What little historical scholarship exists on children and mood-altering drugs focuses largely on the rise in the stimulants for what has been variously known since the early twentieth century as minimal brain dysfunction, hyperkinetic reaction of childhood, and attention deficit hyperactivity disorder. While these drugs play an important role in the history of pediatric psychopharmacology, they are only one part of a broader story. This chapter interweaves the history of other psychoactive agents into that of stimulants. It analyzes the ways in which psychotropic drug-related issues were similar to—and different from—those for other prescription drugs for the child patient. The history of pediatric psychopharmacology also provides a unique lens through which to consider temporally derived political and social definitions of “normal” and “abnormal” children, parenting, and family life and the role drugs have played in those determinations.

Like all pharmacotherapeutic agents, the development, testing, and use of mood-altering drugs in children is at once a story of commerce, research, technological and scientific change, politics, and evolving parental and societal expectations regarding the medical encounter and American childhood. Unlike other medications such as antibiotics, however, psychotropic drugs treated more contested, and relative to infectious diseases, poorly defined conditions. By the 1930s when the sulfonamides came to the market, for example, experts agreed on the major diagnostic criteria for bacterial pneumonia and
its clinical presentation in an infant or child. Differentiating child mental illness from neurological problems such as epilepsy or developmental disorders remained less clear until much later.

In some ways, the story of pediatric mood altering drugs is a very old one. Arguably, Mrs. Winslow’s Soothing Syrup, which arrived on the American market in the 1830s, represented one of the nation’s earliest domestic blockbuster drugs. Heavily advertised for its success at quieting the crying, restless infant or young child, the narcotic-laced product and its many competitors generated millions of dollars in profits. But there is only a superficial similarity between soothing syrups and their mid-twentieth-century successors. Soothing syrups were not targeted at children believed to be suffering from behavioral disorders.2

Like elite pediatricians in the 1930s, those who specialized in the emerging field of child psychiatry largely eschewed pharmacological therapy. Leo Kanner, for example, who originated the nation’s first child psychiatry department in 1930 at the Johns Hopkins Hospital’s Harriet Lane Home, did not sanction their use. When, in 1935, he published the first child psychiatry textbook, he advised against the use of drugs. But his reason differed from that of J. P. Crozer Griffith and A. Graeme Mitchell, who argued in their 1933 text The Diseases of Infants and Children that few drugs benefited youngsters. Rather, Kanner reasoned that children’s behavior often reflected parental “carelessness” or “overindulgence.”3

Child and adult psychiatry evolved differently from one another. Although certainly influenced by Freudian psychoanalysis, child psychiatry was solidly rooted in the early twentieth-century child-saving and juvenile justice movements. The field also reflected the thinking of pioneering developmental psychologists such as Arnold Gesell, who argued that universal and timed patterns defined normative emotional, social, and cognitive maturation in children. Interest in child mental health by the Children’s Bureau as well as private foundations such as Rockefeller, Grant, and the Commonwealth Fund in the interwar period provided resources to unify these ideological threads. The “child guidance clinics” that emerged emphasized a team-based approach that brought together nurses, social workers, psychologists, and psychiatrists in ways not common in general pediatrics.4 Nonetheless, child psychiatry was heavily influenced by pediatrics’ growth as a medical specialty. Pediatricians’ emphasis on universal well child care did not just provide a referral base for psychiatrists, it offered a roadmap for how the specialty could achieve legitimacy. Just as pediatricians could make use of height and weight tables to chart children’s physical development, Gesell’s research yielded a parallel set of tools believed to differentiate the child maturing normally from one harboring psychopathology.5

The modern history of pediatric psychopharmacology begins in the 1930s. It was then that psychiatrist Charles Bradley alerted his colleagues to a finding
that surprised him. Smith Kline & French’s amphetamine, benzedrine sulfate, calmed many of his young patients at the Emma Pendleton Bradley Home in Providence, Rhode Island. Children Bradley diagnosed with “neurological and behavioral disorders” improved after receiving amphetamines for headaches associated with one of their medical procedures.6 The “spectacular” change he documented in many of the children was “paradoxical” because, rather than “stimulating” them as the drug did adults, it had the opposite effect.7 They appeared to learn better after receiving amphetamines, behavior that disappeared as soon as Bradley withdrew the drug.8

Another foundational event in the history of pediatric psychopharmacology included the 1946 National Mental Health Act. The growing federal interest in hospital funding and medical research extended to mental health. This important legislation led to the creation of the National Institute of Mental Health (NIMH) and the first large-scale public investments in training and research for mental health-related issues.9 Organizers for the 1950 White House Conference on Children capitalized on the founding of NIMH and its initiatives by setting as the conference’s main theme the mental and emotional well-being of American children.10 While few in number in the early 1950s, child psychiatrists argued that pediatricians’ expertise did not extend to managing the mentally ill child or one with severe behavioral problems. As such, a small group of them founded the American Academy of Child Psychiatry in 1953. But these early leaders also recognized that they faced a challenge that their pediatrician and general practitioner peers who treated children did not. Kanner’s descriptions of “autistic differences of affective contact” and its symptomatology, for example, lacked the diagnostic specificity of cancer, pneumonia, or other diseases considered physical in nature.11 Moreover, few psychiatric conditions included age as a relevant variable in assessment or diagnostic criteria, so there was less evidence to justify the need for a pediatric focused specialty within psychiatry. The new resource for classifying and defining psychiatric conditions published in 1952, *Diagnostic and Statistical Manual of Mental Disorders*, for example, made no distinction between children and adults.12

**The Child Patient and the Psychopharmacology Revolution**

One of Kanner’s former colleagues, Lauretta Bender, grew fascinated by childhood schizophrenia which she characterized as a maturational disorder of the central nervous system. By the time Bender published her first description of the condition in 1942, she was already famous for her Bender-Gestalt Visual Motor test, a measure of neurological and cognitive damage. As lead psychiatrist at New York City’s large public Bellevue Hospital Child
Psychiatric Division, Bender oversaw both its outpatient clinics as well as its inpatient unit. Bender was also influenced by her mentor at Johns Hopkins, psychiatrist Adolf Meyer, especially his conviction that biology played an important role in psychopathology. Like Bradley, Bender too experimented with stimulants in children. As she grew more interested in psychopharmacology, Bender hypothesized that psychoactive medications served as both a diagnostic and a therapeutic tool in children. She believed that a child’s response to a drug revealed important clues about the disordered developing brain. This thinking bound her less to child psychiatry’s child-saving roots and more to Meyer’s psychobiology framework.

Bender must have realized another benefit to psychopharmacology. While she did not state this point explicitly, it was clear by the ways in which she described drugs’ importance that she also appreciated that they differentiated her practice from that of psychologists. Psychopharmacology validated child psychiatrists’ claim that they possessed a unique body of knowledge because prescription medications fell solely in physicians’ domain. While the clinicians on her unit included nurses, social workers, teachers, and psychologists just as in the child guidance model, Bender’s enthusiasm for drugs meant that the Bellevue unit operated firmly within a biomedical model that placed physicians at the top of the hierarchy. As tranquilizers started pouring onto the market in the 1950s, Bender and her trainees prescribed them to their children. Her unit soon developed a reputation as the nation’s premier site for pediatric psychopharmacology research and therapy.

The inpatient Bellevue Child Psychiatric Unit’s fifty beds housed children under the age of twelve years. Bender estimated that she had enrolled 350 children into her drug studies by the middle of the 1950s. They arrived at Bellevue through different pathways and with a variety of symptoms, but most were poor. In 1950, for example, 24 percent of children came through social service agencies, 23 percent came from the juvenile justice system, and 17 percent had been brought to Bender directly by their parents. The rest were referred by schools or transferred from hospitals or other institutions. Like other 1950s psychiatrists, Bender was struck by the transformation wrought by the new tranquilizer Thorazine (chlorpromazine). The drug’s manufacturer, Smith, Kline, & French, stressed its potential uses for troubled children and juvenile delinquents. All Bender’s patients carried one of these broad labels, and she started using Thorazine as soon as it became available in 1954. Just as it did for adults, the drug transformed the care of the most behaviorally challenging children at Bellevue. Until Thorazine, Bender later recalled, children’s “severe tension states might become so uncontrolled that they would be put in the adult ward temporarily to prevent danger to themselves or to others.”
But after receiving Thorazine, their behavior could be managed on the pediatric unit.

In 1955 Bender, along with Alfred M. Freedman and Abraham S. Effron, colleagues at New York University’s medical school, where she held a faculty appointment, published the first pediatric psychopharmacology review article in the United States. The physicians reported their three-year study in which they had randomly assigned boys between the ages of seven and twelve years admitted to Bellevue to receive one of six new psychiatric drugs. Another group of boys received only a placebo. One of the major benefits of an inpatient unit was that staff could completely control children’s environment. Bellevue’s nurses and teachers spent months monitoring children for side effects and drugs’ impact on symptoms such as anxiety, agitation, or attention. Freedman, Effron, and Bender concluded that all the drugs influenced behavior on the 195 youngsters in some way, leading them to conclude excitedly that “Pharmacological agents have an indisputable role in the management of children in a psychiatric hospital setting.” They did not tease out the impact of particular medications on specific disorders. Nonetheless, they concluded that psychiatry was about to benefit from pharmacology in the same way as had other areas of medicine, noting enthusiastically: “in the last two decades advances in pharmacological therapy in medicine have been noteworthy and, in certain instances, spectacular. Antibiotics, sulfonamides . . . have wrought impressive changes in clinical practice. . . . Yet the application of this new information has had, until very recently, very little utilization in the field of psychiatry.”

But Bender faced challenges her general pediatrics colleagues did not in terms of her drug studies. First, unlike many of her colleagues, she lacked ready access to a comparison group of healthy children. Second, a disproportionate number of her patients were boys. Where concern existed regarding behavior problems in female children, it was usually in those who were pubertal and considered to be acting out sexually. Because Bellevue did not accept youngsters over age twelve, the unit admitted few girls. Without acknowledging the ways in which gender, race, and class may have influenced her diagnostic patterns, Bender pathologized those behaviors that did not fit her preconceived expectations. For example, she thought that many Puerto Rican and African American children cared for in New York City’s child guidance clinics had low IQs and “development problems” associated with “hereditary and family patterns.” She also believed that Jewish children were overrepresented in the city’s psychiatric centers, hypothesizing that the reason was that Jewish parents were overly anxious: “About one-third of the clinic population would be Jewish children brought in very young by very concerned parents, both parents coming and absolutely devoted to their children and seeking medical advice as early as they possibly can because their child is not ‘achieving.’ This is the major problem with the Jewish child in New York City.”
Bender presented more of her Bellevue pediatric drug research the next year at the 1956 annual meeting of New York’s state medical society. By now she estimated that at any given time multiple investigations exploring four or five different drugs were underway on the ward. She provided great detail with regard to her research procedures: “Some medications were deliberately discontinued at the height of clinical improvement to produce changes” in an effort to understand how the drugs worked. In other words, Bender blurred her roles of researcher and physician, making no real effort to differentiate between them. In this way she differed from most others who undertook pediatric drug research in this era. While Julius Richmond administered sulfonamides to healthy newborns to better map out dosing patterns, there is no evidence that he or any other pediatric antibiotic researchers in this era stopped the drug in an ill child to see what happened. But Bender was far from alone in her research endeavors on testing mood altering drugs in children. As one eminent psychologist later noted about this era, “any drug that happened to be used [in adults], we thought we should try with children.”

Within a year of Thorazine’s 1954 availability, another drug, Miltown (meprobamate), arrived on the market. Miltown hailed from the drug class called minor tranquilizers because it treated conditions such as anxiety rather than psychosis like Thorazine, classified as a major tranquilizer. Manufactured by Wallace Laboratories, a division of Carter Products, Miltown was quickly recommended for children. A 1955 *Cosmopolitan* magazine feature story extolled the new drug as “not habit-forming” and benefiting “restless, tense children with behavior problems.” After trying Miltown on some of his young patients, Brooklyn, New York, physician Harry R. Lichtfield reported to his colleagues that he found the agent useful in “one of the foremost pediatric challenges,” treating the “markedly restless, irritable, aggressive, or tense child who has become a problem both to himself and to his family.”

Although Lichtfield did not specify the frequency with which he prescribed Miltown, such a broad description of its benefits suggested he used it to treat a wide range of normative behavior in the healthy infant or child. Wallace Laboratories’ promotional materials targeted physicians like Lichtfield, emphasizing that many company-funded pediatric studies demonstrated the drug’s success with children. One summary, for example, concluded that “delinquent” youngsters “showed continued improvement on prolonged meprobamate therapy.” According to the company, another study suggested Miltown was “the drug of choice in child psychiatry.” In an attempt to capture the pediatric market, Wallace Laboratories formulated a small sugar-coated tablet “especially suitable for use with children” that could be crushed and placed on children’s cereal. Interestingly, the FDA-approved label for Miltown in 1956 makes no mention of its potential uses for children with behavioral problems,
despite the fact that the company included pediatric dosing guidelines in its published guidelines.30

Other psychiatric drugs also quickly found their way into general pediatric practice. New York pediatrician Milton W. Talbot alerted his colleagues to the fact that he found the antipsychotic drug reserpine useful for the “unhappy infant, with its accompanying problem of distraught and unhappy parents,” a problem he saw in his practice “all too frequently.”31 Psychoactive drugs also showed promise in treating pediatric conditions considered to have both a psychiatric and nonpsychiatric component. Miltown, for example, was suggested as a therapy for the child who wet the bed.32 Finally, some argued that tranquilizers had an important role to play in the nation’s civil defense plan in terms of child protection. Lists of stockpiled supplies families needed to keep handy in their bomb shelters included tranquilizers to keep rambunctious children calm during the weeks the family would need to spend underground in the event of a nuclear attack.33

How and when to use the new mood altering agents in general practice reveal the era’s cultural anxieties about what constituted the normal child. On the one hand, Americans differentiated their country from the Soviet Union by maintaining that the culture nurtured children’s individuality in ways the communist nations did not. On the other hand, the child who did not conform behaviorally risked becoming labeled a juvenile delinquent or behaviorally disordered. Marketing materials for Miltown, for example, capitalized on worries about the normal child by urging physicians to study the behavior of children and parents in their practices and make such assessments. Wallace Laboratories compiled a litany of pediatric symptomatology for which the drug might be prescribed, including children with sleeping problems and those with uncooperative behavior. But left unclear, and exacerbated by the unstable diagnostic categories characteristic for pediatric mental illness in this era, was how to determine when children’s sleeplessness met the threshold of a condition needing treatment with a powerful medication. That most of the physicians prescribing the drugs were pediatricians or general practitioners, not child psychiatrists, arguably led to even more confusion.34

The 1958 Child Research in Psychopharmacology Conference

In October 1956, the American Academy of Child Psychiatry and the American Psychiatric Association tried to bring more intellectual coherence to child psychiatry as well as the issues regarding psychotropic drugs for the pediatric patient. With funding from the National Institute of Mental Health and U.S. Public Health Service, the two organizations convened a conference. Perhaps implicitly acknowledging that psychiatrists could exert little control over their non-psychiatrist colleagues, the meeting focused on children
admitted to inpatient child psychiatry wards. As director of the nation’s largest such unit, Bender was invited to detail her therapeutic programs. While she described the many interventions she employed to treat children, she reserved special enthusiasm for psychopharmacology and how Bellevue had “pioneered” its use.\(^{35}\)

That same year, Congress appropriated funding to establish a Psychopharmacology Service Center (soon renamed the Psychopharmacology Research Branch or PRB) within NIMH to help organize testing for psychiatric drugs arriving on the market.\(^{36}\) In October 1958, the Institute sponsored an invited conference, “Child Research in Psychopharmacology.”\(^{37}\) Echoing Abraham Jacobi and, by now, generations of pediatric leaders, director R. H. Felix stressed in his opening remarks that he understood that the child was not a “miniature adult.”\(^{38}\) He also admonished the pediatricians, child psychiatrists, psychologists, pharmacologists, and one social worker in attendance that “these drugs when used with children may not only be tools of tremendous value but also may contain elements of danger.”\(^{39}\) Felix and PRB staff believed clinicians needed better measurement tools to assess the need for, and response to, psychoactive drugs in the pediatric population.

Divisions among the child psychiatrists in attendance about how and when to employ drug therapy became clear from the conference’s start. Johns Hopkins Hospital psychiatrist Leon Eisenberg expressed concern about what he saw as the overuse of mood-altering agents in children. Eisenberg was certainly not averse to medication. He and his mentor Leo Kanner had just published an article summarizing their pediatric tranquilizer experiments.\(^{40}\) But Eisenberg was very worried about the loose prescribing practices of physicians such as Lichtfield and Talbot. He believed better research design would provide guidance to help doctors with drug-related decision-making. At the same time, he believed that pediatric psychopharmacology research presented challenges, a number of which he synthesized in his remarks. First, since the child “comes to [psychiatric] attention because of his family’s or his community’s initiative,” not on his or her own, he pointed out that it could be hard to identify whether the disturbance was in the child, parent, or family. Second, “the lack of a commonly agreed upon system of classification” within child psychiatry, other than labeling children “emotionally disturbed,” made it difficult to compare treatments or define “improvement” in ways that met an agreed upon standard.\(^{41}\) Third, too often “clinical investigation can proceed without a theoretical commitment” or is undertaken to “see what happens.”\(^{42}\) All these factors made it hard for the psychiatrist to have a firm sense of what he or she was treating as well as to interpret the drug response, “Is the child improved . . . only because he is less troublesome to others if he is in a chemical straitjacket?”\(^{43}\) Without better diagnostic criteria and pediatric behavioral measurement rubrics, he believed it was difficult for physicians to interpret
children’s responses to psychoactive medications. Eisenberg argued that the best solution to the problems was for psychiatrists to embrace randomized controlled trials just as their colleagues in other areas of medicine were doing.

Lauretta Bender, a former Kanner colleague herself, responded to Eisenberg. At this point in their respective careers, Bender had significantly more seniority. She had just moved from twenty-two years as Bellevue’s director of child psychiatry to an advisory position with the New York State Department of Mental Hygiene. She also served as research scientist in child psychiatry at Creedmoor State Hospital in Queens, New York. Bender bristled at what she perceived as Eisenberg’s criticism of her approach to pediatric psychopharmacology investigations. She questioned his reliance on the idea that research questions needed to be theoretically framed or hypothesis driven, “wonder[ing] whether one man’s biases are not the other man’s theories.” Bender maintained that drug research approaches that worked in other areas of medicine could not be translated to child psychiatry. She believed that randomized trials in pediatric psychopharmacology introduced “error” because such research was inherently reductionistic, and, as such, an anathema to studying the child as a “unique” individual.

Other speakers avoided directly weighing in on the controversy, but seemed to agree with Eisenberg that psychoactive drug “misuse” was occurring in at least some American children. Yale School of Medicine child psychiatrist Milton J. E. Senn emphasized this point when he concluded the conference by urging the drug companies in attendance (no names were provided) to be more judicious in terms of their sales tactics, “I think the drug houses are aiding and abetting this [over-prescription of mood-altering agents in children] by their looseness of advertising and by the frequency by which they send out literature and samples.” He acknowledged that pediatricians faced a dilemma because parents’ expectations of pediatricians had evolved from earlier eras. Now they were “often called upon to deal with children who are not psychologically sick in terms of mental illness,” but whose parents were concerned about their conduct or demeanor. Senn indicated that pediatricians sometimes faced pressure from parents, teachers, and society to medicalize children’s behavior: the “pediatrician and the nonpsychiatric physician are now attempting to use drugs as short cuts they have been seeking for years to bring about changes in behavior that parents expect the physician to bring about.”
The 1960s: New Frontiers in Pediatric Psychopharmacology

Felix and others at NIMH clearly supported Eisenberg, not Bender. Soon after the conference ended, the Institute funded Eisenberg to undertake the first randomized controlled trial in pediatric psychopharmacology.\(^5^1\) In keeping with the casual norms of informed consent during this era, one of Eisenberg’s earliest NIMH-funded studies compared children with behavioral disorders who were followed at Johns Hopkins Hospital. Youngsters received one of three different treatment regimens, Miltown (meprobamate), Com- pazine (prochlorperazine), or a placebo in addition to their psychotherapy. Eisenberg did not inform families that they and their children were enrolled in a research study. Rather, parents were told that the drugs had been prescribed to help their children “feel better” or “make the world seem happier.”\(^5^2\) A frustrated Eisenberg found the results difficult to interpret because of subjects’ disease heterogeneity. He considered another experiment more successful. For this study he enrolled institutionalized African American youngsters labeled delinquent. The stimulant dextroamphetamine significantly improved many boys’ scores on behavioral rating scales, encouraging him to express cautious optimism that drugs might treat juvenile delinquency.\(^5^3\)

As the 1950s ended, some Americans began to criticize the widespread use of tranquilizers and other mood-altering agents. One Chicago mother wrote anonymously about her experiences in the February 1960 issue of *Ladies Home Journal*. She characterized her ten-year-old son as a “normal, bright, healthy boy.”\(^5^4\) Because he “occasionally had bad temper tantrums” she and her husband took him to see a child psychiatrist for advice.\(^5^5\) Aghast that the doctor wrote a prescription for tranquilizers, the mother traveled to a medical library and read whatever she could find about them. She wanted other *Ladies Home Journal* readers to know what she found. Mood-altering drugs could cause numerous side effects of which her doctor had not informed her and she felt betrayed. She warned other mothers that no long-term data existed as to how tranquilizers might affect the developing brain. Her findings led her to wonder “Is this the kind of medicine to give to a child—any child?”\(^5^6\)

In 1961, one of Bender’s former child psychiatry trainees, Barbara Fish, took charge at Bellevue. Like Bender, Fish ardently believed in psychopharmacology, administering Thorazine and similar drugs to youngsters between the ages of one and six years, for example, to observe their behavior as part of her early research into severe childhood mental illness. Unlike Bender, however, Fish believed in randomized controlled trials and the importance of designing investigations that employed structured, state-of-the-science research methodologies. This embrace brought her a large NIMH grant for Bellevue’s program. Renamed the Children’s Psychopharmacology Research Unit, Bellevue
became the only federally funded psychopharmacology research unit with a dedicated pediatric focus.57

At about the same time, Bender embarked on what many would later consider her most controversial research, studying children’s responses to lysergic acid diethylamide (LSD). While a number of investigators were experimenting with the agent on adults, Bender and her colleague Gloria Faretra at Creedmoor State Hospital were interested in its effects on children.58 Bender believed that LSD might have a therapeutic impact on children with autistic or schizophrenic symptoms because it increased cerebral vascular tone. She hypothesized that “in childhood schizophrenia, all boundaries are lost, not only of the psychological and personality experiences, but also those of the visceral functions, autonomic nervous system, vascular tone, muscular tone, and perception.”59 As such, Bender reasoned that an agent that made the brain’s blood vessels less permeable might help them, or at least reveal data to extend her knowledge of the condition. She acknowledged that the New York City commissioner of the Department of Mental Hygiene initially opposed her plan to experiment with LSD on young children, but ultimately acceded when she lobbied him vigorously. In one of her earliest pediatric LSD studies, in 1961, children between the ages of five and eleven years received it every day for up to several months. Staff administered the agent daily to at least a few youngsters “for a year or two.”60 Based on her personal observations and those of the Creedmoor staff, Bender concluded that the children seemed to have a “general improvement in well-being, appearance and lift in mood.”61 In addition, they “all showed a tendency to become ‘high’ and lively,” although LSD had been withdrawn in two children who became “panicky and anxious.”62

In another study, the team first subcutaneously injected epinephrine and pilocarpine, potentially risky agents known to stimulate and inhibit vascular tone, into thirty boys between the ages of seven and twelve years. Bender used these drugs to better understand individual children’s baseline vascular functions. Next, youngsters received either LSD, Sansert (an investigational LSD derivative developed by the Sandoz company), or psilocybin (a psychedelic compound produced by mushrooms). All three drugs affected children’s blood pressure, pulse, and respiration. Bender and her team repeated this study in ten younger (five to ten years old) boys whose psychological tests revealed they were sicker than the first group. After seven weeks of therapy using LSD, Sansert, or psilocybin, Bender reported a broad range of encouraging results, among them “improvement in interpersonal relationships, more awareness and response to their environment.”63 Taken together, these investigations convinced Bender that such agents stimulated mentally ill children’s central nervous systems in a way she deemed “remarkable.”64

Bender later estimated that she prescribed LSD to eighty-nine children in the years between 1961 and 1965.65 Although most of her funding for the
research came from the New York state health department and Sandoz, she
did manage to obtain one small NIMH grant in the wake of late 1960s reports
that LSD could cause chromosome damage. Since she had administered it or
the Sandoz investigational LSD derivative for a protracted period of time to so
many children, Bender had a ready supply of subjects on which to study this
hypothesis. She and her team studied cells harvested from children who had
participated in her experiments. They found no chromosomal breakages and
concluded that they had not suffered any ill effects from LSD. Interestingly, in
the publication resulting from this research Bender claimed she had adminis-
tered LSD or Sansert to some children for as long as three years, not the two
she had previously stipulated. She also wrote that her work had ended in 1966,
not 1965, as she noted elsewhere.66 For years after she was forced to cease her
LSD-related work because she could no longer obtain the agent from Sandoz
by the mid-1960s, Bender expressed hope that it could be resumed because
“it is one of the most effective methods of treatment we have for childhood
schizophrenia.”67

There was little likelihood that Bender’s methods at Creedmoor would be
questioned by hospital employees. Her research staff managed the unit, over-
seeing the nurses and other staff who carried out the protocols. Although she
never disavowed her LSD research, perhaps in an effort to stem criticism as
ethical norms evolved, Bender included details omitted from her publications
in an extensive, but unpublished, 1968 summary of her Creedmoor research.
For the first time, Bender went out of her way to stress that her work had been
approved by the unit’s “Research Committee and [had received] informed
parental consent.”68 She did not, however, describe these processes further.
Although largely forgotten today, Bender’s work was no secret at the time.
She published widely in prestigious journals without challenge. No colleagues
whose questions and comments accompanied many of her published presen-
tations seemed concerned. Nor did the New York Times, which reported on
Bender’s work in 1963: “LSD Drug Found to Aid Children.”69 This is not sur-
prising given that most Americans during this era knew little about LSD, and
the publicity surrounding its use by members of what became known as the
youth counterculture had not yet occurred.

At the same time Bender undertook her LSD-related work in the early
1960s, Eisenberg, joined now by psychologist C. Keith Conners, continued to
build his NIMH-funded program of pediatric stimulant research. In the late
1950s, Eisenberg became Leo Kanner’s successor as chief of child psychiatry at
Johns Hopkins Hospital.70 Just as Harry Shirkey, Helen Taussig, John Nestor,
and others sought to use the thalidomide crisis to move policymakers to con-
sider a broader set of pediatric-related drug safety issues, so, too, did Eisenberg,
who wanted to draw legislators’ attention to questions specific to mood-
altering agents in children. During Hubert Humphrey’s post-thalidomide
Capitol Hill hearings into how to improve federal oversight of American drug policy, Eisenberg wrote to the senator reiterating the concerns he had raised at the 1958 conference. Informing Humphrey that he was “impressed with the discrepancy between the wide use of these [tranquilizers] drugs in pediatric practice and the meager evidence of their value,” Eisenberg argued for new regulatory protections for children.71 He also warned Humphrey about the “extensive advertising campaign of the drug companies,” whose claims regarding psychoactive drug safety and efficacy fell “just short of open deception.” The letter found its way into the published hearings but with no formal comment from Humphrey.72

In an effort to reach practitioners outside child psychiatry, Eisenberg expanded on these and related concerns the following year in the Children’s Bureau periodical, Children. Without identifying Bender, but surely with her in mind, he lambasted “physicians who consider drugs the agents of choice.”73 In lay terms, Eisenberg outlined the issues as he had to Humphrey. He also walked readers through the ways in which research into child mental illness differed from other pediatric research. Describing the paucity of child-focused measurement tools, he lamented the fact that he lacked a “psychiatric thermometer” to assess youngsters’ mental health.74 Officials at NIMH clearly agreed with Eisenberg. In the years following its late 1950s and early 1960s support for him and Bellevue’s Barbara Fish, the Psychopharmacology Research Branch ceased supporting any new pediatric drug studies. Staffer Ronald S. Lipman acknowledged that the “hiatus . . . reflected not an absence of applications” but “the unsophisticated state of methodology in pediatric [psycho] pharmacology.”75

Eisenberg and Conners both left Johns Hopkins for Harvard in 1967 and were by then well on their way to establishing the efficacy of stimulant medications for what was now called hyperkinetic reaction in childhood. They had also just successfully petitioned the updated version of the Diagnostic and Statistical Manual of Mental Disorders, published in 1968, to include the diagnosis.76 Recognizing the need for better pediatric psychometric tools and assessment rubrics, NIMH funded Conners to develop them. Significantly, Eisenberg’s and Conners’s success at defining diagnostic criteria for hyperactivity, validating assessment measures, and quantifying situations in which the stimulants worked made this area of research the most attractive to NIMH. When it once again approved pediatric psychopharmacology research grants in the late 1960s, most of the successful applicants aimed to extend the work of Eisenberg and Conners in some way.77

The second half of the 1960s also saw a number of legislative and policy discussions surrounding child mental health in which psychopharmacology had no direct immediate role. As part of President Johnson’s War on Poverty and other Great Society initiatives, the government launched new programs
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aimed at studying and addressing ways in which poverty affected children emotionally and academically. The National Institute for Child Health and Human Development (NICHD) funded research and training programs related to developmental disability (often referred to in that era as mental retardation), a condition frequently confused with mental illness in children. Within NIMH, new centers for child and family mental health and juvenile delinquency received robust support. As the decade ended, NIMH drew together leaders in child mental health, creating the Joint Commission on Mental Health of Children. The Commission aimed to synthesize a cohesive national action plan for child mental health in the 1970s.78

Pediatric Psychopharmacology:
Conflict and Consensus in the 1970s

The ways in which the climate surrounding the use of mood-altering drugs in children had shifted since the 1950s became evident early in 1970, when the Commission issued its report, Crisis in Child Mental Health: Challenges for the 1970s. Whereas Bender had once been considered a leader in pediatric psychotropic drug research, she was now an outlier. Although the report did not mention her by name, it included pediatric LSD research in its examples of “fringe” practices.79 The Commission said very little about medication as a therapeutic modality for mentally ill children. In only one place was there mention that, under the right circumstances, drugs could supplement individual child or family therapy.

In summer 1970, just as the Commission’s report was published, the Washington Post featured an article that attracted widespread public and congressional attention. The piece alleged that as many as 10 percent of Omaha, Nebraska, school-aged children, many of them poor and black, had been prescribed “behavior modification” drugs, especially Ritalin (methylphenidate hydrochloride).80 The newspaper noted concerns by parents who felt pressured to medicate their children. They and community leaders alleged that the aim was to “drug black children into quiet submission.”81 A few days later, the New York Times followed the Post story with one of its own. The article in the New York Times presented a more sympathetic view of stimulants. It emphasized Eisenberg’s and Conners’s research and quoted Eisenberg, who reassured parents that when used in the right circumstances, the drugs helped youngsters and was “remarkably safe—even safer than penicillin.”82 Extending the antibiotic analogy, the story cited pediatric neurologist Eric Denhoff, who observed that some called stimulants the “penicillin of children with learning disabilities.”83

The dueling newspaper stories only fueled the controversy. Within a few weeks, New Jersey Democrat Cornelius E. Gallagher convened a hearing in
the House of Representatives seeking a “full public discussion” about “prescribing speed for children.” He referencing the drug catastrophe everyone remembered, Gallagher mused that the nation might be facing a “mental thalidomide” situation. He questioned whether prescribing stimulants sent mixed messages to American youth at a time when adults increasingly worried about substance abuse in the younger generation. Was it illogical, he queried rhetorically, to steer junior high and high school students away from “speed” at the same time their younger siblings were having it prescribed to them? Gallagher also wanted to initiate a national conversation about what constituted normal behavior in the average American child and who made that decision. How, he pointedly asked Ronald Lipman, an FDA clinical studies section chief, did one differentiate the child with “hyperkinesis” from “just a bored, bright, creative pain-in-the-neck kid?”

The thoughtful overviews of hyperkinesis and stimulant research summarized by NIMH and FDA staffers somewhat mollified Gallagher, but he remained concerned about how society decided who was, and who was not, a typical American child. Beyond the grandstanding and hyperbole at the hearing, one of its most notable features was how little Gallagher and the other legislators seemed to know about basic issues surrounding American drug policy. No one mentioned, for example, the fact that their questions about pediatric drug development were similar to those raised earlier by Kefauver, Humphrey, and others. Moreover, Gallagher seemed to lack basic information about ongoing FDA efforts to address pediatric safety and efficacy-related questions, nor did he seem clear on what the agency actually did. Dorothy Dobbs, Director, Division of Neuropharmacological Drug Products at FDA, for example, had to explain to Gallagher that NIMH, not FDA, funded drug research into the stimulants. She noted that the issues raised by the the Washington Post regarding stimulant use in Omaha children were not even research-related since no investigation had been underway. When Gallagher continued to press FDA to engage in ways outside the agency’s regulatory domain, Dobbs’s superior, Elliot L. Richardson, secretary of Health and Human Services, subsequently wrote to Gallagher, explaining to him that the FDA had no oversight of physician practice.

Finally, Gallagher did not seem to understand that his concerns about psychoactive medications and children were not a problem isolated to behavioral drugs. For example, he expressed concern about doctors prescribing stimulants and other psychoactive drugs for children outside the age range stipulated on the label without acknowledging that this practice occurred for virtually every drug on the market. Only a very few pediatric dosing metrics were backed by scientifically derived safety and efficacy data. Gallagher’s lack of knowledge is not surprising. His interest lay primarily in issues related to the right to privacy in American life. He correctly surmised that a Capitol Hill hearing regarding
government overreach wherein school personnel seemed to be intruding on parents’ rights would garner significant media attention.\textsuperscript{92} Even if he agreed with the racism charges leveled by Omaha parents, emphasizing it did not advance his larger privacy-related concerns. But it was a missed opportunity. Had Gallagher chosen to do so, the hearings could have delved into broader issues, potentially synergizing Harry Shirkey’s and Sumner Yaffe’s parallel efforts during this time period. While the hearing was awash in rhetoric regarding child protection, their needs were in reality not its primary focus.

In December 1970, Leon Eisenberg took the stage at the American College of Neuropsychopharmacology. Hoping to bring nuance and balance to the past year’s media-fueled drug controversy, he reminded his colleagues that “Drugs promise neither the passport to a brave new world nor the gateway to the inferno.”\textsuperscript{93} Eisenberg drew on Harry Shirkey’s therapeutic orphan concept as an organizing framework for his talk, subsequently published in a landmark article.\textsuperscript{94} He stressed the fact that most of the challenges in pediatric psychopharmacology differed little from general issues surrounding children and drugs. His discussion of the knowledge deficit regarding pediatric dosing, data extrapolation from animal models, and research design-related issues specific to children’s evolving development sounded identical to the problems articulated simultaneously by Shirkey and Yaffe.\textsuperscript{95}

But Eisenberg also outlined the additional obstacles faced by those in his field, ones that spoke to the differences between child psychiatry and general pediatrics. When most children were prescribed medications, it was for a discrete period of time and to treat a specific illness. But the rationale for psychoactive drugs in children was not as clear. Moreover, they received the drugs for extended periods of time and information regarding long-term effects was virtually nonexistent. This was true for adults as well, but children risked potentially stunted growth or impeded brain development, issues older people did not face. Finally, Eisenberg noted, as he had in the past, that the perceived need to medicate a child was sometimes the result “of disturbed mothers, inadequate teachers or uninformed judges.”\textsuperscript{96} Reflecting his growing interest in how social and economic circumstances shaped health and clinical practice, Eisenberg urged his colleagues to consider nonmedical variables that might result in prescribing mood-altering medication to children, such as poverty, racism, and other structural problems.

Now a national leader, Eisenberg was a well-funded NIMH researcher, professor at Harvard Medical School, and chief of psychiatry at Massachusetts General Hospital. His efforts with Conners had made hyperactivity a discrete psychiatric diagnosis, one differentiated from the older, more diffuse “disturbed child” entity. Eisenberg had less success, however, stemming the tide of drug advertisements in medical journals. Ironically, his work provided evidence that companies like CIBA, which manufactured Ritalin, could use
to increase their focus on children. As Ilina Singh has shown, until the early 1970s most stimulant advertisements featured a picture of an adult. Eisenberg’s research demonstrated, however cautiously, that stimulants improved the behavior and cognitive performance of appropriately diagnosed children. His research meant that CIBA increasingly devoted more attention to children. By the 1970s, in addition to promoting Ritalin to physicians, the company was sending brochures and movies to educators and parent-teacher associations extolling the many ways children benefited socially and academically from stimulant drugs.

The year 1973 brought optimism and fresh challenges to issues surrounding pediatric psychopharmacology. A new set of NIMH Psychopharmacology Research Branch–approved standardized pediatric psychiatric measures for evaluating psychotropic drug outcomes in children provided meaningful tools for researchers. At the same time, Senator Ted Kennedy’s highly charged hearings into human experimentation publicized abuses involving institutionalized mentally ill and developmentally disabled populations. A number of the cases involved children. In the aftermath of the Kennedy hearings, lawsuits involving the use of antipsychotics and sedatives in vulnerable populations followed. Although drugs’ widespread use in such situations was certainly not limited to children, the litigation filed by public interest law firms made an especially strong argument on their behalf.

More Capitol Hill hearings arose from the flow of lawsuits, repeatedly bringing FDA staffers to Capitol Hill. In one instance, for example, petitioners demanded that the “disturbed child” indication on the package insert for Thorazine be replaced with “more precise language which indicates that the drug is approved for the treatment of only those children who have been diagnosed as having a specifically identified psychotic condition . . . for which the drug has been previously approved.” Alexander M. Schmidt, FDA commissioner, reassured litigants and Congress that the agency agreed that more clarity regarding children and psychoactive drug prescription was needed. He empaneled an FDA group to work with stakeholders within NIMH, industry, and the American Academy of Pediatrics (AAP) to do just that. The FDA had recently begun asking for American Academy of Pediatrics Committee on Drugs (COD) consultation regarding psychoactive agents. Whereas few of the COD meetings in the 1960s discussed behavioral drugs, issues regarding their safety and when they should be prescribed now occurred frequently, and the COD issued guidelines for stimulant use in 1973. And just as the agency asked the COD for general guidelines concerning pediatric drug testing, so, too, did FDA want COD assistance for scientific and methodological issues specific to pediatric psychopharmacology.

The mid-1970s creation of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, aimed at codifying
issues surrounding medical ethics and informed consent, slowed behavioral drug investigations in children just as it did for other research, as everyone awaited its findings. Given the negative publicity surrounding the Kennedy hearings, anyone who wanted to undertake such work faced difficult obstacles finding subjects for studies. This made it even more difficult to answer a fundamental question: did all children respond to stimulants or just those who were hyperactive? If the attention span improved in all children who received Ritalin, what condition, exactly was the drug treating? Leon Eisenberg had long worried about this issue, but saw no ethical way to address it. He had admitted as much in a 1968 letter to a Harvard colleague, copied to Henry Beecher, whose influential 1966 article about experimentation ethics had ignited much debate within medicine: “I have never been able to persuade myself that it would be legitimate to give drugs to normal children, even were their parents to consent.”

One young Harvard-trained child psychiatrist at NIMH, Judith Rapoport, decided to study this question using a novel strategy. Before arriving at NIMH, Rapoport practiced at a clinic where she was struck by stimulants’ effects on children who had accidently ingested pills meant for a sibling: “These calm children just got calmer on stimulants!” Now an NIMH staff scientist, Rapoport decided to study their effects in normal children. Perhaps recognizing how difficult it would be to undertake such an investigation in a traditional clinical setting, she decided to approach her NIMH colleagues with children. In an effort to reassure them that the drugs were safe, her own two sons were the first subjects enrolled in her study. Twelve other boys between the ages of six and twelve years whose parents worked at NIMH received one dose of a stimulant or placebo, after which their performance on a variety of psychometric and self-report measures was assessed. Rapoport made sure that none of the families involved fit anyone’s definition of powerless: “the parents were doctors, lawyers, and, in one case, president of the local ACLU.” Her findings confirmed what she had observed empirically: nonhyperactive children also responded with decreased motor activity and improved test performance. While her research did not yield new information about whether stimulants worked in hyperactive children, she concluded that their “lack of specificity” was “no argument against . . . use.” As an example, she reminded readers that diuretics increased urine output in everyone who took them, not just those with congestive heart failure.

As the 1970s ended, those interested in pediatric psychopharmacology grew more optimistic. The perceived need to understand psychoactive drugs in the context of the pediatric patient had helped create a unique niche for child psychiatrists. Newly refined psychometric measures created by Conners and others now allowed clinicians to more clearly differentiate the mentally ill youngster in ways beyond the older “disturbed child” category. Better
assessment tools and greater diagnostic specificity meant that outcomes in response to medication could be more reliably evaluated. Moreover, by 1979, just as the FDA accepted the COD scientific guidelines for pediatric drug research, so, too, did the agency distribute its supplement specific to pediatric psychoactive drug investigations. Child psychiatrists who argued that mental illness was rooted in organic causes believed they were on the cusp of a new era. The first pediatric psychopharmacology text, influenced heavily by biology and genetics, had just been published. The third edition of *Diagnostic and Statistical Manual of Mental Disorders*, due out in 1980, reinforced this perspective and significantly expanded the pediatric section. For those who believed in a more biologically oriented framework for child psychiatry, one in which drug therapy played an important role, these changes seemed destined to facilitate the specialty’s shift away from the child guidance model even further.⁴⁰⁹