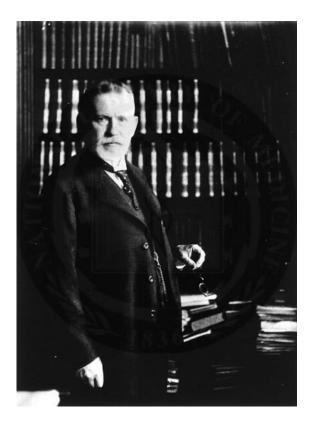
Dr. Ehrlich and Dr. Atomic: Beauty vs. Horror in Science



Paul Ehrlich, 1854-1915.

Sometimes it seems as if horror is the only story that science has to tell, or the only one we want to hear. Somebody has a gadget they have to build, an experiment too sweet to resist... The tug of war between beauty and horror is the theme of "Doctor Atomic."

Dennis Overbye, The New York Times, 2008 (1)

When I was a boy, I looked out into the star-filled sky one night and was awestruck by its beauty... A few days later, I happened on a book called "The Microbe Hunters" and became equally enchanted by the stories of microbes and their role in disease. It dawned on me that I wanted to explore this hidden universe.

Stanley Falkow on his Lasker Award in Medical Research, 2008 (2)

I KID YOU NOT...

It's a rare event when a neglected work of popular literature, Paul de Kruif's *The Microbe Hunters*, is linked to the birth of recombinant DNA. It's also a rare event when a 17th century sonnet, John Donne's "Batter My Heart," becomes an aria in a new opera sung by a



Left, J. Robert Oppenheimer, 1904–1967; right, General Leslie Groves, 1896–1970. Courtesy Los Alamos National Laboratory.

poetically inclined physicist at the birth of the atom bomb. Both events took place in mid-Manhattan last fall and the coincidence is more than geographic. It was also mid-election, 2008. One recalls that Paul Ehrlich, the Microbe Hunter, and J. Robert Oppenheimer, of "Batter My Heart," underwent shameful public trials fueled by notions resurrected by Joe the Plumber. Ehrlich and Oppie became targets of nativist, neo-Luddite rhetoric directed not only against their persons, but against science itself: "I kid you not" as they say in the sub-Arctic (3).

MICROBE HUNTERS AT THE LASKER AWARDS

Stanley Cohen evoked Paul de Kruif's 1926 book, *The Microbe Hunters* as he presented a 2008 Lasker Special Achievement Award in Medical Research to his Stanford colleague, Stanley Falkow. He hailed Falkow's discovery that bacterial plasmids determine antibiotic resistance and virulence, explaining how they had made the revolution in molecular biology possible. Cohen proposed his colleague for a new "pantheon of great Microbe Hunters," recalling that in 1972 Falkow contributed to a discussion at a Waikiki beach delica-

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tessen "over corned beef and pastrami sandwiches and very cold beer" that resulted in the invention of recombinant DNA by Herb Boyer and Cohen himself (4).

Evoking that now legendary birth of biotechnology in Hawaii, Falkow traced the roots of his own career to the heroes of de Kruif's *The Microbe Hunters*—Pasteur, Koch, Dr. Ehrlich and his Magic Bullet, *et al.*—who "became my heroes, and I dreamed of becoming a bacteriologist, doing research on the bacteria that cause disease (1)." Falkow's discovery of how R plasmids help bacteria dodge today's magic bullets made his dreams come true. He also played a role in the 1974 Asilomar conference (5) at which the first whistle of bioethics was blown on gene splicing, and served on the first NIH Recombinant DNA Advisory Commission (1). His place seems secure in that new "pantheon of great Microbe Hunters."

Paul Ehrlich is well established in the older pantheon: he made three discoveries that opened up new fields in science. He was the first to classify cells and microbes according to their affinity for azo-dyes (cytochemistry); he gave weight and number to toxins and antitoxins (immunochemistry), and he developed salvarsan, that "magic bullet" as a cure for syphilis (chemotherapy) (6). Ehrlich won his Nobel in 1908 for work on humoral antibodies, the mediators of acquired immunity. He shared the prize with Ilya Metchnikoff, who discovered that phagocytosis was the basis of cellular, or innate immunity (7). Ehrlich elaborated his prescient model of how toxins interlock with their antitoxins, the side-chain theory of humoral immunity. He concluded that these lock-and-key reactions obey the laws of chemistry and physics, a reductive notion that did not endear him to the nativist philosophers of Geist (spirit). Against the Geist-hunters, he proposed his own "four Gs" as the path for scientific achievement: "Geld, Geduld, Geschick und Glück" (Money, Patience, Skill, and Luck) (6).

The discoveries of three other 2008 Lasker awardees—Victor Ambros, David Baulcombe, and Gary Ruvkun—are prime examples of why Ehrlich's 4 Gs beat the babble of Geist every time. The "unanticipated world of tiny RNAs that regulate gene function in plants and animals" is a world of lock-and-key reactions. You can't get more reductive than those micro RNASs, the magic bullets of molecular biology (8).

THE MICROBE HUNTER ON TRIAL

Two years after the notoriety of his Nobel prize, and within a year of Salvarsan's use in the clinic, attacks on Paul Ehrlich ended in calumny and the courts (9). The German vigilante pack was led by a nationalist physician, Dr. Richard Dreuw of Berlin and a zealous Frankfurt pamphleteer, Karl Wassman, a "strange-looking man dressed in a dark monk's habit, with a rope around his waist...who believed in curing all diseases by Nature alone...(6)" Wassman's pamphlet "Die Warheit" (The Truth) accused Ehrlich and his Japanese co-worker Sahatschiro Hata (1873–1938) of concocting a dangerous, unreliable drug (called 606 at that!) and the Frankfurt hospital of shoddy record

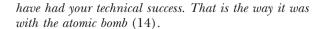
keeping. Schadenfreude and racism became an integral part of the story: "Die fachliche Kritik an dem Heilmittel wird mit antisemitischen Angriffen auf Ehrlichs Person verbunden." (Technical critique of the drug went hand-in-hand with antisemitic attacks on Ehrlich himself.) Lutheran clerics argued that the wages of sin was syphilis and that Ehrlich *et al.* were disrupting the natural order of crime and punishment (10).

Other familiar notes were sounded by populists. Ehrlich had signed over manufacture of the drug to the Hoechst corporation, which charged 10 Marks—sixty or so dollars-for a course of Salvarsan. The critics complained that Ehrlich was getting rich, that Hoechst was profiting from basic research funded by the government, and that clinical trials of Salvarsan had been carried out on the prostitutes of Frankfurt without their consent. Things came to a head in a lengthy, drawn-out libel suit brought by the hospital against Wassman on behalf of Ehrlich and Hata. The proceedings turned into a circus as inflammatory witnesses for the defense were corralled from the red light district and shadier areas of town. In the end, however, Wassman lost, was sent to prison and a worn-out Ehrlich was finally exonerated. But soon the First World War supervened and the Guns of August 1914 silenced the uproar in Frankfurt. Ehrlich died a year later, spirits shattered by the public scandal. Wassman was pardoned, changed the name of his pamphlet to "Die Liebe" (Love) and never mentioned 606 again (6). Salvarsan went on to set the gold standard for the treatment syphilis until 1937.

Sentiments that had fueled the Ehrlich trial reemerged in the Nazi era. In August of 1938, the Nazis removed the street sign for Paul Ehrlich Strasse in Frankfurt. The 1940 Warner Brothers' film *Dr. Ehlich's Magic Bullet* was Hollywood's response to the year of Kristallnacht. The film's screenwriter, Norman Burnside, admitted that "the reason for picking Ehrlich as a protagonist had very little to do with syphilis and its cure," and its producer Hal Wallis agreed that the film was a visceral response to Hitler's 1938 diatribe in which he proclaimed that "a scientific discovery by a Jew is worthless." The 2008 Lasker Awards in the year of Obama are a measure of what defeat of the Nazis made possible. They are also a measure of why the atom bomb was built.

ATOM BOMB AT THE MET

Three weeks after the Lasker Awards ceremonies at the Hotel Pierre, John Adams' opera *Dr. Atomic*, made its debut at the Metropolitan Opera, just across Central Park from the hotel. The setting of the opera is Los Alamos in July of 1945 as the first atom bomb is about to tested. Adams casts J. Robert Oppenheimer, the lab director, as a Faustian hero "equally in love with the Bomb and his own inscrutability (2)." The music is stunning, the sets are striking, and the libretto blends Oppenheimer's favorite poetry—John Donne, Muriel Rukeyser, Charles Baudelaire—with actual wartime texts. Beauty mixes with horror in two astonishing acts.





Edward G. Robinson as Paul Ehrlich in "Dr. Ehrlich's Magic Bullet" (1940). Image © John Springer Collection/CORBIS.

Adams celebrates completion of the "Fat Man," an implosion-design plutonium bomb, in what critic Alex Ross describes as an "inexplicably lovely choral ode to the bomb's thirty-two-point explosive shell, with unison female voices floating above lush string and wind chords and glittering chorus of chimes and celesta (11)." The climax of the drama is the explosion of the Fat Man over a desert site named "Trinity" by Oppenheimer in homage to the three-personed God of John Donne's sonnet "Batter My Heart." In *Dr. Atomic*, the poem is set as an aria for the Age of Anxiety:

BATTER my heart, three person'd God; for, you As yet but knocke, breathe, shine, and seeke to mend; That I may rise, and stand, o'erthrow mee,'and bend Your force, to breake, blowe, burn and make me new. I, like an usurpt towne, to'another due, Labour to'admit you, but Oh, to no end, Reason your viceroy in mee, mee should defend, But is captiv'd, and proves weake or untrue...(12)

As the bomb explodes and the lights go out, Oppenheimer evokes Vishnu in the Bhagavad-Gita: "Now I am become Death, the destroyer of worlds." *Dr. Atomic* closes with the amplified cries of Japanese bomb victims echoing over a pitch-dark auditorium. The tug of war between beauty and horror ends in horror.

Oppenheimer had assumed the task of building the bomb as head of the Manhattan Project's Weapons Design and Research laboratory in Los Alamos. The lab was in a race to build an atom bomb before the Nazis had gotten theirs, and Oppie had recruited a group of the most accomplished physicists of his day, including Hans Bethe, Richard Feynman, Enrico Fermi, Edward Teller, and Victor Weisskopf, along with scores of others. As things turned out, by 1945 the Nazi bomb project had fizzled, while in Los Alamos success became imminent (13). But the bomb had grown into an attractive technical problem of its own. Oppenheimer recalled later how one can become blinded to horror:

It is in my judgment in these things that when you see something that is technically sweet you go ahead and do it and you argue about what to do about it only after you

DR. ATOMIC ON TRIAL

It's difficult, in retrospect, to know whether it was the technical "sweetness" of the project that persuaded Oppenheimer to agree to dropping an atomic bomb on civilian populations. But, he persuaded himself that a dropped bomb was by no means certain to explode and that an unexploded bomb could perhaps be turned against America by an enemy. He worried that an advance warning might prompt the enemy to move POWs to the area (as in Saddam Hussein's use of unwilling hostages in Gulf War I). Finally, he reasoned that no "demonstration" site would be as effective in forcing an end to war as those which Germany and Japan had used to show what "shock and awe" could accomplish: Guernica, Rotterdam, and Pearl Harbor.

Doctor Atomic ends on the 16th of July, 1945, with the explosion at Trinity. On the July 18th, Japan refused an Allied ultimatum issued at Potsdam for unconditional surrender—no warning of a possible bomb accompanied the ultimatum. On August 6, a uranium bomb with a force of 15,000 metric tons of TNT destroyed Hiroshima and, no response being received, on the 9th of August the "Fat Man" was dropped on Nagasaki. The two bombs killed close to 250,000 people—almost all civilians. The war ended on the 10th of August 1945 (14, 15).

The next stage in Oppenheimer's career was perhaps the most difficult. President Truman had awarded him the Presidential Medal of Merit in 1946 for his work at Los Alamos; a year later was appointed director of the Institute for Advanced Study at Princeton where he served until 1966. Simultaneously, he served as chairman of the General Advisory Committee of the Atomic Energy Commission (AEC) from 1947 to 1952. But soon pressure mounted to build the ultimate weapon, an H-bomb, a move supported not only by the military, but also by scientists such as Edward Teller and a coven of "nuclear strategists (16)." Oppenheimer opposed it, as he opposed stockpiling more A bombs: "I do not think that a country like ours can be based on the fear of what its people can do . . . I have a sense of impending disaster and a sense of frustration (17)." But by 1953, the H bomb was a reality and Oppenheimer's resistance was considered unpatriotic. Major General Kenneth D. Nicholas of the AEC branded Oppenheimer as "the leader of a calculated movement in opposition to the hydrogen bomb program even after President Truman had decided as a matter of high national priority to go head with it (18)." This charge, joined to earlier charges that he had hobnobbed with communists and supported the "socialist" side in Spain, resulted in his being hauled before an AEC personnel hearing. The charges of the proceedings became headline news nationwide; the McCarthy-era press had no scruples about reminding folks that Oppenheimer's "communists and fellow-travelers" included names like Isaac Folkoff, Max Friedman, Giovanni Lomanitz,

Frank and Jackie Oppenheimer, William Schneiderman, and Joseph Weinberg (19, 20). Contemporary press and radio accounts carried nativist overtones that echoed the Ehrlich trial (and the campaign rhetoric in the fall of 2008). On June 29, 1954, Oppenheimer's security clearance was revoked and his contract with the Atomic Energy Commission canceled:

The Atomic Energy Commission announced today that it had reached a decision in the matter of Dr. J. Robert Oppenheimer. The Commission by a vote of 4 to 1 decided that Dr. Oppenheimer should be denied access to restricted data.... Certain members of the Commission issued additional statements in support of their conclusions. These opinions and statements are attached (21).

A decade later the political tides had shifted. Anti-Viet Nam war activists, honoring Oppenheimer's resistance to the hydrogen bomb and to nuclear stockpiling, made him a symbol of academic protest against the military. His example was frequently cited as biological scientists worried about their own Manhattan Project: recombinant DNA. Nobelist George Wald was one of many in that period who supported Oppie even as he told students striking against the war at MIT that "Dropping those atomic bombs on Hiroshima and Nagasaki was a war crime...Our business is with life, not death (22)." The moral ambivalence of Oppenheimer and his Los Alamos colleagues toward the products of physical science were a goad to the organizers of the Asilomar conference itself. If the biologist's business is life, the question becomes as to how far life science dare go (5).

One of Oppenheimer's heroes was Galileo Galilei, another physical scientist torn by the ambivalence of power. A passage in Bertold Brecht's *The Life of Galileo*—written in August of 1945 after Hiroshima—sums up what could have happened, had not biologists developed something like a Hippocratic oath for science at Asilomar. Galileo regrets his abjuration, and the earth still moves:

As a scientist I had a unique opportunity. In my day astronomy emerged into the market place. Given this unique situation, if one man had put up a fight it might have had tremendous repercussions. Had I stood firm the scientists could have developed something like the doctors' Hippocratic oath, a vow to use their knowledge exclusively for mankind's benefit. (23)

Gerald Weissmann Editor-in-Chief doi: 10.1096/fj.09-0101ufm

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