Chapter Four

The historical back drop for 20th century obstetrical practices

The historical back drop for 20th century obstetrical practices was the stunning inability of *pre-modern* medicine to effectively treat disease, combined with the universal human hope that some day a magic potion would be found and all illness and disease eliminated. After eons of little or no progress, a quick series of world-changing discoveries in the late 1800s triggered a popular enthusiasm for medical science, something akin to our preoccupation in the 1960s and 70s with the US space program and the moon landings. Space exploration was exciting to hear about and interesting to contemplate, but did not immediately change the day to day lives of the general population, at least not initially. However, the scientific discoveries of the late 1800s made a big impact on the practice of medicine and inspired the emerging profession of obstetrics to be on the cutting edge of modern medicine science.

The second major element was the fact that historically the obstetrical profession had very little experience with normal childbirth in a healthy population. Obstetricians were experts in the use of medical methods to treat *abnormal* conditions, since they were only called when forceps or other obstetrical interventions were needed. Medical schools did not even teach the principles of physiological management, which was considered to be 'woman's work' -- the job of midwives and not the practice of medicine. The other reason the obstetrical profession made no attempt to learn physiological principles was their (wrong) assumption that the biology of female reproduction was a sacrificial system designed to produce progeny at the expense of the mother. Other examples of this are seen in nature, for instance, the way that salmon are sacrificed when they spawn. A frequent expression by obstetricians, then and now, is that "Mother Nature is a bad obstetrician", which meant that leaving things up to normal biology was a bad and even dangerous idea. Medicalizing normal childbirth was seen as the best way to keep a pathological biology at bay.

Last in this list was an inflated expectation of technology and medical science that far exceeded its actual abilities. For all the wonderful advances made by modern medicine in the last 120 years, science still has not been able to eliminate all human suffering. But in 1910, scientific medicine was the new kid on the block. Convinced of its unlimited potential, people fervently believed that the key to a universal cure-- the mythical 'panacea' of legend – was just around the corner. This produced an all too familiar form of groupthink best described as 'irrational enthusiasm'. The new obstetrics promised the moon and people lined up to buy a ticket. When the dust settled, childbirth was accidentally trapped on the wrong side of history.

Since the early 1900s normal childbirth, even in healthy women, has been assumed to be a dangerous and dysfunctional biology that requires the increasingly aggressive use of obstetrical intervention. Ever since, childbearing women have been defined in late 19th terms: helpless victims whose safety is totally dependent on invasive obstetrical manipulations.

However, it became obvious that promising people the moon wasn't just a problem for the childbearing half of the equation. The obstetrical profession itself got trapped by their own belief that they *could and should take over the total control* of reproductive biology and that doing so

could and *would* save all mothers and babies from the "dangers of childbirth". This reinforced the notion that pregnancy and birth were a cruel fate imposed by an uncaring Mother Nature and it also generated unrealistic expectations of obstetrical medicine and the idea that it could take away all of the unpleasantness of laboring and having a baby. The idea that every baby delivered by an obstetrician would be perfectly healthy became (and remains) very popular. Whenever this impossible promise could not be kept, somebody got sued.

Since the malpractice crisis started in 1976, obstetrics has become organized by the need to view everything in legal terms. Risk management is all about reducing the likelihood of litigation, while increasing the likelihood of winning *when* the obstetrician gets sued. This is inevitable in the current dysfunctional system, where ten percent of obstetricians have a malpractice suit filled against them every year, with two-thirds of all obstetricians getting dragged into court at least twice during their professional career. The nicest people often can't stand the strain and leave obstetrics.

The obstetrical answer to the threat of litigation is a sort of obstetrical arms race, one that tries to stay ahead of the lawyers with an escalating model of intervention and ever-increasing use of technology. As of the year 2000, this process reached its inevitable conclusion. Since total responsibility requires total control, the 21st century solution is to electively schedule Cesarean surgery is offered at 39 weeks (a week or more before normal labor would be expected). For pregnant women who resist the idea of a planned surgical delivery, induction of labor is routinely scheduled shortly after the 40 week due date is reached. This aggressive style of obstetrical practice is being promoted as safer and better than anything Mother Nature could accomplish and the only way to deliver on its historic 20th century promise. Unfortunately, this is based on incorrect assumptions.

This historical baggage burdens us with 19th century assumptions, locking all our maternity care providers into a very narrow, obstetrical definition of childbirth. This makes obstetricians unable to consider any other possibilities. As long as normal childbirth in healthy women is trapped behind the unexamined policies of 1910 obstetrics, defined and billed solely as surgical procedure, the obstetrical profession will be unable to change or evolve to meet the unique challenges and new opportunities presented by 21st century medical science.

To understand how and why this happened, it's necessary to follow the trail back from 1910 to the very beginning of what we now refer to as modern medicine – microscopes, wee beasties and the 200 years that changed everything. Then it's possible to examine obstetrical policies in context and figure out why things happened as they did, how normal childbirth wound up on the wrong side of history and what can be done to remedy the problem.

1910 ~ The Best and the Worst of Times:

The last two decades of the 19th century and the first three of the 20th were a time of stark contrast between the pre-scientific days that were passing away, and the soon-to-be era of modern medicine officially defined by the introduction of sulfanilamide in 1935-- the first effective antibacterial drug.

During the 50 years of transition, from 1895 to approximately 1945, medical science rushed into popular culture at a breakneck speed and changed the way people thought about the human condition. For the first time ever, the human hope for effective cures was not just a pie-in-the-sky dream, but the real probability that the medical profession would be able to end human suffering. The most extraordinary scientific discovery was the *germ theory of disease*, which for the first time identified the role of bacteria in causing infection and illness and lead doctors to understand the transmission of disease. While many scientific advances during this time had little or nothing to do with microbiology, the germ theory of disease was certain the most profound change to date in the history of medicine as a rational scientific discipline.

Other major scientific advances during this 50 year revolution included antiseptic and sterile technique, clinical laboratory services, x-rays diagnosis, better surgical techniques, safer anesthesia, blood typing which made transfusions safer, discovery of insulin to keep diabetics alive, an understanding the Rh factor for childbearing women, routine prenatal care and finally, the last and the most extraordinary -- antibiotics for fighting infection.

In the centuries before scientific medicine, the universal response to disease was confined to hope, hand wringing and prayer. Attempts to treat disease used superstitious charms, herbs and dangerous substances such as arsenic, mercury and animal dung. Also included were useless (at best) or harmful activities such as bleeding, purging and sealing up the house to keep out the 'vapors' or bad air (miasma) thought to be the cause of infection.

Conspicuously absent from these 'healing arts' was the basic science of investigation and the technological abilities that eventually lead to a therapeutic understanding of human biology. It wasn't until the 17th century that anyone attempted to use magnification to better understand the natural world. The notion that organisms such as bacteria could just arise out of nothing -- the 2000 year-old wrong idea of known as 'spontaneous generation' – wasn't debunked until the early 1880s. The medical profession did not universally adopt the simple precaution of hand washing until the 1890s.

Microscopes, 'Wee Beasties' and Hope – the 200 years that changed everything

A discovery is said to be an accident meeting a prepared mind - Albert von Szent-Gyorgyi

The miracle of 'modern' medicine was preceded by an impressive list of successive inventors and inventions. These discoveries are a curiously interrelated story and more recent than one might expect. The story of accidental discoveries meeting prepared minds starts with the English biologist **Robert Hooke**. He was the first person to build and used a simple microscope to observe the structure of plants and insects. This allowed him to see previously invisible details on materials such as fabric, cheese and the common flea. His rudimentary equipment was only able to magnify objects10 to 20 times, but that was enough to see the tiny walled chambers that made up a piece of cork. He called them "cells", since they reminded him of monks' cells in a monastery. We have used his descriptive term ever since.

In 1665 Robert Hooke published his finding in an illustrated book called '*Micrographia'*. Shortly thereafter, his book fell into the hands of an unschooled 17th century Dutch drapery merchant, **Antony van Leeuwenhoek**, who was already making magnifying glasses as a hobby.

Van Leeuwenhoek was so fascinated by the detailed drawings that he made himself a microscope so as to see these things for himself. This was one of humanity's luckiest days.

Van Leeuwenhoek was born in Delft on October 24, 1632. His father was a basket-maker, his mother's family were brewers of beer. Before becoming a drapery fabric merchant; he worked as a surveyor and as a minor city official. At one time he served as the trustee for the estate of the famous painter Jan Vermeer, the deceased and bankrupt artist who had had been born in the same year as Leeuwenhoek. Van Leeuwenhoek is thought to have been a friend Vermeer's before he took on the role of trustee.

In 1673, at the age of 41, van Leeuwenhoek used his simple one-lens microscope to peer into a drop of rainwater and became the very first person to ever see the world of microorganisms. His skill at grinding lenses produced the best microscopes of his time, with magnifications ranging up to 200th power. This allowed him to observe tiny "animalcules" under his microscope, which appeared as wiggling threads, long strings of undulating rods and beads and twilling spirals. These living bacteria and protozoa were referred to by van Leeuwenhoek to as "wee beasties".

Van Leeuwenhoek took meticulous notes and later described his findings in letters to some of the most renowned scientists of the day. What started out as a curiosity and part-time hobby turned him into one of the first persons to use what is now called the "scientific method" -- a clear ability to construct experimental procedures that are both rational and repeatable. His talent at analyzing problems produced the philosophy of biological investigation and he developed many of the ground rules still used for scientific experimentation.

Letter of June 12, 1716 Antony van Leeuwenhoek:

> " . . . my work, which I've done for a long time, was not pursued in order to gain the praise I now enjoy, but chiefly from a craving after knowledge, which I notice resides in me more than in most other men. And therewithal, whenever I found out anything remarkable, I have thought it my duty to put down my discovery on paper, so that all ingenious people might be informed thereof."

Before the microscope came into common use, the world of microorganisms was unknown and unthinkable. There were many fanciful explanations for disease, including divine retribution for sins, malevolent spirits, evil spells cast by a sorcerer, unfavorable astrological influence and swampy air. Physicians thought that infectious disease could be spontaneously generated from non-living things, a 2000 year-old wrong assumption known as *the theory of spontaneous generation*. This held sway until Pasteur was able to provide a scientific replacement -- the germ theory of disease -- in 1864.

The world of van Leeuwenhoek's "wee beasties" was mostly a curiosity during the two centuries between the invention of the microscopic and the discovery of bacteria as the origin of infectious disease. There were a few physicians who theorized that somehow microorganisms might be responsible for contagious disease, but the medical world dismissed this as an unproven theory that was of no value to them. The exception was Joseph Lister, a 19th century London physician and surgeon to Queen Victoria. He was certain that something invisible to the naked eye was responsible for post-operative infection. In 1865 he discovered that spraying a dilute solution

of carbolic acid around the operating room dramatically reduced the post-operative infection associated with surgery. The vast majority of the medical profession thought him very odd indeed.

Then a serendipitous series of events occurred that kicked the slow progress of medical science into high gear, where it has remained ever since. The next 'prepared mind' in our story is **Louis Pasteur**, a now famous French chemist employed by the wine industry. The happy accident of discovery occurred in 1864 when Pasteur identified that the process of fermentation (resulting in beer and wine) and putrefaction (such as the rotting of meat) were the result of microorganisms -- invisible bacteria. Discovery of the fermentation process put an end to the idea of spontaneous generation as an explanation of diseases. Pasteur, who was himself the son of a vintner, was able to prove that heating wine to a temperature slightly below the boiling point prevented bacterial spoilage. He developed a way to kill harmful bacteria by slowly raising the temperature of liquids to about 180 degrees and maintaining that temperature for a predetermined length of time. This process is referred to as 'pasteurization'.

Pasteur was an inspired scientist whose experimental methods provided the ability to make milk and other organic liquids safe to drink through pasteurization. This is one of the most important public health measures ever discovered. The theory and techniques of pasteurization could be immediately used by anyone; its goal of rendering liquids safe for human consumption could be accomplished with simple, affordable equipment already at hand. Whenever used, it was instantly able to prevent diseases such as TB from being passed from the cow to humans, diarrheal diseases caused by E. coli in commercially bottled fruit and vegetable juices, botulism in raw honey and many other uses.

Pasteur's experiments demonstrated a causal relationship between bacteria and disease but in 1864 (when he first published his scientific paper) he was unable to prove that a specific strain of bacteria was responsible for a specific disease. However, Pasteur's momentary failure was the stuff of greatness for two contemporary physician-scientists – Joseph Lister and Robert Koch. Each of these men carefully studied Pasteur's work and each took a separate element of Pasteur's theory to make the focus of their own scientific investigation. Each greatly advanced the goals of modern medical science as we know them today.

One of those was Sir Joseph Lister, a 19th century British surgeon referred to above, who applied Pasteur's germ theory at a practical level to surgery in 1865, just a year after Pasteur published his original paper on the germ theory of disease. Lister is often identified as the father of modern surgery but what he did that was so unique was develop the antiseptic and aseptic techniques and the process of sterility that we still use today to make surgical procedures safe from infections.

The other scientist is Dr. Koch, a German country doctor who came on the scene in 1871. He did what Pasteur had not (yet) achieved, which was to prove that a specific strain of bacteria was responsible for a specific disease. Dr Koch became the first person to establish that microorganisms taken from a diseased animal would cause the same disease in an uninfected one. This enabled the medical profession to understand the basic bacteriology behind the germ theory,

bringing medical science ever closer to being able to both prevent and eventually treat infectious disease. Dr. Koch deserves his place as father of bacteriology.

Both men did their most important work within a few years of each other (1867 and 1871 respectively) but for sake of following the pure thread of the scientific discovery before its practical application, I will tell Dr. Koch's story first. Later I will return to Dr. Lister and the others who dealt with the practical end of these scientific principles.

Even though Dr. Robert Koch was 'only' a country doctor, he know of Louis Pasteur's germ theory of disease and was intensely interested in these ideas. He knew that Pasteur had been unable to prove that it was the bacteria themselves -- not other types of cells or unseen toxic substances – that was responsible for causing the contagious illnesses. Koch recognized this as a major stumbling block to scientific advancement of Pasteur's germ theory. Working alone in a small village in the rural countryside and using equipment that he fashioned out of ordinary farm and medical supplies, Dr. Koch used the scientific method to identify the anthrax bacteria and prove that anthrax in sheep and cows was being caused by a specific strain of bacteria. His work became well known and was enthusiastically embraced by other scientists. Eventually he became a famous bacteriologist with his own well-equipped laboratory and went on to develop the standard still used to establish absolute proof of a causal relationship between a specific strain of pathogen and the disease ascribed to it.

Dr. Koch was also able to overcome one of the major stumbling blocks in the emerging filed of microbiology, which was the inability to grow a pure strain of bacteria under controlled laboratory conditions. He accidentally discovered that a sliced potato left on a table in his lab had grown a colony of a single strain of bacteria on its surface. He immediately recognized this as the missing step in the isolation of the uncontaminated strains of bacteria necessary to track a specific disease. A technician in Dr. Koch's lab whose last name was Petri was given the job of developing a reliable method to grow pure colonies of bacteria. He came up with the agar-agar concoction that used the Japanese agar-agar seaweed, gelatin and meat broth in a flat dish. This is still known as the Petri dish and still used in modern labs to grow out cultures.

The ability to isolate and grow pure strains of microorganism permitted Dr. Koch to establish that each infectious disease was caused a specific type of bacteria. The human family is much indebted to Dr. Koch for his meticulously constructed and performed experiments that were so vital to the development of medicine as solid science.

Then in **1881, Louis Pasteur**, who had continued his research on pathogenic organisms, identified that a particular bacteria -- hemolytic streptococcus pyogenes -- was the source of childbed fever, a potentially fatal disease that killed many new mothers and their babies. Hemolytic strep also caused other types of virulent wound infections and "hospital fever" -- a contagious, hospital acquired disease now recognized as iatrogenic (medical practitioner) or nosocomial (hospital-acquired). At a prestigious medical meeting in Paris, the French chemist and microbiologist Louis Pasteur drew a picture on a chalk board of what the streptococcus bacteria looked like under a microscope -- a line of organisms that looked like a miniscule string of tanker cars on a train track -- and said "Gentlemen, this is the cause of childbed fever". While Pasteur didn't mention it, streptococcus pyogenes is also responsible for necrotizing fasciitis, toxic shock

syndrome, scarlet fever, otitis media, meningitis, endocarditis and pneumonia. The human family continues to be indebted to this French vintner's son turned scientist extraordinaire.

The Eve of the 20th century -- Birth Pangs' of Medical Science

The scientific brilliance of Robert Hooke, van Leeuwenhoek, Pasteur, Robert Koch and Dr. Paul Ehrlich (more about him later on) was directly responsible for the modern science of bacteriology. As the 19th century faded into the 20th, the art of medicine was turned into a credible science, at least at the theoretical level. It would take decades more for these improvements to be put into practice in every small town and rural hospital. But in 1910, even the most sophisticated medical centers at Harvard or Johns Hopkins had no effective way to treat bacterial infections. Physicians could put a drop of fluid from the patient under a microscope and accurately identity the offending pathogen – Staphylococcus, Streptococcus pyogenes, E. coli, etc., but this did the patient no good. Doctors could only write the bacteria's unpronounceable Latin name on his chart and provide supportive care while the patient's immune system rose to the occasion and he got better or it didn't and he died.

While Pasteur's germ theory of disease and pasteurization were medical science's equivalent of a moon landing, they still fell short of the home run that was everyone hoping for. Without an effective way to cure bacterial infections, humanity was back to hope and hand wringing. In spite the heartfelt prayers of desperate families, tens of thousands of their loved one died anyway. With the exception of the placebo effect (a major blessing!), digoxin for heart disease, quinine for malaria, morphine for sever pain and aspirin for fever and body aches, there was no body of effective drug therapy. More to the point, there was no drug or substance of any kind that could selectively kill bacteria without also killing the patient. This gapping hole in the fabric of modern medicine continued to defy the best efforts of scientists for another 50 years.

Antibiotics – Jewel in the Crown of Modern Medicine, Home Run for Humanity

But Lady Luck smiled on us in the person of a talented and tireless German pathologist. Dr. Gerhard Domagk (pronounced 'doe-mock') devoted is professional life to searching for an antibacterial drug that could kill pathogens without damaging healthy human tissue. In 1932 Dr. Domagk and the two organic chemists that worked with him discovered the antibiotic properties of sulfanilamide. All three industrial scientists were employed by the pharmaceutical division of the Bayer Corporation in Germany's Rhineland. Scientists at Bayer had been actively searching for an antibacterial drug – what they referred to as 'chemotherapy' -- since 1909. Their eventual discovery of a laboratory chemical that was safe to ingest but could selectively kill harmful microorganisms was a hard won victory that followed years of searching for a substance referred to as an 'internal antiseptic'.

Dr. Domagk was hired by the Bayer Corporation in 1927 to work on this project but discovering such a drug was a much bigger problem than you'd think. Since the time of Pasteur and Lister, scientists had ways to kill bacteria in the laboratory and in life -- pasteurization, sterilization and antibacterial chemicals. Germicides such as chlorinated limewater (bleach) and products made from carbolic acid chemicals (early cousins of Lysol and Listerine) were used to clean instruments and disinfect physical surfaces. But the very thing that made these substances effective against germs could easily kill the person who ingested them.

Finding an internal antiseptic was very different than ones used to wash hands and disinfect sick rooms. Those chemicals could be tested in *vitro,* that is, put in a test tube with a mixture of bacteria and the newest chemical solution. If the germs died, a successful new antiseptic had been discovered. But anything that was going to be ingested or injected in the body had to be safe and at the same time, effective against pathogens. This meant that antibacterial drugs required in *vivo* testing – two groups of lab animals infected with a virulent pathogen, one test group that got the most recent antibacterial compound and a control group also infected with the same pathogens that didn't get any treatment.

Before their success with sulfanilamide in 1932, Domagk and his team had already tried over 3000 chemicals, alone and in various combinations, each tested in vitro and in vivo. Like any good scientific project, meticulous records were kept, listing the exact molecular composition, the types of bacteria used to infect the mice, and comparing outcomes between the treated and untreated group of mice. Thousands of pages of Dr Domagk's surviving lab notes provide the minute details, in his own neat penmanship, of each of these 3000 false starts and dead ends.

Domagk's breakthrough started when the researchers decided to combine a sulfa compound with the basic chemical they'd been investigating for the previous two years. As with everything they'd done before, their eventual success was preceded by hundreds of failed combinations. That first antibacterial drug, later to be named Prontosil, started out as Kl-730, which is to say it was preceded by 729 previous failed attempts. Each new variant was tested against a variety of bacterial infection in animals to see if it worked, a total of 730 tests before they hit the home run. This type of meticulous, repetitive research taxed the patience of the researchers and was an expensive proposition for Domagk's employers, who had no guarantee that any such drug would or even *could* be developed. If they failed, all would be for naught.

This family of antibacterial drugs owes its existence to research underwritten by a large German chemical company that originally made artificial fabric dyes out of coal tar. Bayer started out in the 1860s as a fabric dye company founded by Fredrick Bayer, the son of a silk weaver. By the early 1900s Bayer manufactured synthetic dyes, as well as other chemicals. In 1924 it merged with BASF (now a manufacturer of audio tapes) and another dye-making firm to become part of the conglomerate IG Farben.

Prontosil had the distinction of being one of the first synthetic drugs ever created by an industrial model of research, a method already used by organic chemists hired by corporations to discover new synthetics fabric dyes. The idea that drug research on an industrial scale could discover, develop and profitable market pharmaceuticals was itself an untested business model and a bold leap forward for humanity.

Another Unsung Hero in the Battle Against Bacteria

The connection between artificial dyes and bacterial infections in humans arose out of the observation by another unsung hero of medical science, **Dr Paul Ehrlich**. Dr Ehrlich was a German Jew born in the 1850s in Silesia, a part of Germany that now belongs to Poland. As a university student, he was fascinated by the news that infectious diseases were caused by tiny one-cell organisms invisible to the naked eye. He was eager to see these microscopic bacteria for himself. But at that time, much of the cellular world – blood, sperm, other biological tissue and

bacteria -- were virtually transparent under a microscope, since everything was equally colorless. This made it impossible to distinguish the discrete parts of a cell or determine how those parts functioned. However, when these tissues were exposed to the new synthetic dyes, their parts popped into view under the microscope. Properly stained with the right dye, minute details of nuclei of the cell, its walls and other inner structure became instantly apparent. The study of cellular biology owes its very existence to synthetic dyes made from coal tar derivatives.

As a med student, Dr. Ehrlich continued to be interested in bacteriology and the biological effects of synthetic dyes on tissue. While still an undergraduate, he invented new dyes specifically for staining bacteria and developed combinations of dyes to differentiate between the various different parts of the tissue being studied. Eventually he wrote his doctoral dissertation on the use of dyes to stain animal tissue and soon was the top expert in his field. During his research, he noticed that certain dyes had a preference for certain cells or biological structures, while adjacent tissue might not take up any of the color. Knowledge of the preferential nature of fabrics for particular dyes was something that cloth dyers took advantage of in their work all the time but no one could explain the chemistry behind this serendipitous reaction. Dr. Ehrlich devoted his life to discovering and using these chemical principles to develop therapeutic substances.

He was particularly impressed by his experience with nerve tissue and the methylene blue dye. This synthetic chemical turned the spidery network of nerves and the intricate mesh of fine synaptic filaments a bright indigo blue, while leaving all the tissue around these neural pathways pristinely unaffected. For the first time he was able to see something that was nearly as startling and important to humanity as van Leeuwenheok's 'wee beasties'. Dr Ehrlich recognized an important therapeutic potential in the molecular ability of dyes to make a distinction between different types of cells within organic tissue. What if he could find a chemical dye able to latch on to disease-causing organisms and kill or disable just the pathogenic bacteria, while leaving surrounding healthy tissue unaffected? At that time, no one knew of any chemical substance that could be injected into the body and then pick out and kill bacteria while leaving the tissues around it unharmed. However, that didn't mean that one couldn't be created and intended to try.

From Dr Ehrlich's observation that specific dyes stained some tissues preferentially, while having no effect on surrounding tissue, came the idea that certain molecules from chemical dyes might be able to directly target and kill pathogens while leaving the rest of the 'host' (i.e., the person) untouched. This how the idea of antibiotics as 'wonder drugs' or a 'magic bullet' got stared. A magic bullet is one that a police officer in pursuit of a killer can shoot into a crowd and be certain that his bullet will only hit the criminal, even though the bad guy is surrounded by a sea of innocent people.

All the pharmaceutical industry had to do now was: (a) find out if Dr Ehrlich's theory was valid and (b) find that elusive 'certain' dye. It was this search for the right dye that informed Dr. Domagk's life as an industrial scientist. He was hired to look for a supply of magic bullets made out of chemical dyes with antibiotic properties.

Red Azo Dyes and Azo-Grantricin -- a well-known sulfa drug for kidney infections

Building on the solid foundation laid by Dr Ehrlich's 19th century discoveries, Dr Domagk started working with red azo dyes early in 1931. Of all the chemical dyes available to them, the

azo family of dyes was chosen because they were less toxic that previous compounds tested. The azo dyes had a number of other advantages, including early indications that they could kill bacteria. The core of the dye molecule is like the frame of a bicycle, that is, two carbon rings linked by double-bonded nitrogen atoms. The double bond between the nitrogens is an azo link, which is what gives the family of dyes its name. This chemical structure allows a talented chemist to easily attach thousands of chemical variants to its core structure. The goal was to place the right molecule in the right position on the azo core to bring out its therapeutic properties – the ability to latch on to the bacteria and stop it in its tracks, while leaving the patient healthy or with only minor and temporary side effects.

The team tried one chemical after another by adding a single new molecule to the double bond on the azo core. The list of possibilities was long and they tried hundreds of unsuccessful combinations, including chlorine, iodine and mercury. On their 730th try, they attached a compound form of sulfur known as "sulfanilamide" and a home run hit straight out of the ballpark. Here was another serendipitous event, in that this sulfa compound was cheaply available in bulk quantities only because the patent had expired. Had this sulfa compound still been under patent, the world might well have been deprived of this dramatic discovery.

But Lady Luck continued to smile on Domagk's research. The results for KL-730 were extraordinary. The lab mice not only did not die of the virulent strep they had been infected with, but according to one of Domagk's top lab assistants, they were "jumping us and down very lively". The mice were in perfect health, with no indication of any adverse side effects. At first it seemed too good to be true. To be sure the science was sound, they had to repeat the test again and again to be absolutely certain that it wasn't an error or fluke of some sort. But the tests ran true and in three months, the Bayer Corporation was ready to apply for a patent for their new antibacterial drug.

On Christmas day 1932 the patent was filed in Berlin. It would take almost two years to be approved; KL-730 was being manufactured and distributed under the trade name Prontosil by 1935. Readers who are over fifty, especially those in the nursing or medical field, will remember (and perhaps have taken) an oral drug for urinary tract infections call Azo-Gantrisin. The big round pills were a bright brick red and when ingested, turned the patient's urine a bright orange. That was Dr. Domagk's red azo dye and sulfanilamide.

The discovery of a family of drugs that could actually *cure* fatal infections with few if any side affects was a gift to all humanity. It was better than space travel, landing on the moon and the Internet all rolled up together. The full story of sulfa drugs is fascinating – historical background, the people, the national politics, the process of discovery, the serendipitous events that made the research possible. Anyone interested in knowing more about this fascinating topic should read Thomas Hager's excellent book "The Demons Under the Microscope" (also available as an audio book through Audible.com).

It should be noted that scientific theories, no matter how elegant, rarely result in over night miracles, whether the new discovery is something simple like hand-washing or capital intensive like pharmaceutical drugs. Science has saved us again and again, but often it is the next generation who actually reaps its benefits and not us. For example, virulent drug-resistant bacteria are a fact of modern life. New and better drugs may well solve this perplexing problem (for example, DNA-

specific drugs) but 19,000 people died last year from the MRSA, which is just *one* of the superbugs lying in wait.

While awaiting the next magic bullet, there is one safe, simple, effective, and economical thing that everyone can do. Like pasteurization, it requires no special equipment. It is what I was taught by my nursing instructor on the first day of nursing school. Miss Etta's mantra and answer to everything was: "soap, running water, and friction". As a student nurse I was expected to make frequent and diligent use of soap, running water, and friction, which meant mechanical washing one's hands with soap for at least 15 seconds before rinsing. The best soap is cheap dishwashing liquid, as it has the viscosity of motor oil. This means it will take you at least 15 seconds to wash the stuff off your hands. Whatever kind of soap you use, count to 15 while you scrub, even if you have to silently recite a line of poetry, the verse of a favorite song, a prayer or a nursery rhyme -- whatever it takes to become mindful that the best defense against getting an infectious disease or giving one to someone else is *literally in our own hands*. The accident of discovery is worthless without the prepared mind.