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My Battle Against Gonorrhea

The familiar white urinals, puce-colored walls, and the queasy odor of disinfectant in M207—the men's room on the mezzanine floor of the University of Pittsburgh's medical school. I remember standing in a ragged line of seven young men across from the toilet stalls, pants stripped to my ankles. This was the moment, the crux of the clinical trial, the procedure that had seemed so trivial a few weeks earlier when I had agreed to participate.

Two men wearing long lab coats busied themselves arranging a sequence of labeled catheters on a metal cart near the sinks. The short one looked like a Marine drill sergeant; the other, older one reminded me of Marcus Welby, television's kindly general practitioner. But this time Welby wasn't curing the sick. He snapped on a pair of latex gloves as the drill sergeant turned toward me and the other half-naked subjects and barked, "Okay, gentlemen, we're ready to inoculate."

I looked from side to side. My colleagues' faces were mostly indeterminate. One guy, a graduate student from some department across the campus managed a macho smile. My pediatrician friend had turned green. I told myself there was absolutely nothing to be afraid of—a sharp stab in the urethra, yes, but no danger, no side effects, and, best of all, a walloping reward. One thousand dollars! For a newly minted junior faculty member in 1975, this amount was nothing short of miraculous.

My participation in the experiment had begun when my department chairman, Ken Rogers, invited me one morning to meet with his colleague, Charlie Brinton, whom I remembered as a fatherly but somewhat boring microbiology lecturer. Dr. Brinton was actually a top-notch scientist who had discovered that protein filaments called pili, which cover *Neisseria gonorrhea*'s cell wall, are responsible for attaching the organism to human mucosal cells. The pili also inhibit leukocytes' ability to ingest the bacterium, thus contributing to its pathogenicity. Moreover, Brinton's laboratory had recently created an antipilus vaccine that produced significant antibody responses in rats, as well as in two human volunteers. In the grand tradition of medical self-experimentation, the two volunteers were Brinton himself and my boss, who was an old hand at vaccine trials, having worked on polio with Dr. Jonas Salk at the old Municipal Hospital for Contagious Diseases.

The Army had awarded Dr. Brinton a contract to pursue further work on his vaccine. This was a high-priority project for the military. Gonorrhea infected many thousands of personnel every year and lowered their productivity and morale. An effective *N. gonorrhea* vaccine had the potential to prevent all that if given to recruits during basic training. The next step was for Brinton and his coworkers to embark on a small pilot study of vaccine efficacy in healthy adult men, which was precisely where I came in—they needed a seventh and final subject.

The protocol was straightforward. Each volunteer would first receive a parenteral vaccine injection. The subjects' antibody responses would then be monitored over the ensuing several weeks. The project definitely did *not* involve going out and contracting gonorrhea in the traditional way. Rather, each subject would be given an intraurethral inoculation. Four subjects were randomly assigned to receive a pathogenic dose of *Neisseria gonorrhea*; the other three, a saline solution. Subjects would keep track of symptoms, if any, and undergo a daily examination. Subjects who became ill with gonorrhea would be treated immediately; their nonsymptomatic colleagues would receive antibiotics at the end of the study as a cautionary measure. The inducement was a check for $1000.

This sounded like the key to a new car to me.

We had been nursing along our romantic but utterly undependable Jeep Cherokee for weeks. We desperately needed a new family car. Having recently arrived in Pittsburgh with two small children and two mortgages—our house in North Carolina was still on the market—we had only one salary of $26,000 per year.

"Gonorrhea!" My wife exploded later that night when I described the study to her. "You must be out of your mind!"

"No," I assured her. "This makes a lot of sense. It'll prove I'm a team player. What will Ken and the others say if I turn it down? They'll think I'm not committed."

"But isn't it dangerous?" she asked.

"Absolutely not," I insisted. "If I develop an infection, they'll give me penicillin right away. You, too. There'll be no problem. Really, it's perfectly safe."

In the end we agreed that I'd sleep on the sofa until the study was safely over.

I don't remember the consent form, but it was certainly a far cry from today's complex and highly regulated legal documents. In the mid-1970s, the modern era of ethics in human research had hardly begun. As a result of public outrage over revelations about the Tuskegee Syphilis Study, Congress had passed the National Research Act in 1974, which authorized the creation of a National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research. Ethical requirements for human research, including informed consent procedures and evaluation by institutional review boards, would not be fully established until several years later when the Commission issued its final recommendations, in the Belmont Report, in 1979.

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I cleaned out some boxes not long ago that had remained unmolested in the basement since we moved into the house in 1991. Several of them contained files from my office in Pittsburgh, among which was an accordion folder labeled "GC Vaccine." The folder included mimeographed sheets that summarized the protocol; a crude drawing of a gonococcus with hair-like projections sticking out in every direction; a tattered article from *Chemical Abstracts*; and a brief story from the *Pittsburgh Press* dated April 28, 1975. The story indicated that Dr. Charles Brinton and his colleagues at the University of Pittsburgh had developed a vaccine against gonorrhea, a potential breakthrough that would undergo "intensive testing" in the very near future.

If the folder once contained additional material, it had long since been filed away in a wastebasket, leaving only a series of questions and ambiguities. Given today's standards, could my participation be considered voluntary? Or was there coercion involved? The stipend certainly influenced my decision, but I suspect my desire to impress the boss and be accepted by colleagues played as great a role, or greater, because I realize how emotionally difficult it would have been to say "no." I'm sure Dr. Rogers viewed my participation as entirely voluntary and would have been offended by the idea that our relationship might change if I declined.

How about disclosure of relevant information? I remember very little disclosure, as such. Of course, the investigators assumed that I knew the score. I had plenty of experience treating patients with gonorrhea. But what about privacy and confidentiality? What if there were complications? Who was responsible for providing follow-up medical care, if needed? Considering the time lag, the most interesting questions were obvious: What ever happened to that medical breakthrough? Where is the vaccine?

The traumatic event in the men's room lasted only a moment. I remember how grateful I felt when Charlie Brinton handed me a slip of paper with follow-up instructions before I opened the door and stepped—presumably with pants in place—across the hall and into my office. I spent the next few days in something like a caffeine jag. A twitch here, a burning there. A state of jangled alertness. Exhausted, but unable to sleep.

But nothing happened; the same with the two other guys in our department. I wondered, What about the graduate students? What about the research assistant from Charlie Brinton's laboratory? I didn't know any of them, and it felt a bit awkward to phone and ask, "By the way, do you have any urethral discharge?" Nobody was talking, but it was a double-blind study after all, so we'd just have to wait until some designated point when everything would be revealed. We waited. A week passed; the check arrived. I went to clinic. A triumphant announcement surely must be just around the corner. Two weeks. Nothing happened. When I finally asked Ken Rogers about the results, he suggested I talk to Charlie Brinton, who sounded unusually distracted and said, "Yes, you're right. We'll have to get everyone together."

As far as I know, that meeting never took place, but Ken Rogers called me into his office one day. As usual, he sat at one end of his plasticized sofa that was otherwise stacked with papers and books. He looked up, leaned forward, hands clasped over his knee, and announced in his drill sergeant voice, "Coulehan, this (blank) thing is a (blank-blank) mess."

So that was it. An inexplicable technical failure. Somehow the organisms in our *N. gonorrhoea* inoculations had died off, or the preparations were too diluted to initiate clinical infection. When the laboratory folks attempted to verify bacterial concentration by plating residual effusion on culture media, few colonies had grown. Dr. Rogers didn't know the exact nature of the error, or how it had occurred. Worse yet, our antibody responses had been mediocre and far less impressive than Brinton had anticipated from earlier studies, which, except for the two senior researchers, were done entirely on rats. Leave it to humans to screw up a good theory.

What a washout!

Many developments in medicine have occurred over the 35 years since that fateful day in the medical school men's room. One development that did *not* occur was the creation of an effective vaccine for gonorrhea. What happened? Discovering that old accordion folder led me to spend a few minutes doing a literature search that probably would have taken days in 1975. Interest in pilus peptide–based vaccines continued for a while, and one such vaccine even progressed to the stage of a large clinical trial conducted in Korea among Army personnel. The results of that study were published in 1991 and showed unequivocally that the vaccine didn't prevent naturally acquired gonorrhea, but it did stimulate considerable antibody response. It turned out that the problem was that pilus peptides have innumerable antigenic variants that frequently mutate from one form to another—a bait-and-switch game. Although gonococcal pili initially appeared to be ideal vaccine antigens, in reality they are unpredictable, moving targets.

My "GC Vaccine" folder raises a number of other difficult questions—questions about hope, enthusiasm, ethics, and romance. Why did I participate in the study? I was excited about the idea of playing a role in the development of an important new vaccine. But I'm sure the biggest motivators were the easy money and my sense of duty as a member of the department. Would I do it again under these circumstances? I suppose so. I don't recall having any serious ethical questions, only emotional ones. Yet, in retrospect, it's obvious that the circumstances were unethical. The investigators created a coercive situation by selecting subjects from among junior faculty, students, and laboratory personnel, and paying such a large stipend. They didn't intend to do so, but the effect was inevitable.

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Likewise, the unstructured consent process with its lack of defined commitments and responsibilities was not "informed." We were treated like junior partners who should trust their seniors, rather than subjects with explicit, enforceable rights.

Do I regret my role in the battle against gonorrhea? Of course not. It's an interesting memory, a good story, and there's also the stub from the University of Pittsburgh that documents a check for $1000—no strings attached.

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