NATURAL HISTORY
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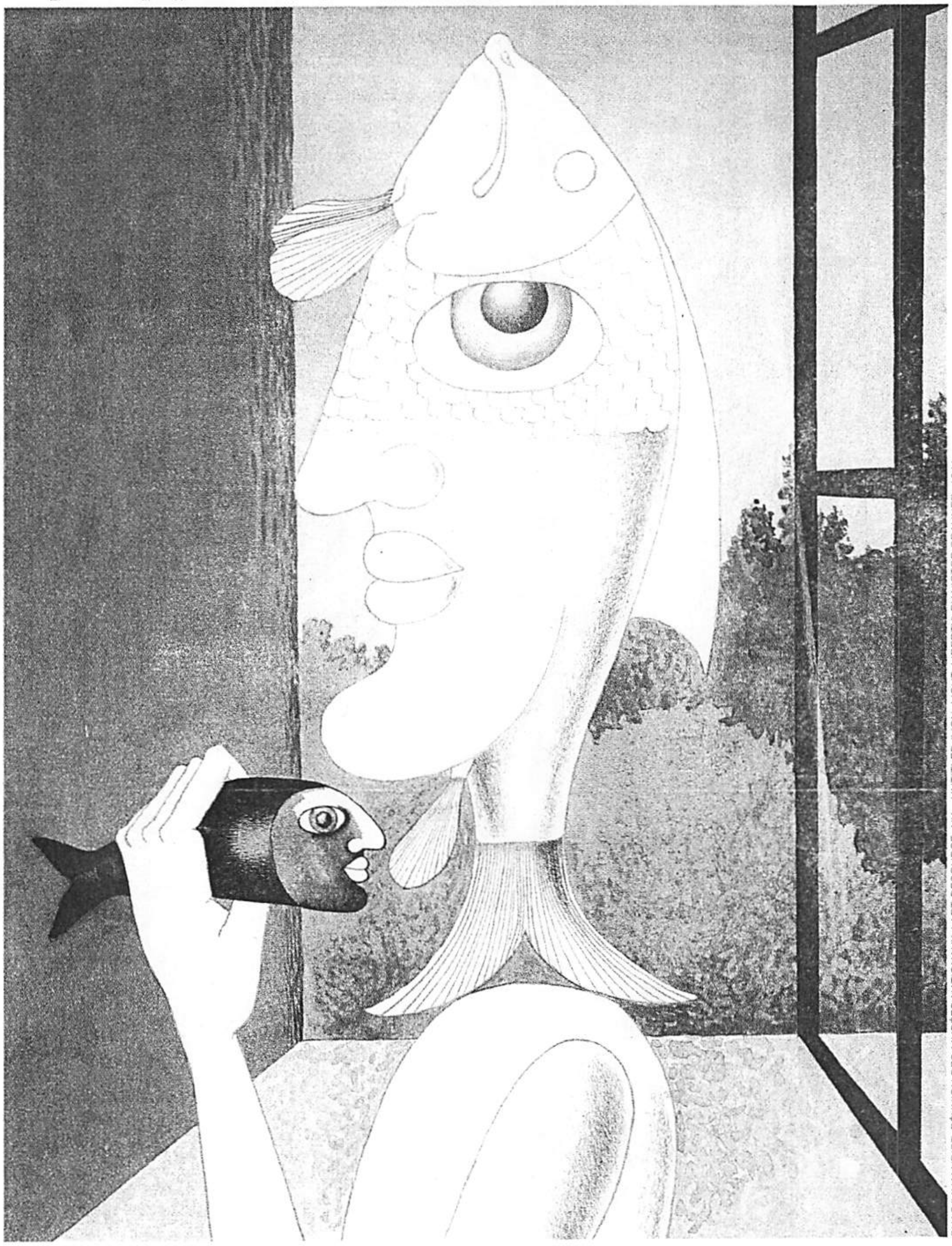
FISH OUT OF WATER



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Human ailments as varied as hernias, hiccups, and choking are a legacy of our "fishy" ancestry.

BY NEIL SHUBIN

HUMANS MAKE MUCH of what distinguishes us from the apes, but we actually share so much with fish that the comparison with apes feels almost trivial. Once you see our similarities to fish, all mammals start to look alike. And our very ancient evolutionary kinship with other animals has an impact on our lives today. The exceptional combination of things we do—talk, think, grasp, and walk on two legs—comes at a cost, the inevitable result of the tree of life inside us.

Imagine trying to jury-rig a vintage Volkswagen Beetle to travel at speeds of 150 miles per hour. In 1933, Adolf Hitler commissioned Ferdinand Porsche to develop a cheap car that could get forty miles per gallon of gas and provide a reliable form of transportation for the average German family: the result was the Volkswagen, a car that remained substantially the same throughout its many years of production. Its original design placed constraints on the ways it could be modified—engineers could only tweak it so far before major problems arose—and it ultimately was replaced by a completely new Beetle.

In many ways, humans are the fish equivalent of an old Beetle turned hot-rod. Take the body plan of a fish, reconfigure it to be a mammal, then tweak and twist that mammal until it walks on two legs, talks, thinks, and has superfine control of its fingers—and you have a recipe for trouble. In a perfectly designed world—one with no evolutionary history—we would not have to suffer from hemorrhoids or easily-damaged knees. Indeed, virtually every illness we suffer has some historical component that can be traced back from mammals to amphibians to fish and beyond.

You can dress up a fish only so much without paying a price.

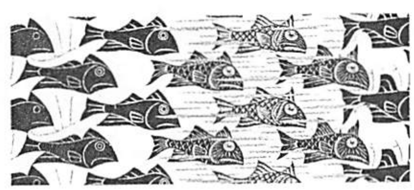
SPEECH COMES AT JUST such a price: sleep apnea and choking are high on the list of problems we have to live with in order to be able to talk. We produce speech sounds by controlling motions of the larynx, the back of the throat, and the tongue. All those structures are relatively simple modifications to the basic design of a mammal or a reptile. The human larynx, for example, is made up mostly of cartilages that correspond to the gill arches of a shark or fish [*see diagram on page 29*]. But in humans, the back of the throat, extending from the last molar tooth to just above the voice box, has flexible walls that can be widened and narrowed by relaxing and contracting a number of muscles. The human tongue, too, is woven of multidirectional muscle fibers that give it a remarkable range of movement. By changing the size and shape of the mouth cavity and the softness or rigidity of the throat, we are able to modify sounds from the larynx.

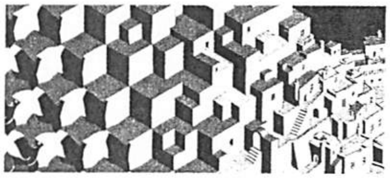
Unfortunately, that flexible throat, so useful in talking, makes us susceptible to a form of sleep apnea that results from obstruction of the airway. During sleep, the muscles of the throat relax. In most people, this does not present a problem, but in some, the passage can collapse so that relatively long stretches pass without a breath. This, of course, can be very dangerous, particularly in people who have heart conditions. Snoring is a symptom of the same underlying problem.

Another trade-off of speech is choking. Our mouths lead both to the trachea, through which we breathe, and to the esophagus, so we use the same flexible passage to swallow, breathe, and talk. Those functions can be at odds, for example when a piece of food "goes down the wrong pipe" and gets lodged in the trachea; our fishy ancestors had no such worries. Other mammals, and reptiles too, use the same structures for eating, breathing, and communicating but the back of the mouth does not need to be so vertically spacious and flexible as ours. The basic mammalian structures are arranged so that nonhuman animals can safely swallow while breathing. Tweaking the engineering to enable us to talk has left us peculiarly vulnerable.

THE ANNOYANCE OF HICCUPS also has its roots in our fish and amphibian past. If there is any consolation, we share that misery with others. Cats and dogs, like many other mammals, also get hiccups. A small patch of tissue in the brain stem is thought to be the center that controls that complicated reflex.

The hiccup reflex is a stereotyped twitch that involves a number of muscles in the body wall, diaphragm, neck, and throat. A reflexive firing of one or two of the major nerves that control breathing causes those various muscles to contract. This results in a very sharp inspiration of





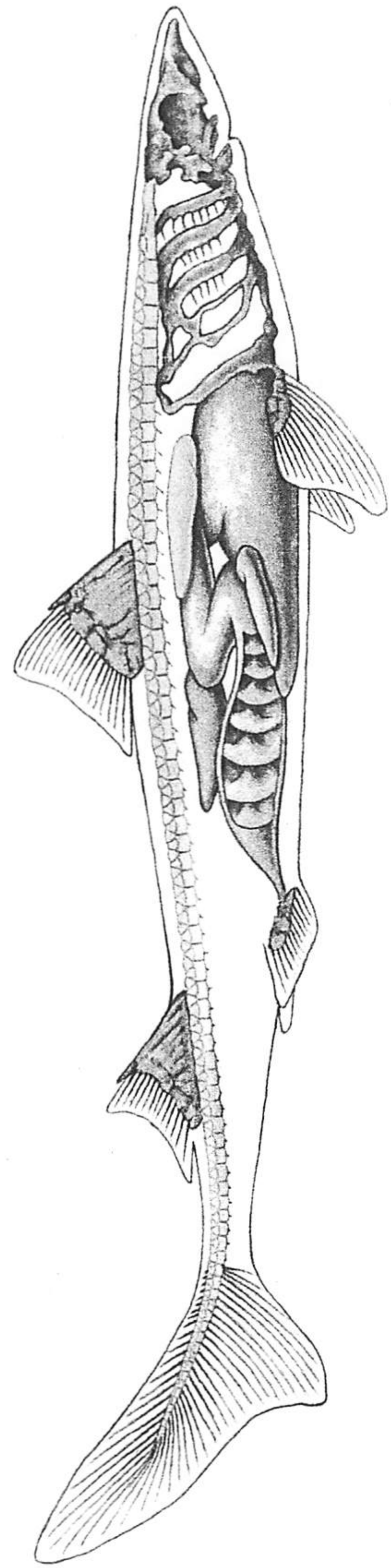
air. Then, about thirty-five milliseconds later, a flap of tissue in the back of the throat (the glottis) closes the top of the airway. The fast inhalation followed by a brief closure of the air tube produces the "hic."

Our tendency to develop hiccups is another influence of our past. There are two issues to think about. One is what causes the reflexive firing of nerves that initiates the hiccup. The other is what controls that distinctive hic—the abrupt inhalation and the glottis closure. The nerve action is a product of our fish history, while the hic is an outcome of the history we share with tadpoles.

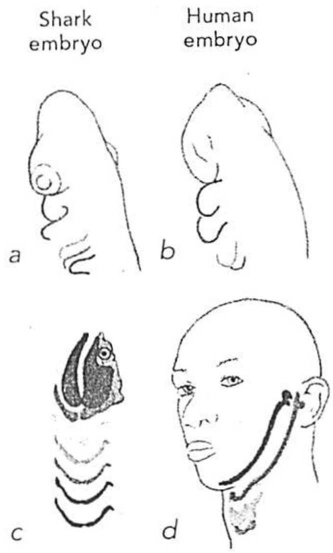
Fish first. Our brains can control our breathing without any conscious effort on our part. Most of the work takes place in the brain stem, at the boundary between the brain and the spinal cord. The brain stem sends nerve impulses to the main breathing muscles. Breathing happens in a pattern: muscles of the chest, the diaphragm (the sheet of muscle that separates chest from abdomen), and the throat contract in a well-defined order. Consequently, the part of the brain stem involved is known as a "central pattern generator." It can produce rhythmic patterns of nerve and, consequently, muscle activation. A number of such generators in the brain and spinal cord control other rhythmic forms of behavior, such as swallowing and walking.

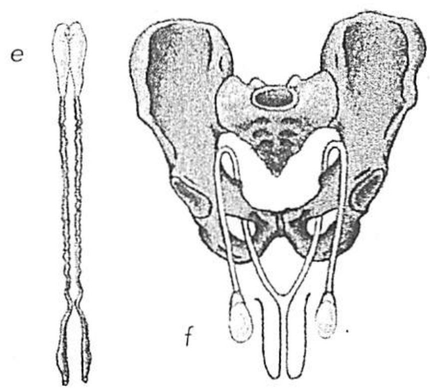
The problem is that the brain stem, originally controlling breathing in fish, has been jury-rigged to work in mammals. Sharks and bony fish respire using muscles in the throat and around the gills. The nerves that control those areas all originate in a well-defined portion of the brain stem. We can even detect that nerve arrangement in some of the most primitive fish in the fossil record. Imprints of ancient ostracoderms, from rocks more than 400 million years old, preserve casts of the brain and cranial nerves, and just as in living fish, the nerves that control breathing extend from the brain stem.

That works well in fish, but it is a lousy arrangement for mammals. In fish, the nerves that control breathing do not have very far to travel from the brain stem. The gills and throat generally surround that area of the brain. We mammals have a different layout; our breathing is carried out by muscles much farther away. For example, the major nerve that controls contraction of the diaphragm—the phrenic nerve—exits the brain stem from the base of the skull, just as it does in fish. Then, however, it extends all the way down through the neck and the chest cavity to reach the diaphragm. That long path through soft tissue is exposed and vulnerable; a rational design would have the nerve travel through the protective spinal column and

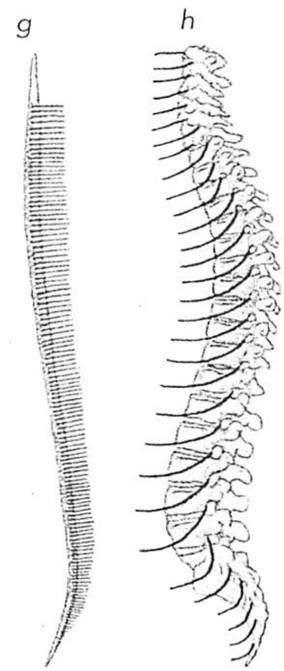


Both shark and human embryos (a, b, at right) have similar gill arches (brightly colored elements). In sharks, the cells in these arches become bones, nerves, arteries, and muscles that support the gills (c); in humans, they form the jaw, ears, larynx, and parts of the throat (d).

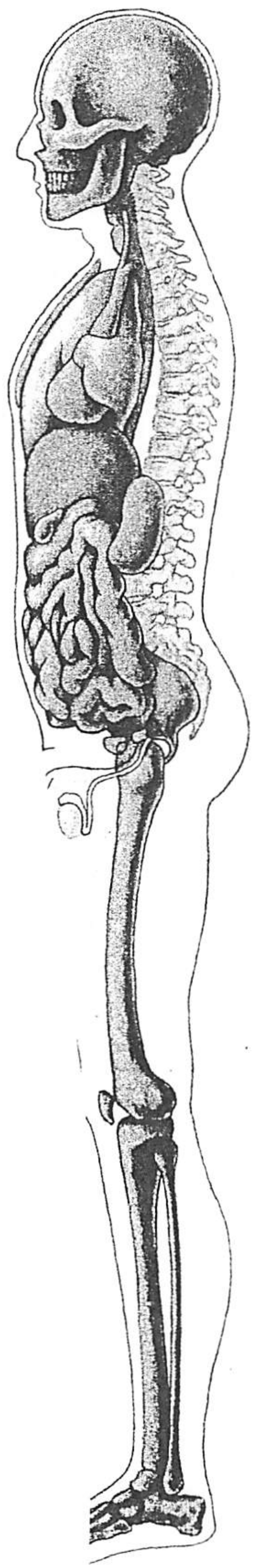




Shark gonads (testes shown here, e) extend above the liver toward the front of the animal, as they do in early human fetuses. In male humans, and other male mammals, the testes (f) descend during further development; the spermatic cords take a detour to loop over the pelvic bone, and the scrotum emerges as an extension of the body, making a weak spot where hernias can form.



Nerves that control sensation and movement exit the spinal cord between the vertebrae in both sharks (g) and humans (h). This arrangement works fine in a fish, which is largely supported by water, or in an animal that walks on four legs, so that the body's weight is dispersed among front and back limbs. Humans, who walk on two legs, often experience severe pain or loss of movement when vertebrae in the lower back shift, or when the disks between the vertebrae change shape or rupture with age and/or disease.



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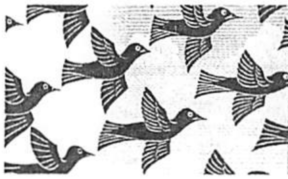


THE FREQUENT KNEE INJURIES PEOPLE SUFFER ARE CLEAR EVIDENCE OF THE PITFALLS OF HAVING AN INNER FISH.

emerge nearer the diaphragm. Unfortunately, anything that interferes with one of these nerves, such as a tumor in the chest cavity, can block their function or cause reflexive firing.

If the odd course of our nerves is a product of our fishy past, the hiccup itself is likely the product of our history as amphibians. Hiccups seem to be controlled by their own pattern generator in the brain stem: stimulate it, and you stimulate hiccups. It turns out that this pattern generator is virtually identical to one found in amphibians—and not in just any amphibians, but specifically in tadpoles. Tadpoles use both lungs and gills to breathe, and this pattern generator is active when they breathe with gills. In that circumstance, a tadpole needs to pump water into its mouth and throat and then out across the gills, but it must also prevent the water from entering its lungs. To keep out the water, it closes the glottis, the flap that can seal off the breathing tube. The central pattern generator in the tadpole brain stem ensures that an inspiration is followed immediately by a closing glottis. They can breathe with their gills thanks to an extended form of hiccup.

There are additional parallels between gill breathing in tadpoles and our hiccups. Gill breathing can be blocked by carbon dioxide, just as hiccups can (one home remedy, breathing into a paper bag, helps concentrate carbon dioxide). Experimentally stretching the wall of a tadpole's chest is another way to block gill breathing, just as inhaling deeply and holding one's breath can stop hiccups. Perhaps we could even block gill breathing in tadpoles by having them drink a glass of water upside down.

THE HAZARDS OF TAKING a fish body and morphing it into a mammal show up in other specific ways. One is our propensity for hernias, at least for hernias near the groin.

If you were to slit the belly of a shark from mouth to tail, the first thing you'd see is liver, a lot of it. The liver of a shark is gigantic. Some zoologists believe that a large liver contributes to the buoyancy of the shark. Move the liver away, and you'll find the gonads extending up into the "chest" area, near the heart [*see diagram, page 28-29*]. This arrangement is typical of most fish: the gonads lie toward the front of the body. In mammals, the location of the gonads is quite different, and therein lies the problem.

This article was adapted from *Your Inner Fish: A Journey into the 3.5-Billion-Year History of the Human Body*, by Neil Shubin, ©2008. Reprinted with permission of Pantheon Books, a division of Random House, Inc. All rights reserved. On sale in bookstores in January.

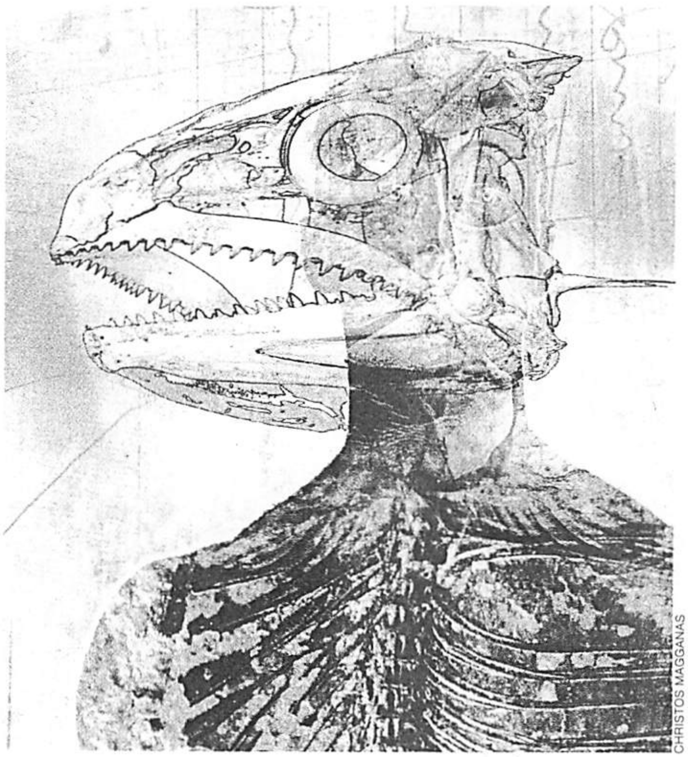
Now, it is a very good thing that our gonads are not near our hearts (although it might make reciting the Pledge of Allegiance a different experience). If our gonads were in our chests, we wouldn't be able to have babies. For males in particular, it would be a disaster. Males continuously produce sperm throughout their lives. Sperm are finicky little cells that need exactly the right range of temperatures to develop correctly for the three months they live. Too hot, too cold, and they die or become malformed. Male mammals have a neat little device for controlling the temperature of the sperm-making apparatus: the scrotum.

As we know, the male gonads sit in a sac. Inside the skin of the sac are muscles that can expand and contract as the temperature changes. Hence the cold shower effect: the scrotum will tuck close to the body when exposed to cold. The whole package rises and falls with temperature. This is all a way to optimize the production of healthy sperm. The dangling scrotum also serves as a sexual signal in many mammals. The problem with this arrangement is that the plumbing that carries sperm to the penis is circuitous. Sperm travel from each testis through a spermatic cord. The cord leaves the scrotum, travels up toward the waist in front of the pelvis, loops rearward over the pubic bone, and doubles back and down through the pelvis to reach the ejaculatory duct, which empties into the urethra. The reason for this absurd roundabout route lies in our developmental and evolutionary history.

Our gonads begin their development in much the same place as a shark's: up near the liver. As they grow and develop, our gonads descend. In females, the ovaries descend from the midsection to lie near the uterus and fallopian tubes. This ensures that the egg does not have far to travel to be fertilized. In males, the descent goes farther.

The descent of the gonads, particularly in males, creates a weak spot in the body wall. To envision what happens when the testes and spermatic cords descend to form a scrotum, imagine pushing your fist against a stretched rubber sheet. In this example, your fist becomes equivalent to the testes and your arm to the spermatic cords. The problem is that where once the rubber sheet was a simple wall, you've now made another space, between your arm and the rubber sheet, where things can slip. This is essentially what happens in many types of inguinal hernias in men. Some inguinal hernias, or hernias of the groin, are congenital, created when a piece of the gut travels with the testes as they descend. Inguinal hernia can also be acquired: A weak spot in the body wall—the muscular wall of the abdomen—can be breached, if pushed by a strong muscle contraction, and a loop of gut can be squeezed to lie next to the spermatic cord.

Females are far tougher than males, particularly around that part of the body. Because females do not have a giant tube running through the abdominal wall, it is much stronger than a male's. That is a good thing, when you think of the enormous stresses that female body walls go through during pregnancy and childbirth.



CHRISTOS MAGGANAS

HURT YOUR KNEE, and you will almost certainly injure one or more of three structures: the medial meniscus, the medial collateral ligament, and the anterior cruciate ligament. So frequent are injuries to those three parts of the knee that they are known among doctors as the "unhappy triad." They are clear evidence of the pitfalls of having an inner fish. Fish do not walk on two legs.

Rocks about 380 million years old preserve the first knees—in the pelvic fins of fish. They look like a simple hinge made of three bones. The animals that had them were mostly aquatic, so their "knees" didn't bear much weight. Consequently, the fin is relatively flat and shaped almost like a paddle. Our legs look the same way when we are in the womb, at six to seven weeks of age. After about eight weeks of development, a remarkable thing happens: our knees rotate so that they face forward, flexing backwards. We can see evidence of this shift even in our adult bodies, where many of the nerves that supply the lower leg wrap backward at the knee.

What does this mean in our daily lives? That rotation of our knees is essential to our ability to walk: imagine trying to amble about with your kneecap facing to the rear. It is also a prescription for disaster. Most of the weight of our body when we walk, run, and jump gets borne on a simple hinge. To make matters worse, the hinge is held together by a handful of strap-like ligaments, with two cartilage pads inside. Our "unhappy triad" is another example of the revenge of our inner fish.

LOOKING BACK THROUGH BILLIONS of years of change, we see that everything innovative or apparently unique in the history of life is really just old stuff that has been recycled, repurposed, or otherwise modified for new uses. Human hands are a modified version of mammalian ones, which are ultimately modified fish fins. Bones in our ears originally helped ancient sharks and reptiles chew. The genes that control all of this structure were originally used to build the bodies of ancient worms, flies, and fish. Every part of us tells this story: our sense organs, our heads, even our entire body plan.

While the evolutionary history we carry within us causes problems, it is also a treasure trove of potential solutions. Answers to fundamental questions we have—about the inner workings of our organs, about possible cures for disease—will come from understanding how our bodies and minds have emerged from parts common to other living creatures. Already, the study of a little worm called *Caenorhabditis* has led to the discovery of a new mechanism for gene regulation. That discovery, for which the Nobel Prize was awarded in 2006, has spawned some of the most promising technology for tumor suppression and reduction ever discovered. If a cure for cancers is to be found, it will likely be derived from that little worm. I can imagine few things more beautiful or intellectually profound than finding the basis for our humanity, and remedies for many of the ills we suffer, nestled inside some of the most humble creatures that have ever lived on our planet.

A paleontologist, **Neil Shubin** has found fossils, such as *Tiktaalik*, "a mosaic of primitive fish and derived amphibian," that throw new light on key transitions in evolution—from water to land, from reptile to mammal—and that clarify the origins of salamanders, dinosaurs, and their relatives. His expeditions have taken him to Greenland, the High Arctic of Canada, Argentina, China, Morocco, Nova Scotia, and the deserts of the United States. Shubin is the provost of Chicago's Field Museum as well as the associate dean and Robert R. Bensley Professor of Anatomy at the University of Chicago. *Your Inner Fish: A Journey into the 3.5-Billion-Year History of the Human Body*, is his first book for a popular audience.

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