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INJURY

When Huck Finn's drunken "Pap" fell over a tub of salt pork and barked both shins, he

> fetched the tub a rattling kick. But it warn't good judgment because that was the boot that had a couple of his toes leaking out the front end . . . and the cussing he done then laid over everything he had ever done previous.

Pap acted as if the tub wanted to hurt him, as if kicking and cursing it could deter future harm to his shins. But the kicking and cussing were wasted effort. The tub was not a rival trying to steal Pap's mate, a predator trying to catch him, or even a microorganism stealthily trying to devour his tissues. It was merely inanimate wood.

In discussing such things as tubs of salt pork as sources of injury, we leave behind the conflicting interests, strategies, and arms races that complicate contests between living opponents. The problems associated with injuries are conceptually simpler than those of infectious diseases, but there is complexity aplenty. Some dangers, like being struck by a meteorite, have always been so rare and unpredictable that we have no evolved defenses and can repair the damage

only by using general-purpose mechanisms. Others, like exposure to high levels of gamma rays, are so new that we have not had time to evolve adequate defenses. But some dangers, like drowning or attack by predators, have happened often enough in evolutionary history that we have evolved ways to avoid them. This chapter is about the ways we avoid, escape, and repair damage from sources of injury such as mechanical trauma, radiation, burning, and freezing. It is also about why these adaptations do not always work as well as we might wish.

Avoidance of Injury

Cooled by milk, the coffee needed to be warmed up just a bit. The microwave oven sounded its three pleasant beeps, and, as one of the authors opened the door, the air filled with the aroma of steaming café au lait. As he grabbed the handle of the ceramic mug, searing pain struck in a fraction of a second, too soon, too intense even to get the hot-handled mug to the counter. It crashed to the floor, splattering hot coffee for yards. After he got his painful hand under cold water, the victim realized that this mug must be different from others, which stay cool to the touch after microwaving. In fact, its handle must have had a metal core. The pain prevented the worse damage that would have resulted from more prolonged contact. The fearful memory of the pain, months later, still makes him shy away from using that particular mug.

Pain and fear are useful, and people who lack them are seriously handicapped. As noted already, the rare individuals who are born without the sense of pain are almost all dead by age thirty. If there are people born without the capacity for fear, you might well look for them in the emergency room or the morgue. We need our pains and our fears. They are normal defenses that warn us of danger. Pain is the signal that tissue is being damaged. It has to be aversive to motivate us to set aside other activities to do whatever is necessary to stop the damage. Fear is a signal that a situation may be dangerous, that some kind of loss or damage is likely, that escape is desirable.

Here we come to a distressing insight. Pain and fear, the sources of so much human suffering, the targets of much medical intervention, are not themselves diseases or impairments but instead are normal components of the body's defenses. Blocking pain and fear in any

way other than eliminating the cause may make the damage worse. For instance, people with syringomyelia, a degeneration of the central part of the spinal cord where the pain nerves are located, experience no pain in their hands. A person with syringomyelia would have picked up that hot cup of coffee and drunk it calmly as the flesh curdled on his fingers. If he smokes, his fingers are likely to be charred. Pain is useful, and its link to fear is no accident. When the body is damaged, pain motivates rapid escape and fear prevents recurrence.

But our adaptations for avoiding injury are more subtle than the mere avoidance of pain and its portents. Avoidance can be conditioned more easily to some cues than to others, depending on what kind of harm occurs. Psychologist John Garcia easily conditioned dogs to avoid a peppermint smell associated with gastrointestinal illness but found it much more difficult to use such sickness to condition avoidance of a tone. Dogs also readily learned to avoid an electric shock that was preceded by a tone but had much more difficulty when the cue was an odor. This makes eminent evolutionary sense. Auditory stimuli are more likely than odors to be good cues to the danger of impending injury, while odors are far more reliable indicators of toxic food. Like so many good ideas, Garcia's was difficult to get published, was ridiculed shortly thereafter, and has been praised ever since.

Some cues—for instance, snakes, spiders, and heights—readily elicit fear in ourselves and other primates. It should not surprise us to discover that we instinctively avoid certain cues that have long been associated with such dangers as falling and dangerous animals. After all, a rabbit that learned a fear of foxes only by being bitten would pass on few of its genes. Rabbit brains are preprogrammed to avoid foxes, and it should not be surprising to find that our brains have some similar capacities. But the price of innate behavior is its inflexibility. Better than a fixed innate response would be a more flexible system that induced fear only to stimuli shown to pose a threat. A newborn fawn will stand and stare at an approaching wolf until it sees its mother flee. Then it too flees, and the flight pattern is set for the rest of its life, ready to pass on to the next generation by imitation. Our fears of snakes, spiders, and heights are prepared but not hardwired. They are partly learned and can be unlearned.

Psychologist Susan Mineka carried out an ingenious series of experiments at the University of Wisconsin Primate Center to demonstrate the development of such fears. Monkeys raised in the laboratory have no fear of snakes and will reach over a snake to get a banana. After

watching a single video that shows another monkey reacting with alarm to a snake, however, the monkeys develop a lasting phobia of snakes. They will no longer even approach the side of a cage closest to a snake, much less reach across it. By contrast, if the video shows another monkey apparently recoiling in fear from a flower, no phobia to flowers is created, even though the response the monkey sees is otherwise identical. Monkeys readily learn fear of snakes, but not fear of flowers.

Generalized Learning and Understanding

In addition to the simple conditioning discussed above, we humans have more subtle adaptations: our capacities for communication, memory, and reasoning. Drivers can imagine that speeding down an icy mountain road is dangerous, even if they have never actually seen it cause an accident. Even those who haven't personally known anyone killed by a fire can understand that a burning building is a serious hazard that a smoke detector can reduce. People can even avoid dangerous things they cannot perceive, such as radon gas, dioxins, and dietary lead, thanks to learning and reasoning. Our capacity to create and manipulate mental representations has many benefits, and the ability to foresee new dangers is clearly one of them. This capacity also helps us to avoid repetitions of actual experiences of danger or injury without creating unnecessary phobias. If we see someone get a shock while wearing suspenders and working carelessly with household wiring, we can reason that the wiring, not the suspenders, caused the misfortune.

Repair of Injury

Injury cannot always be avoided. Whether at the tenth or the ten thousandth stroke, the hammer eventually comes down on the thumb. The resulting injury brings a whole battery of repair mechanisms into play. Blood platelets secrete clotting factors that soon stem the bleeding, whether external or internal (in the form of a bruise). Other cells secrete a complex variety of substances that cause inflammation, thus raising the temperature of the tissue and making it harder for any invading bacteria to grow. They also keep the thumb

painful, thus protecting it from minor stresses that might disrupt the healing process. Simultaneously, the immune system rushes specialized infection fighters to the site. They either attack any bacteria that the injury might have introduced or take them to lymph nodes, where they can be more easily destroyed. Fibrin strands link the tissues together, and, as healing proceeds, they slowly shrink and pull the sides of the wound together. Eventually nerves and blood vessels grow anew into the damaged tissue, and the hammering can proceed as before, albeit more cautiously. These repair processes show a precise, complex coordination that a symphony orchestra might well envy.

Unfortunately, no one has yet written the score for the healing symphony. Many individual parts are described at great length by pathology books, and some attention has even been paid to coordination among the parts, especially the different roles of several groups of immune cells. What we lack is an adaptationist story for the overall process. Such an account would have a plot—the effort to achieve the best possible repairs in as short a time as possible—to which all the details could be related. It would be a tale of optimal trade-offs in the allocation of scarce resources such as time and materials, and between such conflicting values as continued effective use of the damaged part and its protection from stresses that could slow the healing. It would deal with the optimal timing of events, with no job being started until those that must be finished first are completed. It would recognize the need for cooperation and effective communication, not only within such systems such as the immune but also in the participating hormonal, enzymatic, and structural adaptations. It would deal not only with events at the site of injury but with hormonal and other adjustments of emotion and behavior and of physiological processes throughout the body. We hope the score of this well-crafted symphony will be written in the not-too-distant future.

Burns and Frostbite

Even instantaneous pain was not quick enough to save the tens of thousands of skin cells burned by the hot handle of that coffee mug. Two small regions on the thumb and index finger turned white in seconds. Curdled like an egg white dropped into boiling water, the skin cells formed a mass of denatured protein, a kind of injury more difficult to repair than a minor cut. This is, no

doubt, why heat so quickly causes intense pain. Skin with a minor burn heals readily because the mechanism that replaces epidermal cells remains ready to work, but deeper burns pose more difficult problems. If a burn destroys the cells that replace the epidermis, special mechanisms are required to protect the site from infection, clear away the dead tissue, and infuse the region with new skin cells that can grow and gradually resurface the site of the burn. We can do it, but only with time and risk of infection. Far better to avoid the burn.

We have used and abused fire for a hundred thousand years or more. Even before people learned to make fire, they took burning materials from natural sources and maintained fires for cooking and other uses. Has this long association sharpened our reactions to fire's dangers? It would be interesting to learn if we are better defended against hot objects than closely related species are, perhaps by being more sensitive to hot objects or by more rapid healing of burns.

Heat is not the only cause of thermal damage. Freezing can leave cells just as curdled and dead, a condition known as frostbite. Although this was not a routine danger during most of human evolution, it may have shaped our avoidance of extended exposure to cold air and especially to cold water, which is hundreds of times as effective a heat conductor as still air. Liquid nitrogen and dry ice are novel dangers that were entirely absent in the Stone Age. They can be as harmful as fire, but we have not evolved reactions to make us recoil instinctively from liquid nitrogen or dry ice as we do from hot coals.

RADIATION

The most important radiation damage has always been from the sun. Dark-skinned races are fully equipped with the primary defense against the sun's rays, the pigment melanin in the outer skin, which protects the underlying tissues simply by shading them. A few thousand generations of freedom from sunshine, as may happen to animal populations living in caves, results in a loss of the ability to make pigment. The continuous presence of pigmentation in dark-skinned races shows the benefits of its protection against sunshine.

People of European descent pose a special evolutionary problem. Their pale skins show that protection from sunshine has not been

such a consistently important factor in their history, and they are especially vulnerable to sunburn. The first warm, sunny days of spring tempt some of them to bare their skins for many hours. Maybe they know from painful experience that this is not wise, but it feels so good after the winter chill. If fear of repeating the previous year's sunburn does not deter them, the pain of this year's will not either, because it comes too late. Only hours after exposure does the sunburned area become sore, red, and feverish. For several days, sheets of dead skin peel off. Recovery can be complete in a week or two, but this may not be the end of the story, because getting even a few serious sunburns greatly increases the risk of skin cancer years or decades later.

Gradually increasing one's exposure to the sun is less harmful, because all but the most fair-skinned individuals can develop a sufficiently protective layer of melanin. Suntan is a fine example of an inducible defense that is developed only when needed. The fact that fair-skinned people are not heavily pigmented all the time suggests that for their ancestors pigment production had important costs to fitness. In Chapter 9 we will explore the possibility that pallor may be adaptive in shady and cloudy environments.

Everyone knows that it is an excess of solar ultraviolet that causes sunburn, but ordinary visible light, while far less destructive, is also photochemically active and potentially harmful. It does not normally harm us, because natural selection has provided almost everyone with enough melanin and enough enzymes that counter photochemical alterations. Organisms that do not ordinarily live with bright illumination are much more sensitive to sunshine or even to some artificial light sources. For instance, when fluorescent lighting first replaced incandescent light in trout hatcheries, it caused massive mortality in trout eggs. Hatchery biologists knew that in nature such eggs develop under a shady layer of streambed gravel. They hypothesized that the mortality resulted from the greater brightness and shorter (blue) wavelengths of fluorescent light. Experiments showed that this explanation was right: when the trout eggs were shielded from the harmful rays, they did just fine.

Sunlight kills skin cells not by thermal damage but by photochemical alteration of essential substances. The resulting abnormal compounds and dead cells invite attack by the immune system. To some extent this is desirable. It is wasteful to devote resources to supporting dead or inevitably dying cells that ought to be efficiently

cleared away. It is equally important not to eliminate cells that can adequately repair themselves. Distinguishing between these categories may not be easy. For an injury that doesn't involve pathogen invasion, such as sunburn or perhaps a simple fracture, it may be best to suppress some aspects of the immune response so as not to interfere with healing.

The immune cells themselves, like any others, can be damaged by radiation. At the moment it is not at all clear which of the ultraviolet-induced changes in the immune system are adaptive adjustments and which are impairments. The Langerhans cells in the epidermis, which take up foreign substances and present them to the immune system, react to the ultraviolet wavelengths from 290 to 320 nanometers (UV-B) in complex ways. These cells are intimately associated with nerves that secrete a hormone that blocks their action. UV-B radiation depletes the skin of these cells, thus blocking its ability to react to contact with foreign proteins. Such a lack of sensitivity is characteristic of almost all people who get skin cancer. But UV-B is not the only culprit. There is some evidence that some commercially available sunscreen lotions block UV-B and prevent sunburn but still allow the passage of the longer-wave UV-A, which may damage the skin's immune cells. People who get a rash from being in the sun are often advised to use sunscreens, but sunscreens might in fact make the problem worse by encouraging more exposure to UV-A than they could otherwise tolerate.

An alarming increase in the occurrence of melanoma, a potentially fatal skin cancer, is causing a justified fear of excessive exposure to the sun. The rates in Scotland have doubled in the past decade, and the rates among fair-skinned people are increasing at a rate of 7 percent a year in many countries. Explanations for the increase range from the new cultural desire to be tan to the thinning of the ozone shield, which has always blocked much ultraviolet light. While both of these factors need to be considered, an evolutionary view suggests other explanations too. We do spend more time at beaches, but we spend far less walking in the sun without clothes on. The loss of ultraviolet blocking resulting from ozone depletion is more than counterbalanced in most areas by the local air pollution. What is new is not sun exposure or ozone inadequacy but our *pattern* of sun exposure. People now spend most of their time indoors and then go outside on weekends for intense bouts of unaccustomed exposure. People who are outdoors for hours every day adapt to their amount

of usual exposure and are unlikely to get sunburnt. The risk of melanoma is related more closely to the number of sunburns than to the total amount of time spent in the sun.

Another novel environmental factor is the use of chemically complex sun lotions. Blocking ultraviolet radiation does curtail the development of cancerous lesions. A recent controlled study of 588 Australians found that those who used an active sunscreen developed significantly fewer precancerous skin lesions than those who used a cream that did not block much ultraviolet light. But might the chemicals in sunscreens also cause problems? They don't just sit on the surface of the skin but are absorbed into it. What effects do they have on skin cells, and how might they be transformed after binding to tissue proteins and being bombarded by strong light? The answers are very much in doubt. How ironic it would be if we were to discover that skin cancer can be caused, directly or indirectly, by suntan lotions! Attention should also be given to the products used to inhibit the inflammatory process of sunburn. Such inhibition might prevent cancer by preventing unnecessary damage from autoimmune reactions, but it might also protect damaged and potentially cancerous cells from being naturally destroyed by the immune system.

We emphasize that these are not facts but mere speculations that arise from our lack of understanding. Why do we understand so little about sunburn despite the abundance of available information? Understanding that provides a reliable basis for protection and therapy will be reached when researchers well versed in evolutionary reasoning and with a detailed knowledge of the cellular and molecular events of sunburn put together an explanation that: (1) distinguishes UV impairment of skin function from its adaptive responses to UV stress; (2) distinguishes UV impairment of the immune function from the adaptive immune response; (3) distinguishes impairment of Langerhans cell function from adaptive responses; (4) delineates the special components of the repair processes and their coordination; and (5) shows the positive and negative effects of protective lotions applied before exposure and anti-inflammatory medications used afterward.

Sun damage also appears to contribute to cataracts, a clouding of the lens in the eye. While most sunglasses now block ultraviolet light, older models often did not. Instead they reduced the total amount of visible light, so that the pupil actually opened more widely and admitted more ultraviolet light. Worse yet, many of the cheap sunglasses

that children are likely to wear still transmit large proportions of the ultraviolet. We wonder whether some of today's cataract patients might owe their misfortune to sunglasses they wore decades ago.

Regeneration of Body Parts

Children often ask the most intelligent questions. "Why," asks an inquisitive child, "can't Uncle Bob grow a new leg like a starfish does?" Why not indeed? If lizards regrow lost tails, starfish lost arms, and fish lost fins, why can we not even regenerate a lost finger? It is remarkable that this question seldom bothers adults, even biologists. The answer, in general evolutionary terms, is that natural selection will not maintain capacities that are unlikely to be useful or that have costs that would exceed the expected benefits. Thus, as noted in Chapter 3, serious damage to the brain or heart was uniformly fatal before the era of modern medicine, and the ability to regenerate these tissues could not be selected for. An individual who lost an arm in a Stone Age accident could bleed to death in a few minutes. If the bleeding were somehow controlled, the victim would likely soon die of tetanus, gangrene, or other infection. Any process that might have allowed our remote ancestors' arms to regenerate has gradually been lost by the accumulation of mutations that have not been selected against.

But what about the loss of a finger? This would not be as likely to cause death as the loss of a whole arm, and such injuries often do heal under Stone Age conditions. Why not regenerate the finger instead of merely healing the wound? The explanation given in the previous paragraph will not suffice here. We suggest instead two other factors. The first is merely that this regenerative ability would not be used very often and would not produce a major benefit. Most people do not lose fingers, and if they do, the long-term impairment need not be serious. A nine-fingered Neanderthal might live to the ripe old age of fifty. Another reason, which we have already repeatedly emphasized, is that every adaptation has costs. The capacity to regenerate damaged tissue demands not only the cost of maintaining the machinery to make this possible but also the cost of a decreased ability to control harmful growths. A mechanism that allows cell replication increases the risk of cancer. It is dangerous to let mature, specialized

tissues have more than the minimum needed capability to repair likely injuries, as we will discuss in the chapter on cancer.

A different kind of explanation is often offered for our inability to regenerate a missing finger. Regeneration would require growth hormones, control of cell movement, and many other processes, and they are simply not there. This is another way of saying that, after an early stage of fetal development, the machinery needed for producing a finger is missing. This is the sort of proximate explanation, based on the details of the mechanism, that most medical researchers would think of first. But we also need an evolutionary explanation of *why* the needed machinery is missing, whatever that machinery might be. Such an evolutionary explanation is more likely to satisfy a child's curiosity, and it can lead researchers to fruitful ideas on what sort of repair machinery we might expect to be activated by the loss of a finger. We suggest that the machinery will conform to an optimal trade-off between the advantages of rapid and reliable repair, the costs of the needed machinery, and the dangers of cancer.