, so we need to seek the patient's perspective on stressors they experience. This inherent instability means that "watchful waiting" is a viable approach in some patients because illness may resolve without intervention. It also means that we need to be watchful for signs of an unhealthy trajectory developing in patients even after minor stressors.

Second, sensitivity to initial conditions implies that nonlinear behaviors can change with minor but well-timed interventions. The importance of chronotherapy (timed dosing based on biological rhythms) is receiving increasing attention. Drug efficacy often varies with the time of day.[16,17] Though focused on matching circadian rhythms, chronotherapy may be valuable in nonlinear systems if, through our in-depth knowledge of the patient and context, we can identify a point of leverage

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when an otherwise "ineffective" treatment may be effective for the patient at a specific point in time. There may be justification for re-administering a previously ineffective treatment if you believe the responsiveness of the patient may have changed. Sensitivity to initial conditions may also explain the effectiveness of placebos.

- *For the patient above,* minimizing the impact of sensitivity to initial conditions requires immediate access to the patient during a subsequent sensitive time. If the patient has a family history of panic disorder or has had panic attacks in the past, you could anticipate that the patient may experience a panic attack in the future and prepare her for it by discussing the chemical basis for panic (and its lack of serious physical consequences) and by encouraging her to contact you day-or-night immediately after experiencing one so that you can help her to identify a nonthreatening (even if illogical) cause for it, thus preventing the fears that lead to agoraphobia.
- *For the practitioner,* sensitivity to initial conditions emphasizes the need to understand the details surrounding a stressor by asking patients about their perceptions of the events, the circumstances, and how they are being affected by the stressor. Using this sensitivity for treatment implies focusing on the *timing* of interventions, and considering re-administration of treatments or even the use of placebos.

Case 2: Effects of attractors

A.T. is a 47-year-old factory worker with a 30-year history of alcohol consumption. His daily intake consisted of a case of beer until he quit 3 years ago. He has periodically suffered relapses consisting of 3 or 4 days of binge drinking followed by prolonged abstinence. Although his wife and 2 children are supportive of his efforts at abstinence, his son dramatically increased his alcohol consumption when his father stopped his daily consumption. In addition, his teenage daughter began experimenting with drugs 2 years ago.

Alcoholism serves as an *attractor,* controlling not only the patient's behavior, but the behavior of the family.[18] Attractors limit the range of possible behaviors and thereby resist or limit changes in a patient's course. Attractors may be internalized models or belief systems that lead to recurring patterns of behavior, even though sensitivity to initial conditions prevents one from predicting the specific path the system will follow; patterns are predictable, the path followed is not. The combination of attractors and sensitivity to initial conditions ensures nonlinearity.

Alcoholism is not the only example of a factor that molds behavior and resists change. Our lives are governed by repeating patterns of behavior. Lifestyle routines are deeply ingrained and resist change even for medically important reasons. These lifestyle patterns may be due to attractors and may explain the resistance to change that many of our diabetic patients exhibit. Similarly, dysfunctional families often display counterproductive patterns of behavior that are resistant to even the best counseling.

Implications for management. The presence of attractors suggests several implications for patient management.

First, we should anticipate resistance and not be frustrated when it occurs.

Second, we can attack the attractor itself,[19] by identifying another, more positive attractor in the patient's life and reinforcing it to diminish the negative attractor's impact. For example, instead of simply criticizing the inactive lifestyle ingrained in a hypercholesterolemic patient, we reinforce the positive attractor of the patient's affection for his grandchildren and use that attractor to get the patient to exercise.

For strongly negative attractors (eg, alcohol use), we could simply attack the attractor itself without providing an alternate attractor. Though this approach is more risky because of the unpredictability of what the patient will substitute, if the attractor is bad enough, we may be willing to allow the patient to choose any other attractor, assuming that it must be more positive than the original.

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Patterns are predictable; the path that will be followed is not

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Sudden dramatic changes can occur in a nonlinear system as it reaches a "tipping point"

• *For the patient above*, simply attacking the negative attractor may lead to other negative behaviors (eg, smoking). The best approach may be to focus on positive attractors (ie, wife, children, social relationships, hobbies), perhaps even positive attractors for the entire family, to move him or them away from the negative attractor.

• *For the practitioner,* it is imperative to identify the attractors producing recurrent detrimental behaviors that need to be changed. Using attractors for management means that potential positive attractors need to be identified through exploration with patients and reinforced while attacking the negative attractors currently producing the unhealthy behavior.

Case 3: Bifurcation effects

B.I. is a 50-year-old plumber who has had type 2 diabetes for more than 10 years. Though he has regularly seen his physician and taken his medications, his diabetes control has been poor (hemoglobin A_{1c}=10.2). He admits that compliance with his diet and exercise has been "spotty" at best. Six months ago, his older brother began dialysis for end-stage renal disease secondary to diabetes. Within 1 week of his brother's first dialysis session, B.I. began walking 30 minutes each night and eliminated evening snacks. Consequently, he has lost 22 pounds, and his hemoglobin A_{1c} has dropped to 8.1.

Sudden dramatic changes (*bifurcations*) can occur in nonlinear systems as the system reaches a "tipping point." In this case, chronic noncompliance suddenly changed to compliance after a meaningful event.[20] These bifurcations represent a qualitative change in behavior linked to a change in an attractor. Hence, epiphanies may represent behavioral bifurcations.[21] Such epiphanies are important in premature menopause[22] and initial family decisions to hospitalize a mentally ill relative.[23]

Bifurcations have been best documented in cardiovascular disease. Pulsus paradoxicus, pulsus alternans in congestive heart failure (CHF), and cardiac movement in tamponade reflect bifurcations in the system as minor changes cause the system to cross a "tipping point" and produce sudden drastic effects.[10] Similarly, bifurcations in heart rhythm are seen in sick sinus syndrome and ST-T alternans in ventricular tachycardia.[24] Paradoxical behavior of the PR interval[25] and the disastrous effect of the R-on-T phenomenon are other examples. However, bifurcation dynamics are also important in psychosocial behavior. Sudden drastic changes in mood have been documented in patients with generalized anxiety disorder.[26]

Implications for management.

• *For the patient above,* we can first look for events that could serve as epiphanies (eg, development of lung cancer in a relative of our tobacco-dependent patient) and use them to alter behavior. Many physicians already look for consequences of diabetes in friends and relatives to motivate their patients.

Second, we can help patients "brainstorm" several consequences of nonadherence and several benefits to control as a means of assisting them in identifying bifurcation points. In addition, detrimental behavior may diminish by moving it away from the bifurcation point; detrimental behavior may respond to the alteration of resource availability (eg, providing greater or lesser freedom to a patient in midlife crisis who exhibits sudden unhealthy lifestyle changes).

• *For the practitioner,* the existence of bifurcations implies that sudden unforeseen behavior should be expected and should not be a source of frustration. From a management perspective, drastic changes in patient behavior can be achieved by exploring patients' lives and recognizing and reinforcing epiphanies.

Case 4: Self-organized behavior

S.O. is a 40-year-old housewife with a long history of intermittent anxiety, usually in response to a family stressor. She presents with extreme apprehension and insomnia. On examination, she is

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restless and mildly tachycardic. Upon further questioning, she denies any recent adverse events but, in fact, reports that her husband recently received a promotion including a significant increase in salary. In reviewing her chart, you notice that you have diagnosed her with adjustment disorder with anxious mood on 3 previous occasions after adverse family stressors. However, her reactions have often been out-of-proportion to the level of stress and she has occasionally reported significant stressors (eg, death of a sister) without subsequent anxiety.

Neurologic systems tend to organize themselves in response to external events and internal models. These *self-organized systems* consist of tenuously linked parts at the edge of stability balanced between periodic and chaotic behavior. They react to stressors in patterned ways, but the magnitude of the reaction can vary from little or no response to a catastrophic reaction. Because such self-organization can be temporary, with groups periodically forming and dissolving, behavior over time is random without recurrent patterns.

With this patient, varying degrees of stress (even positive events) result in varying degrees of dysfunction with little relationship between the magnitude of stress and the magnitude of dysfunction. The periodic collapse in response to cumulative stress is not the only example of self-organized behavior.

Self-organization is believed to be critical in a variety of neuropsychiatric conditions from personality disorders[2] and conversion reactions to adult consequences of childhood adversity.[27] Patterns of detoxification in groups of alcoholics demonstrate self-organized behavior.[28] Self-organization is important to understanding self-regulation and behavior in families.[29,30] Even social interaction patterns among groups of patients on psychiatric wards show self-organized behavior as unstable groups form, dissolve, and reform.[31]

Implications for management. If nonlinearity indeed reflects health and helps to keep patients in good health, we should be promoting nonlinear behavior. Studies have shown that frequent small interventions can keep a system that is prone to periodic behavior in nonlinearity.[32,33] Similarly, because nonlinear systems can display a spectrum of behaviors from periodic-to-self-organized behavior-to-chaotic dynamics depending upon their resources and interconnectedness, social systems exhibiting periodic behavior may move into nonlinearity in response to increased resources and decreased restraints,[5] or to increased interconnectedness.[34]

Perhaps we can train systems to maximize their variability. For example, exercise programs that used variable intensities and durations may promote a cardiovascular system capable of responding to whatever stressor comes along.

- *For the patient above,* the self-organized behavior is detrimental, producing overreaction to stressors; a more chaotic mood pattern would minimize the impact of stressors. The best approach to achieve this may be to increase resources and decrease restraints. Thus, providing the patient with several ways of dealing with stress (ie, multiple treatment modalities including relaxation techniques, self-hypnosis, meditation, PRN anxiolytics) while promoting connectedness with others (ie, support groups, internet, church contacts, meditation) may increase chaotic variability.
- *For the practitioner,* self-organized behavior may explain the apparent random response to stress in patients. Such unstable behavior can be managed by providing multiple interventions simultaneously (ie, behavioral, pharmacological, social) or temporally (eg, frequent reinforcements of desired behavior) to encourage healthy nonlinearity.

Nonlinearity of primary versus specialty care

Do patients in primary care exhibit a different degree of nonlinearity than those seen in specialty care settings? Generally, yes. Mental illness, for instance, tends to be more severe among psychiatric patients than

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Unstable behavior can be managed by providing multiple interventions simultaneously

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among primary care patients,[35–37] and CHF is more severe among cardiology patients.[38]

Differences in severity of illness are important because, in some cases, the more severe the illness, the more periodic the dynamics.[9,39,40] Thus, the nonlinearity decreases as the severity increases. Because diseases exhibiting periodic dynamics should have a more predictable response to therapy, we would expect more severe illnesses to respond more predictably.[41] This pattern has indeed been observed. Prognosis and predictability of treatment response is related to severity of illness in CHF, acute myocardial infarction, depression, and agoraphobia.[38,42–47]

Thus, for both biomedical and psychosocial problems, predictability of treatment response correlates with the severity of illness. If patients seen in specialty settings have more severe disease, then we should expect that primary care patients exhibit more nonlinear behavior and are thus less predictable in their response.

Learning to see differently

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Expect the unexpected, seek epiphanies, use positive attractors

Though trained to approach medical problems looking through "linear lenses," we see nonlinear behavior all the time in our patients. If nonlinear processes represent health, then when systems are using healthy, nonlinear dynamics, they are resistant to disruptive external stressors. However, when such systems transition into periodicity due to illness, they may become predictable and more amenable to intervention, permitting physicians to treat them and hopefully restore the healthy, nonlinear dynamics.

Sensitivity to minor changes in their environment, resistance to change, sudden dramatic change in behavior, and intermittent collapses characterize behaviors in many patients. If we understand the nonlinear nature of these behaviors, we will be better able to help our patients.

Expect the unexpected, reduce unpredictability by learning about patients and their contexts, attack resistance by seeking epiphanies or using positive attractors, recognize the sensitivity of our patients' trajectories and use or anticipate it when possible, and promote the healthy benefits of nonlinearity. ■

CONFLICTS OF INTEREST

The author has no conflicts of interest to report.

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