prostaglandin inhibitors, and the molecular challenge is substantial as well. The molecular delineation of the genetic defects that result in tubulopathies can lead to a better understanding of their physiology. However, the DNA sequencing of the genes that encode transporters and channels (as well as their subunits) is not a trivial matter and must be complemented by experiments determining expression patterns. The Xenopus oocytes that have been used for such studies are transfected cells rather than “real” polarized cells of the thick ascending limb of the loop of Henle surrounded by the sophisticated hypertonic environment of the renal medulla.

The complex polyuria–polydipsia syndrome described by Schlingmann et al. is attributable to the concomitant loss-of-function mutations in both CLCNKA and CLCNKB; the syndrome results in ion selectivity, demonstrating the means whereby a renal tubular cell lets one type of ion (chloride) through the lipid membrane to the exclusion of others. It thus provides yet another example of the molecular basis of Bartter’s syndrome (see Figure).

The contributions of Roderick McKinnon and Peter Agre to solving these two complementary problems of the resorption of renal solute and renal solvent earned them the 2003 Nobel Prize in chemistry.

We live in a fascinating time in which clinical syndromes can be deciphered at the molecular and even the atomic level.

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Recently at large in the hospital, they told me, have been a rotavirus, a Norwalk virus, several strains of multidrug-resistant pseudomonas, a super-resistant klebsiella, and not surprisingly, the ubiquitous scourges of modern hospitals, methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococcus (VRE). The hardest part of their job, they say, is not the variety of contagions they encounter, or the fears the staff have about some of them, or even the press, which can cause panic to spread faster than any biologic infection. Instead, their greatest difficulty is getting clinicians like me to do the one thing that consistently halts the spread of most infections: wash our hands.

There isn’t much they haven’t tried. They showed me the admonishing signs they have posted, the sinks they have repositioned, the new ones they have installed. They have made some sinks automated. They have bought special $5,000 “precaution carts”
that store everything for washing up, gloving, and gowned in one ergonomic, portable, and aesthetically pleasing package. They have given away free movie tickets to the hospital units with the best compliance. They have issued hygiene report cards.

Yet, still, we do not mend our ways. Yokoe and Marino’s statistics show what studies everywhere have shown—that we wash our hands one third to one half as much as we are supposed to. Having shaken hands with a sniffling patient, pulled a sticky dressing off someone’s wound, pressed a stethoscope against a sweating breast, most of us do little more than wipe our hands on our white coats and move on—to see the next patient, to scribble a note in the chart, to eat a sandwich.

This is, of course, nothing new. Sherwin Nuland’s recent book, The Doctors’ Plague: Germs, Childbed Fever, and the Strange Story of Ignác Semmelweis, recounts the sad and disturbing tale of the Viennese obstetrician’s failure to persuade his colleagues to scrub their hands before delivering babies.1 In 1847, at the age of 28, Semmelweis famously deduced that, by not washing their hands consistently or well enough, doctors were themselves to blame for puerperal fever, the leading cause of maternal deaths in hospitals. On his wards, he mandated scrubbing with a nail brush and chlorine. The rate of death from puerperal fever immediately fell from 20 percent to 1 percent—incontrovertible proof, it would seem, that he was right. Yet doctors’ practices did not change. Some colleagues were even offended by his claims: it was impossible that doctors could be killing their patients. Far from being hailed, Semmelweis was dismissed from his job.

Semmelweis’s story has come down to us as Exhibit A in the case for the obstinacy and blindness of physicians. Nuland discovered, however, that the trouble was partly that 19th-century physicians faced multiple, seemingly equally powerful explanations for puerperal fever—there was, for example, a strong belief that miasmas were the cause. And Semmelweis strangely refused either to publish an explanation of the logic behind his theory or to prove it with a convincing experiment in animals. Instead, he took the calls for proof as a personal insult and attacked his detractors viciously. “You, Herr Professor, have been a partner in this massacre,” he wrote to one University of Vienna obstetrician who questioned his theory. To a colleague in Würzburg he wrote, “Should you, Herr Hofrat, without having disproved my doctrine, continue to train your pupils [against it], I declare before God and the world that you are a murderer and the ‘History of Childbed Fever’ would not be unjust to you if it memorialized you as a medical Nero.” His own staff turned against him, Nuland found. In Pest, Hungary, where he relocated after losing his post in Vienna, he would stand next to the sink and berate anyone who forgot to scrub his or her hands. People began purposely to evade, sometimes even sabotage, his hand-washing regimen. Semmelweis was a genius, but he was also a lunatic, and that made him a failed genius. It was another 20 years before Joseph Lister offered his clearer, more persuasive, and more respectful plea for antisepsis in the Lancet.

One hundred and thirty years of doctors’ plagues later, however, you have to wonder whether it will take a lunatic to stop them. Consider what Yokoe and Marino are up against. No part of human skin is spared from bacteria. Bacterial counts on the hands range from 5000 to 5 million colony-forming units per square centimeter. The hair, axillae, and groin harbor greater concentrations. On the hands, deep skin crevices trap 10 to 20 percent of the flora, making removal difficult, even with scrubbing, and sterilization impossible. The worst place is under the fingernails. Hence the recent Centers for Disease Control and Prevention guidelines requiring hospital personnel to keep their nails trimmed to less than a quarter of an inch and to remove artificial nails.

Plain soaps do, at best, a middling job of disinfecting. Their detergents remove loose dirt and grime, but 15 seconds of washing reduces bacterial counts by only about an order of magnitude. Semmelweis recognized that ordinary soap was not enough and used a chlorine solution to achieve disinfection. Today’s antibacterial soaps contain chemicals such as chlorhexidine to disrupt microbial membranes and proteins.

Even with the right soap, however, proper hand washing requires a strict procedure. First, you must remove your watch, rings, and other jewelry (which are notorious for trapping bacteria). Next, you wet your hands in warm tap water. Dispense the soap and lather all surfaces, including the lower one third of the arms, for the full duration recommended by the manufacturer (usually 15 to 30 seconds). Rinse off for 30 full seconds. Dry completely with a clean, disposable towel. Then use the towel to turn the tap off. Repeat after contact with the patient.

Almost no one, of course, adheres to this procedure. It seems impossible. On morning rounds, our surgery residents may visit 20 patients in an hour. The nurses in our intensive care unit typically have
a similar number of contacts with patients requiring hand washing in between. Even if you get the whole cleansing process down to a minute per patient, that’s still a third of staff time spent just washing hands. Such frequent hand washing can also irritate the skin, which can produce a dermatitis, which itself increases bacterial counts.

Less irritating than soap, alcohol rinses and gels have been in use in Europe for more than a decade but for some reason are only now catching on in the United States. They take far less time to use — only about 15 seconds or so to rub a gel over the hands and fingers and let it air-dry. Dispensers can be put at the bedside more easily than a sink. And at alcohol concentrations of 50 to 95 percent, they are more effective at killing organisms, too. (Interestingly, pure alcohol is not as effective — at least some water is required to denature microbial proteins.)

Still, it took Yokoe more than a year to get our staff to accept the 60 percent alcohol gel we have recently adopted. Its introduction was first blocked because of the staff’s fears that it would produce noxious building air. (It didn’t.) Next came worries that, despite evidence to the contrary, it would be more irritating to the skin. So a product with aloe was brought in. People complained about the smell. So the aloe was taken out. Then some of the staff refused to use the gel after rumors spread that it would reduce fertility. The rumors died only after the infection-control unit circulated evidence that alcohol is not systemically absorbed and a hospital fertility specialist endorsed the use of the gel.

With the gel finally in wide use, the compliance rates for proper hand hygiene improved substantially: from around 40 percent to 70 percent. But — and this is the troubling finding — hospital infection rates did not drop one iota. Indeed, the MRSA and VRE infection rates have continued to rise. As of the day I write this, 63 of our nearly 700 hospital patients have become colonized or infected with MRSA, and another 22 have acquired VRE — unfortunately, typical numbers for an academic hospital.

We have all become inured to infection rates like these. But hospital outbreaks of VRE did not even occur until 1988, only 16 years ago, when a renal dialysis unit in England became infested. By 1990, 4 in 1000 patients in intensive care units (ICUs) in the United States had become colonized with VRE. By 1997, a stunning 23 percent of patients in ICUs were colonized. What will happen if — or rather, when — an outbreak of a considerably more dangerous organism such as vancomycin-resistant staphylococcus occurs? “It will be a disaster,” Yokoe warns.

Anything short of a Semmelweis-like obsession with hand washing has begun to seem inadequate. Yokoe, Marino, and their team have now resorted to doing random spot checks on the floors. On a surgical ICU, they showed me what they do. They go directly into patients’ rooms. They check for unattended spills, toilets that have not been cleaned, faucets that drip, empty gel dispensers, overflowing needle boxes, inadequate supplies of gloves and gowns. They check whether the nurses are wearing gloves when they handle patients’ dressings and catheters. And, of course, they watch to see whether everyone is washing up. Neither hesitates to confront people, though they try to be gentle about it. (“Did you forget to gel your hands?” is a favored line.) Staff members have come to recognize them. I watched a gloved and gowned nurse come out of a patient’s room, pick up the patient’s chart, see Marino, and immediately stop short. “I didn’t touch anything in the room! I’m clean!” she blurted out.

They hate this aspect of the job. They don’t want to be infection cops. It’s no fun, and it’s not necessarily effective, either. With 12 patient floors and four different patient pods per floor, they can’t stand watch the way Semmelweis did, leering over the lone sink on his unit. And they risk having the staff revolt as Semmelweis’s staff did. But what other options remain?

The Journal of Hospital Infection and Infection Control and Hospital Epidemiology, two leading specialty journals, read like a sad litany of failed attempts to get us to change our contaminating ways. The situation has prompted one expert to propose — only half jokingly — that the best solution may be to give up on hand washing and get people simply to stop touching patients.

It is striking to consider how different the history of the operating room after Lister has been from that of the hospital floor after Semmelweis. In the operating room today, no one pretends that even 90 percent compliance with scrubbing is good enough. If a single doctor or nurse fails to wash up before coming to the operating table, we are horrified — and certainly not shocked if an infection develops in the patient a week or two later. It is a fundamental difference in culture. And I would trace a large part of that difference to a single institution: the circulating nurse. In surgery, at some point, it became obvious that keeping the operators from
contaminating patients required not only drapes and autoclaves and sterile gowns and gloves, but also an extra set of hands. Every time an unanticipated instrument was needed for a patient, the team couldn’t stand around waiting for one member to break scrub, pull the thing off a shelf, wash up, and return. So the circulator was invented — a person whose central job is, essentially, to keep the team antiseptic. Circulators get the extra sponges and equipment, handle the telephone calls, do the paperwork, get help when it’s needed. And every time they do, they’re not just helping the case go more smoothly. They are keeping the patient uninfected. By their very existence, they reemphasize that sterility is a priority in every case.

Would it be impossible to bring the same idea at least to ICUs? One can imagine someone whose role is to get nurses the medicines, dressings, and equipment they need, perhaps fill out the forms, tap in the numbers that must go into the computer — whatever is necessary to keep the nurse at the bedside rather than going back and forth everywhere, picking up and spreading organisms. Circulators might even improve care. And their presence might keep the rest of us in line, too.

This proposal is likely to be too expensive. It probably violates licensing rules in one place or another. But after 130 years of failure, neither exhortation nor technology seems capable of stopping the epidemics that are spreading in our hospitals.

I have tried lately to be more scrupulous about washing my hands. I do pretty well, if I say so myself. But then I blow it. It happens almost every day. I walk into a patient’s hospital room, and I’m thinking about what I have to tell her concerning her operation, or about her family, who might be standing there looking kind of angry at me, or for that matter, about the funny little joke a resident just told me, and I completely forget about getting a squirt of that gel into my palms, no matter how many reminder signs have been hung on the walls. Sometimes I do remember, but before I can find the dispenser, the patient puts his hand out in greeting and I think it too strange not to go ahead and take it. On occasion, I even think, well, screw it — I’m late, I have to get a move on, and what difference does it really make what I do this one time?

Later in my tour with Yokoe and Marino, we walked through a regular hospital unit. And I began to see the ward the way they do. Flowing in and out of the patients’ rooms were physical therapists, patient care assistants, nurses, nutritionists, residents, students. Some were good about washing. Some were not. Yokoe pointed out the three rooms with precaution signs on the doors because of MRSA or VRE. Only then did I realize we were on my own patient’s floor. One of those signs hung on his door.

He was 62 years old and had been in the hospital for almost three weeks. He had been transferred in shock from another hospital where an operation had gone awry. I performed an emergency splenectomy for him and then had to go back in again when the bleeding still didn’t stop. He got through it all, though. Three days after admission, he was recovering slowly but steadily. Surveillance cultures were completely negative for resistant organisms. Ten days after admission, however, repeated cultures came back positive for both MRSA and VRE. A few days after that, he became septic. His central line — his lifeline for parenteral nutrition — had become infected, and we had to take it out.

Until that moment, when I stood there looking at the sign on his door, it had not occurred to me that I might have given him that infection. But the truth is I may have. One of us certainly did.

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