HORIZONS OF SCIENCE

By Waldemar Kaempffert

The Coming Revolution in Medicine

Of the four and a half million soldiers in the Revolutionary and Napoleonic armies from 1792 to 1815 about two and a half million died in hospitals and 150,000 were killed in action. In the Crimean War 8,250 Frenchmen were killed and 59,815 died of sickness. In our Civil War the Union forces lost 67,058 on the battlefield, 43,012 who died of wounds and 224,586 who succumbed to disease. Until World War I infections were always deadlier than bullets. Today disease is under control and surgeons regard the appearance of infection in soldiers on whom they have operated as little short of a disgrace.

The sulfa drugs are partly responsible for the medical showing made by all armies in the field. Before they were introduced six hours was considered the maximum waiting period if massive lacerations were to be successfully handled. Today many of the wounded wait much longer, a shot of antitetanus in the veins, powdered sulfanilamide in their wounds. Every American soldier's first-aid packet contains eight tablets of sulfadiazine, with instructions that read: "If wounded take the contents of this package at once."

The sulfa drugs are more than so many new additions to the pharmacopeia. Blood-poisoning, streptococcal sore throats, childbed fever, scarlet fever, erysipelas, gonorrhea, pneumonia, peritonitis, mastoiditis (infection of the middle ear), trachoma (which once ended in blindness), bacterial dysentery, a score of other afflictions are now under scientific control. A revolution is under way, and a dream has come partially true — the dream of the specific which will seek out deadly germs in the body or heal an internal injury and leave everything else alone.

Primitive savages, who are supposed to be ridden by superstition but who are actually as practical as plumbers when faced with the hardships of the wilderness, had made more progress in realizing the dream than supposedly scientific physicians of Europe up to the

early nineteenth century. Pre-Columbian Incas had discovered that quinine in the crude form of cinchona bark was a specific against malaria, but Jesuits who returned to Europe from Peru found it hard to convince physicians that it was so. When Jacques Cartier's men were afflicted with scurvy, a disease caused by deficiency of a vitamin, Canadian Indians cured them with infusions of leaves. Snake venom, dried toads, curare, extracts of herbs and roots — the savage remedies at which the medicos once scoffed turn out to have their virtues.

Like the savage the civilized physician has always wanted an agent which would be highly selective, a specific, in other words, which would cure a sick organ or tissue without injuring anything else or which would kill the germs that cause disease without destroying the tissues affected. He had a few specifics — very few. One of them was mercury, long used in the inefficient treatment of syphilis at the risk of killing the patient. Quinine was another. And now there are scores — all chemicals.

Though it played no part in their thinking it was Pasteur and Koch who encouraged hope in the specific. Both had demonstrated the bacterial origin of many infections. Both killed bacteria and cured diseases, always with implications of specific action. But where was the disinfectant which would be swallowed or injected in large doses and which would attack only deadly bacteria? Lister used carbolic acid (phenol) with good effect in surgical operations to prevent infection, but no physician in his senses would prescribe it to kill bacteria in the stomach or inject it into the blood stream.

It was Paul Ehrlich who placed the specific on its scientific feet. Like thousands of physicians he knew that dyes do not color all textiles with equal facility. A dye that is fast for wool can often be washed out of cotton or linen. Particularly is this true of the coal-tar colors, which are highly selective. If they can act in this way on animal and plant fibers, why not on microorganisms and tissues? The question was penetrating. Ehrlich had no thought of African sleeping-sickness or syphilis when he propounded it. He was thinking of bacteria which were all but invisible under the microscope — invisible because they were as clear as the watery medium in which they lived. If a dye could be found which would stain only a germ or a living cell, bacteriology would re-

ceive an immense impetus. The germ, the cell would stand out like a red cloth on green grass. After much work Ehrlich found his dyes and devised the modern method of staining microscopic specimens. Bacteriology and the diagnosis of many diseases leaped forward. A bit of tissue could be studied not as a slice of dead meat cut out of the body but as a collection of living cells.

All this was enough to send any scientist's name ringing down the ages. But a trigger had been pulled in Ehrlich's mind. If a dye can pick out a certain kind of cell or germ, stain that, but not touch anything else, why not hook a killing chemical to it? The dye ought to creep up on its quarry and the chemical ought to kill. Out of this reasoning came the attack on the microorganisms of African sleeping-sickness, which are transmitted by the bite of the tsetse fly, and then on the spirochetes of syphilis. Dyes linked to killing chemicals sought out the germs in both diseases. The jungle became safer for settlers; syphilis was stripped of its old terror.

Until twelve years ago not much progress had been made in applying Ehrlich's theories. There was no lack of industry. Ehrlich had simply tried dyes by the hundreds before he found the right ones. A man might work all his life in this fashion and have nothing to show. Then an accident happened: sulfanilamide. An obscure Austrian student, P. Gelmo, had discovered it in 1908, when Ehrlich was immersed in his researches. Gelmo determined the chemical properties of his compound, won a doctor's degree from the University of Vienna, published his thesis in a chemical journal and then disappeared. Was he a casualty of World War I? He has never been heard of since. Because he was a chemist and not a bacteriologist he had not the faintest inkling that he had discovered something as important as Ehrlich's mode of combatting African sleeping-sickness and syphilis.

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Though he had disappeared, though his thesis had been embalmed in a chemical journal without making any impression, Gelmo was no forgotten man. In searching chemical literature Rockefeller scientists stumbled on his buried sulfanilamide, saw possibilities in it, hooked it to quinine, but got nowhere. Chemists of the German chemical trust also dug up the bones and decided that they had possibilities — but only for textile

dyes. Dr. Gerhard Domagk, head of the German trust's pathological institute, pricked up his ears. Suppose this compound of Gelmo's were hooked to an appropriate dye. Bacteria might be killed in the selective Ehrlich way.

Out of experimenting that matches Ehrlich's in the search of specifics against sleeping-sickness and syphilis came an orange-red dye to which Gelmo's sulfanilamide had been coupled. A Dr. Foester rose before a meeting of physicians to tell of his almost miraculous success in curing what was a hopeless case of blood-poisoning in a child with the combination. No one paid much attention. After all, what is one case? The German trust knew better. It banked on Domagk's unpublished results with animals. It patented "prontosil," Domagk's linkage, and handed out samples to physicians.

The American public first heard of prontosil when it was used to treat President Roosevelt's son, James, for a streptococcal sore throat. James and prontosil made the front page, much to the displeasure of physicians, because they wanted more information. The facts were forthcoming soon enough. In Great Britain exhaustive experiments were made in cases of childbirth fever with dramatic success. Though both the English *Lancet* and the *Journal of the American Medical Association* were editorially pessimistic, the tide of opinion turned. It was plain enough that a whole series of globular germs called "cocci" could be reduced to helplessness without killing the patient.

Because prontosil was patented the German chemical trust had the world by the throat. It was either pay the price or die of blood-poisoning, childbirth fever or one of a dozen coccal infections. Patented preparations have never been popular in medicine. Could the prontosil patent be evaded? It struck French chemists in the Pasteur Institute of Paris that prontosil was much too complex and that it might be reduced to something simpler. It was therefore torn apart, and each part was tested separately. Gelmo's sulfanilamide proved to be the active portion; prontosil simply gave it up in the body. Sulfanilamide was effective without any selective dye at all. Almost overnight a patent which could not have been bought for millions dropped in value to the price of yesterday's newspaper.

All this wrought havoc to the prevailing theory. Domagk had preached Ehrlich's doctrine. In other words, the dye selected the

cocci to be attacked, whereupon the sulfanilamide destroyed them. It was shown that sulfanilamide was no true specific, and that it combatted infections not by killing "cocci" but by preventing them from multiplying, so that they could be destroyed by their natural enemies, the white cells of the blood.

There are now several thousand sulfa compounds, of which not more than a score are of any medical use as yet. All act like Gelmo's. It is rarely now that sulfanilamide is given by mouth, and this because it nauseates and it attacks the kidneys. If we hear of sulfanilamide on the battlefield and in the operating room it is because it is an effective dressing for wounds. For the treatment of pneumonia, childbirth fever, gonorrhea, and coccal infections in general other sulfa compounds have taken its place because they do not make patients sick to their stomachs or because they are not absorbed by the intestines. So we have sulfapyridine, sulfathiazole, sulfaguanidine, sulfadiazine and others.

Though the sulfa drugs are not true specifics, though they check bacterial growth without actually killing, their introduction marks an extraordinary advance in what Ehrlich called "chemotherapy." For the first time in medical history it is possible to introduce enough of a powerful disinfectant into the human system to overcome a bacterial disease. The sulfa compounds place the physician in the position of a sharpshooter. Except in African sleeping sickness, a few deadly jungle infections and syphilis, all treated in accordance with Ehrlich's selective principle, he had to use a shotgun and hope for the best. Now he is a crack shot armed with a rifle when he stalks the coccal infections.

Ehrlich restricted his term "chemotherapy" to the chemical treatment of bacterial infections by the crackshot method. There is no reason why the term should be so limited. The process whereby the body converts food into muscle and energy is essentially chemical. A needle pricks the finger and at once all the chemical and physical resources of the body are marshalled to repair the injury. The transmission of pain along a nerve is largely an electrochemical phenomenon. If we are enraged the adrenal glands, which lie above the kidneys, pour out chemicals that rouse the fighting spirit. All the glands secrete chemicals that have their uses in keeping the body healthily alive. Turn where we will we find chemistry at work. Medi-

cine is of necessity applied chemistry in the large sense. Properly developed, chemotherapy must include much of medicine.

Flesh, bones, blood, nerves and brains are highly complicated chemical structures. It follows that sickness simply upsets the chemical balance and that it is the business of chemistry to restore it. Why does an antitoxin check diphtheria? Because of some obscure chemical action. Why do bacteria lay us low? Not because they are like knives or bullets, but because they release poisons — chemicals. Why do minds go awry? Because the brain has been chemically upset. The successful administration of insulin to shock the brain in early cases of schizophrenia proves as much. We take a dose of luminal, sodium amytal or one of a hundred similar compounds and fall into a sound sleep. Evidently the chemistry of the nervous system has been influenced. Why do we grow old? Because the body's chemistry has changed.

Some day medicine will do away with serums and vaccines. It is a complex chemical in the serum of vaccine that cures. When that chemical is discovered it will be synthesized and used directly. The serums which were once the only means of dealing with pneumonia are already giving way to the sulfa compounds. Radioactive phosphorus and calcium are used in the experimental treatment of some forms of cancer because of their selective action — more proof of the validity of the chemical approach. Even when we massage the muscles of the body we stimulate chemical processes and induce a sense of well being.

Good as our doctors are, they are still "medicine men" in the savage sense. Fully half of their practices are based not on scientific knowledge but on tradition. The age-old wheeze that "medicine is an art as well as a science" speaks for itself.

We want more science and less art in medicine. Crude as chemotherapy may be, it is the harbinger of a new medical day.

THE bad man wants to kill those who disagree with him; the good man merely wants them to go to hell.

— ANONYMOUS

▶ *Enthusiasm for the Statue of Liberty did not run too high.*

WHEN LIBERTY WAS IMPORTED

By Francis Rowsome

A driving rain whipped flags and bunting into limp tatters. Seven hundred spectators huddled under umbrellas, listening damply to speeches and a brass band. A reporter observed that the umbrellas tipped in magic unison to oppose new gusts of wind from New York harbor. At last the speeches were done, the great cornerstone was derricked up a few inches, and a copper box inserted beneath. Within the box were coins, newspapers, the Declaration of Independence, and a history to date — August 5, 1884 — of this, the Statue of Liberty, the biggest and grandest statue the world has ever seen. When the block had been lowered, a master mason tapped it three times with his mallet, and ceremoniously poured over it oil, wine and grain. Hastily the crowd broke for the ferries to Manhattan. The reporter noted that throughout the cornerstone-laying, "rain came down with wildly enthusiastic fury."

Wild enthusiasm was something the backers of the Statue of Liberty had often had to get along without. The story of the colossal Liberty begins some twenty years before, when a few friends gathered for dinner in the Versailles home of Edouard Laboulaye, historian and writer. The conversation turned upon foreign relations; the Italians, having borrowed a large sum from France, had just repudiated the debt. America, in contrast, was a fine country, and France loved her. As an American testimonial later recorded: "Having at the table congenial spirits, the poetic and sublime idea was then and there conceived" of presenting America with "the figure of Liberty in colossal proportions. . . ."

The dream might have been forgotten had there not been present a young, bearded Alsatian sculptor, Frédéric Auguste Bartholdi. Colossal statuary fascinated Bartholdi. But since the other guests displayed

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