PANDEMIC

TITLES BY ROBIN COOK

CHARLATANS CONTAGION HOST ACCEPTABLE RISK

> CELL FATAL CURE

NAND TERMINAL

DEATH BENEFIT BLINDSIGHT

VITAL SIGNS CURE

INTERVENTION HARMFUL INTENT

FOREIGN BODY MUTATION

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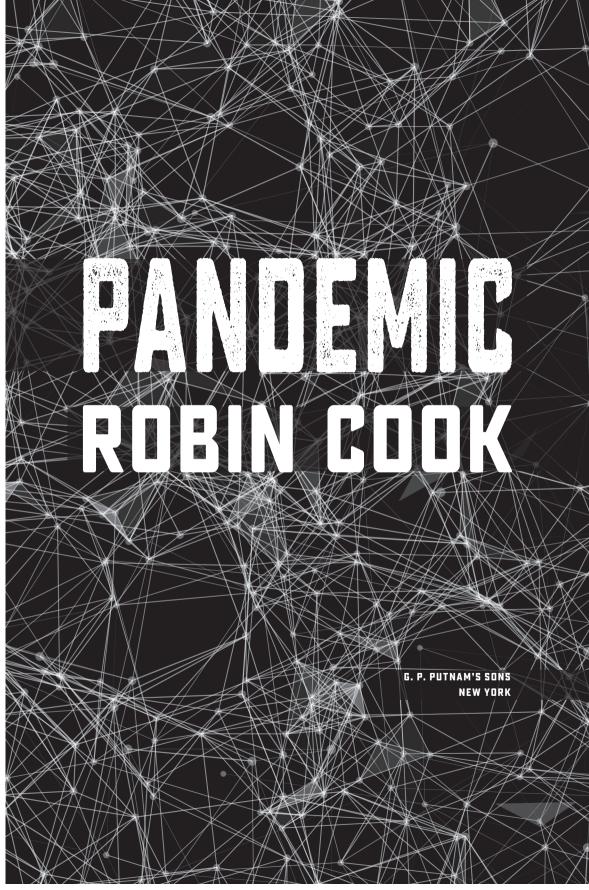
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This is a work of fiction. Names, characters, places, and incidents either are the product of the author's imagination or are used fictitiously, and any resemblance to actual persons, living or dead, businesses, companies, events, or locales is entirely coincidental.

This book is dedicated to the mystical clairvoyance that some gifted scientists have, which allows them to look at data available to all and see diamonds in the rough, resulting in a scientific quantum leap forward.

Such is the case with Jennifer A. Doudna and Emmanuelle Marie Charpentier, who are responsible for the gene-editing technology CRISPR/CAS9 and its evolving permutations.

PANDEMIC

PREFACE

On the warm summer day of August 17, 2012, the newly released issue of *Science* magazine contained an article about bacterial immunity with a title so esoteric that late-night talk-show hosts could have used it in their monologues to make fun of scientific gobbledygook. But the article's publication has turned out to be an enormously important biological watershed event, despite the modest prediction offered in its concluding sentence that the mechanisms described therein "could offer considerable potential for gene targeting and genome applications."*

Seldom has there been such an understatement, as the potential has already become a virtual explosion of applications. The *Science* article was the first to introduce to the world a biologically active chimeric molecule called CRISPR/CAS9, which had been engineered from a bacterial immune system that had evolved to counter viral invaders. This extraordinary molecule made up of three easily produced and inexpensive bacterial components can be custom-tailored to seek out and alter genes in plants or animals. All at once, even a high school student armed with

^{* &}quot;A Programmable Dual-RNA-Guided DNA Endonuclease in Adaptive Bacterial Immunity" by Martin Jinek, Krzysztof Chylinski, Ines Fondara, Michael Hauer, Jennifer Doudna, Emmanuelle Charpentier, *Science*, vol. 337, pp. 816–21.

readily available low-cost reagents and a little instruction could learn to modify the genetic makeup of living cells, which can pass on the changes to daughter cells. With CRISPR/CAS9, any gene whose sequence is known can be removed, replaced, turned on, or turned off, and all this can be done in the equivalent of someone's garage. It is that easy. Heretofore, such a capability existed only in the futuristic dreams of academic molecular biologists with huge, expensive laboratories at their disposal. In other words, rather suddenly, CRISPR/CAS9 has emerged as an enormously powerful, democratized gene-editing mechanism capable of rewriting the fabric of life, including human life. There is no doubt that this capability will revolutionize medicine, agriculture, and animal husbandry.

But there is a dark side. The ease and availability of this versatile and powerful tool that puts the power of the creator in the hands of so many unregulated players beget as much peril as promise. With so many potential actors involved, the situation is even more worrisome than it was in nuclear physics following the splitting of the atom, because in that instance few people had access to the necessary raw materials and equipment to experiment on their own. With CRISPR/CAS9 the question becomes whether future experimenters, be they world-renowned biologists, well-funded entrepreneurs, or high school students, will be more moved by ethical concerns or by the opportunity to maximize their own individual advantage or on a whim with little or no concern for the consequences to the planet and to all of humanity. *Pandemic* is the story of such danger.

PROLOG<u>UE</u>

PART 1 WEDNESDAY, APRIL 7, 1:45 P.M.

Twenty-eight-year-old David Zhao took the cloverleaf exit off Interstate 80 onto New Jersey 661, heading south toward a small town called Dover tucked away in the relatively rural northwestern part of the state. He knew the route well, as he had traversed it hundreds upon hundreds of times over the previous five years. With relatively light midday Saturday traffic it had been a quick trip, accomplished in a little more than an hour. As per usual, he'd picked up the interstate right after crossing the George Washington Bridge. He'd come from the Columbia University Medical Center in upper Manhattan, where he was a Ph.D. student in genetics and bioinformatics at the Columbia University's Department of Systems Biology.

David was driving alone, as he usually did when he went to Dover. Also as per usual, it was a command performance by his imperious father, Wei, who, if truth be told, was somewhat of an embarrassment for David. Like a lot of successful Chinese businessmen, Wei had been given the opportunity to ride the crest of the economic miracle that modern

China represented. But now that he'd become a billionaire, he wanted out of the People's Republic of China, as he had come to much prefer the more laissez-faire business environment of the United States. To David, such attitude smacked of treason and offended his sense of pride in his country's extraordinary progress and uninterrupted history.

David's real given name was Daquan, but when he was sent by his father to the United States nine years ago to study biotechnology and microbiology at MIT, he needed a westernized name, as Zhao Daquan wasn't going to suffice, especially in the normal Chinese order of family name first. He needed an American name so as not to confuse people or stand out, as he knew how much discrimination played a role in American society. To solve the problem, he Googled popular boys' names in the United States. Since David started with the same two letters as Daquan and also had two syllables, the choice was simple. Although it took some time to adjust to the new name, now that he had, he liked it well enough. Still, he was looking forward to reverting to Zhao Daquan when he returned to China. His game plan was to move back there when he finished his Ph.D. the following year and eventually run his father's Chinese biotech and pharmaceutical companies, provided they were still there. David's biggest fear was that his father might succeed in moving the totality of his operations out of the People's Republic.

On the secondary road, David made himself slow down. He knew he had a heavy foot, especially when it came to the new car that his father had given him for his last birthday, a matte-black Lexus LC 500 coupe. David liked the car but wasn't thrilled with it. He had specifically told his father that he wanted a Lamborghini like another Chinese graduate-student friend of his had been given, but in typical fashion, his father had ignored the request. It was similar to how the decision had been made for David to come to the United States for college. David had expressly said that he preferred to stay in Shanghai and attend the Shanghai Jiao Tong University, where his father had gotten his graduate degree in biotechnol-

ogy. But his father had ignored David's feelings. David doubted that his father ever realized that David might have a different point of view on any subject. In that sense, his father was very old-school, demanding unquestioning filial piety.

Turning off NJ 661, David slowed down even more. He'd already gotten more than his share of speeding tickets in New Jersey, so many that his father had threatened to take away his car. That was the last thing that David wanted, as he enjoyed driving. It was his escape. He was now on a rural road surrounded by fields that were just beginning to turn green interspersed with stands of leafless forest. Within a few miles the first part of his father's considerable entrepreneurial domain came into view. Dover Valley Hospital was an impressively modern private hospital currently nearing completion after a total renovation. In its previous incarnation, it had been a small, aging community-hospital-cumnursing home that David's father had purchased out of bankruptcy. Once Wei owned the property he began pouring capital into it, to the surprise and delight of the surrounding towns.

David motored past the nearly finished hospital that he knew now had state-of-the-art operating rooms, among its other modern assets. David was well aware that it was his father's intention to turn the institution into a world-class cancer treatment, gene therapy, in vitro fertilization, and transplant center, all to capitalize on the incredible financial opportunities being opened up by CRISPR/CAS9 technology.

Next to the Dover Valley Hospital, another modern architectural complex loomed. This was his father's GeneRx company, which was the American equivalent of his similarly named company in Shanghai. Here were the brains of the American operation manned by a large workforce of mostly Chinese biotech engineers and technicians that David's father had imported, including a considerable bevy of interns coming from all of the major biotechnology programs at China's many universities. Surrounding the spacious complex was a high chain-link, razor-wire-topped

fence that angled off into the surrounding forest from both sides of a security booth that stood in the middle of the access road, partially hidden by tall evergreens.

Generally, David would merely drive to the gate and expect it to be raised by the duty officer, but since his car was relatively new, he pulled up to the security booth and lowered the window. He was immediately greeted by one of the guards, who addressed him in Mandarin, welcoming him back to GeneRx.

"Are you heading to the main building?" the guard asked.

"No," David said. "I'm going to the Farm for a performance."

The guard laughed, saying it was going to be well attended. He then raised the gate.

Passing the entrance to the multistoried parking lot, David drove around the right side of the main building and into a wooded area. After a few twists and turns, the road opened up into another clearing and another parking area. Beyond it was another matching three-story structure comprised of three wings in the form of *T*'s with hip roofs that stuck off the back. There was a sign on the front that said: FARM INSTITUTE, but David knew that no one called it that. It was known merely as the Farm.

David knew he was a little late, so he quickly found parking and jogged up to the front entrance. Five minutes later he was in the central wing, changing into clean clothing and donning a mask and surgical cap. He was heading into a sterile area that had air flow going only out, similar to a patient isolation room in a hospital. When he was fully decked out and after being checked by a technician to be certain he was adequately covered, David pushed through swinging doors and entered the sterile area. This was the part of the Farm that housed the cloned and sterile pigs whose genomes had been modified by CRISPR/CAS9. There were multiple other areas for various other types of animals, including goats, sheep, cows, monkeys, dogs, mice, rats, and ferrets. The Farm Insti-

tute represented a new direction of "farmaceuticals," with large-molecule, protein-based biopharmaceuticals being manufactured by animals rather than by chemical processes or fermentation vats.

After descending a perfectly white hallway to a door marked INSEM-INATION ROOM, David pushed inside. The square room with a central depressed area was occupied by a large, mostly white pig in heat, a tall individual David could tell was the Farm's head veterinarian, and a handful of his assistants, who were restraining the sow. Grouped around the periphery were some twenty people. David recognized only two, as everyone was in the same getup as he was, their identities obscured beneath facemasks, caps, and gowns. The two people he recognized were his father, Wei Zhao, and his father's man Friday, Kang-Dae Ryang. It was easy to recognize his father because of his unique silhouette. For one thing, his father was tall and commanding, at six feet five inches. David himself wasn't too far behind, at six-three. But his father's build was what really stood out, particularly the breadth of his shoulders and the waist that was still remarkably narrow, despite his advancing years. When Wei Zhao was a university student in the seventies he picked a unique hero, Arnold Schwarzenegger, and became a bodybuilder. Although it had started as a fad, it morphed into a lifelong addiction, and he was still currently doing it in his sixties, albeit in a much-reduced fashion. Kang-Dae's appearance was the exact opposite, thanks to his pencil-thin frame. His gown appeared as if it were hanging on a wire clothes hanger and his eyes had a beady look that brought to mind a bird of prey.

David made it a point to sidle up to his father to make sure that his presence had been noted. It had, but he could immediately tell Wei wasn't happy that David was later than he had been told to arrive. David had done it on purpose, as he derived a modicum of pleasure from his passive-aggressive behavior.

The veterinarian, who was wearing a headlamp, straightened and motioned to Wei with the syringe he was holding that all was ready. A

speculum had been inserted by one of his assistants, so presumably the cervical os was visible.

Wei cleared his throat and spoke first in Mandarin and then in English for all to hear. "Welcome, everyone! We're represented by the whole team, including the CRISPR/CAS9 molecular biologists, the stem-cell experts, the geneticists, the embryologists, and the veterinarians. We're all here to witness this 'one small step for man and one giant leap for mankind."

There was a little forced laughter at the reference to the United States' landing on the moon. "As you all know, GeneRx is in great need of an additional revenue stream now that my financing plans for our American operations have been interrupted by XI Jinping, the Politburo, and the People's Bank of China, all conspiring to generally restrict capital outflow. I am convinced that what we are doing here today will minimize that problem by helping GeneRx be first out of the gate, so we can corner crucial patents and reap the benefits. As you all know, today we are implanting ten cloned bespoke embryos, and we only need one to succeed to ensure our success. Next week we will do the second implantation to answer our crucial question as to which is better: a chimeric pig or a transgenic pig. Thanks to CRISPR/CAS9, we have a choice. Thank you all for pushing ahead so diligently to make this day happen. This will be the first immunologically custom-designed pig. I'm totally confident it will soon lead to hundreds and ultimately thousands of such creations."

After concluding his brief remarks, Wei stepped down into the "pit" to observe firsthand the insemination. Kang-Dae stayed where he was, and David moved next to him. David eyed the man out of the corner of his vision, keeping Wei in sight. He didn't want his father seeing them talking together. In David's estimation, Kang-Dae couldn't have weighed more than eighty pounds, or a bit more than thirty-six kilograms. David attributed the man's rawboned frame to his having grown up in North Korea and starved as a child. Although he had managed to defect to

China thirty-eight years ago, he'd never gained the weight he would have had he not been severely malnourished when young. David had known Kang-Dae for as long as he could remember, as Kang-Dae had been sent by the Communist Party to work for Wei in Wei's very first biotech company, where he proved to be a tireless and totally dedicated worker. He'd even taught himself biology and biotech. Devoid of a family, he ended up living in a tiny room in Wei's home despite Wei knowing he was essentially a spy. As a consequence of proximity, David and Kang-Dae had become close and remained so, particularly after they both unexpectedly and somewhat unhappily ended up in the United States. There, in New Jersey, they learned that they shared a wish for Wei's American enterprise to fail so they could all return to China.

Leaning toward the Korean man and speaking sotto voce, David said: "Did you do what I suggested?"

"Yes," Kang-Dae said. He was a man of few words.

"Once or several times?" David asked. As Wei's trusted aide, Kang-Dae had unparalleled access to the entire complex. He still lived at Wei's nearby private estate. He was more like an appendage than an aide.

"Three times, like you suggested," Kang-Dae said. "I put it in the drinking water. Will it work?"

"There's no way to know for sure," David said. "This whole project is breaking new ground for all of us. But it was definitely toxic to human kidney cells in tissue culture, so if I had to guess, I'd say it is going to work very well: maybe too well!"

PART 2 SEVEN MONTHS LATER . . . MONDAY, NOVEMBER 5, 9:10 A.M.

"Wait! Hold on!" Carol called out. She'd just entered the subway station at 45th Street in Sunset Park, Brooklyn, to see that the R train was

already there. To her shock, it had arrived early, something New Yorkers did not expect the subway to do. Holding on tightly to her new miniature Gucci backpack, Carol started to run. It wasn't easy, for reasons that had less to do with her attire, which was one of her favorite dresses and relatively high heels, than with her physical stamina. Any running was a feat that, until recently, she hadn't been able to accomplish for more than a year. As she ran, she frantically waved her free hand in the hopes of catching the conductor's attention to keep the doors ajar.

As out of shape as she was, the effort was Herculean for Carol, and as she leaped onto the train she was seriously out of breath. She could also feel her heart pounding in her chest, which gave her a touch of concern, but she trusted it would soon subside, and it quickly did. Over the last month she'd been religious in her trips to the gym and was now up to twenty minutes every other day on the treadmill, which she considered fantastic progress. If someone had predicted four months ago that she'd be doing that much exercise at this point in her life, she would have considered them certifiably crazy. Yet, needless to say, she was thrilled. In many ways, being able to run again was like being reborn.

No sooner had Carol gotten on the subway than the doors slid closed, and the train lurched forward in the direction of Manhattan. To keep her balance, Carol grabbed one of the upright poles that ran from floor to ceiling and glanced around for an appropriate seat. Since it was only the sixth stop from the train's origin at 95th Street in Bay Ridge, and since it was now 9:11 and hence mostly after the morning rush hour, there were plenty of openings. But as an experienced subway rider, she knew that certain seats were better than others. Being hassled on the subway was not an infrequent event, and a bit of attention to detail was worth the effort. She quickly spied an auspicious spot only ten feet away.

As soon as the train reached its desired speed, Carol made her way to the seat she had her eye on. There were no immediate neighbors. The closest people, each an empty seat away, were an elderly, well-dressed African American man and an attractive white woman Carol guessed was close to her own age of twenty-eight. The slender woman impressed Carol with her style and the quality of her casual but elegant clothes. She had a haircut not too dissimilar to Carol's, with a dark-brown-base undercut that was mostly covered by a bleached-blond combover. It made Carol wonder if they went to the same hairdresser. As Carol sat down she exchanged a quick glance and smile with the woman. It was a part of New York that Carol loved. You never knew who you might see. Life here was so much more interesting than it was in the boonies of New Jersey where she'd grown up. There people became set in their ways as teenagers and never tried anything new and exciting.

Making herself comfortable, as she had a long subway ride ahead of her, Carol pulled her iPhone out of her backpack to go over the disturbing texts she'd been exchanging of late with Helen, the woman she had expected to marry if and when Carol's serious health problems had been put behind them. The sad irony was that the health problems were almost resolved, whereas the relationship had been challenged and had taken a turn for the worse, so much so that Carol had recently moved from their shared apartment in Borough Park, Brooklyn, to her own studio in Sunset Park. It had all happened rather suddenly. Almost three months ago, while Carol had been in the hospital for her life-saving operation, Helen had invited a dear old high school boyfriend, John Carver, to stay with her as he happened to be in New York and was in need of an apartment. She'd been looking for emotional support, someone to comfort her while she battled the fear that Carol might die, but then the unexpected had happened.

Between the trying emotional circumstances and their close proximity, Helen and John's old romantic relationship reawakened. When it had become clear that Carol was going to live, Helen had hoped she would be understanding and would embrace Jonathan as a permanent third party in their relationship.

Although Carol was initially dismayed and shocked, her desperate need for love and acceptance after the stress of her hospitalization and

near death inspired her to give the unconventional arrangement a good try over several months. But it wasn't for her. At age thirteen she'd come to accept her sexual preference and adjusted, and had just become more certain as the years had gone by.

Rereading all the texts and reexperiencing the emotion they represented didn't help Carol's mindset. It also made her look at the tattoo she had got together with Helen six months ago. It was hard for her to ignore, since it was on the under surface of her right forearm. The image was of a puzzle piece next to a matching image of the puzzle piece's supposed origin. Both were drawn in perspective to make them look all the more real, and the base of the origin was done in a rainbow of colors. Helen's name was on the puzzle piece, as Carol's was on Helen's tattoo. Carol had always loved the tattoo and had been proud of it until now, but her current goal on this trip was to return to the tattoo parlor in Midtown Manhattan where they had gotten the ink and have something done to erase the painful reminder of all that had gone wrong between them. Carol didn't know what the options might be but assumed the tattoo artist would have some ideas. Besides, the trip gave her something to do, as she still had not gone back to her career in advertising. That wasn't going to happen for another month. It had been a deal she'd made with her doctor.

As Carol's train made its way north through Brooklyn, people boarded at each of the many stations, with far fewer people getting off. By the time they were approaching the tunnel to Manhattan, the train was almost as packed as if it were rush hour. It was then that Carol got the first disturbing symptom—a shudder-inducing chill, as if a blast of arctic air had wafted through the subway car. It came on so suddenly that Carol instinctively looked around to see if other people had experienced it, but it was immediately apparent that it had come from within her own body. Her first impulse was to feel her pulse. With relief, she determined it was entirely normal. For a moment she held her breath, wondering if the unpleasant sensation would return. It didn't, at least not at first.

Instead she felt a sense of weakness, as if she might have trouble standing up if she tried.

Still holding her mobile phone, Carol checked to see if she had a strong signal. She did, and she contemplated calling her doctor out in New Jersey. But she hesitated, wondering exactly what she would say. Sudden weakness hardly seemed like an appropriate symptom to tell a doctor. It was much too vague. She was certain he would tell her to call back if it didn't go away or if the chill returned. She decided to wait as she raised her internal antennae to seek out any abnormal sensations. She looked around at the faces she could see. No one was paying her any heed, as everyone was pressed together cheek to jowl.

As the train entered Manhattan, she began to relax a degree. There was still the sense of weakness, but it hadn't worsened, and although she got several more chills, they were nothing like the first. They were just enough to let her know she had probably developed a slight fever. When the train stopped at Canal Street she thought about getting off but was afraid to try to stand up. If she were to fall, it would be much too embarrassing. She felt the same at Prince Street, and then things went downhill. She began to experience difficulty getting her breath, which worsened quickly. By Union Square station, where there was to be a mass exit and mass boarding, she was beginning to feel desperate. She needed air, but her legs seemed not to want to respond.

As the train's doors opened, her phone slipped from her grasp and fell to the floor. In the blink of an eye it was snapped up by a scruffy sort who had been eyeing Carol's behavior. The second he had the phone he melted into the people departing the packed car. Carol tried to call out that she needed help, but no words emerged as she attempted to breathe. A bit of froth appeared at the corners of her mouth. Pulling her legs under her, she marshaled her remaining strength and tried to stand, but as soon as she pushed off the seat, she collapsed, falling against the legs of the people standing immediately adjacent to the bench seat she was on. People tried to move to give her more room, but there was no place to go.

One person tried to arrest her fall but couldn't, as Carol was like a dead weight. Mercifully, she lost consciousness as she slumped like a rag doll, partially propped up against the legs of fellow riders.

As quickly as her phone had disappeared, it was now time for her Gucci backpack to follow suit. Several of the other passengers tried to grab the offending individual, who also departed before the doors closed, but their attention was quickly redirected at Carol, who was twitching uncontrollably and turning blue. It was obvious to everyone that she was desperately ill and struggling for air. Nine-one-one was dialed on multiple phones. As the train lurched forward, another knowledgeable passenger notified the conductor. She came pushing through the crowd as she communicated the bad news to the engineer. As the conductor reached Carol, the intercom sprang to life to announce that a sick passenger was on the train and the train would be stopping at the upcoming 23rd Street station for an indeterminate amount of time. There were a few audible groans. It was a problem that happened far too often on the NYC subway system, inconveniencing thousands upon thousands of passengers who were not sick.

The gravity of Carol's condition was immediately apparent to the conductor, who was confused as to what she should do. With almost no first-aid training other than CPR, which didn't seem to be indicated, since Carol had a pulse and was breathing, she felt helpless. It was quickly apparent to everyone present that there was no good Samaritan with medical training available. Meanwhile, up in the first car, the engineer alerted the rail control center to the emergency and was assured an EMT team was being dispatched to the station.

Once at the 23rd Street Station, it took more than twenty minutes for masked EMT workers to arrive. Many riders had departed the train by then, seeking other transportation, and so the paramedics had a relatively clear path to Carol. What they found was a livid patient with an undetectable heart rate and blood pressure who was barely breathing, if at all, and had lost control of her bladder. After putting a mask on the patient

and attaching her to an oxygen source, they quickly lifted her onto a gurney. They then whisked her off the train, up to the street, and into the waiting ambulance.

With the siren blaring, they rapidly weaved their way across town to pull up to the ER unloading dock at Bellevue Hospital. As they unloaded her from the ambulance, a triage nurse corroborated that there was no heartbeat. One of the EMTs leaped up on the gurney as the others rapidly propelled it into the depths of the Emergency Department and ultimately into one of the trauma rooms, calling out a cardiac arrest in the process. This unleashed a resuscitation team poised for such an emergency, which included a medical resident, a nurse practitioner, and a resident in anesthesia. With the history of breathing difficulty obtained from fellow subway passengers, the patient was intubated and given positive pressure. The assisted respiration required a shocking amount of pressure, suggesting the lungs were possibly consolidated, meaning ventilation was impossible.

With no heartbeat and no ventilation, Carol was declared dead on arrival at 10:23 and covered with a sheet. The only trouble was that no one knew her name was Carol. When the ER clerk called the NYC Medical Examiner's Office she gave the deceased the temporary moniker of Jane Doe, explaining there was no identification and the patient was unaccompanied. At that point, Carol's gurney was unceremoniously parked in a corner to await the medical examiner's van. Under the white sheet, she was still dressed in her finery, and the endotracheal tube still protruded from her mouth.

LATER THAT MORNING . . . MONDAY, NOVEMBER 5, 10:30 A.M.

By 10:30 in the morning all eight autopsy tables at New York City's Office of the Chief Medical Examiner, known colloquially as the OCME, were in use, as the team tried to catch up with demand. Over the weekend there had been a backup of ten bodies that had not been considered forensic emergencies and had been left for Monday morning. Besides those ten, six new cases had come in between late Sunday afternoon and early that morning. Table #1, the table farthest from the stainless-steel sinks, had seen the most action. This was the table favored by Dr. Jack Stapleton. Since he was almost always the first doctor in the "pit" in the morning, he got to choose his station, and he always told Vinnie Ammendola, the mortuary tech with whom he usually teamed, to nab it. Situated at the periphery, it was a little bit separate from the main commotion in the autopsy room when all the tables were in use. At that time Jack was already starting his third case. Most of the other tables were still on their first.

"So!" Jack said, straightening up. He had just carefully shaved away the blood-soaked, matted hair from the right side of the victim's head.

He had been very careful not to distort the wound he wished to expose. What was now obvious was a completely circular dark-red-to-black lesion an inch or two above the woman's right ear, surrounded by a narrow circular abrasion. The patient was on her back with her head rotated to the left and propped up on a wooden block. She was naked and so pale she could have been mistaken for a wax-museum model.

"Is the entrance wound round or oval?" Jack liked a didactic style and frequently used it even when other people weren't listening, as often happened when he was working with Vinnie. Vinnie had a habit of zoning out on occasion. But this morning Jack had an attentive audience. Lieutenant Detective Lou Soldano, an old friend of Jack and Jack's wife, Laurie, had shown up. Over the years Lou had come to truly appreciate the enormous benefits forensic pathology could provide to law enforcement, particularly when it came to homicide investigation, which was his specialty. Whenever there was a case that Lou thought could be helped by forensics, he made it a point to observe the autopsy. Although there hadn't been any such cases for a number of months, that morning there had been three.

"I'd say circular," Lou said. Lou was standing across from Jack on the patient's left side. Also on that side was Vinnie. Next to Jack was a second mortuary tech, Carlos Sanchez, who had been newly hired by the OCME and was now at the very beginning of his orientation and training. As one of the more experienced techs, Vinnie generally broke in newbies by having them work closely with him. Jack was accustomed to the routine and usually didn't mind, provided it didn't slow him down too much. Jack was one of those people who didn't like to waste time and had little patience with incompetence. So far, he wasn't all that impressed with Carlos. It wasn't anything specific, more an attitude thing, as if the man wasn't all that interested.

"I agree," Jack said. "Vinnie?"

"Circular," Vinnie said, rolling his eyes. Vinnie and Jack had worked with each other so many times over so many years that they could anticipate each other. Vinnie knew the tone of voice Jack used strongly suggested he was about to start a "teaching" session, which invariably meant the autopsy would end up taking considerably longer than otherwise, keeping Vinnie away from the coffee break he always took after the third case was over. Vinnie was a coffee addict and his last cup had been just after seven that morning.

"Mr. Sanchez?" Jack asked, ignoring Vinnie's mild acting out.

"Huh?" Carlos blurted.

Jack turned to look into the eyes of the new hire, just visible through the man's plastic face shield. "Are we keeping you from some other, more interesting engagement, Mr. Sanchez?" he asked sarcastically but then let it go. He turned back to Lou. "It is definitely circular, meaning the bullet entered perpendicular to the plane of the skull. More apropos, it is certainly not what is described as stellate or jagged. Now, do you see any stippling around the periphery of the wound?" The little red dots in the skin that sometimes surrounded gunshot wounds resulted from gunpowder residue emerging from a gun barrel along with the bullet.

"I don't see that much except on the ear," Lou said, trying to be optimistic.

"There is a bit on the ear and also some on the neck," Jack said, pointing. "Obviously the full head of hair absorbed most of it."

"I don't think I'm going to like where you're going with all this," Lou said. The victim was the wife of one of Lou's detective colleagues who also worked out of the NYPD's Homicide Division.

Jack nodded. There was no doubt that Lou had become quite forensically knowledgeable over the years of their friendship. "There's more. Let's use a wooden dowel to align this entrance wound above the right ear with the exit wound below the left mandible."

Vinnie handed Jack the wooden rod he had leaned against the autopsy table. Grasping it at both ends, Jack held it so that it rested on the crown of the patient's head but lined up with the two wounds.

Lou reluctantly agreed. "I'm getting the picture: The pathway of the bullet is definitely downward."

"I'm sorry to be the bearer of bad news," Jack offered, hearing the disappointment in his friend's voice. "Unfortunately, what we see here is not a contact wound. My guess at this point would be that the gun barrel had to have been about two feet away and maybe as much as thirty inches. And the trajectory was definitely oriented caudally. Are you aware of the statistics about this?"

"Not exactly," Lou said. "But I know it's not what I was hoping. Jesus, I've known this guy for more than twenty years. I've even had dinner in their home out in Queens a dozen times, especially after I got divorced. They had their problems like all couples. But hell! They have two grown kids."

"Ninety percent or more of small-arms suicides are contact wounds, meaning the barrel of the gun is up against the skull when discharged. In only about five percent of suicides is the bullet path downward, and an even smaller percentage where it's directed from the back to the front, both of which we see here."

"So you don't think this was a suicide?" Lou asked, almost plaintively. Jack shook his head.

"Can we get on with this freakin' autopsy," Vinnie complained.

Jack flashed a dirty look at his favorite mortuary tech. Vinnie ignored it. "I'm having caffeine withdrawal."

"Was there a suicide note?" Jack asked, returning his attention to Lou.

"Clutched in her left hand," Lou said with a nod. "One of Walter's service automatics was in her right hand. She was lying on their bed on her back. It was a mess."

"And he had called you?" Jack said.

"Yeah," Lou said. "We'd been together most of the evening after being called out on that first autopsy we did. Walter found her dead when he got home, or so he said. I was the one who put in the nine-oneone call as I was leaving my apartment on my way over to see him. I got there before anyone else, and the man was beside himself. It was godawful. Not that I haven't seen worse." "Well, we'll have to see how it plays out," Jack said. "Maybe there was a third party involved. But I certainly will not be signing this out as a suicide. I'm definitely thinking homicide. But let's do the autopsy and go from there."

"Hallelujah," Vinnie said, making a rapid sign of the cross in the air in appreciation.

"Let's not be blasphemous," Jack chided sardonically.

"You should talk," Vinnie scoffed. More than anyone at the OCME, Vinnie knew just how irreverent Jack Stapleton could be. Jack was not a religious man after his first wife and two young daughters had been killed in a commuter plane crash. He couldn't imagine a Christian God would let such a terrible thing happen.

The postmortem went quickly. Other than a number of uterine fibroids, the woman's general health had been excellent and there was no pathology. The part of the autopsy that took the longest time came after Vinnie had shown Carlos how to remove the skull cap. With appropriate exposure, Jack had carefully followed the bullet's transit through the brain, where it had wreaked complete havoc. While Jack was busy, Vinnie exposed the underside of the skull cap to photograph the beveled edges of the inner aspect of the entrance wound.

When Jack's third autopsy was complete, he left Vinnie and Carlos to clean up and return the cadaver to the walk-in cooler. Although Lou usually departed as soon as the main part of the autopsy was over, on this occasion he stayed until the bitter end. Jack sensed he was reluctant to head back to his lonely apartment in SoHo. The implication was that he needed to talk more about the disturbing autopsy results, even though he was plainly exhausted from having been up all night.

After changing out of their autopsy gear, Jack took him up to the so-called lunchroom on the second floor, which wasn't much with its blue-painted concrete-block walls, cheap molded plastic furniture, and a handful of vending machines. For a modern medical examiner's office with a staff of highly trained, world-class forensic pathologists, it was

pathetic. But there was a light at the end of the tunnel. A brand-new high-rise NYC medical examiner's building had been constructed on 26th Street, four blocks south of the sad, existing six-story structure that had been built almost a century ago at 30th Street and First Avenue. Most of the Manhattan office's hundreds of employees had already moved to the palatial new location. Those who had yet to go were the toxicologists and the entire bevy of MEs. The problem was that the new building did not have an autopsy room. A new state-of-the-art autopsy facility was still in the planning stages, to be built as a separate structure next to the new high-rise. Until it was operational, Jack and his colleagues had to remain in the old, outdated structure.

"Knowing the choices, what can I get you?" Jack asked. He regarded his friend of almost twenty years. As his name clearly suggested, Lou was distinctly southern Italian, with thick, reasonably long, mostly dark hair and equally dark eyes and decidedly olive skin. A handsome, heavy-featured man of medium height and musculature, with a girth that suggested too much pasta and not enough exercise. As usual, he was wearing a dark blue suit that didn't appear to have been pressed in the previous year. His rumpled white dress shirt was open at the collar and his gravy-stained silk tie was loosened and appeared never to have been untied, but rather slipped over the head at the end of each and every day.

The comparison with Jack was stark, especially when the two were standing right next to each other as they were now. Jack's hair was a light brown, cut moderately short, with a blush of gray over his temples. His eyes were the color of maple syrup and his complexion suggested he had a slight tan even when he hadn't been in the sun for months. At six feet two inches tall, with an athletic build from bike riding and street basketball, he seemed to tower over Lou, whose habit was to hunch over as if his head was far too heavy.

"I don't know," Lou admitted. He was having trouble making up his mind.

"How about a water," Jack suggested. He knew the last thing Lou needed was more coffee. What he really needed was sleep.

"Yeah, water's fine," Lou said.

Jack got two waters and sat down across from Lou.

"You'll let me know what toxicology shows on the second case," Lou said.

"Absolutely," Jack said. "As soon as I know." All three cases that Lou had come in to watch that morning involved the NYC Police Department. The one Lou was currently referring to was a "death in custody" case. During the autopsy Jack had been able to show Lou that the prisoner's hyoid bone had been fractured, which was a clear demonstration that a lethal choke hold had been used. It had happened during an arrest. The question now was whether the force was justified or whether it was excessive. The neighborhood where it had happened was up in arms and wanted answers.

Lou was also awaiting final word on the first case he had watched Jack handle that morning. It, too, was an arrest that had gone bad, resulting in a shootout with the victim holed up in his car, where he was hit four times. Several bystanders claim that the victim had yelled "enough" and had stopped firing, yet still the police shot him. Once again it was a potential PR nightmare for the police department, and a tragedy if it proved to be true. To get answers, Jack had painstakingly tracked all four bullets in the man's body and now wanted to re-create the scene in the special laboratory in the new high-rise building to figure out exactly what had happened and when.

"It's been an interesting morning," Jack said. "I'm especially sorry that I couldn't be more help for your buddy. Probably the case is going to turn on the suicide note and whether it's authentic. Divorce isn't fun, but it is a lot better than homicide, if that's what the case turns out to be."

"Enough about me and my problems," Lou said with a wave of dismissal. "What's up at the Stapleton-Montgomery household these days?

I haven't talked to you or Laur for ages." Lou had met Laurie Montgomery, Jack's wife, before Jack had been hired by the NYC OCME. Lou and Laurie had even briefly dated until they both sensed it wasn't to be and became fast friends instead. When Jack came on the scene, Lou had been his advocate. *Laur* had been the name one of Lou's daughters had used when she'd first met Laurie, and, thinking it cute, Lou had adopted it as well.

"Please," Jack said. "Let's not go there."

"Uh-oh." Lou leaned forward over the table. "Knowing you as I do, I don't like the sound of this. What's up?"

"I don't know if I want to get into it," Jack told him.

"If you don't talk to me, who are you going to talk to?" Lou arched a brow. "I love both you guys."

Jack nodded. Lou was right. He was the only person Jack could talk to about what was going on. The question was whether he wanted to talk at all. Ever since the plane crash that annihilated his first family more than twenty-five years ago, Jack had more difficulty than the typical male in talking about emotional issues. When problems arose, he much preferred to work harder and play harder, which meant more hours at the OCME and more hours playing evening basketball. But even he knew such a strategy had the major drawback of not contributing to a possible solution. It was like sweeping dust under a rug or sticking your head in the sand.

"Whatever it is, it has to get solved," Lou said. "Listen. You and Laurie are my last holdout for belief in the possibility of marital bliss, especially with this new possible homicide disaster with my buddy, Walter. One of the reasons I haven't been in touch with you two over the last month or so is that I have met a new woman, and I'm actually toying with the idea of tying the knot once again."

"Congratulations, my friend." Jack's tone didn't hold a lot of enthusiasm. "I hear the reservation in your voice," Lou said. "Come on! Talk to me. Does it have something to do with Laur's becoming the chief here at the OCME?"

Two months ago, Dr. Harold Bingham, the chief medical examiner, had passed away following a heart attack, and an ad hoc NYC search committee had recommended Dr. Laurie Montgomery take over the reins. The offer had surprised both Jack and Laurie, but particularly Jack, especially after Laurie accepted. Jack had always hated what he called the bureaucratic bull crap that was a necessary adjunct to being a medical examiner, having little patience for kowtowing to powers-that-be in any form or fashion. It had taken years to establish a degree of political independence for the OCME, particularly from the police or the people who controlled the police, so as to become an unbiased voice for the dead. The importance of such independence was obvious from the three autopsies Jack had done that very morning. All too often in the distant past, the mayor or the police commissioner would tell the medical examiner what he was to find on his autopsies. Jack prided himself on his ability not to let the opinions of others influence him. But with his wife as chief and the line between his personal and professional lives suddenly blurring, his hard-won impartiality had taken on a whole new complication.

"I can tell you this," Jack said. "I was shocked when she took the job. Between you and me, she's not having all that much fun. Not only is she now beholden to some degree to her bosses, meaning the mayor and the Commissioner of Health, she rarely gets to do what she does and likes best—namely, forensic pathology. Those two politicos have her running ragged just to maintain funding. She doesn't like confrontation, nor is she good at it, thanks to her autocratic cardiac surgeon father, who tortured her when she was a teenager."

"So is she bringing home her frustrations and taking them out on you?" Lou asked.

"Well, you know Laurie. Whenever she does something, she does it one hundred and ten percent. She's the boss now both here and at home."

"I'm sorry to hear it," Lou said. "Have you tried to talk with her about it all?"

Suddenly Jack put down his water with such force on the table that Lou started, spilling some of his own. Jack then threw up his hands and shook his head in disbelief. "I don't believe myself," he admitted. "I don't know why I'm even saying all this."

"I think it's pretty obvious," Lou said. "It's bothering the hell out of you. I can tell."

"No, it's not," Jack snapped. "Oh, it's bothering me some, especially when Laurie has been trying to dictate how much basketball I should be playing or telling me I shouldn't be riding my new Trek road bike to and from work. But her bringing her CEO problems home isn't the issue that's driving me up the wall. Laurie is a big girl, and I'm a big boy. It's Emma who's turned me into a basket case."

"Oh, no," Lou said. "What's with Emma?" It had been a while since he'd seen Jack and Laurie's daughter, who'd just turned three.

"Two weeks ago our pediatrician tentatively diagnosed her with autism."

"Good God," Lou said.

"We've known something has not been right, but we didn't want to hear it was autism. She'd been doing fine with her babbling and relating to us and JJ but then started going backward."

"I hate to admit to my ignorance, but I'm not all that sure what autism is. I've heard about the condition, but I don't know anyone whose kids have it."

"You're not alone," Jack said. "It's a mysterious affliction. It can cause describe autism as difficulties for the kid in terms of social interaction and communication. would revise this It's not even a specific diagnosis, as far as I'm concerned. It's a spectrum thing, with some kids seriously afflicted and others not so much. Even the so-called experts have no idea of the specific underlying pathology."

"What causes it?"

"There again, nobody really knows." Jack shook his head. "They

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talk about environmental factors, genes, and epigenetic factors. It could be some mysterious combination of all three."

"What the hell are epigenetic factors? You doctors love to make us normal people feel like idiots."

"Sorry," Jack said. "Epigenetic factors refer to inheritable characteristics that don't depend on the DNA sequence of a gene."

"Sorry I asked," Lou said. "Is there any treatment for autism?"

"Not really. There's a range of behavioral interventions and specialeducation programs that have some promise but not a lot of evidencebased results. The uncertainty of it all is what's driving me bananas."

"How is Laur taking it?"

"In some ways she's doing better than I in that she's taken it on as an intellectual challenge, willing to read everything and anything as the way to deal with it. I'm the opposite. I get almost immediately fed up with the vagueness and wordiness of it all and want to rail against the gods. It's my surgical personality. But the downside for Laurie is her feeling of guilt. She keeps beating herself up about not having taken a maternity leave sooner, thinking that all the weird chemicals we're exposed to around here could have played a role."

"Has that been proven to cause it?"

"No, of course not," Jack said.

"Then she shouldn't blame herself," Lou pointed out.

"Yeah, well, you tell her that," Jack said. "I've been saying the same thing until I'm blue in the face. Besides, I have my own struggles with guilt."

"How can it be your fault?"

"I'm a total jinx on kids," Jack said. "You know my daughters from my first marriage were killed in a plane crash, but did you know they were on the plane to begin with because they were on the way back from visiting me when I was training in Chicago? And look at JJ. The poor kid had neuroblastoma as a baby. I wouldn't want to be my kid."

"I never thought of you as superstitious," Lou said.

"I didn't, either," Jack said. "But it's hard to argue with the facts."

"Talking about JJ, how is he doing?"

"Terrific," Jack said. "He's the bright light in all this."

"How old is he now?"

"Eight and a half," Jack said. "He's in the third grade. No sign of a recurrence of his tumor, and you should see him dribble a basketball. The kid's a natural."

"Does he get along with Emma?"

"He does. He has the patience of a saint despite Emma's retrogression. I wish Laurie's mother, Dorothy, was half as cooperative and understanding."

"What's with Laur's mother? Is she making things worse?"

"Inestimably worse. If it weren't for her having invited herself to move in during this trying time, I might not be such a wreck. And it's not just me. She's driving our live-in nanny just as crazy. You remember Caitlin O'Connell, don't you? We were lucky to find her after JJ's kidnapping."

"That I'll never forget. Seems like yesterday."

"Well, she confided in me that she's thinking of moving out if Dorothy stays. I've tried to talk to Laurie about it, but Laurie has always had trouble dealing with her parents, especially her father, but her mother, too."

"What's the mother doing that's so bad?"

"She's the one who's been critical of Laurie not taking a maternity leave as soon as she knew she was pregnant, and she won't drop it. Plus, she's a conspiracy theorist of sorts and continues to insist that Laurie and I are to blame for letting Emma get the MMR vaccine."

"Wait a minute," Lou said. "Now, that's something I have heard about. Don't they think the MMR vaccine causes autism? Did I read that someplace?"

"That was years ago, when there was a medical-journal article that said so," Jack snapped. "But the study was totally disproved as bogus, and the medical journal that published the article retracted it. Simply put:

Vaccines in general and MMR in particular do not cause autism, period, end of story."

"Okay, okay," Lou said soothingly. "I didn't know."

"Well, sorry to jump on you," Jack said. "But Dorothy's attitude about this drives me up the wall. And to think she's been married to a doctor for most of her life but prefers to listen to her paranoid, conspiracy-minded bridge friends. And, worst of all, she will not shut up about it. Nor will she shut up about autism and neuroblastoma not being in the Montgomery family, meaning both have to be in my family. Well, as far as I know, neither have been in my family, either. Anyway, I'm being driven to distraction. I even asked Warren if I could sleep on his couch." Warren was one of the neighborhood basketball players with whom Jack had become fast friends.

"I'm sorry about all this, my friend," Lou said. "Do you want me to try to talk with Laur and see if I can help?"

"I appreciate your heart being in the right place," Jack said. "But I think you bringing it up will only make things worse. As I said, Laurie has trouble dealing with her parents. It's just going to have to play itself out—provided Caitlin doesn't act on her threat, because there is no way Dorothy can take care of Emma on her own. As for me, I have to find something here at work to occupy my mind. I had to do the same when JJ got sick. Luckily, back then I got all steamed up about the dangers of alternative medicine with the chiropractor who killed a young woman with a stupid neck adjustment. I need something like that now."

"I'll see if I can rustle up some confusing homicides to tax your skills," Lou suggested, chuckling. "Like the floater that ended up taking you to Africa."

"There you go," Jack said with smile. "That would be perfect." He remembered the case very well, along with the trip to Equatorial Guinea. It seemed like yesterday, even though it was going on twenty years ago.

The sudden ringing of Jack's mobile phone startled both men. Jack

had his ringtone on *Alarm* to make sure he'd hear it when he'd ridden his bike to work that morning and hadn't returned it to its usual setting. It sounded like a firetruck racing through traffic and was particularly loud as it echoed off the snack room's cinder-block walls. Jack snapped the phone up, stopped the racket, and looked at the caller ID. It was Dr. Jennifer Hernandez, this week's on-call medical examiner.

The on-call role rotated among the more junior doctors and included backing up the pathology residents on night call, coming in to the OCME earlier than everyone else to schedule the autopsies involving the cases that had landed during the night, and handling any queries during the day that required a response from a medical examiner. It was busywork for the most part, and Jack had been glad when his seniority exempted him. When calls did come in, they usually were from the in-house MLIs, or medical-legal investigators, whose job was to get the details of all cases referred to the medical examiner. These were all deaths that occurred in an unusual, unexpected or suspicious manner, including suicide, accident, criminal violence, in custody (like the cases Jack had processed that morning), or merely suddenly when the victim was in apparent good health. The MLIs were very experienced and rarely contacted the on-call medical examiner.

"Do you mind if I take this?" Jack asked, gesturing with his mobile phone in his hand.

"Be my guest," Lou said graciously. "You're working. I'm just a free-loader."

Guessing it probably related to an MLI question and therefore might be a harbinger of an interesting case, Jack was eager. "Maybe this is what the doctor ordered," he said.