The literature on the preschool child with ADD-H is so sparse that there seems little enlightenment to offer. However, recognizing that the practitioner is sure to be faced with the problem, some review of what is known of the condition in this age group is needed.

Although most children are brought to the doctor after they have begun attending elementary school, there are certainly children who manifest powerfully deviant, hyperactive-aggressive behavior well before kindergarten age, who are damaging families, bringing out the worst in parents, and being denied the peaceful, secure, protected and seemingly happy world of most middle-class children.

Much of the material about these children is anecdotal.

In an individual case study, 1 a 2-year, 8-month-old child was referred by a pediatrician to a psychiatric group:

On interview the mother reported that the child was beyond her control. He was "on the go" from early morning till night, refused to sit still or play with games or peers for any more than a few minutes at any one time, was destructive of his toys and furniture and was shunned by his peers and sibling because of his unpredictable and physically aggressive behavior. He was negative, stubborn and given to temper tantrums. His sleep was disturbed with initial insomnia and early rising which often resulted in destructive behavior before the family rose.

The description of a preschool child by Cantwell<sup>2</sup> and previously referred to in Chapter 2 is sufficiently impressive (and convincing) to be worth quoting in its entirety:

This boy had distinguished himself shortly before his third birthday by being expelled from nursery school. In itself this was not particularly significant, since the school itself was a very rigid one. What was unusual was the statement to me by his teacher that under no circumstances would they take him back: he was simply too disruptive.

When I interviewed his parents, the history they gave was a disaster. They described a small tyrant who ruled the house: he was up all night running around, had learned to unhook the screen door, and had been found walking down Ventura Boulevard in his Pampers, had put himself in the clothes dryer and turned it on, and so on. [After Dr. Cantwell examined the child] the boy then walked outside my office, where there is a group of secretarial desks. One woman was away from her desk, and he climbed up on her chair and started pounding the typewriter. When she returned and asked him to get down, he jumped down, kicked her in the shins, and yelled—because of his articulation problem—"Duck you, bitch!" He then lay down and began kicking and screaming; it took his mother another 45 minutes to calm him sufficiently to take him home.

But Dr. Cantwell wisely points out that this child was an exception to the usual difficulty of diagnosing the ADD-H child during the preschool years:

In fact, the ADD child is very seldom diagnosed until the early school years, in nursery school, kindergarten, or the primary grades. (not surprisingly, ADD without hyperactivity tends to be diagnosed still later, probably presenting as some sort of learning disability, failure to progress in school, and so on.) The reasons are twofold. First, with a preschool child the physician must inevitably rely heavily on reports of parents, who may be more or less tolerant of deviant behavior, may or may not have personality problems of their own, and often have only a limited basis for evaluating their child in comparison with others—especially now that small families are becoming common. In the more structured schoolroom situation, by contrast, the child is surrounded by many others doing more or less the same thing, so that an alert teacher can usually spot the especially distractible child (and of course, the especially disruptive one) quite easily. The second reason is that in very young children, distractibility and often a degree of hyperactivity do not seem abnormal because the child's repertoire of purposeful behavior is still very limited. It is difficult

to diagnose ADD reliably at age three except in a school situation, and almost impossible before then in any situation.\*

The small group of investigators who have tried to do systematic research on the preschool child have consistently begun the published results of their research by reviewing the difficulties in preschool diagnosis of ADD so cogently stated by Cantwell.

Susan Campbell and colleagues at the University of Pittsburgh have made the untapped arena of the ADD preschool child their special interest:

Diagnosis is particularly problematic with this age group. DSM-III criteria are not all applicable since school behavior is central. Further studies of hyperactivity in school-age youngsters often rely on both parent and teacher reports, thus ensuring some degree of cross-situational, inter-rater consistency in perceptions of problem behavior. Diagnosis of hyperactivity on the basis of both parent and teacher reports helps to exclude children whose main problem is their excessively intolerant parents. Unfortunatey, this dual criterion cannot be used with young children since many are not yet in school. In addition, although the line between normal and problem behavior is blurry at best, objective behavioral criteria which clearly differentiate normal from problem toddlers and preschoolers are virtually nonexistent. Many of the problems of which parents complain-such as tantrums, defiance, restlessness, and difficulty playing alone—show developmental change and are typical of toddlerhood and the early preschool years. Thus, it is difficult to differentiate active and defiant children who are showing potentially chronic problems from those who are merely going through a turbulent developmental phase. . . . 3

Campbell's primary interest at present is the identification of the ADD-H preschooler and the discovery of whether or not the preschool deviant behaviors persist into the school years. She has not yet dealt with therapeutic interventions which, with diagnosis, will be the main focus of the practitioner.

The physician is dependent on the mother for acquiring the information for a diagnosis of ADD-H in preschool children leading to possible intervention. Office behavior in some cases is helpful. However, investigators at the University of Illinois<sup>4</sup> have shown that in 80 percent of cases, the child's behavior in the physician's office is of no diagnostic or prognostic significance in ADD. And surely, the wise pediatrician has learned from experience that, in the general

<sup>\*</sup>In Cantwell DP: The hyperactive child. Hosp Prac 14:65-73, 1979. Reprinted with permission of Hospital Practice, published by H. P. Publishing Co.

evaluation of any child, he or she cannot extrapolate from the child's behavior in the office to the same child's behavior in the larger world. The toddler's behavior in a strange and frightening place with an intrusive stranger tells us very little about how the child behaves in his or her more usual environment.

We need to have some answer, at least in general, of how reliable mothers' reports about preschoolers can be or usually are. Schleifer and associates<sup>5</sup> studied 28 children whose mothers found that the children could not stick to anything for more than a few minutes, did not listen, could not play alone, and neither punishment nor praise made any difference. These children were studied in a variety of ways including a 2-hour nursery school session once a week for 9 weeks with six children (half hyperactives, half controls) and two teachers. Only 10 of the 29 who appeared to be ADD-H by mothers' descriptions were found to be different from the controls in the nursery school situation. Using school behavior as corroboration, it appears that only one-third of the children referred by mothers could be considered ADD-H. However, it must be remembered that the nursery school session in this study was atypical: six children, two teachers—close to the one-to-one situation in which, outside the home at least, ADD children are known to do well.

Campbell and associates<sup>6</sup> reported the early work on 46 preschool children referred with problems characteristic of ADD-H and 22 controls. She plans to eventually include assessment, treatment, and follow-up phases, but this report deals only with initial assessment data obtained prior to and during a home visit and two visits to a laboratory playroom. Here, measures of gross motor activity, activity shifts, and attention to toys and other objects were obtained, as well as evaluation of performance on structured tasks designed to test attention and impulsivity. Her group found good correspondence between the mother's description of the child's problem behavior and the behavior and performance of the child in the situations studied—88 percent of the referred sample were significantly more restless, active, and inattentive than the controls and did poorly on laboratory measures of sustained attention and impulsivity.

One of the two studies suggests good reliability of parental observations; the other found parents reliable in only one-third of the cases

For preschool patients, doctors will have to make up their minds on the severity of the problem and importance of intervention on the basis of their own observations and interviews. In the present state of the art, research has little more to offer. However, the physician can be absolutely confident that severely ADD-H preschoolers do definitely exist and that their parents, and no doubt the child,

desperately need the doctor's help. There is also evidence that these maladaptive behaviors persist into the school years.

Ross and Ross,<sup>7</sup> notable in the ADD research community for impressive compendiums of much of the research in the field, take a hard-line position on the doctor's responsibility toward difficult preschool children:

The hyperactive preschool child generally is not referred for treatment until the point of formal school entry, yet it is clear from the foregoing empirical and descriptive data that he is already exhibiting a set of behaviors that will impede the development of satisfactory peer relations and cause continuous problems in the school setting. Furthermore, outcome data on hyperactive preschool children indicate that in the early school years these children are still perceived by adults as having more behavior problems than non-hyperactive controls have. Consequently, whether or not a diagnosis of hyperactivity is eventually made, it should be clear to the pediatrician that immediate intervention is indicated. We are assuming, of course, that the pediatrician has been taking the time to really listen to the mother. If he brushes aside the mother's attempts to explain the difficulties she is having with her child, it is to be hoped that she will seek help elsewhere.

But what is the "immediate intervention" that Ross and Ross imply has been demonstrated to be helpful in improving the fate of preschool ADD-H children? This is not at all clear.

# Stimulant Drugs in Preschool Children

There is very little information, either anecdotal or systematic, on the use of stimulant drugs in preschool children. Nichamin,<sup>8</sup> commenting on what he calls Minimal Cerebral Dysfunction in the infant and toddler under the heading of "personal view," comments:

When hyperactivity and deviant behavior are excessive, the distracted parents may urgently plead for some relief. In these circumstances I sometimes prescribe methylphenidate in small (2.5 mg) doses twice daily with surprisingly effective and often dramatic results. This stimulant medication paradoxically [sic] quiets these young children, rendering them more amenable to better conformity in intra-family relationships and pursuits. The tensions of family imbalance begin to dissipate. For close supervision, bimonthly visits are recommended. The daily dosage of methylphenidate should rarely exceed 5 to 10 mg. Side effects of anorexia or sleeplessness are occasionally encountered, and these can be curtailed by adjustment of dosage. Should a peculiar stare or exces-

sive quietness develop, this can likewise be controlled by a smaller dose or temporarily stopping the drug. Although experience with methylphenidate in this young age period has been quite limited, it is my impression that it is probably as safe and effective as with the child a few years older. There is need for further study and evaluation of the psychostimulant drugs in the toddler age period.

Although that article was published in 1972, Nichamin's last statement remains correct. However, the one careful, systematic study that could be discovered does not support Nichamin's clinical experiences.

Schleifer and associates<sup>5</sup> carried out a double-blind crossover study on 26 preschool children considered ADD-H on the basis of parents' reports, 10 of whom were also found to be ADD-H in a small experimental nursery school (the "true" hyperactives). The children ranged in age from 3 years 4 months to 4 years 10 months, with a mean of 4 years 1 month. All children were first put on 5 mg bid which was increased or decreased "until the minimum drug dosage producing the most effective clinical change with the fewest negative side effects was obtained." The mean dose was finally 5 mg bid, ranging from 2.5 mg qAM to 20 mg qAM and 10 mg at lunch. Group analysis showed that active medication significantly decreased hyperactivity scores and active medication significantly increased "reflectivity" (as measured by laboratory tasks) as well. There were no significant differences in the way medication affected the "true" or "situational" hyperactives.

Although there was some improvement in behavior, a striking finding of the Schleifer group in the use of stimulants for preschoolers was the high incidence of important side effects:

Clinical observations indicated that methylphenidate very often had a negative effect on the child's mood and also on his relationship with peers, causing less social behavior and interaction. These almost always appeared and were reported as unwanted side effects of the drug, and included sadness, irritability, excessive hugging and clinging, and increased solitary play, as well as the more usual side effects of poor appetite and difficulty getting to sleep, and were determinate factors in the psychiatrist and the mothers deciding that all but three of the 28 children discontinue medication after the experiment ended (italics added).

Two years later,<sup>9</sup> none of the children were still on medication, which seems to confirm the conclusion that, "in general, drugs were found to be unsatisfactory with this age group since negative side effects were pervasive and outweighed any positive drug effects."

### REFERENCES

- 1. Husain A, Chapel J, Malek-Ahmadi P: Methylphenidate, neuroleptics and dyskinesia-dystonia. Can J Psychiatry 25:254-258, 1980.
- 2. Cantwell DP: The hyperactive child. Hosp Prac 14:65-73, 1979.
- 3. Campbell SB, Breaux AM, Ewing LJ, Szumowski EK: A one-year followup study of parent referred hyperactive preschool children. J Am Acad Child Psychiatry 23:234–249, 1984.
- 4. Sleator EK, Ullmann RK: Can the physician diagnose hyperactivity in the office? Pediatrics 67:13–17, 1981.
- 5. Schleifer M, Weiss G, Cohen N, et al: Hyperactivity in preschoolers and the effect of methylphenidate. Am J Orthopsychiatry 45:38–50, 1975.
- Campbell SB, Szumowski EK, Ewing LJ, et al: A multidimensional assessment of parent-identified behavior problem toddlers. J Abnorm Child Psychol 10:569–592, 1982.
- 7. Ross DM, Ross SA: Hyperactivity: Current issues, research, and theory, ed 2. New York, Wiley, 1982.
- 8. Nichamin SJ: Recognizing minimal cerebral dysfunction in the infant and toddler. Clin Pediatr 11:255–257, 1972.
- 9. Campbell SB, Schleifer M, Weiss G, Perlman T: A two-year follow-up of hyperactive preschoolers. Am J Orthopsychiatry 47:149–162, 1977.

# What Happens to ADD Children When They Grow Up?

Assuming the truth of the widely held notion that childhood experiences are powerful determinants of adult behavior, what kind of adulthood should we expect to follow the unhappy, unsuccessful, and sometimes disastrous early years of ADD children?

Even the ADD rather than ADD-H child who is quiet, sometimes withdrawn, and not troublesome must bear the onerous burden in our society of failure to learn: reprehensible to teacher and embarrassing to parents. In addition, the child is often ignored by peers or the object of their contempt.

The ADD child who is also hyperactive and impulsive is not only a learning failure but a constant source of annoyance to teacher, classmates, and parents, and public retributive behavior from these associates is the rule. A kind of pathetic friendlessness is an almost invariable experience of the ADD-H child. He or she is rejected by peers despite awkward, repeated offers of friendship, and the rejection is a source of puzzlement, resentment, and hostility. As for the many children who, in addition to all the above weaknesses, also manifest a "conduct" problem-aggressively defiant, hostile, loud, ready to pick a fight, destructive, and not rarely in trouble with the police even at an early age—it must seem that everything they do elicits the wrath of peers, powerful adults, and most distressing of all, the parents whom all children need to count on for solace in difficult times. And this pervasive failure usually characterizes the child's life, often from the earliest years or the first entrance to day care or kindergarten all the way through high school days.

Clearly the intensity of these experiences varies greatly from child to child, but when, according to Milton, "the childhood shows the man as morning shows the day," then should we not expect a great many of our ADD children to eventually become failed adults: anything from unemployed illiterates, to loners, to panhandlers, alcoholics, depressives, suicides, or criminals?

To compound the ominous portent of such a childhood, the condition we diagnose as ADD (as well as all other behavior disorders) surely falls into Lewis Thomas' category of one of the areas of medicine for which there is no technology. That is, we know neither cause nor cure, and treatment consists of supportive, reassuring, and nonspecific interventions. The examples Thomas provides are rheumatoid arthritis, multiple sclerosis, stroke, cirrhosis, and the other diseases that continue to mystify medicine. Autism and mental retardation are clearly in the same category. How many patients who suffer from these chronic conditions are expected to return to normal with time or after the administration of supportive, nonspecific interventions? Why none, of course. And yet, it is a surprising fact that some investigators who follow ADD children over relatively long periods of time, and those who comment on such work, somehow communicate the idea that it is a remarkable fact that ADD patients are not functioning at the level of their normal peers.<sup>2-5</sup> For example, "At recent meetings of researchers in this field, great concern has been expressed that adult outcomes of this condition, despite successful therapy with drugs, may not be very good."2

To study long-term outcome is necessary, but to expect that ADD children will, as young adults or adults, conform as well to our societal standards as the average child is certainly naive.

Having now claimed that simple common sense demands the expectation of a disastrous adulthood for children diagnosed as ADD, let us look at the actual findings of the intrepid investigators who have ventured into this very difficult area of research.

The reader should be forewarned that the information that will emerge from a look at the current follow-up data will be spotty at best, clouded with uncertainty, and will not provide the definitive answers that the clinician would like to use to inform anxious parents.

The greatest difficulty in acquiring valid predictive information is that the children who manifest the behavioral condition we now call ADD are a heterogenous population. Their problems vary both in quantity and quality. For example, some have only attention problems but are quiet and nondisruptive; others have not only the attention problem but are impulsive, always on the go in one way or another, and consequently disruptive. Some children in both of these groups are obedient, anxious to please, and generally con-

formist. Others are defiant, hostile bullies, seem to take pleasure from the discomfiture of others, and are quick to engage in fisticuffs. What do we learn when children with all of these different characteristics are observed, the outcome results are put in one big statistical pot, and generalizations are made from the results? Not very much.

And most of the studies report outcome results at 10 to 15 years of age. Not only are those ages well known behavioral nadirs, but what really matters is how ADD children function in society as adults. After all, adolescence is of brief duration.

Despite the difficulties, some, shall we say, clues have emerged from the investigations which are at least a little help in the clinical management of ADD.

This review will simply zero in on those aspects of the follow-up literature which, in the opinion of the author, have made a possible contribution to clinical management. Much of the information summarized will have come from the work of the group at McGill University in Montreal whose work has, of course, its limitations, as does all follow-up research, but has benefited from the continuity imparted by the participation of Dr. Gabrielle Weiss, child psychiatrist, since the very beginning of the project.

## PROGNOSTIC FACTORS IN OUTCOME

Is there anything clinicians can learn from observations of the child when he or she first comes for evaluation that will give information about how the child will eventually turn out? In other words, are there, indeed, any useful prognostic indicators?

Certainly the most comprehensive work dealing with prognostic factors in hyperactivity has been done by Dr. Jan Loney and her associates at the University of Iowa. True, her work is retrospective, but it comes as close to being a model follow-up study as is possible to devise from retrospective data. A great advantage her group had was that the intake data at the University of Iowa Hospital were remarkably complete and the follow-up assessment was detailed and comprehensive. She and her colleagues analyzed data of 84 boys who were between 6 and 12 years of age at the time of outpatient evaluation, and between 12 and 18 at the time of follow-up interviewing and testing.<sup>6</sup>

Instead of using teacher and/or patient rating scales as is so commonly done, Loney's group studied in great detail the records accumulated at the time of intake. They looked for 13 symptoms considered to be of special importance in this group of children diagnosed as hyperactive. The symptom ratings were made after review

of the staff, psychiatric, and social summaries and psychological and educational test reports contained in each child's medical chart. Using a statistical technique called factor analysis, they found that two factors emerged from this analysis. The factor that they labeled aggression included the following symptoms: delinquent acts, evasion of rules, excitability, irritability, fighting, and disobedience. The factor that they labeled hyperactivity included restlessness, running around, distractibility, and forgetfulness. Of the 84 boys studied they found 20 exclusively hyperactive—that is, they had low aggression scores and high hyperactivity scores; there were 13 exclusively aggressive children; there were 25 with high scores on both factors, and 2 with low scores on both factors.

Establishing the fact that there are distinct subgroups of ADD children is an important contribution in itself, and characterizing the subgroups with some specificity is a further contribution. That is, it now seems clear that there are some children diagnosed as hyperactive who manifest little or no aggressive behavior. This point is emphasized because there have been those who insisted "the evidence for the independence of hyperactivity as independent from conduct disorder is dubious at best." The experience at the University of Illinois corresponds closely to the findings of Loney and associates. It is reassuring to have her elegant confirmation.

Of special importance in the finding of a fairly clear-cut distinction between the aggressive and nonaggressive hyperactive children, often all lumped together in the past as hyperactive, is that Loney and Paternite<sup>8</sup> have shown that considerable prognostic power rests on this distinction. Using multiple regression analysis, Loney and Paternite found that the presence of aggressive behavior at intake was the most significant predictor of adolescent delinquency.<sup>8</sup> Ecological variables, especially low socioeconomic status, also played a predictive role in adolescent outcome. Looking at offenses against property they found significant prognostic contributions are made by urban residence, number of children in the family, and aggressive behavior at intake. Not surprisingly, the quality of early academic function predicts similar functioning 5 years later.

Loney and Paternite are careful to point out that the multiple regression technique used is predictive pragmatically in that knowledge of a particular variable allows one to make predictions about another variable. "It is not predictive in the causal sense."

In a further study by Loney and colleagues of 22 of their subjects<sup>9</sup> when they reached the ages of 21 to 23, researchers again showed that the outcome of ADD is most likely to be affected by whether or not the child has associated conduct or oppositional disorder. In the later study, initial IQ was also an important prognostic factor.

August and his colleagues, <sup>10</sup> appropriately seeking to validate the accumulating evidence that antisocial aggressive behavior at intake carries important prognostic weight, have at least begun to make headway in that direction. The usual difficulties with follow-up research obtained: in this case the duration of follow-up was short; mean age at follow-up was only 14 years, and there was considerable attrition of subject population during that 4 years. Nevertheless, they have some justification for concluding:

In summary, our findings are additional evidence that there are at least two types of hyperactive children. . . . The boys in one group present a clear picture of aggressive conduct disorder during childhood, . . . tend to continue to be over-aggressive and anti-social as young adolescents. These are the hyperactive boys who are personally at high risk for later delinquency. On the other hand, there are hyperactive boys who show little if any signs of conduct disturbance, who have a relatively higher prevalence of cognitive problems . . . and who show few signs of behavioral deviance at follow-up beyond their difficulties with attention and impulsivity.

The poor prognosis of children with a major aggressive component in their behavior is not a new finding. In a comprehensive review of follow-up studies related to psychopathological disorders of children, Robins<sup>11</sup> states, "the antisocial behaviors of children have been found to be a remarkable persistent set of behaviors. . . . Of all the behaviors observed in the Fels study aggression was the most persistent over time." Robins found juvenile antisocial behavior the single most powerful predictor of adult psychiatric status. However, before the physician abandons hope for all the mean, aggressive, troublemaking children, another conclusion by Dr. Robins is revealing. "We also, for the most part, are still unable to identify which particular children with conduct disorders have poor long-term prognoses. We know about half will continue their difficulties into adulthood, but we are unable to predict with any certainty which children will and which will not." In other words, about half of the conduct problem children will not be delinquent adults, and we may very well never be able to achieve the fine tuning of prognostic factors which will enable us to accurately predict outcome in the individual child.

However, the physician who would like to have at least a "ball-park" estimate on what the future holds for his or her young patient will need to acquire some information about the environment, including socioeconomic status and parenting styles, as well as various behavioral elements characterizing the child. This information, as has been discussed under diagnosis, will have to come from par-

ents, teachers, other school personnel, and sometimes the police or parole office.

In organizing reports of these informants, the behaviors described under "Conduct Disorder" in the third edition of the *Diagnostic and Statistical Manual* (DSM-III)<sup>12</sup> can be useful. Conduct disorder is divided into four main subtypes, though the authors point out that the validity of the subtypes is controversial. The described behaviors certainly include those Loney and associates<sup>6,8,9</sup> and August and associates<sup>10</sup> mentioned when they discussed aggressive behaviors. DSM-III defines conduct disorder as follows:

The essential feature is a repetitive and persistent pattern of conduct in which either the basic rights of others or major age-appropriate societal norms or rules are violated. The conduct is more serious than the ordinary mischief and pranks of children and adolescents. . . . The Aggressive types are characterized by a repetitive and persistent pattern of aggressive conduct in which the rights of others are violated. . . . The Undersocialized types (show) a lack of concern for the feelings, wishes, and well-being of others, as shown by callous behavior. . . . Appropriate feelings of guilt . . . are generally absent. . . . Such a child may readily inform on his or her companions and try to place blame on them. 12

A teacher rating scale that clearly differentiates the subtypes of ADD can be a useful tool. Investigators at the University of Illinois (where the scale was developed) feel ACTeRS is particularly helpful in demonstrating the presence of conduct disorder–aggression, oppositional behavior, or whatever one wishes to call it, and also provides standards for comparison with the average child with respect to the severity of the behavior.

The physician, who can be a powerful figure in molding the all-important expectations of parents, should keep in mind that there are some ADD children who cannot sit still, cannot keep on task, who never seem to finish anything, are unable to control impulsivity, and may not be very popular with their peers, but they are basically good kids: not mean, not malicious, not defiant, and in fact would like to please if they could. If such children also are fortunate enough to have loving and caring parents who are not poor, there is now reason to believe that we can be optimistic about their ability to eventually find a satisfactory niche in the adult world. And, according to Robins, 11 as many as half of those with conduct problems will not carry these seemingly ominous behaviors into their later years. There is enough evidence now accumulated about outcome that the physician can in good conscience avoid gloomy and possibly self-fulfilling prophecies.

### NATURAL HISTORY OF ADD

In a relatively early publication (1971) Dr. Gabrielle Weiss and her group<sup>13</sup> reported a study of 64 children who 5 years previously had been diagnosed as hyperactive. The mean age at follow-up was 13. There had been some drug treatment but it had been sporadic, unmonitored, and usually of such brief duration that these children can be considered untreated children. There had been essentially no behavioral intervention and no remedial teaching. A matched control group for about half of the subjects was picked up at the time the outcome measures were made.

The most striking finding was that although restlessness had been the main problem for all the subjects 5 years earlier, it was no longer a major complaint about any of the children at the 5-year follow-up (after the elapse of 5 years). However, restlessness was still present, although it was no longer considered a severe problem. The restlessness seemed to consist mainly of fiddling around with small objects at their desks—the conclusion was that they really had not outgrown their restlessness but they expressed it in less disturbing ways than had been the case 5 years previously. Distractibility as measured by direct classroom observations was still present. Forty-five percent of the mothers considered distractibility or poor concentration the child's chief problem. And in fact, they found that many of the children themselves complained about this problem. The teachers still found the patients more aggressive than was true of the control group. Seventy percent of the mothers described their children as emotionally immature, lacking in ambition, and unable to maintain goals; 30 percent said their children had no friends; 25 percent manifested antisocial behavior, and 10 percent had had court referrals. The teachers found their behavior and social adjustment significantly worse than the normal controls, and reported poor academic functioning in 80 percent of the children. Seventy percent had repeated at least one grade, and half of these had repeated two or more grades. Only 3 of the 64 were doing aboveaverage school work, and these children had IOs of above 125. When the patients were matched with the controls according to IO, they were still doing significantly worse on oral reading, arithmetic, and writing.

On the whole, the data available on what has happened to hyperactive children first observed in the early primary grades and then restudied again at ages 13 to 15 showed that not much improvement had taken place during that period of time.<sup>3-5</sup> Their restlessness was less obnoxious to observers but poor ability to concentrate, behavioral immaturity, deficient motivation and goal-oriented

behavior, difficulty in making friends, antisocial behavior, and strikingly poor school performance were still significant attributes of these children. Such findings are consistent from one center to another even with the use of different methods of getting the information. Keeping in mind that there are always exceptions, the physician is now in a position to confidently answer the anxious mother who asks if her child will indeed outgrow his or her problems by age 12 as she has so often heard. The honest answer will, unfortunately, be "probably not."

But life goes on for a long time after age 12 or even 15. As many parents of relatively normal children know, the discouragement and despair we feel often ameliorates with time. Dr. Weiss, with her coworker Dr. Lily Hechtman and others, has now published an impressive series of papers on a 10-year follow-up of hyperactive children. 14-17 They were able to collect good data on 75 young adults with a mean age of 19.5 years and a range of 17 to 24 years. These individuals had been assessed originally 10 to 13 years previously when they were 6 to 12 years old. Restlessness and poor concentration were their main complaints, and these difficulties had been present since their earliest years. They presented severe problems both at home and at school. Forty-four control subjects were compared to the hyperactives and were matched for age, sex, and economic class. As in the earlier study by Weiss and associates<sup>13</sup> these 75 hyperactive children were also an essentially untreated group. Some had had brief periods of drug treatment but it had been sporadic and incidental, and despite the fact that many of the children had at one time or another severe behavior problems, there had been negligible behavioral intervention or psychotherapy.

Each subject, as part of the end-point work-up, had an extensive interview with a child psychiatrist which included detailed biographical, school and work histories, a history of court referrals and what they call nonmedical drug use, including abuse and drug dealing. A psychiatric assessment of each individual's behavior during the interview was also made. What did they find?

For the biographical information they found no difference between hyperactives and controls in the number "doing nothing." Fewer of the hyperactives were still living with their parents, there were no differences in sexual history, but the hyperactive subjects had had a significantly larger number of automobile accidents.

In school history, the hyperactives completed significantly less education than the controls, but the mean difference in education was less than one year. Significantly more had received poor grades, had repeated grades, and had been expelled from school. (Remember, "significant" is being use here strictly in its statistical meaning.)

There was a trend, but only a trend, for more hyperactives than controls to have had court referrals in the previous 5 years. However, and this is an important point, there was no difference between the two groups in the number of subjects who had court appearances within the last year before end-point work-up.

Hyperactives used nonmedical drugs significantly more frequently in the past 5 years but—and this is again important—there was no difference between the groups with respect to drug use in the past year. In other words, the hyperactives seemed to be distinctly improving with age year by year in the late teens and early twenties.

The psychiatric assessment showed no significant difference between the two groups in their ability to relate to the examiner and in their verbal ability. The hyperactives had more so-called problems of adjustment, and fewer friends. They were also more restless during the interview, and the hyperactives were more frequently diagnosed as having "personality trait disorders," (that is "impulsive" and "immature—dependent" traits). Two hyperactives were diagnosed as borderline psychotic in comparison to none of the controls, but this difference was not statistically significant—that is, it could have happened by chance. No subjects were psychotic.

What about the work history? This is really the most interesting and important finding. It is an important *new* finding, a rare event in this field. It is also good news—another rare event in ADD research.

There was no difference in job status (using the Hollingshead scale) between hyperactives and controls. There was no difference in vocational aspirations, nor in whether the aspirations were judged by the psychiatrists to be realistic. The job satisfaction of the hyperactives was no different than the controls. Rating scales containing the same questions regarding competence were sent to high schools and employers of the adult hyperactives and the normal subjects. The hyperactives were found inferior by the teachers on all items on the questionnaire but there was no difference between the groups on employers' questionnaires. That appears to be a finding of great importance.

Although some competence in reading and arithmetic is clearly a vital asset in our society, the fact is that some people cannot, perhaps will not, but certainly do not do well in school. That doesn't necessarily mean that there aren't a lot of other things they can do in the world that will give them satisfaction and allow them to be self-supporting. Dr. Weiss has shown that certainly many of the hyperactive children she studied are in this group.

In summary, Dr. Weiss' study of the natural history of hyperactive individuals can be interpreted as showing that if you wait long enough and get them through school with a little learning, many can

indeed be said to be functioning at an acceptable level. Most will not be scholars and professionals, but then, very few people are.

Satterfield and associates, <sup>18</sup> working in the Los Angeles area, reports results in considerable contrast to the Weiss group. The mean age of subjects was 17.3 years (range 14 to 21), and the researchers counted actual police records of genuinely serious crimes in the ADD and control groups. A stunning 48 percent of ADD subjects were found to have arrest records for serious crimes (significantly greater than the arrest records of the controls).

Satterfield and associates contend that the unusually large amount of criminal behavior found can be attributed to actually examining police records instead of using the reports of interviewees. But before it is possible to evaluate the true importance of these seemingly startling finds further information is needed. Satterfield and colleagues describe only the general class of crimes: "Serious crimes included robbery, burglary, grand theft, grant theft automobile, and assault with a deadly weapon." Serious crimes, indeed, but we are not told how many of each of the crimes were committed. That is, it means something different if 15-year-old boys take someone else's car on a joy ride than if 20-year-olds are caught robbing banks or assaulting with deadly weapons. We are not told if the number of arrests varied with age as did the Weiss group. Were the Satterfield arrests diminishing as the subjects approached the age of 21?

Because of the extraordinarily high level of arrests in his group and because, as has been discussed, antisocial behavior at intake is now recognized as an important predictor of future antisocial behavior, surely some information about the aggression status of the Satterfield group at intake could be expected. The only claims Satterfield makes for his teacher rating scale are that it has good test-retest reliability, and validly differentiates placebo from treatment groups. He makes no claim that his scale delineates the different behavioral patterns of his subjects. In order to reconcile the findings of Weiss and Satterfield we must either assume that Satterfield's subjects included a great many children with severe conduct problems in whom delinquent behavior is highly probable, or that their behavior will improve as they mature. The inconsistencies in the findings of these two groups of investigators point up the difficulties of interpreting research results when we do not have an accurate description of the specific behavioral characteristics of this heterogenous group of children. ADD or hyperactivity are convenient and legitimate titles, but that does not tell us, for example, if the child has a large component of aggressive, antisocial behavior. Some do, some do not.

An interesting study which provides pertinent information about the natural history of hyperactivity and seems to confirm Dr. Weiss' findings was done by Borland and Heckman, who examined the records collected in a child guidance clinic between 1950 and 1955. This was before the days when the diagnosis of hyperactivity was made, but by carefully studying all the information in the records they found a number of boys whose history and symptoms clearly conformed to the diagnosis of hyperactivity as now made. They searched for and found 20 of the men who had been worked up 25 years previously and who agreed to participate in this study. The controls used were an interesting choice, brothers of the 20 hyperactive subjects; the hyperactive and normal brothers were compared. The mean age of the subjects was 30 years, and of the brothers 28 years.

Most of the hyperactive subjects had completed high school and each was self-supporting and steadily employed. Significantly more of the hyperactives than their brothers were nervous, restless, and had difficulty controlling their temper. They changed jobs more often than their brothers but they also worked more hours than their brothers—many of them were moonlighting. The additional jobs were partly to earn more money, but also each explained the extra work as a means of avoiding feelings of restlessness and nervousness in periods of inactivity. The hyperactives had socioeconomic levels significantly lower than their brothers.

This report must be considered an optimistic one, showing that men who had had sufficiently severe problems with hyperactive behaviors 20 to 25 years previously that they had been taken to a child guidance clinic, were at maturity not experiencing serious social or psychiatric problems. Most had completed high school, a few had gone to college, they were steadily employed and self-supporting, and most had achieved middle-class status. Many were still nervous and restless and they had not done as well in the world as their brothers. Although this is a less tight study than that of Dr. Weiss and the number of subjects studied is much smaller, the correspondence of findings between the two investigators strengthens the evidence that in very long-term follow-up the fate of the hyperactive child is not nearly as poor as we might have expected from their chronically poor school performance and generally defective behavior in the early years.

The Weiss and Borland grown-up subjects have much in common with some of the young adults who back in the mid-1970s were primary school children who made up the subject population at the University of Illinois. For example, J.L., now age 22 and recently seen by the project physician, is a cheerful, energetic, outgoing

young man who managed to finish high school, kept there only by his enthusiasm for the athletic activities, and is now: (1) a fireman in a local fire department 30 hours a week, (2) a teacher at the local fire service institute 20 hours a week, (3) a volunteer firefighter for several small neighboring communities, and (4) a bouncer at a lively local night spot every Friday and Saturday night. If he does less, he is bored.

Until there are studies which differentiate subgroups of ADD children and carry out well-controlled anterospective research, which, to be realistic, may be too expensive to be done in the present constricted research climate, we must go with the conclusions of the outstanding research group in this field. In summing up the findings on the natural history of this condition we will use the words of Weiss and associates: "However, the differences between groups were generally not significant in the year prior to evaluation, and tests indicate that they had attained similar levels of moral development. Results suggest a more encouraging adult outcome than has previously been expected for hyperactive children."

### EFFECT OF THERAPY ON OUTCOME

# Stimulant Drugs

These are without doubt the most frequently used treatment as well as the most thoroughly investigated. For the instantaneous amelioration of behavioral problems there is almost certainly no other intervention so effective in the short term. The doctor gives the magic potion and can often have the heady experience of rescuing overnight a beleaguered family, teacher, and patient. But is there evidence that in the long run drug treatment helps children make up their learning deficits, helps them to work at grade level, keeps them out of trouble with authorities both in and out of school, and makes them more socially acceptable adults than if they had not taken the medication? The answer is that we do not know and neither are we likely to know at any time in the forseeable future. The necessary research has not been done: a randomized, controlled clinical trial on two large groups of ADD children (both groups made up of drugresponders), one on active medication with meticulous safeguards to guarantee compliance, and the other group on placebo, to be carried out for a minimum of 7 to 10 years, and with no other interventions to muddy the results. Such a trial has not been done and it will almost certainly not be done.

Nevertheless, earnest investigators have tried to do what they can to find out if stimulant treatment makes for better outcome in

the long term. The general tenor of whatever has been done is that, although stimulant drug treatment is in many ways satisfactory in the short term, the outcome over a period of years does not seem to have much effect. In fact, this position is now essentially accepted as proven by many who write on the topic.<sup>20–22</sup>

Such docile, unquestioning acceptance of the results of drug research which does not conform to the controlled clinic trial paradigm now essential in intervention assessment is remarkable. Scientific rigor is certainly expected in all short-term stimulant drug studies. And there is an additional defect in all long-term drug research in ADD which is sufficiently serious that we must conclude the long-term effects of regular treatment of ADD with stimulant drugs are not known. All investigators in this field totally ignore (or, rarely, provide mere lip service to) a cause for therapeutic failure that has been thoroughly studied, found to be "a protean feature of all regimens involving self administration" (most especially in long-term treatment), and very frequently reported with much concern in current medical literature—noncompliance!

Barkley and Cunningham,<sup>24</sup> in an influential review of outcome studies, were greatly concerned about the quality of studies they reviewed, when they found that out of over 120 research reports there were only 5 that could be judged well-designed and controlled. In the review discussing 17 studies using "objective" tests and measures of academic performance, they concluded, "these drug studies indicated that the stimulant drugs do not appreciably improve the academic achievement or outcome of hyperactive children."

Barkley and Cunningham, despite all their emphasis on rigor in research design before they will so much as consider including a discussion of a paper in their review, apparently do not consider attempts on the part of the investigator to find out if the subject was actually taking the drug under study of the least importance. In actuality, it is not merely an important element of rigor in drug assessment research, it is essential, and especially so in the face of negative results.<sup>25</sup>

In a critical review of the Barkley and Cunningham paper, Sprague and Berger<sup>26</sup> demonstrate that the standardized achievement tests which were used in most of the 17 studies reviewed are insensitive to the kind of academic changes one would expect in the circumstances which obtained in this research. In two of the studies which according to Sprague and Berger did show significant academic improvement,<sup>27,28</sup> the subjects under study were institutionalized and there is no doubt that good compliance was maintained. Neither study was of sufficient duration to answer questions about the helpfulness of drugs in the long term. The facts are, however, that when institutionalized children who were very likely to be re-

ceiving daily medication were tested, they did significantly better on the drug than without it.

Further evidence of the indifference of the ADD research community to the importance of compliance in drug assessment research is indicated in discussions by Barkley and Cunningham<sup>24</sup> and Weiss<sup>20</sup> of the possible cause of the seeming paradox between striking short-term effects of stimulant drugs and poor long-term outcome. Barkley gives four possible explanations, Weiss provides six. Yet both fail to mention noncompliance as a possible cause of therapeutic failure, despite the fact that the little research published on compliance with stimulant drug regimens in ADD shows that it is, indeed, very poor.

Conrad and associates,<sup>29</sup> in a project which followed treated ADD children for 4 to 6 months, made a conscientious effort to evaluate compliance by keeping records of the number of daily doses dispensed for each child. Two of their study groups were receiving medication; it was found that 24 percent of one group and 50 percent of the other were getting medication irregularly, in arbitrarily reduced doses, or not at all, at the time of post testing, after only 4 to 6 months of treatment.

Firestone<sup>30</sup> recognizes poor adherence to a drug regimen as a "rarely mentioned" but important problem in the studies of the effects of drugs on hyperactivity when he reported the results of a study to determine "normal drug usage patterns in an outpatient child population."

He found that 20 percent had discontinued medication by the fourth month and 44 percent by the tenth month; "all but three families stopped giving their children medication prior to consulting the project or their physician." One must assume that inevitably as the duration of treatment lengthens, compliance becomes even more unreliable, for it is well known that there is "marked" deterioration in compliance as the duration of therapy continues.<sup>23</sup>

Kauffman and his colleagues<sup>31</sup> in a double-blind crossover study of methylphenidate, d-amphetamine, and placebo were meticulous in their effort to create a method of dispensing medication that might be considered to produce optimum patient compliance. Individual dose packages were stapled to a 7-day calendar; the patients were seen by the same pediatrician once a week when they were given another one-week supply of the medication. They were instructed to return their calendar each week and to leave any unused doses attached to the calendar. A urine sample was obtained at each weekly visit and tested by sensitive quantitative methods for the presence of methylphenidate or d-amphetamine. Using the results of urine testing as their standard they found wide variation in the presence of the proper medication in the urine from patient to pa-

tient and from week to week, but the mean rates were "virtually identical regardless of the way in which they were calculated." The mean compliance rate for methylphenidate was 67 percent, and for d-amphetamine 61 percent. Kauffman also found that the evidence from returned capusles suggested considerably greater compliance than that by drug assay. Returned pills indicated only 13 percent noncompliance during methylphenidate periods and 18 percent while receiving d-amphetamine!

Evidence of "negative compliance" was also found—seven instances of active drug present in the urine when the child was supposed to be on placebo. (These were children who had been on stimulant medication prior to their enrollment in this program and presumably had active medication at home).

This is certainly the most careful compliance study to date on the use of stimulants in ADD. However, Kauffman and associates failed to mention a possible source of exaggerating the rate of compliance even with their method. Although undoubtedly the patients were not informed of the purpose of the urine collection one can probably assume that medication was more likely to be taken on the day of the visit to the doctor than on an ordinary day.

In addition to the general tendency toward noncompliance with almost any medication, stimulant treatment for ADD is undoubtedly more prone to neglect than most drug treatments. As previously reported, 52 ADD children who had been followed carefully at the University of Illinois were interviewed to find out their attitude toward drug taking and to check the reliability of the interview by comparing their statements to known facts about the child.<sup>32</sup> Of the 52 interviewed, 22 stated unequivocally that they disliked taking stimulants. There were 10 additional children who did not admit to objecting, but it was known from repeated episodes recorded in their files that they also disliked the medication and would try to avoid taking it at times.

The children admitted using a variety of methods to avoid taking the medication: deliberately neglecting to remind a forgetful teacher or parent to supply a pill, surreptitiously throwing the medication away, "cheeking" it temporarily until no one was watching, initiating bitter arguments with parents every morning, and refusing to take medication as they became older were common practices. Thirty-four of the 52 subjects interviewed admitted to or were known to try to avoid taking medication by one or more of these methods.

Table 4–1 provides the reasons given by the children for their powerful dislike of taking stimulant drugs.

These findings are, by the way, directly contradictory to the claim by Whalen and Henker, 2,33 based on unverified information

from interviews, that children become strongly dependent on drugs for acceptable classroom behavior. The authors hypothesize that such dependence may interfere with the child's efforts to take responsibility for self-improvement. The verified interviews of Sleator and associates<sup>32</sup> showed opposite results. One fairly typical child (unpublished data), recognizing sadly that he seemed to need the medication to maintain self-control, stated that he tried hard to notice how he behaved when he was on medication so he could act the same way without it. The reward of being taken off medication was a stimulus to many of the children in our efforts to help them improve unmedicated behavior.

The title of this section promises some information on the effects of stimulant treatment on eventual outcome in ADD children. So far we have discussed only, for obvious reasons, noncompliance in stimulant-drug taking. However, if for no other reason than because material published previously has had such an important effect on the thinking of the research community in this field (that is, it is now pretty much taken for granted that in the long run medication is not helpful), some brief mention should be made of the research on which this opinion is based.

Mendelson and associates,<sup>3</sup> Heussey and associates,<sup>4</sup> and Loney and associates<sup>34</sup> could hardly have measured compliance, as they were doing retrospective studies—that is, tracking down children who had been diagnosed as hyperactive and for whom treatment had been started at various points in time before the follow-up data were accumulated. Mendelson and associates<sup>3</sup> in fact, do not claim that their work assesses treatment effects, although it is so interpreted by Barkley and Cunningham.<sup>24</sup>

Loney and associates<sup>34</sup> compared 26 children given only shortterm behaviorally oriented counseling to 25 boys treated with stimulants. There was no relationship found between treatment with stimulant drugs and long-term academic outcome. The *only* information provided about the medication of the drug-treated subjects is that "all but one of the medicated subjects took medication for at least six months, and none of them was still taking medication at the time of follow-up."

Two of the long-term drug outcome papers indicate some sensitivity to compliance problems. Riddle and Rapoport<sup>35</sup> express confidence that theirs was "an unusually drug faithful population." However, the assumption of the physician that this middle-class group was an unusually "drug faithful" population without actual monitoring is not convincing. It has been shown in one study that of 459 children of middle and upper middle class suburban, professional families, only 56 percent completed (as determined by urine tests) a 10-day course of penicillin therapy.<sup>36</sup> It has also been shown

in several studies that physician assessment of patient compliance is little better than chance.<sup>37</sup> In addition, in the Riddle and Rapoport study, when the children were taken off medication prior to testing, only 50 percent of teachers felt the children were more difficult during the weeks off medication than they had been previously. This is a finding that may very well be suggestive of considerable noncompliance.

Weiss and her colleagues<sup>38</sup> also give considerably more specific information about their patient's medication than do other authors. However, the subjects in this study took their noon pills to school in their lunch boxes and were responsible for taking it themselves (personal communication). Interview data (plus recognition by Weiss and associates of the dislike of children for taking medication) suggest that the noon pill may not have been taken very regularly. How regularly the morning medication was taken is simply not known.

Kauffman and associates<sup>31</sup> sum up the situation briefly and clearly:

However, failure of the patient to take medication as dictated by the investigational protocol has gone totally unrecognized as a potential contributor of the confusion and contradiction among studies. This is unfortunate because the relatively high rate of noncompliance observed in this study raised serious questions regarding the reliability of behavioral and learning data obtained from even relatively well controlled studies. Unpredictable patient compliance adds an additional variable to an already confusing area of research and may account, in part, for the highly variable and conflicting results reported over the years. Failure to take medication may substantially reduce the apparent efficacy of an active pharmacologic agent. Likewise, self-medication with active drug while the patient is ostensibly receiving placebo will erroneously exaggerate any placebo effect. Either deviation in medication-taking behavior on the part of the patient will reduce the ability of a study to detect real drug effects no matter how elegant and well controlled the experimental protocol.

Under the circumstances, the conclusion of this section must be that the effects of medication on long-term outcome are not known; the difficulties of good compliance monitoring are so great with methylphenidate (gas-chromatographic analysis of urine at random times) that good data may never be achieved.

Should the fact that stimulant drugs have not proven to be in any sense a cure for ADD preclude their use? Those who have had experience with these medications know full well that they provide at least a crutch when a crutch is desperately needed. Epilepsy is not cured by anticonvulsant drugs, diabetes is not cured by insulin, eczema is not cured by hydrocortisone ointment, nor is asthma cured in those children whose disease is so severe that steroids must be given. Other examples abound. Do doctors therefore spurn these drugs as useless? Indeed not! Stimulants in some restless, inattentive, impulsive children can greatly relieve these disturbing symptoms, and a troubled child (and family) should never be denied this relief because there is no research evidence that the drugs result in a cure.

### REFERENCES

- 1. The President's Biomedical Research Panel Report: The Place of Biomedical Science in Medicine. The Overview Cluster's Observations. Thomas L (chairman). Nutrition Today 2:18–27, 1976.
- 2. Whalen CK, Henker B: Hyperactivity and the attention deficit disorders: Expanding frontiers. Pediatr Clin North Am 31:397–427, 1984.
- Mendelson W, Johnson N, Stewart MA: Hyperactive children as teenagers: A follow-up study. J Nerv Ment Dis 153:273–279, 1971.
- Huessy JR, Metoyer M, Townsend M: 8–10 year follow-up of 84 children treated for behavioral disorder in rural Vermont. Acta Paedopsychiatrica 40:230–235, 1974.
- 5. Dykman RA, Ackerman P: Long term follow-up studies of hyperactive children, in Camp BW (ed): Advances in Behavioral Pediatrics, ed 1. Greenwich, Conn, JAI Press, 1980, pp 97–128.
- 6. Langhorne JE, Loney J: A four-fold model for subgrouping the hyperkinetic syndrome. Child Psychiatry Hum Dev 9:153–160, 1979.
- 7. Quay HC: Classification, in Quay HC, Werry JS (eds): Psychopathological Disorders of Childhood, ed 2. New York, Wiley, 1979, pp 1–42.
- Paternite CE, Loney J: Childhood hyperkinesis: Relationships between symptomatology and home environment, in Whalen CK, Henker B (eds): Hyperactive Children: The Social Ecology of Identification and Treatment. New York, Academic Press, 1980, pp 105–141.
- Loney J, Kramer J, Milich RS: The hyperactive child grows up: Predictors of symptoms, delinquency and achievement at follow-up, in Gadow KD, Loney J (eds): Psychosocial Aspects of Drug Treatment for Hyperactivity. Boulder, Colo, Westview Press, 1981, pp 381–415.
- August GJ, Stewart MA, Holmes CS: A four-year follow-up of hyperactive boys with and without conduct disorder. Br J Psychiatry 143:192–198, 1983.
- Robins LN: Follow-up studies, in Quay JC, Werry JS (eds): Psychopathological Disorders of Childhood, ed 2. New York, Wiley, 1979, pp 483–513.
- 12. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders DSM-III, ed 3. Washington, DC, American Psychiatric Association, 1980.

- 13. Weiss G, Minde K, Werry JS, et al: Studies on the hyperactive child VIII: Five year follow-up. Arch Gen Psychiatry 24:409–414, 1971.
- 14. Hechtman L, Weiss G, Perlman T, Hopkins J, et al: Hyperactives as young adults: Prospective ten-year follow-up, in Gadow KD, Loney J (eds): Psychosocial Aspects of Drug Treatment for Hyperactivity. Boulder, Colo, Westview Press, 1981, pp 417–442.
- 15. Weiss G, Hechtman L, Perlman T, et al: Hyperactives as young adults: A controlled prospective ten-year follow-up of 75 children. Arch Gen Psychiatry 36:675–681, 1979.
- Hechtman L, Weiss G: Long-term outcome of hyperactive children. Am J Orthopsychiatry 53:532-541, 1983.
- 17. Hechtman L, Weiss G, Perlman T: Hyperactives as young adults: Past and current substance abuse and antisocial behavior. Am J Orthopsychiatry 54:415–425, 1984.
- Satterfield JH, Hoppe CM, Schell AM: A prospective study of delinquency in 110 adolescent boys with attention deficit disorder and 88 normal adolescent boys. Am J Psychiatry 139:795–798, 1982.
- 19. Borland BL, Heckman JK: Hyperactive boys and their brothers: A 25 year follow-up study. Arch Gen Psychiatry 33:669-675, 1976.
- 20. Weiss G: Controversial issues of the pharmocotherapy of the hyperactive child. Can J Psychiatry 26:385-391, 1981.
- 21. Henker B, Whalen CK: The many messages of medication: Hyperactive children's perceptions of attributions, in Salinger S (ed): Ecosystem of the "Sick" Child: Implications for Classification and Intervention. New York, Academic Press, 1980, pp 141–165.
- 22. Cowart VS: Stimulant therapy for attention disorders. Medical News IAMA 258:279-287, 1982.
- 23. Sackett DL, Snow JC: The magnitude of compliance and noncompliance, in Haynes BR, Taylor DW, Sackett DL (eds): Compliance in Health Care. Baltimore, Johns Hopkins University Press, 1979, pp 11–45.
- 24. Barkley RA, Cunningham CE: Do stimulant drugs improve the academic performance of hyperkinetic children? A review of outcome studies. Clin Pediatr 17:85–92, 1978.
- 25. Goldsmith CH: The effect of compliance distributions in therapeutic trials, in Haynes BR, Taylor DW, Sackett DL (eds): Compliance in Health Care. Baltimore, Johns Hopkins University Press, 1979, pp 297–308.
- 26. Sprague RL, Berger BD: Drug effects on learning performance: Relevance of animal research to pediatric psychopharmacology, in Knights RM, Bakker DJ (eds): Treatment of Hyperactive and Learning Disordered Children. Baltimore, University Park Press, 1980, pp 167–183.
- 27. Bradley C, Bowen M: Amphetamine (benzedrine) therapy of children's behavior disorders. Am J Orthopsychiatry 10:782–788, 1940.
- 28. Christensen D: Effects of combining methylphenidate and a classroom token system in modifying hyperactive behavior. Am J Ment Defic 80:226, 1975.
- 29. Conrad WG, Dworkin WS, Shai A, Tobiessen JE: Effects of amphetamine therapy and prescriptive tutoring on the behavior and achievement of lower class hyperactive children. J Learn Dis 4:45–52, 1971.

- 30. Firestone P: Factors associated with children's adherence to stimulant medication. Am J Orthopsychiatry 52:447–456, 1982.
- 31. Kauffman RE, Smith-Wright D, Reese CA, Simpson R, et al: Medication compliance in hyperactive children. Pediatric Pharmacology 1:231–237, 1981.
- 32. Sleator EK, Ullmann RK, von Neumann A: How do hyperactive children feel about taking stimulants and will they tell the doctor? Clin Pediatr 21:474–479, 1982.
- 33. Whalen CK, Henker B: Psychostimulants and children: A review and analysis. Psychol Bull 83:1113–1130, 1976.
- 34. Loney J, Kramer J, Kosier T: Medicated versus unmedicated hyperactive adolescents: Academic, delinquent and symptomatological outcome. Paper presented at the annual meeting of the American Psychological Association, Los Angeles, 1981.
- Riddle KD, Rapoport JL: A 2-year follow-up of 72 hyperactive boys. J Nerv Ment Dis 162:126–134, 1976.
- 36. Charney E, Bynum R, Eldredge D, et al: How well do patients take oral penicillin? A collaborative study in private practice. Pediatrics 40:188–194, 1967.
- Gordis L: Conceptual and methodologic problems in measuring patient compliance, in Haynes BR, Taylor DW, Sackett DL (eds): Compliance in Health Care. Baltimore, Johns Hopkins University Press, 1979, pp 23– 45.
- Weiss G, Kruger E, Danielson U, Elman M: Effect of long-term treatment of hyperactive children with methylphenidate. CMAJ 112:159–165, 1975.