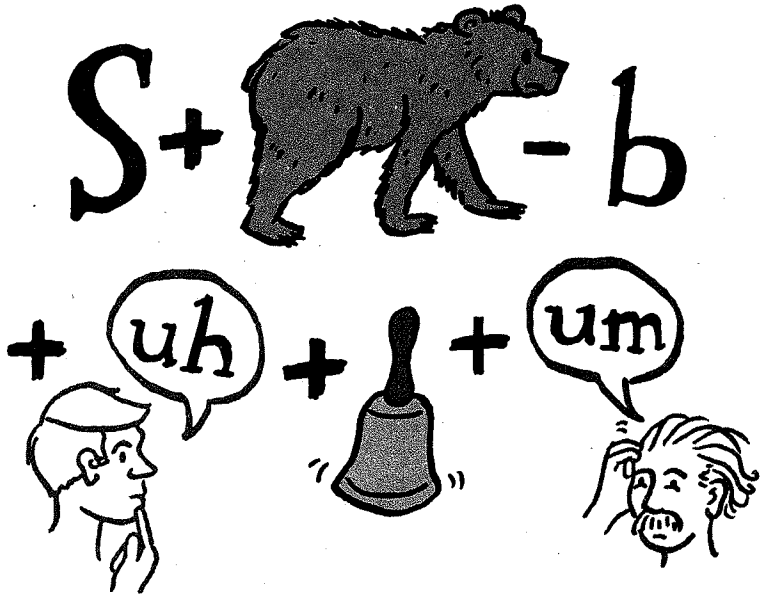
CHAPTER SIX

The Laughing Disease

So far we've mostly considered one-way communication—from brain to body, for example. But the nervous system also uses feedback loops, to tweak commands on the fly and combine signals in new and sophisticated ways.



Toward the end the victims laughed frantically, explosively, on the slimmest pretense, laughed so hard they'd fall over and sometimes almost roll into the fire. Until that point their symptoms—lethargy, headaches, joint pain—might have been anything. Even when they began to stumble about and had to flail their arms in a herky-jerky dance to stay balanced, even those tics might be explained away as sorcery. But laughing could only mean kuru. Within months of the first symptoms, most kuru victims—predominately women and children in eastern Papua New Guinea—couldn't stand upright without clutching a bamboo cane or stake. Soon they couldn't sit up on their own. When terminal, they'd lose sphincter control and the ability to swallow. And along the way, many would start to laugh—laughing reflexively, senselessly, with no mirth, no joy. The lucky ones died of pneumonia before they starved. The unlucky ones were whittled down until their ribs pushed through their skin, and the women's breasts hung deflated.

After a few days of mourning, the local women raised the victim on a stretcher of sticks and bark, and gathered in a secluded bamboo or coconut grove distant from the men. Silently, they started a fire and greased themselves with pig fat to protect against the insects and the nighttime cold of the mountain highlands of Papua New Guinea. They laid the body on banana leaves and began sawing each joint, fraying the cartilage with rock knives. Next they flayed the torso. Out came the clotted heart, the dense kidneys, the curlicue intestines. Each organ was piled onto leaves, then diced, salted, sprinkled with ginger, and stuffed into bamboo tubes. The women even charred the bones into powder and stuffed that into tubes; only the bitter gallbladder was tossed aside. To prepare the head they burned the hair off, gritting through the acrid smell, then hacked a hole into the skull vault. Someone wrapped her hands in fern leaves and scooped out the

brains and filled still more bamboo. Their mouths watered as they steam-cooked the tubes over warm stones in a shallow pit, a cannibalistic clambake. In dividing up the flesh, the victim's adult relatives—daughters, sisters, nieces—claimed the choicer bits like the genitals, buttocks, and brain. Otherwise, people shared most everything, even letting their toddlers partake in the feast. And once they started feasting, they kept stuffing and stuffing themselves until their bellies ached, taking leftovers home so they could binge again later.

The tribe never named itself, but explorers called them the Fore *(For-ay),* after their language. In Fore theology, consuming someone's body allowed his or her five souls to enter paradise more quickly. Moreover, incorporating their loved ones' flesh into their own flesh comforted the Fore, and they considered this more humane than letting maggots or worms disgrace someone. Anthropologists noted another, more prosaic reason for the feasts. For food, the Fore mostly gathered fruits and vegetables and scraped a few *kaukau* (sweet potatoes) out of the poor, thin mountain soil. A few villages kept pigs, and hunters speared rats, possums, and birds, but the men usually hoarded these spoils. The funeral feasts let women and children gorge on protein, too, and they especially enjoyed eating kuru victims. Kuru left people sedentary, unable to walk or work, and those who died of pneumonia (or were euthanized by smothering before they'd starved) often had layers of fat.

Despite the feasts, kuru—from a local word for "cold trembling"—alarmed the Fore, and they concealed its existence from the outside world for decades. Doing so wasn't hard, as they lived in the eastern highlands of New Guinea, among the most isolated places on earth; through the mid-1900s, many tribes there didn't know salt water existed. But soon enough the outside world began wrapping its coils around the Fore and other nearby groups. Gold miners tramped through the highlands in the 1930s, and a Japanese plane crashed there during World War II. Missionaries dribbled in, and in 1951 Australia established a patrol post for men who enjoyed wearing short

khaki shorts and pointing rifles at people who lacked even metal tools. Kuru had reached epidemic levels by then, but most of the outsiders were worried about other things, like the tribes' excessive violence and their outré sex habits. (One-quarter of adult males in the highlands died in raids or ambushes, and some tribes initiated boys into manhood with ritual sodomy.) Some white visitors did catch a glimpse of a kuru invalid being hustled out of sight now and then, or noticed the curious lack of burial grounds in a place with such high mortality. But even the first western doctor to examine a kuru patient arrived at the rather Victorian diagnosis of hysteria, hysteria fueled by colonialism and the erosion of traditional tribal life.

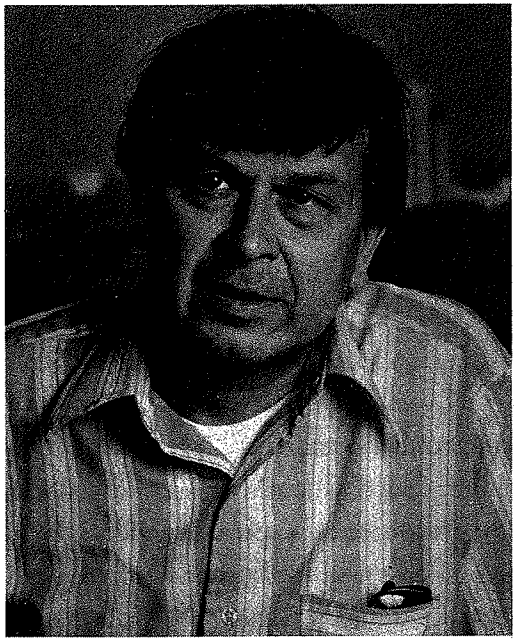
The more cases of kuru that emerged, though, the more empty that diagnosis seemed. How could a seven-year-old with no memories of tribal life come down with hysteria, much less die of it? Kuru was clearly organic, and the movement and balance problems suggested brain trouble. But whether kuru was genetic or infectious, no one knew. To compound the mystery, unlike all other known infections or neurodegenerative diseases, which don't discriminate by race or creed, kuru attacked only the Fore and their neighbors, some 40,000 people; *The Guinness Book of World Records* once named kuru the rarest disease on earth. But exactly because of its oddities, this rarest of diseases soon became a global obsession, with samples of Fore brains speeding across the globe and opening up whole new realms of neuroscience.

~

The highlands attracted a strange breed of visitor. People who laughed off leeches and lice. People who didn't mind that the natives greeted them by fondling their breasts or sprinkling pig's blood on them. People who shrugged when the roads were washed out yet again and didn't blink when told that reaching a village a few miles distant would require an eight-hour hike around gorges and cliffs. You almost had to thrive on hardship, and throughout the 1950s New Guinea

attracted its share of misfits—none more misfit than D. Carleton Gajdusek.

Born to a butcher in New York State, Gajdusek *(GUY-duh-sheck)* proved a science prodigy as a boy. He sailed through school, and on the stairs leading up to his lab in the attic he painted the names of Jenner, Lister, Ehrlich, and other great biologists. (A dubious legend had it that he left the top stair blank, for himself.) Still, he had trouble relating to his peers, to say the least; he once threatened to poison his entire class with the cyanide his aunt had given him to collect bugs. So at age nineteen this young man with icy blue eyes and pitcher ears ran off to Harvard Medical School, where he earned the nickname Atom Bomb for his intensity. He specialized in pediatrics, then did graduate work in California on microbes. His circle of colleagues there included James Watson.



Neuroscientist and adventurer Carleton Gajdusek. (National Library of Medicine)

But just as Gajdusek began to establish himself in American science, he began to chafe at the conventions of bourgeois American life. He finally escaped under the auspices of the army medical corps and set about wandering through Mexico, Singapore, Peru, Afghanistan, Korea, Turkey, Iran. At each stop he hunted out children with rabies or plagues or hemorrhagic fevers, doing pathbreaking work on little-known diseases. He made friends easily and lost them even more easily, often in blowout fights. In fact he had little personal life beyond his pediatric work: a colleague once observed that he had "no interest in women, but an almost obsessional interest in children." Like the Pied Piper, he attracted a coterie of boys in every remote village, and he once wrote in his journal, "Oh, that we might be Peter Pans and live always in Never-Never Land."

In early 1957 he visited New Guinea, planning to cruise right through—until he heard about kuru. Kuru combined his interests in microbiology, neurology, children, and remote cultures, and the colleague who first briefed Gajdusek about it compared his reaction "to showing a red flag to a bull." Gajdusek caught the next bush plane up to the highlands and began tramping from village to village over some of the steepest, slipperiest terrain on earth. He quickly memorized the symptoms—twitching eyes, a staggering gait, trouble swallowing, laughter—and identified two dozen kuru victims within a week, sixty within a month. With growing excitement he also began writing letters to colleagues, alerting them to this new disease.

He spent the next few months conducting a kuru census, visiting every village he could and taking tissue samples from victims. To this end he recruited—with soccer balls and other toys—an entourage of ten- to thirteen-year-old *dokta bois* (doctor boys), dozens of whom might accompany him on a patrol. They marched for hours with Gajdusek every day, clad in white *laplaps* (waistcloth skirts) and carrying boxes of rice, tinned meats, and medical supplies on poles over their shoulders. They had to dodge bees and mudslides and stinging plants. They made tea in streams and wielded bamboo torches after dark.

Their shelters for the night were often barely distinguishable from the surrounding shrubbery, and they lived in perpetual fear of ambushes from neighbors with bows and arrows. Reaching some villages required crossing gorges on bamboo bridges that disintegrated with each step, the chaff flaking off and floating down a hundred feet to the rivers below. Naturally, most boys saw the patrols as grand adventures, the happiest hours of their lives.

At every stop Gajdusek asked about kuru, and the more enterprising *dokta bois* snuck into the bush to rustle out victims who'd been hidden away. Some boys were beaten for this by family members who wanted their mothers and aunts and children to die in peace. But whenever a victim agreed, Gajdusek took blood and urine samples in makeshift bamboo tubes and packed them away in his supply boxes.

After a thousand miles of hiking, Gajdusek had determined just how bad things were. Roughly 200 people were dying of kuru annually, the proportional equivalent of 1.5 million U.S. deaths every year. And things were actually worse than that sounds. Because kuru

Two young kuru victims. (Carleton Gajdusek, from "Early Images of Kuru and the People of Okapa," *Philosophical Transactions of the Royal Society B* 363, no. 1510 [2008]: 3636–43)

targeted women and children, it threatened to extinguish the Fore culture, since the younger generation couldn't replenish itself. More acutely, the chronic shortage of women, a common cause of war among hunter-gatherers, seemed likely to ratchet up tensions even more.

The delicacy of the situation made the ruling Australian government tremble. Australia had acquired the highlands after World War I, and politicians there viewed New Guinea as their one chance to become a colonial power. As with most colonial overlords, Australia was motivated by a patronizing wish to "civilize" the natives, combined with a strong lust for profit, and by 1957 it had achieved both ends. Fewer and fewer natives wore penis sheaths or pierced their noses with pig tusks. Papuans now built rectangular homes instead of traditional oval ones, and they abandoned their simple, bamboo-pipe-irrigated yam gardens to slave away on coffee plantations or in mines. At the same time murder rates had dropped off steeply and centuries-old diseases like yaws and leprosy had disappeared. But kuru threatened to upset this *pax Australiana* by panicking the highlanders and discrediting the government. Colonial officials tried to keep it secret, and they despised Gajdusek for spreading word of it. Hell, for all they knew, Gajdusek himself was spreading the disease by tramping from village to village. So colonial officials tried to restrict his movements within the highlands and even petitioned the U.S. State Department to forbid his travel. They meanwhile played dirty and waged a propaganda war, denouncing him as a "scientific pirate" and threatening other scientists for collaborating with him. One rival taunted Gajdusek that "your name is [now] mud."

But Australia was about to learn that Carleton Gajdusek did not lose stare-downs. After throwing a tantrum over the interference, he decided to simply outwork his saboteurs. He'd penetrate more deeply into Fore territory and collect more gallons of blood, urine, and saliva than any five Aussies. Sure enough, within five months Gajdusek had identified hundreds of kuru victims, and he even sweet-talked some

families—or bribed them, with knives, blankets, salt, soap, and tobacco—into letting him do autopsies on the victims' brains. Like a pseudo-cannibal himself, Gajdusek performed some of these autopsies on the kitchen table in his hut, plopping the brains onto his dinner plates and slicing them up like thick white focaccia with a gray-matter crust. He sent most of this precious tissue back to his lab at the National Institutes of Health, in Maryland, but shrewdly also sent samples to Australian scientists, to placate them and undermine the politicians whispering poison into their ears. Eventually Australia realized it would just have to tolerate Gajdusek.

In the meantime Gajdusek faced another, unexpected obstacle to his work—sorcery. Almost to the last man and woman, the Fore believed that sorcerers caused kuru, and they listened to Gajdusek's lectures on microbes and genetics with amuse- or bemusement. According to tradition, sorcerers worked their necromancy on personal items, including body discards such as hair, fingernails, and feces. Sorcerers first bound these items with leaves, then cast their spells and buried the bundles in swamps; as the items decayed, so too would the victims' health. (To be sure, the Fore considered most spells cast in this manner perfectly acceptable, but "making kuru" went beyond the bounds of decency.) To head off sorcerers, the Fore held bonfires to burn their refuse, and also built some of the deepest latrines on the planet. (After doing their business in the woods, they might even carry the turds back to the latrine, for safety's sake.) And people who had already contracted kuru would hire showy counter-sorcerers, who chanted and dispensed herbs and forbade patients from drinking water, eating salt, or consorting with the opposite sex. Not surprisingly, people who believed so deeply in sorcery weren't thrilled about giving up bodily fluids to a stranger. So to convince people of their security, Gajdusek acquired a reassuringly large lock, which he slapped onto his box of samples.

After Gajdusek collected the samples, they had a dicey future. If he had access to a jeep, he drove them to the nearest patrol station.

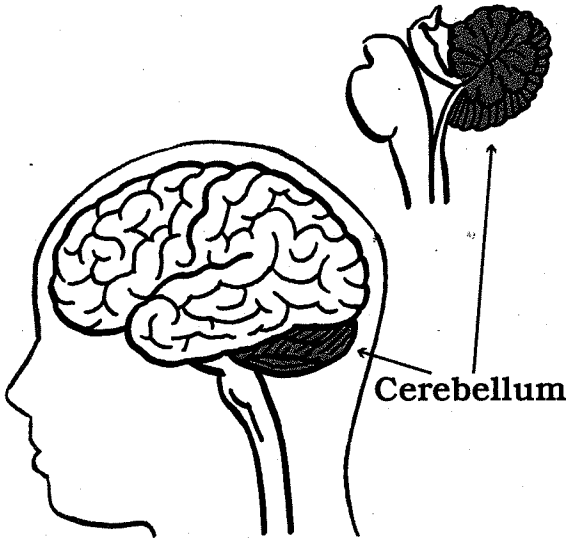
Often as not, though, an axle had broken or the road had washed out, and he had to dispatch a *dokta boi* on a multihour hike. It was then even odds whether the freezer at the station was working. Within a few days, hopefully, the blood or brains got loaded onto a plane en route to a city with an international airport. There, a technician could finally pack the samples in dry ice and dispatch them to Maryland or Melbourne or the dozen other places where labs—goaded by Gajdusek—had taken up kuru.

Neurologists also started trickling into the highlands to examine kuru victims directly and look for signs of brain damage. Some of the tests they administered looked like DUI checkpoint trials, with Fore people walking heel to toe, touching fingers to noses, or standing on one leg and raising both arms. Kuru victims generally failed such tests. Neurologists also tested for certain reflexes. If you tap the skin around an infant's mouth, she'll automatically purse her lips; this "snout reflex" makes it easier to suckle a nipple. Similarly, brushing an infant's palm in certain places will make her fingers curl, a reaction called the hand-grasp reflex. These reflexes disappear during our second or third year as the brain matures and certain other circuits inhibit them. But they can reemerge after brain damage—and often did in kuru victims.

Based on the battery of tests, neurologists traced much of the initial damage in kuru to the brain's movement centers, especially the cerebellum. As we've seen, a few different patches of gray matter in the brain (e.g., the motor cortex) work together to initiate movement. In addition, the brain's motor system has some crucial feedback loops to ensure that movements are carried out properly. One key structure in this feedback circuit is the cerebellum.

As part of the so-called reptile brain, the cerebellum sits way back near the spinal cord, and its wrinkly appearance makes it look like a mini-brain all by itself.* It plays an especially important role in coordinating movement and providing balance. In short, the cerebellum collects inputs from all over the brain, including all four lobes. This

allows it to monitor the body's position in space in multiple ways (through touch, vision, balance, and so on). It then checks to see whether the movement you're executing is anything close to what you intended. If not, the cerebellum pings another brain structure (the thalamus), which passes the message to the motor cortex and tells your muscles how to adjust. *Not so fast,* it might caution, or *a tad to the left.* Without the cerebellum you might get lucky and grab your glass of wine every so often, but it's more likely that you'd flail your arm too far one way, then correct wildly the other way and knock the glass over. In other words, the cerebellum makes grace and precision possible. It helps control the timing of movements, enabling you to walk, talk, jump, and swallow smoothly. Even some involuntary movements, like breathing, depend on the cerebellum to some extent.



When the cerebellum deteriorates, then, your balance falters and your movements become clumsy. Hence the trembling, the eye-twitching, and the jerking gait of kuru victims. Pathological laughter can also arise when a circuit that involves the cerebellum suffers damage. And of course degenerative brain diseases rarely confine themselves to one spot in the brain. The snout and grasp reflexes, and the general cognitive decline of victims, told neurologists that kuru eventually radiated outward and affected structures like the frontal lobes.

Even as the anatomical damage became clear, though, the underlying cause of kuru remained murky, especially on a molecular level. Some scientists jumped to the conclusion that because kuru often ran in families, it must be genetic. But as Gajdusek knew, this theory had holes. For one thing, kuru spread not only within families but also sometimes from one unrelated adult to another, which isn't genetic behavior. Moreover, adult males almost never got kuru, while adult women did frequently. That might suggest something sex-linked—except that the incidence was equal among prepubescent boys and girls. Gajdusek suspected that kuru spread via infection. But that theory ran aground on the fact that the brains he autopsied showed no inflammation and zero other signs of infection.

Nevertheless, the autopsies did reveal other clues. In 1957 an American colleague of Gajdusek's discovered "plaques" in the brains of kuru victims—gnarly black burrs of protein a thousandth of an inch in diameter. The colleague also noticed a proliferation of astrocytes, a type of glial cell shaped like a star. Close to half the cells in the brain are astrocytes, and they play an important role in forming the blood-brain barrier, a protective sheath around blood vessels that blocks foreign material from entering the brain. But for whatever reason, astrocytes also multiply beyond control in the gray matter whenever neurons die off, eventually forming scars. The colleague had no idea what might be causing the protein plaques and astrocyte scars in kuru victims, but he did note a resemblance to Creutzfeldt-Jakob disease (a.k.a. human "mad cow" disease).

Two years later came another clue, from across the Atlantic Ocean. After a friend recommended he visit, an American veterinarian named William Hadlow attended a museum exhibit on kuru in London. He wandered about among the Fore artifacts, interested but hardly engrossed, until some photographic blowups of kuru brains arrested

him. The tissue in the pictures looked oddly spongy, and oddly familiar. Hadlow had studied scrapie, a disease that wrecks the brains (especially the cerebellums) of sheep, causing them to stagger and to scrape their skin raw on trees or fences. Some sheep even hop like rabbits. Scrapie-infested neurons have holes in them, as if tiny carnivorous moths had invaded. Scrapie brains also contain larger holes, where whole bundles of neurons have died. Hadlow noticed that kuru brains had the exact same patterns of holes—the exact same spongy appearance. He quickly wrote a paper, and Gajdusek got in touch with him shortly thereafter. As with the Creutzfeldt-Jakob link, the scrapie connection was a great lead but frustrating, since no one knew what—toxins? genes? viruses? some combination?—caused either disease.

~

The words "slow down" had no meaning for Gajdusek, but with so many other scientists now studying kuru, he did decide to indulge some of his other interests, especially anthropology. He built a bamboo hut for himself in the eastern highlands and began documenting life there, taking thousands of photographs and literal miles of reel-to-reel video. Despite the constant mist and paper-curling humidity, he also filled 100,000 journal pages with field notes about most everything under the sun—local songs, etymology, bawdy gossip, recipes, the inroads made among the locals by communism and Christianity. He used the journals as a diary as well, recording how much weight he'd lost in the field (25 pounds, down to 160) and his fantasy that he could see *Sputnik* circling among the stars overhead.

As a child-development specialist, one subject above all obsessed Gajdusek—sexual initiation rites—and he traveled widely across the highlands, far beyond the Fore tribes, to gather information on them. At around age seven, boys in some highland tribes moved into special domed huts, where they spent their days and nights servicing older adolescents and occasionally grown men. "You should not be afraid of

eating penises," the elders instructed them: they believed that semen strengthened young boys the way breast milk strengthened infants. Oral and anal sex also allowed the boys to "store up" semen, since some tribes believed that men didn't produce semen naturally. Gajdusek recorded every rite he could, down to the details of who got frisky with whom. He also marveled at how some boys even "flirted" with him, batting their eyes and stroking his pasty skin. In his field notes he emphasized that the tribes sanctioned all this underage sex, and argued that it served an important social function in keeping the men from warring over women. (Other anthropologists rolled their eyes at such interpretations.) What's more, the rites helped Gajdusek realize that the "stuffy" sexual mores of the world he'd grown up in were not universal.

In fact the more he immersed himself in highland culture, the more Gajdusek found his past life wanting. He never renounced Western civilization entirely: in particular, he devoured the decadent literature of Henry James and Marcel Proust during his spare hours in the field. But right in the middle of some passage about dukes and duchesses, he might glance up to see Papuan youths dancing outside his hut, wearing feathered headdresses and tusks through their noses. Like Gauguin, this primitive life attracted him, and the dueling impulses—the intellectual and the primal—warred for his soul. One colleague remembered him disappearing into the bush for weeks, then stumbling into a dinner party after his journey in a dirty T-shirt and shorts, one shoe missing. However disheveled, he always dazzled guests with repartee—bouncing until 4 a.m. from Melville to meadow mice to Plato to Puritanism to suicide to Soviet foreign policy—all before disappearing into the wilderness again. Like Kurtz in *Heart of Darkness,* he seemed to be wrestling with all of Western civilization.

Meanwhile, the Fore had their own bone to pick with Western civilization, particularly with Western medicine. Doctors had recently used "shoots"—injections of medicine—to eradicate leprosy in the area. Although thankful, the natives didn't take this as a sign of the

superiority of Western science; rather, they concluded that Western doctors must be powerful sorcerers indeed, far more powerful than the native sorcerers who caused diseases. So when doctors set about trying to cure kuru, Fore expectations were high. Unfortunately, none of the vitamins, tranquilizers, steroids, antibiotics, liver extracts, or other medicines that Gajdusek and company hauled into the field did any good: kuru always killed. After years of futile interventions, the Fore began to seethe. The white men took, took, took, they complained—took bodies, took blood, took brains—but gave nothing back. Even those who believed in Western medicine lashed out. One of Gajdusek's companions fumed that he knew America had "the big microscope" capable of curing any disease, and he couldn't understand why Gajdusek didn't hurry the hell up with kuru.

As the situation unraveled, the Australian government, desperate to stop kuru, considered building a giant fence around the Fore and confining them to a "reserve." (Not only would the fence keep the Fore in, they noted, it would keep Gajdusek out.) Inspired by the genetic theory of kuru, officials also discussed sterilizing the tribe.

But with each new victim, it became clearer that the genetic theory didn't hold water: kuru simply spread too quickly, killing most people before they'd passed on their genes. Plus, some women who were genetically distinct from the Fore and had only married into the tribe had also come down with kuru.

At the same time, no other possible cause made sense. Kuru was neurological, clearly. But scientists had failed to find any bacteria or viruses in the brains of victims. Other experiments ruled out hormone imbalances, autoimmune diseases, metal toxins, plant toxins, insect toxins, alcoholism, and STDs. Some doctors suggested cannibalism as a factor, but the practice had already been outlawed by then. Besides, the Fore had always cooked the bodies thoroughly before eating them, and their customs forbade children from dining on brains anyway, because eating brains supposedly stunted their growth.

With the Fore growing testier and testier, doctors in the field

resorted to bartering treasure for tissue, which made for some ugly scenes. Often the doctors would camp outside a village that had a terminal kuru case, erecting a few poles and throwing up a tarp for a makeshift autopsy clinic. At the first howl of mourning they'd enter the family's hut and start negotiating, offering axes, blankets, tobacco, salt cakes, even American cash. One man argued that if white men took his "meat" (his wife's brain), he should get meat in return. The doctors rustled up a three-pound ham—at which point the husband thanked them, joined the mourners outside, and wailed louder than anyone. The autopsy often took place under kerosene lamps or in drizzling rain, and it could take hours of slicing, cracking, and sawing to liberate the brain and spinal cord—an eon in a place with spotty refrigeration. Doctors wrapped the autopsy up by stuffing cotton balls into the skull and returning the body. They then had the distasteful job of making sure the villagers buried the body instead of eating it.

As for Gajdusek, he continued his anthropologic-cum-medical work, and despite admonishing himself not to, he found himself more and more entangled with the personal lives of his patients. One sad incident involved Kageinaro, a young boy. Although frisky and "flirty" on previous encounters, Gajdusek entered Kageinaro's village one day to find him acting aloof and distant. Gajdusek asked the boy's friend what the matter was. The friend sighed, "Me tink 'e gat sik." *Sick.* "All at once," Gajdusek recalled, "I knew another of my boys had kuru." That night he insisted Kageinaro sleep beside him, for comfort; he wrote in his journal the next morning that "if kuru is contagious I certainly have it." Gajdusek also returned months later to be with Kageinaro as he died, pulling him out of the soiled "lair" where his family had abandoned him. The boy reeked; his eyes flinched from the sunlight; he turned his crusted mouth away from Gajdusek in embarrassment. Gajdusek comforted him as best he could, holding him and giving him water. Most of it ran in rivulets down Kageinaro's cheeks, since he couldn't swallow. Gajdusek, mirroring the boy's face, sobbed.

Scientists soon entered Kageinaro's name in The Book. This pile of

white looseleaf sheets, bound together and carried in an attaché case, acted as a sort of Papuan Doomsday Book, recording every known kuru victim from 1957 forward. As a scientific document The Book is a marvel—scientists had never tracked a disease with such precision. As a social document The Book is simply sad, an unparalleled chronicle of devastation. It records that 145 of the 172 hamlets in the area lost someone to kuru, and some villages lost 10 percent of their women in one year. Reading between the lines, the entire social order was crumbling, and while the *dokta bois* worked and worked, hauling the brains of loved ones to patrol stations and even visiting the villages of enemies to collect samples, The Book just kept getting fatter and fatter. It eventually swelled multiple inches thick.

A breakthrough came at last in the mid-1960s. Although focused on fieldwork, Gajdusek maintained an active research lab back in Maryland. Tantalized by the possible connections among the diseases, he and his team of scientists started to inject cells infected with kuru, scrapie, and Creutzfeldt-Jakob disease into the brains of rodents, to determine whether those diseases were contagious. (Getting scrapie into the United States had required him to flout an international ban and smuggle the tissues in personally, but Gajdusek never considered himself bound by petty laws.) These diseases were indeed contagious, so in 1963 he took the next step, gathering a cohort of apes in an uninsulated cinder-block building in rural Maryland.

Not long before, a boy named Eiro and a girl named Kigea had died of kuru in Papua New Guinea. Near the end both could do little but grunt, and they'd subsisted for weeks on sugar water. (When Kigea's doctor offered her a lollipop, she was too weak to grasp it.) Their families agreed to autopsies, and thanks to a wondrous new material, Styrofoam, their nice, cold brains reached Maryland in pristine condition. On August 17, 1963, Gajdusek and colleagues mixed a thousandth of an ounce of Kigea's brain with water and injected the slurry into the skull of a chimp named Daisey. Georgette the chimp got an injection of Eiro's brain matter four days later.

As they settled in to monitor the chimps' health, the team had to fend off the U.S. Department of Agriculture, which wanted to know why the hell someone was messing around with biological agents in an unsecure building in Maryland farm country. Meanwhile, Gajdusek, never one to sit idle, kept traveling around the world and directing various other research projects from his anarchic NIH laboratory. Visitors remember Bob Dylan blasting on the stereo, psychedelic posters brightening the walls, and lab assistants practicing yoga.

To maintain his connection to New Guinea in between trips there, Gajdusek also began "adopting" Papuan youths, starting with a brash and lively lad named Mbaginta'o in 1963. Among other things, Mbaginta'o had to learn how to use a toilet, wear shoes, and eat with utensils before immigrating to Maryland. Gajdusek nevertheless enrolled him, as "Ivan" Gajdusek, in Georgetown Prep, an elite local high school. Ivan adjusted well, and eventually Gajdusek brought over a "brother" for him. He too thrived, so another brother appeared. Then another. Pretty soon—story of his life—Gajdusek went overboard, and dozens of teens from other tribes followed over the next few decades, some initially against their will. Gajdusek paid to feed and clothe all of them and sent them to good schools. Rather than focus on academics, however, many of his "sons" preferred boozing, racing cars, seducing the daughters of local Rotarians, and generally, as Gajdusek fumed, "fucking around." In short, they behaved like teenagers. Gajdusek did invoke some discipline—his boys did laundry, mowed, cooked, and cleaned their rooms. But it didn't help them adjust when "dad" would jet off for months at a time to track down some exotic disease and occasionally leave them unsupervised.

The breakthrough came in 1966. After years of tedium—and no results—Daisey the chimp developed a drooping lip and a shuffling, stuttering gait, signs of cerebellum damage. Georgette came down with symptoms shortly afterward. After drawing blood and ruling out every disease and nutritional deficiency and poison they could think of, colleagues summoned Gajdusek back from Guam. Gajdusek

arrived grumpy—he hated having his trips cut short—but grew excited when he saw the chimps. The researchers euthanized them and performed autopsies, then sent some brain tissue to a pathologist. She found plaques and spongy holes. Gajdusek's team ripped off a paper for *Nature* in one day, and it appeared in print two weeks later, exploding like a grenade. Not only had they killed the genetic theory of kuru, they'd proved that a degenerative brain disease was contagious in primates, an unheard-of result. Furthermore, they dared speculate on the broader implications of their work for medicine. They proposed that kuru, scrapie, and Creutzfeldt-Jakob—which all cause "spongiform" brain damage and can all lie dormant for long periods before roaring awake—were caused by a new class of microbes, which they dubbed "slow viruses."

The epidemiology of kuru also became clearer in the 1960s. Gajdusek had always balked at linking kuru and cannibalism, since doing so reinforced barbaric "bushman" stereotypes.* Besides, the cannibalism connection had always foundered on a few facts. For one, only women ate the brains at funeral feasts, but children still got kuru, children of both sexes. What's more, Christian missionaries—despite insisting that the Fore eat the body and blood of Christ—had all but eradicated cannibalism by the mid-1950s, while kuru itself had not ceased.

To some people, though, cannibalism still made a lot of sense. The Fore had adopted cannibalism only in the 1890s, when the fad of funeral feasts had diffused down from the north. Intriguingly, the first kuru cases appeared a decade later. And kuru flared up hottest among the tribes most enthusiastic about the feasts. More important, dogged anthropologists determined that the Fore had been lying a little about who ate what. Gooey gray and white matter were supposed to be verboten for the young'uns, but Fore mothers, being mothers, had often indulged them anyway, providing a plausible vector for the infection. And while cannibalism did cease in the 1950s, the chimp experiments explained the lag, since kuru could take years to emerge even when injected directly into the brain. With all these

facts laid in front of them, scientists realized that cannibalism explained everything.

These were the first bits of good news, ever, in kuru research. Thankfully, they weren't the last. By the late 1960s the demographics of kuru had shifted and it was becoming rarer. With no more funeral feasts, the average age of victims in The Book was increasing year by year, as fewer and fewer young people contracted it. Kuru never quite disappeared, but by 1975, when Papua New Guinea gained independence from Australia, the highlanders could finally feel they were putting an awful three-quarters of a century behind them.

What's more, in 1976, their champion, Gajdusek, won a Nobel Prize for his discovery of slow viruses. Gajdusek led an American sweep in the sciences that year, and Milton Friedman and Saul Bellow won as well. Gajdusek got characteristically pissy about all the fuss and formality of the prize. (Friends speculated he'd probably never worn a tie before the ceremony.) But the Nobel affirmed kuru as a disease of major importance. Besides, Gajdusek got a kick out of taking eight of his adopted boys to Sweden. They slept in one of Stockholm's fanciest hotels—on the floor, in sleeping bags.

~

Even with the imprimatur of a Nobel, however, one question kept nagging scientists: what exactly were the slow viruses that caused kuru, scrapie, and Creutzfeldt-Jakob?

One problem with the slow virus theory was the presence of the blood-brain barrier. Scientists have known since 1885 that if you inject, say, blue dye into the bloodstream, the heart, lungs, liver, and pretty much every other organ will turn blue. The brain won't, because the BBB allows only certain preapproved molecules across. (Unfortunately, it also bars most pharmaceuticals we swallow or inject, making common brain diseases like Alzheimer's and Parkinson's difficult to treat.) Microbes have an even harder time crossing the barrier: aside from some exceptions, like the corkscrew-shaped syphilis bacteria

that plagued Charles Guiteau, most bugs cannot penetrate the neurosanctum neurosanctorum.

Furthermore, kuru brains never got inflamed, a fact impossible to square with any known microbe. The purported viruses proved alarmingly resistant to sterilization, too. Tissue infected with kuru remained contagious even after it was roasted in ovens, soaked in caustic chemicals, fried with UV light, dehydrated like jerky, or exposed to nuclear radiation. No living thing could survive such abuse. This led a few scientists to suggest that the infectious agents might not technically be alive; perhaps they were mere scraps of life, like rogue proteins. But this idea ran so counter to everything biologists knew that getting them even to consider it took someone every bit as tenacious and stubborn as Carleton Gajdusek.

That someone was Stanley Prusiner, who initiated the next great phase of kuru research. Not that his career had gotten off to a great start. Prusiner, a neurologist, pretty much flunked out when he first visited the highlands in 1978. Native *bois* practically had to push him up the mountains with two hands on his backside, and not long after seeing his first patients, some intestinal distress waylaid him and villagers had to lug him back down. Nevertheless, Prusiner returned to his lab in San Francisco full of grand plans. In particular he bet big on rogue proteins as the biological vector for both kuru and Creutzfeldt-Jakob. Unlike cells, proteins aren't alive; in fact, most proteins are helpless outside the cell. But maybe, just maybe, Prusiner argued, some proteins could survive independently and even reproduce in some manner. Because they're simpler, proteins should also survive sterilization better, should have an easier time crossing the BBB, and should avoid triggering inflammation in the brain, since they lack the proper markers for our immune cells to recognize.

Somewhat rashly, Prusiner decided—even before he had any evidence that they existed—to name these rogue proteins, calling them prions *(pree-ons),* a portmanteau of *pro*tein and *in*fection. (This fudged the order of the *i* and *o,* of course, but Prusiner felt the ends

justified the spelling peccadillo. "It's a terrific word," he once gushed. "It's snappy." Certainly snappier than *proins.*)

Most scientists disparaged the prion as a vague, fictitious construct—the "p-word," they called it. And in parallel with their dislike of prions, many colleagues developed a pretty healthy aversion to Prusiner himself. In some circles the p-word came to stand for *pushy* and *publicity,* since Prusiner preened and promoted himself and even hired a PR agent. To be fair, Prusiner repeatedly offered to collaborate with colleagues, but most spurned him, including Gajdusek's group. Another time, when Prusiner named Gajdusek as a coauthor on a paper, as a courtesy, Gajdusek hijacked the writing process and refused to allow Prusiner to publish it until he'd deleted all mention of the word "prion." To his credit, Prusiner shrugged these insults off. And after years of laborious work, his team finally isolated a prion in 1982.

The discovery almost ruined him. During follow-up work, his lab determined that normal brain cells manufactured a protein with the exact same amino acid sequence as the prion protein. (Amino acids are the building blocks of proteins.) In other words the healthy brain, as a matter of course, produced something pretty much identical to prions all the time. But if that was true, why didn't we all have kuru or Creutzfeldt-Jakob? Prusiner didn't know, and he brooded over this reversal for months.

Never one to get too discouraged, he soon realized that, far from invalidating his theory of infectious proteins, this new result made it all the more interesting. The key point is that, while the amino acid sequence does help define a protein's identity, proteins are also defined by their 3-D shape. And just as you can rearrange the same sequence of fifty Legos into different structures by snapping the pieces together at different angles, the same sequence of amino acids can be twisted into different proteins with different shapes and different properties. In this case, Prusiner's team determined that a crucial corkscrew-shaped stretch on the normal prions—the ones healthy cells made—got mangled and refolded in the deadly prions, like an untwisted coat

hanger. Clearly, there was a "good" prion and a "bad" prion, and kuru and Creutzfeldt-Jakob seemed to involve the conversion of the former to the latter.

So what causes the conversion? Oddly, the catalyst turns out to be the bad prion itself. That is, the bad prion has the ability to lock onto copies of the normal prion that float by and mangle them, changing their shape until they're clones of the bad one. These bad clones then clump together, forming minuscule protein plaques that harm neurons. That's bad enough, but every so often the clump grows too large and breaks in two. And when it does—here's the key—the rate of converting good prions into bad prions doubles, since each half can now drift off and corrupt others independently. Even worse, those two clumps will both grow too large in turn and split, producing four bad prion clumps. After another round of growth and breakage, those four will become eight, and so on. In other words, prions are a slow chain reaction. The end result is an exponentially growing number of prion vampires—and plenty of dead neurons and spongy holes.*

This prion theory also helped explain where kuru came from. Unlike kuru, Creutzfeldt-Jakob appears in ethnic groups worldwide. It usually starts when a gene mutates in some unlucky person's brain, and he begins to produce bad prion proteins spontaneously. Around 1900 some eastern highlander almost certainly came down with a form of Creutzfeldt-Jakob that attacked the cerebellum, and his equally unlucky loved ones consumed the brain. Prions are indeed immune to cooking and digestion, unfortunately, and can cross the BBB. As a result, the loved ones' brains got infected, and they died. The loved ones were in turn consumed, infecting still more people—who themselves died and were themselves consumed, and so on. Eventually, they started calling the killer kuru. Notice that it wasn't cannibalism per se that caused the outbreak; eating brains isn't inherently deadly. It was the bad luck of eating patient zero. Sadly, then, the very proteins that Fore women had so craved at the funeral feasts ended up killing them.

Since the 1980s prion research has swelled in importance. The outbreak of mad cow disease in the 1990s was basically a case of bovine kuru. British farmers were feeding the ground-up brains of cattle that had a prion disease to other cattle, who in turn infected the humans who ate them. (Not coincidentally, Prusiner won a Nobel Prize for prion research just after the mad cow scare, in 1997.) Disturbingly, some people might still have deadly bovine prions lying dormant inside them.

More recently, prion research has crossed over into mainstream neuroscience. The snarly protein plaques in kuru brains seem to grow and spread in much the same way as the snarly protein plaques that ravage the brains of people with Alzheimer's, Parkinson's, and other neurodegenerative diseases—first turning innocent proteins rogue, then clumping together into plaques that poison neurons and interfere with synapses. (There's even evidence that Alzheimer's plaques in particular require the presence of the normal prion proteins to do damage.) Thankfully, you can't "catch" diseases like Alzheimer's and Parkinson's. But if other scientists can build on this prion work and slow down or even cure these ailments—which affect more than six million people in the United States alone and will grow increasingly common as our population ages—more Nobels will surely follow.

Gajdusek himself had first suggested the kuru–Alzheimer link decades ago but didn't really pursue it. After winning the Nobel, in fact, he got more and more lethargic. There were still plenty of lectures worldwide as well as occasional jaunts to study diseases in places like Siberia. But having gained back the weight (and then some) he'd shed in New Guinea long before, he slowed down a lot, and spent more and more time at home with his adopted children.

Or rather, his adopted sons, since the vast majority of youths he'd surrounded himself with were male. A few colleagues, having noticed the pattern here—*All strapping lads, eh?*—began snickering about this and winking at each other whenever Gajdusek prattled on about "my boys." The FBI found the situation less funny.

As early as 1989, Maryland police had started investigating Gajdusek on charges of sexual molestation. The FBI got involved in 1995, when agents began scouring his published journals and field notes. A number of passages made them cringe. Passages describing various boys' pubic hair; passages about boys who, "with the slightest encouragement to their fondling, [go] searching in my pockets"; passages about him waking up on Christmas morning having "slept well again, like a bitch with her half-dozen pups lying and crawling over her"; passages about fathers who "smile and... indicate that I should let the boys play sexually with me." All of this was vague or ambiguous, though, and it all took place in New Guinea anyway. So the FBI began questioning his adopted sons, and finally found one who claimed that Gajdusek had had relations with him as a teenager in Maryland. (Other victims came forward later.) The young man agreed to call the seventy-two-year-old scientist, and during their conversation he asked him, "Do you know what a pedophile is?" Gajdusek allegedly answered, "I am one," then admitted to having sex with other boys. Gajdusek begged him to keep quiet, but the phone call was being recorded. Just before Easter in 1996, as a pudgy, jet-lagged Gajdusek pulled into his driveway one morning, returning from a conference in Slovakia on mad cow disease, a half dozen police cars whipped out of hiding, their red and blue lights screaming. Arrested and jailed on charges of "perverted practices," Gajdusek ranted from his cell, vowing to "pray to my pantheon of gods" for deliverance and attacking his accusers as "jealous, vindictive... probably psychotic." Eventually, though, he pleaded guilty and served eight months.

In subsequent interviews* Gajdusek more or less admitted everything: "all boys want a lover," he claimed, later adding, "and if I find them playing with my cock, I say good on you, and I play with theirs." He further defended himself by saying that the boys always approached him for sex, not vice versa, and that they came from a culture where sex between men and boys was appropriate, so no harm done. (An intellectual, he also invoked the widespread pederasty of classical

Greece.) In truth, the highlanders weren't the sexual libertines he claimed: they knew full well about other pedophiles who'd settled in their land and taken advantage of their culture, and they despised these men as perverts. Gajdusek also seemed willfully blind to the power he'd held over his boys in America as their guardian and master. Regardless, he never apologized, and fled to Europe after his jail term. He summered in Paris and Amsterdam, and wintered in northern Norway, enjoying the never-ending nights of winter solitude. He died, defiant and alone, in a hotel room in Tromsø, Norway, in 2008.

It's a complex legacy. Gajdusek was one of the outstanding neuroscientists of his era: he alerted the world to a brand-new brain disease, and his experiments on the brains of apes (along with Prusiner's crucial research) opened up a whole new realm of not-quite-living "biology." He also proved that infectious agents can crouch inside the brain for years before springing—a baffling notion then, yet one that foreshadowed the long latency of HIV. Moreover Gajdusek fought harder than anyone to help the victims of this cruel disorder, and it remains the only human disease besides smallpox ever eradicated: since 1977, 2,500 people have died of kuru, but none since 2005. The Book has probably had its last entry. Yet even as he fought to save Fore society, Gajdusek was apparently preying on its most vulnerable members. What's more, for all his sweat and blood, his work on the brain saved exactly no one; missionaries and patrols had largely stopped the cannibalism before he arrived, and every last person who caught kuru died. In the end, neuroscience proved impotent—and even today most Fore people remain convinced that sorcerers caused kuru.

But perhaps that's too bleak a view: the victims of kuru didn't die in vain. Basic biological research serves as the foundation for more and better work, and because of those victims' sacrifices we now know that kuru ravages the brain in ways tantalizingly similar to Alzheimer's, Parkinson's, and other plagues of old age. So perhaps the "world's rarest disease" holds the insight to preventing brain decay in human beings everywhere. If that proves to be so, the Fore will have gotten

inside our brains as surely as they got inside the brains of so many scientists. And as neuroscience continues to expand its scope and map out how the tiny circuits in our brains give rise to higher-level drives and emotions, perhaps even the self-delusions and contradictory desires of someone like D. Carleton Gajdusek will start to make a little more sense.

CHAPTER SEVEN

Sex and Punishment

In addition to nerves and neurons, the brain also sends out signals via hormones. Hormones play an especially important role in regulating emotions, which provide a crucial bridge between brain and body.