Investigation

3.13B: Normal or Abnormal?

Introduction:

We have previously noted that the educational pathway to becoming a physician stretches over many years. But one navigates that journey only one day at a time. Even after one completes medical school and specialty training (called a residency), physicians continue to study to remain up-to-date with the latest information and innovations in their field. That never-ending quest for knowledge would seem too heavy a burden except that the rewards of a career restoring good health to others make the effort worthwhile.

On this Friday evening your role, experiencing different aspects of a career in medical science, sends you to the airport to fly off to a medical conference for the weekend, a symposium that will teach you new concepts to apply in your practice. You have arranged for another physician to cover any emergencies your patients might encounter while you attend the conference.

This trip might feel like a holiday except that this morning you awoke to a freezing cold house. Something you may have learned about life, a broken furnace never happens when you have time to deal with it; things like plumbing appear to always decide to break down when you have no spare time to deal with them. Fortunately you were able to reach your heating system repairman when you got to the office this morning, and he called you back in the early afternoon to say he fixed the problem by replacing a bad thermostat. Your old thermostat was not calling for heat from the furnace when the temperature in the house fell below normal.

As you now settle into your airplane seat before takeoff, your mind dwells on that thermostat. That thermostat could have ruined your trip. Whoever thinks about thermostats? They just sit there patiently on the wall keeping our homes warm in winter and cool in the summer. Thermostats keep the house temperature “normal.”

As you see patients in your medical practice you constantly check all manner of things related to their body and health to see if they appear normal or abnormal. When a physician finds something abnormal that finding becomes a clue in the search for a diagnosis that we hope leads to a treatment. Noting elements of the history and physical examination that appear normal also contribute to reaching the correct diagnosis. We have come to understand that path to a diagnosis in medicine very clearly, but that broken thermostat serves as a reminder of a very important principle that lies behind that methodology. We might define that principle by saying, “Normal does not happen by accident!” Anything we measure, or test, or examine in medicine, anything that we evaluate as normal or abnormal, has some physiologic mechanism that controls that feature. “Normal does not happen accidently!”

[If your love of science happens especially to favor physics, you might view these comments about “normal” findings as having a parallel to the difficult to understand concept of entropy in thermodynamics. Physicists would say that one must do work to create and maintain order. Biological systems appear to also obey the spirit of that edict and must do work to keep things “normal.”]

The furnace does not come on to heat a house accidently. The **thermostat** must sense that the temperature in the house has fallen before a set value and must then signal the furnace to send heat. That series of steps keeps the house at its normal temperature. When the house temperature became abnormal the repairman found the problem did not come from a broken furnace, but from a broken thermostat.

Engineers who design controllers define a **closed loop system** as one that measures its output, compares that measurement to a set point (the desired output), and then uses the difference between the two to dictate what happens next. An **open loop system** would have set inputs but no measure of the output, so the system would have no ability to compensate for any external factors. If you had an open loop heating system in your house, you would expect the house to get too warm on a warm day and feel cold on a cold day.

When you get the flu and your body temperature goes much higher than its normal value of close to 98.6 degrees Fahrenheit, would you say that your furnace has gone wild or has your thermostat failed? Circle your guess about the bad element:

FURNACE or THERMOSTAT

Do you actually have a furnace and a thermostat inside your body? You do, but both certainly look quite different from the components used to heat a house. The chemical process that our cells utilize to **extract** calories from the food we eat, **calories** to power our activities of living, create heat. Muscle cells, especially, use up a lot of energy and thereby also generate a large percentage of our body’s heat. When you go running on a cold day, you do not need a heavy coat to stay warm. When you work hard outside on a hot day, you quickly get very hot. When you feel cold your muscles shiver. That shivering burn calories and thus generates heat. In a real sense your muscles serve as your body’s primary furnace.

How about a thermostat? Where would you look for a thermostat inside the human body? Circle your best guess.

ANKLE APPENDIX EAR TONGUE TOE BRAIN LIVER

If you selected the next to the last choice you picked out the correct answer. Not an easy question. The sensing of body temperature and the control for the body’s response to being too hot or too cold arise in the hypothalamus, a specific region inside the brain.

FOOD FOR THOUGHT

In the paragraphs above, we used a thermostat controlling a furnace as an example of a control system designed to keep the temperature of a house at a specific value. We picked that example because you have seen thermostats and furnaces, but we would not call that control system very sophisticated. The usual home thermostat turns the furnace on full blast until the room temperature reaches the desired level, then it shuts the furnace completely off. Engineers call that type of controller a “bang-bang controller.” “Bang” on, then “bang” off. Guess what happens to the temperature in the room after the furnace shuts off.

Contrast this “bang-bang controller” with the manner in which you might control your bicycle in order to stop precisely where you want to park your bike. You would never pump your peddles at full speed until you reached your destination. Instead you would slow down as you get close and then use your brakes to come to a complete stop at the exact point you desire. If you used the “bang-bang” approach you would expect to fly right by your destination and then have to back up. Exactly that happens each time your furnace gets your house to the desired temperature; it goes a little over and then falls back until the furnace needs to heat up again.

The idea of slowing down or cutting back as you get close to the set point, engineers refer to as proportional control. A proportional controller would represent a more sophisticated or more accurate approach. The design of controllers for all manner of applications has become a specialty in engineering that has a constantly growing set of mathematical tools to guide the design toward ever more accurate and stable controllers. Digital computers make possible controllers that can evoke complex decision making processes and even change their performance as unexpected situations arise. We call these advanced controllers “learning” or “adaptive controllers.” Automobiles that drive themselves would represent an example of a very sophisticated adaptive control system capable of adjusting to a wide range of situations.

One can apply the mathematics of control systems to better characterize and understand the processes the human body uses to control its own functions. The specialty of **endocrinology** in medicine focuses almost exclusively on the way the body regulates itself and the conditions in which disease impacts those controls. Physicians do not routinely use mathematics to model those control systems. All specialties of medicine encounter aspects of natural, human control systems that may go astray and thereby create symptoms and abnormal findings.

Man-made controllers have found uses in medical treatment, for example an implanted electronic **pacemaker** used to control the beating of the heart. Numerous other artificial controllers have been designed to solve specific medical problems in drug administration, movement disorders, neural function, and even replacements for lost arms or legs. Most certainly the future will see more and more opportunities to use man-made control systems to replace or augment the control systems the body uses naturally to keep all of our various processes working properly. The human body must have thousands of control systems, many of which we may not currently understand or perhaps even recognize.

The fact that anything we can describe in medicine as having a normal value must have a mechanism for keeping that feature “normal” represents an important concept to keep in your mind.

MEDICAL INVESTIGATION

Before we started talking about normal values and how they stay normal, you were getting onto an airplane headed to a weekend medical conference. Such **conferences** serve to keep you updated on new information you need to care for your patients. You selected this particular meeting because experts will present new information about how the body controls sleep and on the next day how the body manages aging. Both of these topics come up over and over every day in your office as you deal with your patient’s health problems. You feel eager to get to this particular conference.

You do not have one patient complaining of a sleep disturbance; you have dozens. You do not have one patient affected by aging; you do not have any patients not affected by aging. Bright and early Saturday morning you seat yourself right up front ready to soak up any information you can get to improve your care of your patients.

The first speaker has grey hair, which suggests she has studied the topic a long while. The conference moderator finishes his impressive summary of her academic accomplishments, and she begins, “The need for and the purpose of sleep constitute the least clearly understood areas of our research on human sleep.” Humans spend about a third of our lives sleeping and we do not know why? Can that really be the case?

Fortunately the speaker went on to tell her audience a lot of things we do know about sleep. We once thought sleep only served to rest the body, but now we know better. Sleep plays a significant role in learning and long-term memory. Cells inside the brain communicate with each other using electrical impulses, making the brain somewhat akin to a digital computer. While immediate thoughts and actions appear to result from electrical activity inside the brain, long-term memory appears to have chemical aspects that depend upon protein synthesis for the more permanent storage of information (changes in the way the brain cells influence their neighbors). Sleep appears to facilitate the conversion of new information into long-term memory (backpropogating, we have learned about in this section), but we do not know exactly how. But clearly when mothers insist their children get plenty of sleep so they can do well in school, science backs up that advice.

The speaker also reviewed a massive amount of information on a center in the brain that times our body’s daily activity in sync with the light from the sun and another center that appears to keep tabs on our need to sleep for mind and body rejuvenation. Scientists have studied our brain activity during sleep and defined two main categories of sleep: Rapid eye movement sleep (**REM sleep**) and **non-REM**. The non-REM sleep has three different modes (N1, N2, and N3) and we appear to normally cycle through these stages in steps N1, N2, N3, N2, REM, etc. We dream only during REM sleep. While the think of sleep as a period of resting, during REM sleep some areas of the brain appear to work very hard as indicated by imaging studies that show increases in the blood flowing to those areas, more blood flow than measured when awake.

Sleep seems to occur across the spectrum of animal life. Dolphins, porpoises, and penguins appear able to sleep one half of their brain at a time while the other half remains alert and on guard. Scientists suspect that some birds may have the ability to sleep in flight, but no one has captured direct evidence of this ability. Biologists have studied the sleep patterns of fruit flies and honeybees. Reptiles do not display REM sleep, so they probably do not have nightmares about humans.

But what about those patients who go to their doctor to get help sleeping? The speaker explained that the body has a **biological clock** that readies us to sleep each night. We also have a sense of accumulated physical and mental fatigue that encourages us to sleep. A multitude of factors have the ability disrupt these natural control systems trying to provide us with sufficient sleep, specifically enough rest, refreshment, and memory assimilation. Disrupted sleep in time becomes chronic sleep deprivation, and that condition can actually sometime require hospitalization to restore a healthy mental functioning. Life events, changes in work schedule, medications, diet changes, or travel across time zones, constitute common causes of sleep disruption.

The speaker noted that sleep scientists have observed that study subjects who get plentiful sleep may not always sleep uninterrupted throughout the night. It would appear that an hour of wakefulness about two-thirds the way through the night occurs commonly enough for them to call that "normal." Those who experience this "wake up" period usually find it not unpleasant and indeed report it seems highly productive as they think about events in their life, often gaining new insights. When patients complain about experiencing sleep disruption, physicians should make sure the complaint does not arise from a normal "wake up" phenomena.

Some medications designed to treat a lack of sleep can themselves disrupt the normal cycle of non-REM and REM sleep, so routine use of these medications can easily become a problem itself. Remember we believe that REM sleep allows the brain to structure long-term memory. Medications the physicians prescribe to treat feelings of depression commonly alter sleep patterns, so physicians need to ask about the sleep experience of patients who are using these medications. The speaker also stressed the importance of a stable sleep schedule and a quiet, dark, comfortable bedroom environment for healthy sleep.

In your role as a physician, take a moment to evaluate the quality of sleep of a patient you know very well, yourself.

How much sleep do you get routinely each night? ______ hours

Do you have a specific time to go to bed? YES NO

Do you dream and remember your dreams? YES NO

Do you experience a time during the night of being awake to think? YES NO

Do you commonly find yourself feeling very sleepy during the day? YES NO

Are there things you want to change to improve the value of your sleep time?

Scientists who study sleep report that individuals who keep a written, daily journal that records every dream they recall upon awaking will find in a few weeks that they will remember multiple dreams in detail each morning. The recall of dreams can often help identify sources of stress in one's life and lead to resolution of those stresses. You might wish to experiment by writing down any dreams you remember each morning.

THE FINAL DAY OF THE CONFERENCE -- FOOD FOR THOUGHT

The last day of the conference introduced a totally new topic. Everyone has an interest in the expectation of the length of his or her life. In the United States we currently expect females to live about 81 years on average and males to live about 76 years. The longest documented human life lasted 122 years. The fact that we can talk about a normal life span for people living in our nation evokes our new rule! If we have a normal value for life span, the human body must have some process that controls it.

On the last day of the conference several speakers talked about life span. In 1993, Dr. Cynthia Kenyon, working at the University of California in San Francisco, discovered that she could modify a **gene** in a particular species of worm she was studying and thus double the lifespan of the worm. The worm did not simply live longer, but actually remained active and vibrant twice as long. Apparently Dr. Kenyon had successfully slowed the aging process that she previously considered normal for this type of worm.

In 2013, researchers at the National Institutes of Health modified a single gene in a group of mice and extended their average lifespan by about 20%.

In our study of medical science we have been thinking about medicine and healthcare in terms of diseases that we identify and then treat. But the speakers on this last day of our conference are talking about human aging as a process with a control mechanism we might figure out and modify. Instead of thinking about aging as a normal life process, according to the speakers, medical researchers instead are thinking about aging as a disease we should try to cure.

One of the speakers talked about a drug called **metformin** that physicians use to treat type II diabetes. Studies in animals have demonstrated this drug can slow down aging and studies are underway to test this possibility in humans.

If you were to look up statistics on the average life span of humans in different countries around the world you would find a wide variation. People who live in countries that have limited healthcare and poor living conditions tend to have shorter average life spans. Citizens of wealthier nations currently live longer on average.

Some physicians elect careers in public health. We have not talked about public health as a field of medicine before. Public health professionals primarily focus on the ways that governments or other public institutions can improve the health of their citizens, and the measure of life span can service as a scorecard for public health efforts. The nation of Japan currently appears to lead all others in having the longest average life span among its citizens. Probably many factors contribute to Japan's success, but articles in American medical journals draw attention to a relaxation of mandatory flu shots for school children in Japan between 1987 and 1994, which resulted in higher death rates across Japan. The Japanese Ministry of Health acted to restore an emphasis on flu shots for both school children and at-risk elderly citizens. School children play a key role in the spread of season flu epidemics and Japan's efforts with regard to this group appear to have played a role in their leading the world in life span statistics as of 2012.

As medical science increases our understanding of what controls aging and how medications might **modulate** those controls, public health may become a very exciting field. The extension of life span within a nation would have major economic effects for governments and on a more individual level would certainly change perspectives on work, personal relationships, family life, and social interactions.

As this weekend conference drew to a close everyone in attendance walked away with a great deal to think about as they traveled home. Take a moment to think about how a dramatic change in life span might impact your life. If you know at this moment that you will live an active, vibrant life that will last 120 years, write a couple of sentences to explain your first thought about how your life will differ from the life your parents lead.

If I am going to live to be 120 year old, I think I want to think a lot about __________

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