

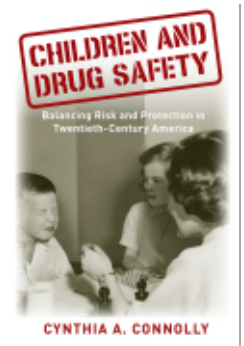


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Chapter 1: Drug Therapy: From “Baby Killers” to Baby Savers, 1906–1933

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1

Drug Therapy



From “Baby Killers” to Baby Savers, 1906–1933

In 2010 the United States Congress commissioned its advisory research body, the Institute of Medicine (IOM), to collaborate with the Food and Drug Administration (FDA) in studying the success of two 2002 initiatives. The Best Pharmaceuticals for Children Act (BPCA) offered a financial incentive for drug companies to study drugs already on the market. The Pediatric Research Equity Act (PREA) required them to provide dosing and drug safety data for all new children’s drugs, which they were already doing for adults.

The first meeting of the IOM committee, comprising internationally prominent pediatricians, researchers, pharmacologists, and ethicists, convened that December 17 with FDA representatives to review their task. Dianne Murphy, director of the FDA Office of Pediatric Therapeutics, began the meeting with a presentation of historical context, emphasizing the era beginning in the 1970s. Her first slide was startling. Although the FDA had been charged decades earlier with assuring that drugs for all Americans, including children, were safe and effective, the slide laid bare a starker reality. “Ignorance is poor public policy,” it read, “and yet it best describes what has been the status of our understanding of how best to use therapeutics [medication] in the pediatric population.”¹ Although Dr. Murphy also traced the BPCA’s and PREA’s successes in her presentation, she tempered any celebration with how much was as yet unfinished, lamenting, “[W]e don’t even know dosing for most [pediatric]

drugs.” Dr. Murphy was not exaggerating the problem. Just two years earlier, in 2008, another IOM workgroup expressed concerns that 50 to 75 percent of medications prescribed for children had not received the full panel of tests for safety and efficacy that the committee believed necessary to protect children.²

How could this situation have happened? Children’s and adults’ unique pharmacotherapeutic differences had been emphasized by the founder of modern pediatrics, Abraham Jacobi, in the Civil War era.³ How could an issue formally identified so long ago remain unsolved so many years later? How could this situation have occurred in a nation in which the FDA, clinicians, and industry had long recognized it as untenable? How especially could this have happened in a nation in which policymakers throughout the twentieth century repeatedly professed agreement that children’s health and welfare represented a high national priority?⁴

This book offers some answers to those questions. To do so, it provides a historical overview of drug therapeutics and policy for children in the United States with an emphasis on the period between the founding of the Food and Drug Administration (FDA) in 1906 and the late 1970s, when major stakeholders such as the FDA, the American Academy of Pediatrics (AAP), and leading pediatric pharmacologists, clinicians, and scientists believed—erroneously—that the tools were in place to solve the problems related to children and drug safety. The story is worth telling for multiple reasons. First, most histories of childhood during this era do not have health as their central focus, and they say little about pharmacotherapeutics. Second, studying children, drugs, and drug policy provides a unique lens through which to examine children’s health without focusing on a single disease, professional group, or care site such as home or hospital. That the story of children and drugs sits at the interface of the state, business, health care delivery, parenting, and childhood makes it especially intriguing.⁵

Third, the issue situates children at the center of drug regulation and drug development history during these years. There are well-regarded studies of therapeutics and drug policy in American society, yet children are mentioned only in passing, usually as having spurred new legislation or an investigation of some kind.⁶ Children’s recognized biological differences, the professional structures and specialties governing their care, and their purported protected place in American society as deserving of a healthy start in life have resulted in a different historical trajectory from adults with regard to drug development and policy. Studying this topic in its historical context is critically important because it illuminates the intended and unintended consequences of past policy decisions and offers a framework for considering what alternative directions might have produced different outcomes. The answers to these questions are important today because contemporary policies, and those contemplated

for the future, reflect an embedded historical context that suggests certain alternatives as more feasible or consequential than other choices.⁷

Fourth, the twentieth-century history of children and drugs is worth exploring because issues surrounding children's health and social welfare are of profound concern to Americans today, no matter where in the country they live and no matter what their political beliefs. The issues embedded in discussions of children and drugs involve considerations regarding society's obligations to children, evolving understandings of their place and protection in American society, and determinations of who should decide what interventions are in the best interest of the child. These topics are no less relevant today than they have been in the past.

One concern that animated child-focused drug policy reformers in all eras was how to make sure children benefited from new legislation. Some argued that children needed policies crafted just for them, while others maintained that they were better served by being included in broader regulatory actions aimed at all Americans. Similar debates continue today. For example, some maintain that the Children's Health Insurance Program (CHIP), a federal health insurance program enacted in 1996 for poor and low-income children, should be phased out in favor of enrolling these children in the 2010 Patient Protection and Affordable Care Act. Others believe strongly that children's health care funding requires a fundamentally different approach from that for adults, one grounded in a growth- and development-oriented model aimed at maximizing well-being, not just preventing and treating disease. As the 117th Congress prepares to dismantle the Affordable Care Act in 2017, these earlier debates are worth considering.⁸

This topic thus provides an especially rich template to study themes of children's risk, rights, and protection in the United States in the changing contexts of childhood, parenting, and health care delivery. The history of children and drug policy is a particularly valuable case study because the issues unique to children have never been fully addressed, although they have been repeatedly raised by parents, drug companies, scientists, pediatric clinicians, government, and politicians. In the early postwar era, for example, physicians interested in prescribing the newly available penicillin to gravely ill children faced the enduring challenge of how best to approximate children's doses, even as an explosion of postwar research amplified the understanding of the physiologic differences between children and adults and among youngsters of different ages. But in the early 1960s, at a historical moment in time when this new knowledge might have resulted in legislation, and at a high water moment of rhetoric regarding the child-centeredness of the United States, it did not. The adult patient remained the norm in terms of defining official dosage guidelines, formulation, and administration of medications. Why and how did this happen?

History is the only discipline that can capture the complexity of this paradox. A historical lens highlights the ways in which evolving policies, scientific knowledge, and clinical practice solve some problems while creating new ones. It reveals the variables beyond science that shape policy as well as the unexpected consequences of well-intended laws. It also shows how notions of parenting, children, and their place in American society are enmeshed with the regulatory state, science, commerce, parenting, and clinical practice in often surprising ways.

Fifth, the history of pediatric drug development during these years provides a nuanced opportunity to study childhood and children's voices, opening a window into opaque corners of the past. Since the advent of social history in the 1960s and 1970s, capturing the agency of individuals and groups traditionally invisible in historical narratives has received new attention. Children are one such historically underrepresented group. Addressing questions regarding children's influence on events in America is notoriously difficult because they leave few personally generated written or oral records. They have often been viewed as lacking a perspective of their own because, medically and legally, parents or other adults make decisions on their behalf.⁹ But this story shows how adults spent much time and energy thinking about how to appeal to children's palate and preferences; thus, children inarguably shaped the postwar drug economy, at least indirectly.

The final reason the history of children and drugs is worth telling is because it is so poorly remembered by scientists, nurses, doctors, pharmacists, parents, and others on today's front lines of pediatric health care, even though it created the context in which they practice. In order to fulfill their obligation to children and families, clinicians need to better appreciate the individuals and events that preceded their era. State-of-the-science studies on pediatric experimentation as well as drug development tend to relegate the pre-1970s era to a few pages or a decontextualized introductory chapter or two. As such, they cannot provide an understanding of the major role earlier events played in constructing the template for late twentieth- and early twenty-first-century pediatric pharmacotherapeutic policy and practice. It is for that reason that this book emphasizes the time period before the 1980s.¹⁰

Worse yet, the history has sometimes been incorrectly represented. In 2010, for example, the best known and most prestigious pharmacology textbook in the United States, *Goodman & Gilman's Pharmacological Basis of Therapeutics*, updated its section on pediatric pharmacotherapy. The authors who drafted the section briefly traced a few pediatric drug-related disasters such as thalidomide. Before moving on to discuss recent regulatory changes, they stated, "Before the 1970s, children and pregnant women were routinely excluded from drug studies."¹¹

This statement was incorrect. In researching this book, I learned that at some historical moments it had been considered in children's best interest for them to participate in drug trials, sometimes with their parents' knowledge, sometimes without it. At different junctures in the past, children were barred from such research in an effort to protect them. In other words, the ethics regarding how best to evaluate drugs in the pediatric population has been dynamic and contingent. Balancing the potential benefits of more pediatric data against the need to expose children to as little risk as possible remains a vexing problem, as do questions about who makes those determinations and how they do so.¹²

Our contemporary sound-bite culture favors descriptions of greedy drug companies or bumbling federal regulators. One of the most fascinating parts of this story, to me, is how far from the truth those labels are. Organizations such as the AAP and the American Pharmaceutical Association (APhA), along with the pharmaceutical industry, the FDA, Congress, and individual scientists, pharmacologists, pharmacists, and pediatricians devoted considerable time, attention, and resources to issues surrounding children and drugs over the years. Almost all were well intentioned, but the same or similar problems arose again and again. As I drew on surviving primary sources, events, and people to weave the larger social, cultural, political, and economic context over time, I have been able to examine the successes, missed opportunities, and consequences—intended and unintended—of decisions made in the past with regard to American children, thus providing guideposts for better decision making in the future.

This book problematizes the issues of children and drug development and safety for both minor and serious conditions. My study does not include a lengthy explication of vaccines, vitamins, or drug development and testing in pregnant women because their historical trajectories differ from those of pediatric medications. Where there is overlap, however, I do address topics related to these concerns.¹³ Drugs for children with cancer receive mention where appropriate, but they are an extremely small part of this story because, as I explain, the funding structures governing cancer therapeutics differed from other drugs with much more widespread use in children, such as antibiotics.¹⁴

My goal is to generate a meaningful synthesis of a broad topic, requiring compromise and omissions. As with all historical research, the data set is incomplete. I have chosen representative events and seminal moments in an effort to provide fidelity to the history and I focus on the United States only. That is not to say that many of the issues raised in this book were not occurring elsewhere. They were, although the narrative and stakeholders differ from country to country; forms of government, regulatory structures, clinical practice, and cultural issues surrounding children, parents, and experimentation

vary widely. A comparative history of pediatric drug development and pharmacotherapeutics in industrialized countries is very much needed.¹⁵

Chapter Outlines

The book is organized both chronologically and thematically. Chapter 1 provides an introduction to the book, presents research questions and themes, and details relevant historical context. It traces late nineteenth- and early twentieth-century baby- and child-saving, using concerns about widespread use of opium-laced “soothing syrups” in infants as a case study. Media campaigns referred to these agents as “baby killers” and helped create the FDA in 1906, ushering in the modern era of drug regulation. Soothing syrups also provided the major justification for the subsequent 1914 Harrison Narcotic Act. This introductory chapter also provides historical background, sketching the rise of experimental science and pharmacology and the evolution of pediatrics as a medical and nursing specialty. It concludes with an exploration of the shifting context of American childhood and child health and social welfare policy debates from the early twentieth century until the early 1930s.

Chapter 2 explores attempts in the 1930s to improve pediatric drug knowledge amid escalating tensions between the American Medical Association and the American Academy of Pediatrics regarding which organization should speak for children on this topic. It charts the rise of the modern era of therapeutic medicinal chemistry in the United States with the advent of the sulfonamides. These new agents profoundly changed the treatment of common, often fatal pediatric conditions such as meningitis and pneumonia. Despite the new drugs’ potential, however, innovation sometimes brought risk. In 1937, the product Elixir Sulfanilamide, which contained the sweet-tasting but poisonous diethylene glycol, resulted in dozens of deaths. Because many of those who died from the tragedy were youngsters, child protection rhetoric helped forge a new law, the 1938 Federal Food, Drug, and Cosmetic Act. This statute stipulated that manufacturers had to provide the FDA with data about drug safety before marketing or selling their products. This chapter also examines sulfa drugs and penicillin in actual use for children during the 1930s and 1940s. This close analysis not only reveals the evolving transformations in medical and nursing practice, hospitals, parental expectations, and the childhood illness experience brought about by these drugs; it also shows how and why the template for pediatric drug discovery, testing, dosing, and monitoring of adverse reactions evolved the way it did.

Chapter 3 traces the way antibiotics dramatically reduced pediatric morbidity and mortality in the early Cold War era, a time rife with discourse regarding American commitment to child well-being. At the same time, the absence of formal rules for informed consent engendered a “trial and error” approach

to pediatric drug research, just as with other medical experimentation during this era. The ongoing debates about how to systematize pediatric drug knowledge and what group should take the lead stalemated any potential for an easy solution. This chapter also explores antibiotics' unintended consequences. For example, as media coverage announced penicillin's successes, parents began to demand antibiotics for their children, bringing unprecedented challenges to physician authority. The introduction of broad-spectrum antibiotics demonstrated how important the drug industry believed the pediatric market was to a full product line in a competitive marketplace. Yet the discussion of the two pediatric chloramphenicol catastrophes of the 1950s reveals the inability to protect children from risks of some antibiotics, the most widely used drugs for children in this era.

Chapter 4 begins in the early 1960s, chronicling how reformers used the thalidomide disaster, the sleeping pill linked to birth defects, to mobilize support for the bill that became the landmark 1962 Kefauver-Harris Amendments to the Federal Food, Drug, and Cosmetic Act. This legislation codified evaluation standards for measuring drug efficacy and mandated new rules for research ethics. The statute arrived at the same time that rhetoric about the importance of the child to American society soared. Within the year, however, fears that the new law was not fulfilling its safety promise to children led pediatrician and pharmacologist Harry C. Shirkey to coin an evocative and Dickensian term, calling children "therapeutic orphans." The FDA could approve a new drug application submitted without pediatric data, even if there was reasonable expectation that the drug would be prescribed to children. Pediatricians and others treating children were then required to modify the adult dosage for children, using whatever method they chose.

Shirkey argued that the lack of formal consideration of children's needs disenfranchised them. Other leading pediatric pharmacologists and physicians agreed with Shirkey, as did the AAP, FDA staffers, and some drug company representatives. A number of national conferences and meetings brought stakeholders together in an attempt to resolve the pediatric drug discovery and testing issues. The 1970s ended on a high note, with optimism that everything was in place to generate better pediatric drug knowledge and safety going forward.

Chapters 2, 3, and 4 focus almost exclusively on prescription drugs, especially antibiotics, the most widely used prescription drugs in children during this era. But analysis of these drugs does not tell the full pediatric story. Chapter 5 moves from a largely chronological order to examine the over-the-counter pediatric drug market, using as a case study the postwar creation, distribution, and marketing of an old chemical agent, aspirin (acetylsalicylic acid), in a small dose flavored to appeal to a child's palate. Advertisers of "candy aspirin," as it was often called in the 1950s and 1960s, strove to convince

mothers (any emphasis on fathers is notably absent) that parental competence was linked to the purchase of a particular aspirin brand. Tactics were often grounded in racial, class, or gender stereotypes. But the popularity of candy aspirin quickly resulted in a dramatic increase in the rate of children's aspirin poisoning. One perceived solution, child safety caps, fomented much contentious debate, resulting in decades of stalemate. The 1966 Child Protection Act Hearings, which debated safety cap legislation, weighed the benefits to youngsters' health from such a mandate against the aspirin industry's resistance to greater governmental intrusion into private enterprise. This case study reveals what can happen when recommendations for reducing risks to children's health challenge corporations' economic well-being.

Chapter 6 begins in the 1930s with the discovery that amphetamines calmed children with behavior disorders, rather than stimulating them the way the drugs did in adults. It interweaves the history of pediatric psychopharmacology into that of child psychiatry in the United States in the years between the late 1930s and 1970s. The chapter also analyzes the similarities and differences in drug development, testing, and use when the agents in question were to be used for a child considered to be suffering from a "mental" disease and not a "physical" one. Using the research of Leon Eisenberg and Lauretta Bender as case studies, it also traces the different ways prominent child psychiatrists perceived the role of drugs in diagnosing and treating the behaviorally disordered child. Finally, given the lack of diagnostic specificity in child psychiatry for most of this time, pediatric psychopharmacology also provides a lens through which to study cultural anxieties regarding the "normal" American child and the ways the use of mood altering agents in children encoded prevailing notions of race, gender, social class, and ethnicity.

Chapter 7 begins in the late 1970s, when the FDA, AAP, and other stakeholders believed that technical, scientific, and ethical processes were in place to improve pediatric drug safety. But their optimism quickly faded as drug companies continued to submit new drug applications to the FDA without pediatric data and the agency approved them. At the same time, the political context shifted as a result of the antiregulatory philosophies of the newly elected President Ronald Reagan. But in what came as a surprise to many, President Reagan did sign the 1983 Orphan Drug Act (ODA). The ODA offered companies who manufactured and sold drugs for conditions with relatively few sufferers lucrative patent extensions. The law benefited children disproportionately because so many rare diseases afflict youngsters. Interestingly, while the AAP and FDA played important roles in helping enact the ODA, it was parental activism, particularly that of one mother, Abbey S. Meyers, that made the difference.

Chapter 7 also summarizes the changing context of American childhood in the 1980s and 1990s, when the imperative to address the problems of children

and drugs began to accelerate. In an era in which parents were becoming more fearful regarding child safety, the rising incidence of chronic illness in children and the growing use of behavioral drugs meant that more children received drugs on a regular basis than in the past, a trend that began to receive significant attention in the 1990s. This phenomenon coincided with the acquired immunodeficiency syndrome (AIDS) epidemic. Activists successfully strove to hasten the drug approval process and increase adults' access to experimental therapies. Whether this course of action was or was not in the best interests of children with AIDS weighed heavily on families, clinicians, activists, and the FDA. Also during this decade, the market supremacy afforded to children's aspirin for fever and pain was challenged again. But this time it was not in the context of concerns about aspirin poisoning. Rather, by the early 1980s, aspirin became linked to a terrifying condition, Reye's syndrome. The aspirin industry responded by employing all the tactics it had been drawing on since the early 1950s.

Food and Drug Administration rules crafted in the 1990s created what became known as the "Pediatric Rule," mandating manufacturers to conduct studies and provide adequate labeling for use of the products in children. When the FDA's authority to write such a guideline was successfully challenged in federal court, stakeholders, among them the AAP and FDA, pressured Congress to write new legislation. This effort culminated in the 2002 Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA). In 2012, President Barack Obama signed legislation making these laws permanent. Chapter 7 closes with a description of these laws, their impact on pediatric drug safety and knowledge today, and an analysis of what we can learn from this story.

Baby Killers, Child Saving, and Regulation

The August 27, 1900, edition of the *Pittsburgh Press* carried an advertisement for a new medicine, Dr. James' Soothing Syrup Cordial. The language was designed to capture parents' attention in an era of expanding literacy. "Little Folks Love it," the promotion proclaimed. Touted as a "cure" for cholera infantum, an antiquated term for infectious diarrhea, the elixir, promised the ad, also "relieves colic, corrects sour stomach, [and] eases the pain of teething," common ailments suffered by almost every baby at one time or another. For the parent who worried about safety, the ad reassured in big letters:

Clear as crystal,
 No laudanum.
 Nothing that could
 Possibly harm.

Just a pure wholesome
Cordial, that soothes the
Little nerves and gives them natural rest.¹⁶

Dr. James' Soothing Syrup may not have included laudanum, an opiod compound such as morphine or codeine, sometimes blended with alcohol—but it did contain heroin. Synthesized in 1897 by a scientist from the German company Bayer, heroin attracted great attention in both Europe and the United States. Within a year Bayer marketed it as a more effective cough suppressant than codeine. Another benefit, the company claimed, was that heroin was not habit-forming.¹⁷

Today we know that heroin is an addictive and dangerous substance, and, as such, Dr. James' Soothing Syrup caused the same high rates of infant death as the other opiate-laced soothing syrups did. Like Dr. James's, these sweetened narcotic products were advertised as treatments for a number of minor conditions. Parents could purchase soothing syrups at local stores or from trained apothecaries, who began calling themselves professional pharmacists in the latter part of the nineteenth century. They could even order them through mail-order services.¹⁸ The soothing syrups were so widely available and penetrated culture so thoroughly that, in 1879, composer Edward Elgar named a composition for the well-known Mrs. Winslow's Soothing Syrup.¹⁹



FIGURE 1 Advertisement for Mrs. Winslow's Soothing Syrup for Children, 1885.
(Credit: Courtesy of the National Library of Medicine.)

Some reformers argued against direct selling of soothing syrups to parents, but there was no consensus on the issue. The controversy over how best to balance ideals of free enterprise with consumer protection resulted in a rift in the nineteenth-century feminist movement. In their women's rights periodical, *The Revolution*, editors Elizabeth Cady Stanton and Susan B. Anthony, warned women about patent medications, especially those dangerous to children, such as soothing syrups. Cady Stanton and Anthony could not keep *The Revolution* profitable, however, and Laura Curtis Bullard, whose large family fortune relied on the invention and successful marketing of Mrs. Winslow's Soothing Syrup, purchased the journal, and the product subsequently received aggressive promotion in its pages.²⁰

Physicians also worried about the indiscriminate sale of narcotics, although they, too, often recommended them liberally for young children. But just as with all drugs, they worried about how to titrate doses for children of different ages and sizes. One doctor, Abraham Jacobi, argued that nowhere were the differences between children and adults more profound than when it came to considerations of drug therapy. As early as 1861, he maintained that "for the purpose of attending the diseases of children, it is not sufficient to diminish and sweeten the doses administered to adults."²¹ Although he could not articulate quite how, Jacobi believed that children's needs were more complicated than the age- or proportion-based dosing schemes such as Young's Rule, which dated to at least the early nineteenth century.²² Pioneers in the evolving field of experimental pharmacology also struggled to understand what children's small size relative to adults might mean in terms of their ability to process or metabolize drugs.²³

By the 1870s and 1880s a small number of children's specialists, led by Jacobi, institutionalized pediatrics as a specialty within medicine. They founded a pediatric section within the nation's leading physicians' organization, the American Medical Association (AMA). Some practitioners from the newly inaugurated nurse training schools also focused their efforts around the needs of sick children. Like Jacobi, nurses and doctors who specialized in pediatrics believed that children needed their own health care providers because youngsters were wholly different in terms of disease presentation and course, rather than just "miniature men and women."²⁴

Soothing syrups were just one of the numerous health threats to children in the early twentieth century. An industrializing economy led many rural Americans to relocate to overcrowded and polluted cities to work, sometimes alongside their children, in factories or textile mills. Many of them, as well as a large influx of new immigrants, resided in tenements on the narrow, dirty streets of cities such as New York, Philadelphia, and Chicago, where diseases spread quickly, especially among the youngest, most indigent children. The growing trend to track vital statistics in the latter part of the nineteenth

century documented the frighteningly high infant mortality rate, making the problem increasingly visible to scientists and public health reformers.²⁵

One hope to reduce morbidity and mortality from infectious disease lay in preventive measures such as vaccines. But after a number of pediatric deaths from smallpox vaccine and diphtheria antitoxin (an antibody treatment aimed at neutralizing the bacteria), public health reformers insisted that biological agents be manufactured according to set standards to protect the public. They persuaded Congress to pass the Biologics Control Act of 1902. Under this law, the Hygienic Laboratory of the Public Health Service oversaw the manufacture and distribution of biological agents such as vaccines.²⁶

Advocates of the Biologics Control Act effectively used child protection to build support for the law, and those who sought new drug and food safety laws took notice. Over the course of the next few years, muckraking journalist Samuel Adams Hopkins and the women's magazine *Ladies' Home Journal* railed against the risks to infants from soothing syrups. Hopkins's polemical 1905 *Collier's* magazine articles, subsequently published in book form as *The Great American Fraud*, strengthened public support for new laws to protect consumers from unsafe drugs and adulterated foods. Within a year of Hopkins's blistering exposé of the patent drug industry, Congress passed the Federal Food and Drugs Act, which in 1906 created the modern FDA.²⁷ The AMA, too, framed its support for the 1906 law in terms of child advocacy, at least in part. The organization's periodical, the *Journal of the American Medical Association (JAMA)*, published letters from physicians who described infant deaths from soothing syrups. In the wake of the Federal Food and Drugs Act's success, the AMA became a major broker in American pharmaceutical policy. Its Council on Pharmacy and Chemistry, comprising expert physicians in pharmacology and therapeutics, advised the FDA and served as physicians' primary drug resource through its regular *JAMA* updates.²⁸

The new law, however, did not actively ban soothing syrups, nor did it require premarket approval from the FDA before a medicine could be sold; it merely stipulated that drugs needed to be labeled correctly and meet specified standards. If they did not, the FDA considered them misbranded. For example, opium-containing products had to be manufactured in compliance with the standards of strength and purity set by the United States Pharmacopeia (USP) and the National Formulary (NF). Any variation from the USP-NF-approved formulation needed to be noted on the label. Therefore, opium needed to be correctly labeled but was not prohibited.²⁹

Although members of the public could still legally purchase opium for themselves or their children whenever they chose, the 1906 Federal Food and Drugs Act also stipulated that manufacturers could not make false or misleading statements. In other words, in addition to quantifying the amount of heroin in Dr. James' Soothing Syrup, Bayer could no longer maintain on the

label that it contained “Nothing that could possibly harm,” since physicians and public health reformers had widely documented the risks of opiate overdose in infants and young children. The FDA could take legal action against any company continuing to advertise the safety of opium products for children. But building a case against an individual company and bringing that case to court took time and resources. Some companies simply flouted the law and, in the short term, opium-laced products marketed for children remained readily available.³⁰

The attempt to protect children from soothing syrups and other dangerous patent medications between the 1890s and World War I, a period of structural change and bureaucratic expansion known today as the Progressive era, was one component of a much larger “baby-saving” or “child-saving” movement. Child-saving causes spanned a range of issues, from infant mortality prevention to mandatory schooling, juvenile justice reform, and a ban on child labor. The movement’s early twentieth century high water moment arrived in 1909, when, after an intensive lobbying effort by professional and lay child savers, President Theodore Roosevelt sponsored a White House Conference that brought together hundreds of specialists across a number of disciplines to study the needs of orphans and children whose parents were too poor to keep them at home.³¹

Capitalizing on momentum from the 1909 conference and societal enthusiasm for child saving, public health reformers in a number of cities began educational campaigns that attacked soothing syrups as “baby killers.” Hoping to heighten parents’ awareness of their dangers and to counter manufacturers’ aggressive advertising, they posted placards that implored, “Don’t make a dope fiend of your baby.” The next year, prominent doctors and nurses gathering in Baltimore to discuss ways of reducing infant mortality in the United States made a point of denouncing soothing syrups.³² The FDA also worked to educate the public about soothing syrups. In addition to publishing articles in *Good Housekeeping* and other women’s magazines, FDA staff used the mostly agricultural periodical, the *Farmers’ Bulletin*, to issue one of its earliest public warnings about addictive medications, noting that “soothing sirups [*sic*], naturally occupy the first place” on any warning list of habit-forming drugs.³³

The ongoing activism from initiatives such as these helped spur another law, the Harrison Narcotics Act of 1914, which codified the amount of opium a proprietary drug could contain. It further mandated that the public could obtain legal narcotics only through physician sanction, that is, a prescription. The newly created Federal Trade Commission would file suit in the event of violations.³⁴ Despite these laws, educational efforts, and health care provider activism, at least some mothers remained confused by proprietary drug manufacturers’ advertising tactics. They wrote letters to a new federal agency, the Children’s Bureau, revealing their confusion regarding claims made on behalf of medications such as soothing syrups.³⁵ The bureau joined the fight against

soothing syrups, adding information about their dangers in educational pamphlets written by its nurses and doctors.³⁶

At the same time that reformers worked to protect children from soothing syrups and other dangerous drugs, new understandings of infant and child physiology and biochemistry began to improve the fluid and electrolyte management of acutely ill infants and young children. Potentially life-threatening clinical problems such as dehydration, for example, could now be more effectively managed, even in newborns. Outcomes for acutely ill, hospitalized children began to improve by the 1910s and 1920s. Better treatments helped children's hospitals transition from facilities aimed at providing moral and environmental care to indigent children who were often well but had no place to live to institutions that increasingly emphasized technologically driven care to acutely ill youngsters from all social classes.³⁷

The 1921 Sheppard-Towner Maternity and Infancy Act created a federal role in maternal, infant, and child health in the United States. The federal funds distributed to states through Sheppard-Towner enabled communities to screen thousands of children for health defects and deliver well-child care, considered by pediatricians, public health, and school nurses essential to their well-being.³⁸ But the Sheppard-Towner Act fomented controversy within the AMA when, in the late 1920s, the law needed reauthorization. The pediatric section strongly supported the initiative, but the organization's policymaking House of Delegates did not. The AMA broader membership worried that the law, with its public funding for health promotion and disease prevention, represented an "imported, socialistic scheme unsuited to our form of government" and, as such, was anathema to the AMA's preferred private practice, fee-for-service health care delivery model.³⁹ The disagreement resulted in two AMA resolutions regarding the reauthorization, the pediatric section in favor and the House of Delegates in opposition. The AMA leadership ended the impasse by reminding the pediatricians that they could not issue independent policy endorsements. Partly as a result of the AMA's intense lobbying effort, Congress allowed Sheppard-Towner funding to expire in the late 1920s. In response, in 1930, a small group of outraged pediatricians broke away to form a new group, the American Academy of Pediatrics. Its central mission included political engagement on children's behalf.⁴⁰

While there was less controversy among physicians about the need to remove unsafe drugs from the market, most American courts through the 1920s set a high bar to prove fraudulent claims of drug safety. This hampered efforts to remove potentially dangerous products from the market and led some to believe more stringent drug laws were needed.⁴¹ One significant expansion of FDA authority came in 1927, when Congress enacted the Federal Caustic Poison Act. Focused largely on protecting children, the law

mandated warning labels for potentially dangerous household products such as cleaning agents.⁴²

The onset of the Great Depression in 1929 dampened enthusiasm for new drug legislation. President Herbert Hoover's administration, however, forged ahead with a White House–sponsored children's conference scheduled before the economic downturn. Whereas the 1909 meeting had largely addressed issues surrounding indigent and orphaned children, the 1930 White House Conference on Child Health and Protection focused on the needs of all American children. Its most visible outcome was the nineteen-point manifesto of children's rights, the Children's Charter. But delegates to the conference carefully avoided taking a position on whether the obligation of fulfilling the charter, which focused heavily on health, fell to parents, the government, voluntary organizations, or some combination of the three. The tangible results of the 1930 conference were nominal and overshadowed by the deepening financial crisis.⁴³ But the combination of the 1930 White House Conference and the founding of the AAP did make an impact on a group of pediatricians in Philadelphia. They decided the time was right to amplify their long-standing baby- and child-saving efforts by focusing on an issue they monitored with mounting alarm—the lack of pediatric dosing and drug safety information.⁴⁴