CLINICAL TUNING: RHYTHMS, RESONANCE, AND HARMONY

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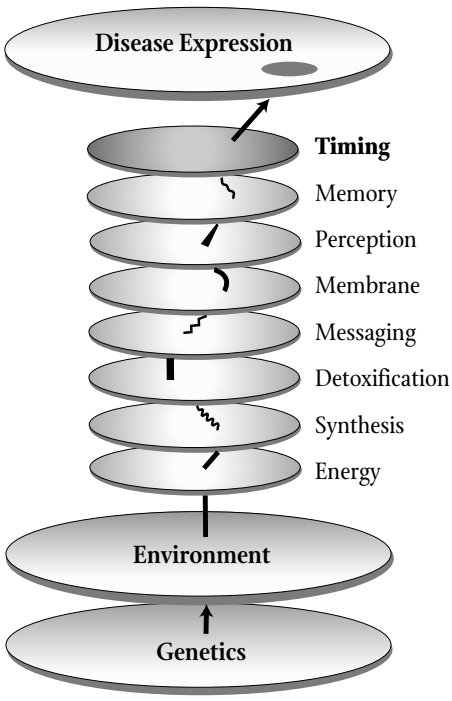
INDIVIDUALITY IN HEALTH AND DISEASE

The previous essays in this *Lenses* series describe clinical options for intervening with genetic and environmental influences that are expressed as illness. These essays have inventoried diagnostic and therapeutic approaches to treating chronically ill patients by considering ways to improve balance in the physiology of the following:

- Energy metabolism
- Anabolism
- Detoxification
- Molecular messaging
- Membranes and boundaries
- The unified neurology and immunology of perception and memory

The demands of ranking the importance of each of these fields of investigation are increased by their individual complexities and their mutual interplay. The difficulty of our clinical efforts is magnified enormously by the unavoidable fact of clinical life: *each patient is an individual*. And, as it turns out, the person who is sick enough to consult us is more likely than others to have a quirky imbalance as embodied in unmet special needs or sensitivities to allergens or toxins.



Individuality is the integrative medicine practitioner's special burden, in that we are patient-oriented, not disease-oriented. How much easier would be the life of a clinician who simply dispenses the average treatment for the average patient with the average depression, hypertension, inflammatory bowel disease, asthma, acne, or the rest of the list of disease entities that many of us were taught were the causes, not just the names, of symptoms?

BIOCHEMICALLY DIFFERENT, RHYTHMICALLY THE SAME

This essay, the last in the *Lenses* series, brings us to an issue that provides relief from the quandaries of individuality. It deals with an aspect in which we are all alike. Acknowledging integrative medicine's respect for individuality, it may be safer—and avoid semantic arguments—to say that "normal" is a statistical concept that can only loosely embrace a single person's biochemistry or immunology. Just as no individual patient is average, he or she is also not normal, except in a statistical sense. When it comes to the temporal domain, however, we are bound by rhythmic imperatives that command humans to heed the universal rules of harmony. We all dance to the same beat. Biochemically, we are all different, but rhythmically, we are all the same. In matters of rhythm, "normal" is not a statistical range, but rather a *relationship* embraced by the rules of harmony.

Let's start where this essay will finish—with the notion of tuning. Turn your radio dial just a tad to the left or right and you encounter a disagreeable noise and then lose the station. Turn it back, and you satisfy the condition for hearing the station, as your receiver resonates with the station's frequency. A satisfaction of a different kind comes in music when a dissonant chord is followed by a consonant chord. The consonant chord has a feature called harmony, which we can both feel and define in terms of the relationship among the frequencies of its composite oscillations.

Tuning, harmony, consonance, and dissonance are terms we apply to notions of vibration, oscillation, and waves. Resonance is a sympathetic vibration produced in response to oscillations in systems with the same natural frequency.

The Problem of Dyschronism

Do our physiological systems have natural frequencies that are of concern to physicians who may be interested in the "tuning" of their patients? Consider the familiar frequency of days. Except for individuals engaged in rapid transmeridianal travel, days come in one size: 24 hours. This is the beat to which we all must dance. The time patterns of sleeping, eating, and bowel movements—so called vegetative functions—indicate how well we are tuned to the 24-hour cycle of planet Earth, which establishes, for each of its inhabitants, an identical standard for normative synchronization. How many of our patients start out with irregularity in their vegetative functions?

Dietary requirements for calcium may vary by more than 200-fold. Sensitivity to mercury may vary by more than 1,000-fold. However, human requirements to keep in step with the planet are the same for all of us (as they are for all creatures whose need to live by the clock and the calendar is evident in their diurnal, nocturnal, and seasonal behavior). Sickness results from falling out of step. Losing the beat set by Earth's day-night cycles may result from external influences such as jet lag and shift work. Improper or proper timing of food, activity, or exposure to light may function as either cause or remedy for *dyschronism*—the technical term for being out of synchrony with the 24-hour cycle. Whether dyschronism is caused by recognized external or mysterious internal disruptors of synchrony, morning and evening exposure to full-spectrum light; morning consumption of protein and evening consumption of carbohydrates, and avoidance of light, food, and activity during night hours have remedial effects.[1]

Three Mile Island and Monday Night Football

On the other hand, abuse of such signals can produce harm, sometimes of dramatic proportion. In the disaster at Three Mile Island, operators were shift workers on a poorly designed schedule in which they rotated evening to day to night instead of the other way around. At 4:00 AM on the day of the disaster, the workers were at the least optimal time for swift thinking and were confused by being out of circadian synchrony. Disarray of the workers' physiological timing produced difficulties with the timing and sequence of turning dials or pushing buttons in the control room of their nuclear reactor, with historic consequences.[2]

Sequence is as important a reality in our physiology as timing. Our bodies do not perform all tasks simultaneously. Each task is compartmentalized in time. Each lowly, specific molecule—such as melatonin—has a specified interval for its production, just as the most exalted general functions, such as consciousness, do. Melatonin blood levels peak significantly soon after midnight. If melatonin production is suppressed—by night exposure to light, for example, melatonin production is not delayed—it is cancelled for that night, only to reappear at its scheduled time slot the next night. Consciousness is a daytime activity, so nighttime is a bad time for it, especially around 4:00 AM. At this time, an individual is 50% more likely to make an error, and early afternoon provides a second low point of dulled senses and cognitive efficiency. The times of day when most people are most conscious are around 8:00 AM and 6:00 PM. The peak for muscular performance is also around 6:00 PM—something to think about when you see Olympic figure-skating competitors performing at midnight.

Athletic performance is particularly susceptible to the effects of East-West travel. Athletes, whose performance is enhanced if they travel from West to East for night games, experience degraded performance if they travel from East to West. Before the start time of National Football League Monday night games was changed to 8:00 PM (from 9:00 PM) in the mid 1990s, East-coast players would begin playing at midnight on their internal clock, and could still be playing as late as 3:00 AM (the interval of lowest human athletic performance). West-coast teams traveling to the East-coast to play were playing at their internal-physiological-circadian optimum (6:00 PM) against players who were entering their zone of suboptimal performance at a game time of 9:00 PM. West-coast teams won more often and by more points than East-coast teams, and West-coast teams performed significantly better than the predicted Las Vegas point spread for each game.[3]

The time slots for the biochemical details that underlie performance peaks serve as a guide to the timing of administering supplements or drugs. Detoxification and regeneration are nighttime activities. The right time and sequence of medications to suppress, and then rescue, cell replication and detoxification make a critical difference in the outcome of cancer chemotherapy. Timing and sequence will achieve more importance in all therapies as more attention is paid to circadian chemistry as revealed by research. Meanwhile, clinicians can depend on feedback from patients with informative responses to a change in the timing of administering supplements. For example, I have a patient who had a dramatic response to methyl-B_{12} when she started her injections in the evening, after having a negligible effect from morning doses.

Menstrual Periodicity

Our ancestors internalized the lunar cycle as the 28-day menstrual cycle. A woman may "normally" be 50 or 70 inches tall, but no such range of normal can be attributed to a menstrual cycle. Exactly 28 days is normal. Period. If we knew how to reset a woman's irregular menstrual clock with measures as convenient as those available for correcting cir-

cadian dyschronism, we would be more inclined to make a fuss over a patient's departure from a 28-day cycle. As it stands, the best we can do is promote good rhythmic functioning in general, and expect that it will spill over to normalizing menstrual periodicity. I expect menstrual irregularity to repair itself as a response—if not a specific target—of improved health in my patients. Then again, efforts to synchronize circadian and other rhythms have mutual effects that tend to tune the body's whole harmonic system.

Getting Sick From Looking Fit

One of the most accessible of the body's rhythms is breathing. Its timing is uniquely susceptible to abuse, as it also is to remediation. On magazine covers and on television, we see model humans with chests pushed out and guts sucked in. It appears to be our culture's voluntary expression of a posture that would otherwise seem to be an involuntary response to stress. Stress invokes tension in the accessory respiratory muscles, which tend to appropriate diaphragmatic breathing. Whether they are pushed by the example of the chest-out posture of Mr. and Ms. Universe or by anxieties of everyday life, we can help our patients' rhythmic systems by teaching them diaphragmatic breathing and reminding them to catch themselves in traffic or standing in line, and to relax and let their diaphragm do its natural rhythmic activity. Yoga teachers, players of wind instruments, and singers can help them in this exercise of relaxation. Dancing, running, swimming, martial arts, and other activities that call for integration of mind, muscle, and breath benefit from favoring the diaphragm's natural connections and minimizing chest breathing.

Unlike the chest muscles, which communicate with the higher centers of the brain, the diaphragm communicates with the control centers for cardiovascular rhythms. The synchronization of pulse and respiration provides the best example of my definition of normal rhythmic functioning as relational rather than statistical. You may have already raised the question of whether the "normal" pulse rate of 72 is simply a statistical norm. It is, but its relationship with other rhythms yields ratios that illustrate "normal" in the sense of optimal. The partnership of pulse and respiration is a relationship that illustrates the body's similarity to music and invites consideration of the meshing of all the rhythms of the body in ways that signal health when harmony reigns. A simply designed study by Hildebrandt showed that the fitness of human subjects was superior when their resting pulse:respiration ratio was a whole number (eg, 3, 4, or 5).[5] In other words, a pulse:respiration ratio of 72:18 = 4 (or 68:17 = 4, or 60:15 = 4, or 100:20 = 5, or 75:25 = 3) is associated with a higher level of fitness than, say, 75:17 = 4.4, 60:14 = 4.3 or 82:17 = 4.8. In musical terms, the whole-number relationships between pulse:respiration are consonant, and the non-integral relationships are dissonant. The consonance of integral relationships between rhythmic physiological functions may be neither the cause nor the effect of fitness. It is intuitive that harmony works better than disharmony. The principle illustrated by the results of Hildebrandt's study must govern the mutual relationships among all of the body's rhythms.

What are "all the body's rhythms," and how can we encourage harmony among them? Respect for the nutritional needs of growth and detoxification that occur at night and the demands of consciousness during the day can be reflected in the timing of our intake of protein, carbohydrates, and the micronutrients most related to the dominant day or night activity. We can practice diaphragmatic breathing, and we can be careful with our exposure to light and activities that mesh with our circadian cycle. We can permit sleep, meditation, rhythmic exercise, dance, and music to help us resynchronize.

Molecular Buzz and Tuning

A few years ago while at dinner with Dr Jeff Bland and Dr Candace Pert, a leading molecular biologist and discoverer of the opioid receptor site, I asked Dr Pert a question that came to me when I read her book, *The Molecules of Emotion*. In the book, she described the opioid receptor site as having two configurations between which the molecule alternates. I wanted to know if she thought that the receptor site's flip-flops were along the lines of something that buzzed or something that went bumpity-bump. She voted for buzz. Then I wondered if the buzzing might have anything to do with the ligand finding its receptor site, given that the concentrations involved (eg, below 10^{-10}) might require facilitation beyond random contact. Such facilitation, I speculated, might be due to a resonance between the natural frequency of the receptor site and its ligand, based on the naïve observation that we usually can hear approaching things before we can see them. I pictured the resonance opening a channel, so to speak, in the watery medium through which the ligand passes to find its mate. Dr Pert's assent to the concept gave me confidence in my image of a lot of very complex but orchestrated buzzing taking place at the molecular level of all living things.

Since then, I have made the acquaintance of Richard Deth, PhD, whose work has been cited in previous essays in this *Lenses* series. Dr Deth discovered the site on the dopamine D4 receptor site that carries out methylation. He proposes that the D4 receptor, acting via membrane methylation, has the role of modulating resonant synchronization between brain regions, thereby facilitating an interaction upon which attention, and probably consciousness, is based. The frequencies of the participating neurons in the resonance couples are in 30-80 cycles per second (gamma) range, which increases during attention. Synchronization is impaired in autistic people.[6] Parents of autistic children regularly describe their children as going in and out of "synch" or "tuning." Dr Deth's research is moving in a direction that

should give us a better understanding of the molecular—and rhythmic—basis for the feeling one gets in the presence of autistic children that their timing is off.

Tuning at high molecular frequencies, or at the lower frequencies of neuronal firing, is no different in concept from the integrated timing of physiological functions of cardiac and respiratory rates or the meshing of light, nutrients, and activity to our circadian rhythms. It's just a difference in frequency. All of these rhythms are part of a harmonic system, similar to an orchestra, with its integration of frequencies of acoustic phenomena from the notes of strings and woodwinds to the beats of the percussion instruments. Like an orchestra, we may create different complexities in our lives, but we are all bound by the same rules of synchrony.

Summary

The temporal domain is a dimension that we neglect at the peril of our full understanding of fitness. The relationships between rhythms obey simple rules that are manifest in our notions of synchrony, resonance, and tuning. The laws of harmony and the day-night cycle of our planet are shared by all of us. However, we may differ in the ways our biochemistry, environment, or activities and our will permit obedience to those rules and rhythms. Awareness of timing is the first step to remediation.

The details of rhythmic integration and related therapeutic opportunities for the healthy meshing of our various rhythms will play a larger role in medicine's future. In that future, medicine will encounter its past, when, in ancient times, the harmonies of the world were a more conscious part of perceived reality. That reality was one that we now consider to be connected more to a spiritual than a scientific perception of the world.

Post Script

In this series of commentaries, now ending, I have tried to offer a way of thinking about each patient as an individual—in the context of eight physiological domains that offer therapeutic leverage on the ways that genetic and environmental factors are expressed as health or disease. The underlying clinical assumption of the kinds of strategies I have touched upon has been materialistic. That is, our strategic questions and answers all lie within the domain of biochemistry and immunology—with the added feature of temporality.

Beyond any religious considerations is the question of whether there is a spiritual reality that lies in and beyond our perceived experience, except when we glimpse through chinks in the wall of our day-to-day existence. To me, a grasp of the notions of harmony and tuning sends me in the direction of interconnections and leads across the boundary to spiritual considerations. Forty years of listening to my patients' stories of their lives and deaths has convinced me that clinical decisions should heed the reality of the spiritual world as, at least, a source of information and perhaps more so the origin of the energy that shapes our lives.

A decade ago, I faced an audience of clinicians who were attending a conference on biochemistry and immunology. Seizing the privilege of the podium, I asked for a show of hands: "Please raise your hand if you have personally had an experience such as Maslow described as 'ineffable, ephemeral, noetic, and transcendent,' in which you were persuaded of the existence of a reality that lies beyond the realm of everyday experience, but not normally accessible to your senses." Eighty percent of the audience members raised their hands. In bringing up spiritual issues to the readers of *Integrative Medicine*, I know that I am preaching to the choir. I also know that I am in over my head, except to assert that I believe it's important for us as clinicians to confront and answer for ourselves the question, "Are humans spiritual beings?" and to consider the implications of a positive answer, at least in terms of access to information.

Others will do a better job than I on this topic. I wish, however, not to close this series of commentaries on the medicine we are evolving and the eight lenses without a final acknowledgment. The lenses provide, for me, a prescription for thoroughness that is incomplete without adding spiritual considerations for finding the answers to the question posed in the villages of Kathmandu, Nepal, by my mentor, Dr Edgar Miller, in the spring of 1959: "Have we done everything we can for this patient?"

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