Paul Ehrlich and His Magic Bullets—Revisited

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1. A Forgotten Classic

In 1940 Warner Brothers Studios released a film, Dr. Ehrlich’s Magic Bullet, which starred Edward G. Robinson (1883–1973), who was born in Romania as Emanuel Goldenberg and who—at a time when the beginning Holocaust threw its shadow over Germany—was sufficiently familiar with prejudice and discrimination to play convincingly the role of Paul Ehrlich, whose own career suffered because of open and latent anti-Semitism, even in the time before World War I. In this memorable masterwork Ruth Gordon (1896–1985) impresses the viewer in her part of Mrs. Ehrlich, who in 1929 secured the memory of her husband by establishing the Paul Ehrlich Prize. Ten years later she barely escaped the coming disaster by fleeing to Switzerland, whence she moved to the United States in August 1941.

At the time of her exile, when she was practically destitute, Warner Brothers appointed her a consultant for their film in progress. She was helped by her daughter Stephanie Schwerin (1884–1966), and recent research in the Warner Brothers archives shows that the Ehrlich family received more than fifty thousand dollars for their guidance. The title of this film was probably influenced by the last chapter of the popular book Microbe Hunters.4

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1 Read 13 November 1998.
2 This lecture honors the memory of Paul Ehrlich’s grandson, Gunther Schwerin (1910–1997), a longtime friend, who helped me to serve and observe the legacy of his grandmother, Hedwig Ehrlich (1864–1948), in the Paul Ehrlich Foundation, Frankfurt, as a member of the Stiftungsrat, 1979–97, selecting candidates for the Paul Ehrlich Prize, the most prestigious award for scientists, given annually in the Paulskirche in Frankfurt, on 14 March, Ehrlich’s birthday.
2. Magic Bullets

Ehrlich used the English expression “magic bullet” for the first time in his Harben Lectures. The German word Zauberkugel, comparable to the Freikugel of Weber’s opera Der Freischütz, appears earlier in his thoughts and publications, based on his view of “sidechains,” the precursor of our concept of receptors, and on the desirable properties of drugs that must not harm the host but must attack the parasitic invader, in other words, curatives must be parasitotropic and not organotropic.

Ehrlich’s first magic bullet was Salvarsan or arsphenamine, discovered in 1909, which provided the only cure for syphilis until it was superseded and replaced by penicillin and all the other magic bullets of the family of antibiotics. Ehrlich thought of attaching toxins to antibodies, in modern parlance a kind of “cruise missile” in which the antibody carries the deadly freight to the site of the invading parasite. His
idea lives on in the development of immunotoxins. In the fifth Paul Ehrlich Lecture at NIH in 1992, Manfred Eigen (Nobel Prize 1967, Paul Ehrlich Prize 1995), spoke about interfering with intercellular transfer of information as a new kind of magic bullet against viral infections. Finally, genes as therapeutic agents are now in the forefront of pharmaceutical research, and promise to be of help in diseases that appeared incurable.

What is now called biotechnology is a vast enterprise that produces biopharmaceuticals that have reached worldwide sales of 14 billion dollars. Some of these new drugs listed in the following table, from the point of view of Paul Ehrlich, might be called “magic bullets.”

<table>
<thead>
<tr>
<th>Product</th>
<th>Biological basis</th>
<th>Activity/use</th>
<th>1997 worldwide sales ($ millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epogen</td>
<td>Erythropoietin</td>
<td>Red blood cell growth</td>
<td>1,161</td>
</tr>
<tr>
<td>Neupogen</td>
<td>Colony-stimulating factor</td>
<td>White blood cell growth</td>
<td>1,056</td>
</tr>
<tr>
<td>Procrit</td>
<td>Erythropoietin</td>
<td>Red blood cell growth</td>
<td>1,000</td>
</tr>
<tr>
<td>Humulin</td>
<td>Insulin</td>
<td>Diabetes</td>
<td>936</td>
</tr>
<tr>
<td>Intron-A</td>
<td>α-Interferon</td>
<td>Anticancer, infections</td>
<td>598</td>
</tr>
<tr>
<td>Engerix-B</td>
<td>Hepatitis B</td>
<td>Vaccine</td>
<td>584</td>
</tr>
<tr>
<td>Cerezyme</td>
<td>Glucocerebrosidase</td>
<td>Genetic deficiency</td>
<td>333</td>
</tr>
<tr>
<td>Activase</td>
<td>Tissue plasminogen activator</td>
<td>Heart attack/stroke</td>
<td>261</td>
</tr>
<tr>
<td>Humatrope</td>
<td>Somatropin</td>
<td>Growth deficiencies</td>
<td>260</td>
</tr>
<tr>
<td>ReoPro</td>
<td>GPIIb/IIIa antibody</td>
<td>Prevents blood clots</td>
<td>254</td>
</tr>
<tr>
<td>Avonex</td>
<td>Interferon beta-1a</td>
<td>Multiple sclerosis</td>
<td>240</td>
</tr>
<tr>
<td>Protropin/Nutropin</td>
<td>Somatrem/somatropin</td>
<td>Growth deficiencies</td>
<td>224</td>
</tr>
<tr>
<td>Pulmozyme</td>
<td>Dornase alpha</td>
<td>Cystic fibrosis</td>
<td>92</td>
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<tr>
<td>Proleukin</td>
<td>Interleukin</td>
<td>Cancer</td>
<td>71</td>
</tr>
<tr>
<td>Leukine</td>
<td>Colony-stimulating factor</td>
<td>White blood cell growth</td>
<td>53</td>
</tr>
</tbody>
</table>

3. EHRLICH HONORED BY A BANKNOTE

In 1989 the Federal Bank of Germany, Deutsche Bundesbank, issued new banknotes, among them the new denomination of DM 200 that—belatedly—memorializes and honors Paul Ehrlich. The design of this bill was the result of a close collaboration of the bank with

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Figure 2. In 1989, the Federal Bank of Germany (Bundesbank) issued new banknotes (with the novel denomination of DM 200) honoring Paul Ehrlich. His grandson Gunther Schwerin provided the portrait with the quizzical look. The inset reveals the structure of arsenobenzene, the basic prototype of Salvarsan.
Ehrlich’s grandson⁷ and myself.⁸ Gunther Schwerin selected his favorite picture of his grandfather with the slightly slipped glasses behind which lurks an unquenchable humor, because he found the portrait by Max Liebermann (Fig. 3) too formal and too stern.

At the left of the portrait is a formula, viz. arsenobenzene, the parent structure of the magic bullet, arsphenamine or diamino-dihydroxyarsenobenzene, against a background of old Frankfurt, with the Dom (left back) and the Paulskirche, the solemn location for the award of the annual Ehrlich Prize. More than six hundred compounds had to be synthesized, before Ehrlich-Hata 606 could be entered in the Laboratory Journal under the name of “Salzsauers Aminoarsenophenol”.⁹

![Structure of 606](image)

This structure differs from the trimeric ring structure on the banknote by connecting two arsenic atoms with a double bond, a structure that was not known until 1983.¹⁰ When commercial samples of arsphenamine were subjected to modern analytical methods, they turned out to be mixtures of linear and cyclic oligomers and polymers. In view of this revelation the magic bullet should be termed “magic buckshot,” and the Zauberkugel becomes Zauberschrot.

The reverse side of the banknote (Fig. 4) displays Ehrlich’s favorite tool, the historical Zeiss microscope, against a background of decorative cell types. His first discovery was the “mast cell,” which he

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⁹ Ehrlich’s view of the structure of Salvarsan, as pictured in an entry in his laboratory journal dated 7 September 1909.
Figure 3. Paul Ehrlich, painted by Max Liebermann
Figure 4. The reverse side of the banknote shows Ehrlich's favorite working tool, the historical Zeiss microscope with a background of decorative cell types, and, in the upper left corner, the function of the mast cells that he discovered, which is repeated on the inset on the right for better recognition.
found in Freiburg as a young student in 1877, a cell that is involved in the immune response and the anaphylactic shock.

4. Ehrlich’s Family and the Holocaust

Ehrlich summed up his experience of setbacks and discriminations in a letter to his protector and sponsor, Associate Minister Friedrich Althoff, dated 27 July 1907:11,12

I personally am indebted to you for my entire career and the opportunity to develop my ideas in a fruitful fashion. When I was an assistant I was shoved around, deprived of laboratory space and completely ignored by the University. I felt useless and unwanted at that time. Never have I received an offer to occupy even the smallest academic position and was looked upon as a person without any special expertise, in other words absolutely unemployable. If at this point you would not have stood up for me with a firm hand and admirable initiative, if you had not secured for me new opportunities to do my research and done so with untiring zeal and gracious benevolence, I would have stagnated and remained completely unproductive.

The Holocaust forced all of Ehrlich’s surviving family (Fig. 5) into exile, first in Switzerland, then England and the United States. Some of the descendants of Ehrlich’s four sisters, who did not flee, became victims of the tragedy, including a father, a mother, and their baby, who perished in Auschwitz.13

5. The First Nobel Prize in Medicine

The first Nobel Prize in Medicine and Physiology was awarded to Emil von Behring in December 1901 for his development of a serum against diphtheria. A search in the archives of the Nobel Foundation shows that Paul Ehrlich was a strong competitor, as a letter (translated

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Figure 5. Ehrlich’s granddaughter, Susanne von Schueching, née Landau (1908–1982), daughter of Marianne Landau, née Ehrlich (1886–1963), upper row left, and the famous mathematician Edmund Landau (1877–1938), standing next to his wife, pointed out that she, her mother, her aunt Stephanie Schwerin, née Ehrlich (1884–1966), seated left and her husband, Dr. Ernst Schwerin (1869–1946), standing far right, as well as her grandmother Hedwig Ehrlich, née Pinkus (1864–1946), seated far right, all sought refuge in the United States and became American citizens. Max Pinkus (1877–1934), standing left with hat in hand, Mrs. Ehrlich’s brother, was a friend of Gerhart Hauptmann, famous writer, Nobel Prize 1912, who in 1934 had the courage to attend his friend’s funeral as the only non-Jewish participant; cf. Kurt Schwerin, “Die Juden in Schlesien,” Bulletin des Leo Baeck Instituts (1980), 19 (56–57), 1–84; see 44.
from German) from Professor Theodor Langhans in Berne, dated 12 January 1901, and directed to the Nobel Committee, attests:

As far as Paul Ehrlich is concerned, we need to select his most important contributions, his investigations on ricin (the “toxalbumin” or Lectin of the castor bean), and on abrin (a powerful phytotoxin of the precatory bean) going back to 1891 and following directly those of Behring’s. Both of these toxins are related to the toxalbumoses of bacterial origin and can be prepared in large quantities and sufficient purity, which made it possible for Ehrlich to investigate the problem of the immune response with almost mathematical precision. He arrived at the most interesting result that the peak of immunity is reached after repeated doses on the sixth day, comparable to the crises in pneumonia or measles, and Ehrlich drew attention to the analogy of the two situations. Better known are his experiments in which he studied the transfer of immunity from mother to child through lactation or inheritance, investigations that he extended to tetanus and swine erysipelas (Schweine-Rotlauf). But even more important and most original are Ehrlich’s views on the origin of antitoxins (antibodies), his determination of the strength of the serum against diphtheria in 1897 which he expanded to tetanus. He considers antitoxin (antibody) a normal component of the cell with special “sidechains” (Receptors) as part of the operational cellular apparatus. The toxin of tetanus combines with such a side chain with a profound effect on the entire cell including the nucleus. As soon as the “sidechain” is occupied by the toxin, a compensatory formation of many new sidechains results, in Ehrlich’s views, in an incredible abundance in which the excess sidechains are ejected from the cells, enter the blood stream and thus form the antiserum which neutralizes the invading toxin. . . . This explanation is vastly different and much more innovative than anything that has been thought or written on the origin of antibodies so far. Ehrlich’s ideas on toxoids (attenuated toxins) and epitoxoids prove him to be an ingenious and highly original thinker. His earlier hematological work, the discovery of the mast cells, the histo-chemical staining of living nerve fibers with methylene blue, his vital staining, have by now been fully accepted and clinically applied.

In short, I would like to nominate Behring in Marburg and Paul Ehrlich in Frankfurt as prime candidates for the first Nobel Prize.

I consider the two candidates as the most original and felicitous investigators in the field of medicine.

It took seven long years until in 1908 Ehrlich finally received his overdue Nobel Prize for his signal contributions to immunology. His
principal opponent on the Nobel Committee was Svante Arrhenius (1859–1927) who, after his own Nobel Prize in 1904, mellowed somewhat. As a physical chemist with an unusual interest in immunology, he felt that Ehrlich was wrong when he postulated that one molecule of antigen or toxin leads the immune system to the production of millions of molecules of antibodies. His belief was that the “mass action law” should govern this process.

There has never been a more dramatic conflict and such a drawn-out discussion within the Nobel Committee. Both scientific and personal differences fed the controversy. Arrhenius returned from a visit to Frankfurt somewhat alienated by Ehrlich’s dictatorial leadership and by the “markedly Jewish atmosphere of the Frankfurt Institute.”

In retrospect, it is clear that a shared Nobel Prize for Behring and Ehrlich would have saved much needless chagrin.

6. EHRlich AND BEHRING

Althoff, in his powerful position as associate minister of education in the Prussian government, lent his support to his two favorite protégés, Ehrlich and Behring, and often tried to reconcile the growing personal differences between them. As early as 1899 these problems are described in a letter of Ehrlich written to his cousin and closest friend, the well-known pathologist and histochemist Carl Weigert (1845–1904):

Lieber Carolus:

Finally I am getting around to write you confidentially about our tiff with Behring. Not long ago we had a terrible row which, of course, he will use to denigrate me. To quote Bismarck: I have a spotless waistcoat and view what comes with equanimity.

As you well know, there has been enough tinder for quite some time. You may recall the behaviour of Behring—who is indebted to me for his entire financial success—how ungrateful and boorish he was when he discontinued our contract. I don’t want to talk about it, because I am anxious to forget the whole affair. Also I am quite happy to be rid of all these business transactions and now enjoy a position which allows me to serve the

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public to the best of my ability. But to atone for this, I must enjoy utter independence and be no longer exposed to Behring’s crass egotism and money-grabbing. I am not in the least inclined to accompany him on his parforce tours and be subservient to his business shenanigans. I have no mind whatsoever to convert my Institute into a branch establishment or business venture of Behring’s. I would rather abandon the whole caboodle.

The real reason for his distemper—which, of course, he did not disclose—has to do with the *tuberculin problem*. First of all, I rubbed him the wrong way when I proved that his tuberculin D—with which he wanted to wow the world and to eclipse Robert Koch—is nothing else than a terrible bust. On closer inspection, he should have shown gratitude to me, because I was the one who explained to him the utter uselessness of his investigations so far for which he has spent frightening amounts of money. Without my dissent he would have lost himself in this unholy swamp over the years.

What follows next was that it dawned upon Behring that Koch with his tuberculin D—which he thought he had bypassed and improved—was absolutely right. As a consequence of this insight tuberculin D vanished with hardly a trace and, all of a sudden, there were courtesies and sunny comments on Koch’s tuberculin R. The real trouble came when he tried to convert Koch’s discovery into financial gains by applying for a patent. But then the majority of decent people raised such a racket against this shameless exploitation of another person’s intellectual property that Behring felt moved to withdraw his patent application, as it happened before his departure for Italy. Of course, this was not a pleasant wake-up for him who had already dreamed of geese and swans as sources of antitoxins for making a fortune of millions. In sum, his troubles in Berlin did not leave him as the victor, so he preferred to leave the capital and tried to wend his way toward Italy.

Of course, everybody knew my position, since I decidedly pleaded for Koch—*dignum et justum erat*. All this mattered little in the eyes of the public, but under the surface there were complaints about my official activities, but they were baseless enough not to raise any administrative hackles. Even Behring pointed out that tests of my sera would not be in the best interest of Hoechst or himself. All this meant a serious licking for him, since any testing by Dönitz or Bauhof would be unreservedly impartial and

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16 Behring’s share in the profits of Farbwerke Hoecht in the years 1895–1914 are 1,847,000 Gold-Marks, equal to 15–30 million DM in today’s value; cf. Carola Throm, “Das Diphtherie Serum,” *Wissenschaftliche Verlagsgesellschaft* (Stuttgart, 1995). I am indebted to Dr. Arthur M. Silverstein, Institute for the History of Medicine, Johns Hopkins University, for this information.
my entire Institute could expect full confidence from the Minis-

try of Health. Following these events Behring was anxious to gain greater influence on my Institute’s management, such as per-

sonnel and programs, but I had peremptorily stated before, that Behring—whose interests are exclusively mercantile—would ruin the prestige of my entire Institute, if he were to exercise any special influence. An Institute, such as mine, must be free of par-
tisan disturbances, cannot tolerate the wolf as a shepherd or a Behring as a Curator. I don’t want to have any part of such an arrangement and would rather give up the whole show.

In these circumstances the first preliminaries kicked up a row: deeply insulted and injured Behring left the locality in a huff. Of course, he will bad-mouth me now everywhere, but my con-
science is untroubled, and whatever he may be up to, doesn’t faze me in the least. Of course, he will try to block our daily supplies and prevent us from testing sera for foreign consumption which would hurt us. But there will be ways to get around this contin-
gency. In an emergency we expect the (Prussian) State to take care of us, either by raising taxes or by new assignments of sera against tetanus or consumption. My favorite arrangement would consist in support by the State of all salaries and in independence from industry. I am writing you this, so you may get a complete picture of the situation.

Four years after this letter Ludwig Aschoff (1866–1942), the leading German pathologist after Rudolf Virchow (1821–1902), describes a meeting with Behring in Nordhausen17 where, in the presence of Min-
ister Althoff, the rankling differences and discrepancies, as described in Ehrlich’s telling outburst, were to be ended by negotiation and recon-
ciliation, which, however, was of short duration.

Even ten years later in 1914, when the two Nobel laureates cele-
brated their sixtieth birthdays, Ehrlich on 14 March, Behring on 15 March, and their peaceful togetherness was published as the title page of the Berliner Illustrierte Zeitung, the grandson Gunther Schwerin had grave doubts about the authenticity of this double portrait. And indeed, Dr. Thomas Stoeckl, an Ehrlich scholar in Freiburg, established the composite nature of this photomontage (Fig. 6).

7. ERLICH’S MATERIAL AND MENTAL LEGACIES IN THE UNITED STATES

What happened to the considerable wealth that Paul Ehrlich had accumulated by his share in the Salvarsan sales and the holdings of Mrs. Ehrlich’s wealthy Pinkus family? Joshua Lederberg, the president of

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17 Ludwig Aschoff, Ein Gelehrtenleben in Briefen an die Familie (Freiburg im Breisgau, 1966), 161–62.
the Rockefeller University, summed it up in 1993: “Dr. Ehrlich’s life-long work represents the kind of humanitarian spirit toward which this University has always striven. We are deeply grateful to Gunther Schwerin for his generosity in carrying out this fine tradition.”

The Paul Ehrlich Fund at the Rockefeller University exceeds $1.5 million and represents part of the material restitution of property stolen or confiscated as a result of the Holocaust. The first “Paul Ehrlich Scholar” was Professor Alan Anderem, who studies the intracellular signaling pathways that are activated when macrophages (defensive cells of the immune system) encounter invading organisms. It is the same question that occupied Ehrlich more than a century ago, but now it is pursued with the full armamentarium of modern molecular biology.

In August 1904, Ehrlich had visited Johns Hopkins University and his old friend William Henry Welch (1850–1934). The Paul Ehrlich Lecture at Johns Hopkins is a lasting memorial of this close association. A similar lecture was instituted at the National Institutes of Health in 1988, when the first lecturer, Edgar Lederer (1908–1988), professeur emeritus of the Centre National de la Recherche Scientifiques, was introduced on 21 April with the following words:

Professor Edgar Lederer, our first Paul Ehrlich Lecturer, has been following for sixty years in the footsteps of Ehrlich and has

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"The Rockefeller University Today" 1.3 (1993), 2.
forged his own magic bullets, such as his muramyl dipeptides (MDP) which modulate or stimulate the body’s immune defense against hostile bacterial and viral invaders or parasite protozoans. In tumor immunology MDP finds application as immunoadjuvant, when injected simultaneously with tumor antigens. The speaker is also credited with the development of synthetic peptides as vaccines, a new approach to the cure of diseases.

There is also a direct connection of NIH with Ehrlich’s Laboratory: Reid Hunt (1870–1948), an enthusiastic disciple of Ehrlich, returned from his second stay in Frankfurt in 1903 to be named, in 1904, Chief of the Division of Pharmacology in the Hygienic Laboratory of the United States Public Health Service, the precursor of the National Institutes of Health. In 1907 Hunt wrote a letter to the Journal of the American Medical Association pleading that the future therapy of infectious diseases lay in chemotherapy rather than in vaccines and sera. This letter was written before Ehrlich announced the discovery of salvarsan. Carl Voegtlin (1879–1960), Hunt’s student and Chief of the Division of Pharmacology from 1913–1943, studied the mechanism of action of arsenicals on cells.

Subsequent speakers who developed magic bullets were George Hitchings (1905–1998; Nobel Prize 1988, who lectured in 1990) and Manfred Eigen (Nobel Prize 1967, who spoke in 1992, the same year in which he received the Paul Ehrlich Prize). Stanley Prusiner lectured in 1995, received the Paul Ehrlich Prize in the same year, and the Nobel Prize in 1997 for his discovery of prions, dormant magic bullets.

8. Epilogue: A Visit to Ehrlich’s Grave

Ehrlich’s grave in the new Jewish cemetery in Frankfurt suffered some damage during the war but survived the sacrileges of the Holocaust (Fig. 7). Two columns with disparate symbols form the spiritual entrance through which posterity must pass to gain access to the character of the person who rests here. The left column shows the Star of David, a symbol that truly came to life through a fellow Frankfurter, Franz Rosenzweig (1886–1929) in his book The Star of Redemption (Der Stern der Erlösung), which he composed as a soldier in World War I, in the pauses between battles. He attempted a synthesis between German Enlightenment and a new Jewish Humanism (Haskalah), a union he recognized as a source of strength for a new identity and consolidation and—later—a renewed will for survival and the foundation of a Jewish state. From here there is a smooth transition to another leader in philosophy, medicine, and rabbinical scholarship, Moses ben Maimon or Maimonides (1135–1204), who, like Rosenzweig, was a
builder of bridges, in this case between the ideas of Aristotle and the philosophy expressed in his own book *Guide to the Perplexed*. Medieval scholastics, among them Thomas Aquinas, were influenced by this work almost as much as Spinoza, the most famous follower of Maimonides. If we want to find a philosopher and originator of medical ethics comparable to Maimonides, we have to go back to Hippocrates (460–370 B.C.), whose style of writing in aphorisms was copied by Maimonides. And just like the “Oath of Hippocrates,” there is in Israel a comparable “Oath of Maimonides.”
The symbol of the right column is the staff of Asclepios (Cauduceus), a god who was the fruit of a union of Apollo with a nymph, and a student of the centaur Cheiron who healed by putting his hand (cheir) on the sick. According to Plato the true physician attempts to heal not only the body but also the soul, because he is interested in the cause, the etiology, of the disease. Without much difficulty we recognize in this type of physician Paul Ehrlich, who immersed himself in the tradition of Giovanni Battista Morgagni (1682–1771), founder of pathology and author of “de causis et sedibus morborum” or “about causes and seats of diseases.” Ehrlich the healer and almost thaumaturgist is described by his friend Carl Ludwig Schleich (1859–1919) in his moving obituary (1915):

Whoever has seen Paul Ehrlich at a sickbed in one of the spreading wards of a large hospital, must have noticed that this extraordinary man embodied the humanist as physician. I was touched by the tenderness with which he took care of his child patients, how he joked with them and tried to soothe their discomfort by caresses, and yet, at the same time, I noticed his unease to be in the middle of an impersonal machinery whose wheels were turning in his name and by his authority.19

Ehrlich always thought of others more than of himself, so that the inscription “ROPHE VELO LO”—he was a physician, alas not for himself—would fit his tombstone as well as it does that of Julius Preuss (1861–1913), the author of the leading compendium on Talmudic medicine.20

9. The Mill of Time

Ehrlich’s ideas and paradigms, his sidechain or receptor theory, his magic bullets and introduction of chemotherapy, his explanation of the immune response, viz. selection from existing antibodies rather than instruction by a template antigen, his proposal to use antibodies as carriers of drugs or toxins and as “cruise missiles” to reach tumor sites, all these concepts have gone through the mill of time (Fig. 8) and appeared in refined and extended form by a host of followers. As Schiller said of Kant, “When kings build, carters get busy.”

19 Carl Ludwig Schleich, Die Neue Rundschau 26 (1915), 1409–19, see 1419.
**Figure 8.** The birth and rebirth of great ideas is here symbolized in “Le Moulin mystique,” Vézelay, France, ca. 1100. Moses pours the seeds into the mill of time, and many centuries later St. Paul receives the flour.