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ABSTRACT

The study compared the efficacy, side effects, and safety of magnesium pemoline (Cylert) and destroamphetamine (Dexedrine) as compared with placebo. Subjects were 81 children, ages 6-12 years, who evidenced one or more signs of minimal brain dysfunction, and were referred with major complaints of hyperactivity, short attention span, distractibility, poor frustration tolerance, disruptive behavior, and academic problems. Subjects were randomly assigned to the three treatment conditions. During the 8 weeks, medical evaluation occurred four times, psychological testing twice, and parent and teacher ratings weekly. It was found that both drugs significantly reduced symptomatology over placebo controls. Dexedrine produced a more immediate and dramatic effect, with more patients being much improved. Cylert, however, did benefit a substantial number of patients, with fewer anorexic side effects. Neither drug produced hematologic, liver, kidney, or cardiovascular effects of consequence. (KW)

The purpose of this study was to compare the efficacy, side effects and safety of magnesium pemoline (Cylert) and dextroamphetamine (Dexedrine) as compared with placebo. Cylert is a CNS stimulant comprised of pemoline and magnesium hydroxide which has been reported to have significant anti-fatigue and performance enhancing properties in prior studies with adults and children. Dextroamphetamine and the other amphetamines have been successfully used for many years in the treatment of childhood hyperkinesis.

Method

Subjects

Patients were referred from schools, pediatricians and social agencies with a major complaint of severe overactivity, short attention span, distractibility, poor frustation tolerance, disruptive behavior and failure to progress in school at the rate expected on the basis of potential. Patients included in the drug study were to be between six and 12 years of age, to have IQs above 80, and an absence of severe neurotic, psychotic, or neurologic symptoms, or history of family psychopathology sufficient to account for the current behavioral symptoms. In addition, the children were required to have one or more of the following indications of "minimal brain dysfunction": (a) significant history of complications of pregnancy, parturition, delivery, or perinatal complications; (b) delayed or otherwise abnormal developmental milestones; (c) early onset of severe hypermotility; (d) soft neurological signs; (e) abnormal EEG of a non-epileptic type; (f) visual or auditory perceptual impairment; (g) a significant discrepancy between actual school achievement and learning potential.

A medical history, physical and neurologic examination, standardized psychiatric examination, parent and teacher behavior ratings and psychological tests were used to establish conformity with these admission criteria. The physical examination also included a battery of hematologic, chemistry and urinalysis studies.

Eighty-four patients were entered into the study, and 81 completed treatment. There were 74 males and 10 females, all Caucasian except for one Negro. Fifty-nine children had both behavior and academic problems at referral, 19 had only behavior problems, and 6 had primarily academic problems. Fourteen children had adoptive or foster parents, and 46 had a history of severe hyperactivity during the first two years of life. Twenty-four of the children had been retained in school at least once. The children ranged in age from 6 to 12 years, and were largely middle class in social background. The age and social class distributions are shown in Table 1. Thirty percent of the children were left-handed, and about 30% of the parents were left-handed. Twenty-three parents had a history of reading and writing difficulties and 21 parents had a history of hyperactivity in their own childhood.

Design and Procedure

Patients were randomly assigned to the three treatment conditions by consecutive numbers which were precoded by the drug company, utilizing standard randomization techniques. Cylert was administered in 25 mg. tablets, and Dexedrine in 5 mg. tablets. Each patient received two bottles of medication sufficient for an eight-week course of therapy. One bottle with a white label was used for morning administration and the second bottle with a blue label was used for afternoon administration. Because the preliminary studies indicated that

Cylert could be used with a single morning dosage, the afternoon bottles for the Cylert cases contained only placebo. A procedure was followed which required that dosage be adjusted upwards twice weekly in increments of one capsule until improvement was impressive (as judged by parent and teacher phone report), or until side effects required further adjustments. The schedule for drug administration is shown in Table 2. Once an effective dose was reached it was maintained throughout the balance of the eight-week study period. The maximum dosage of Cylert was 125 mg. and for Dexedrine, 40 mg. The actual dosages in the study ranged from 5 to 40 mg. of Dexedrine, with a mean dosage of 20 mg.; and 25 to 125 mg. of Cylert, with a mean of 82 mg. The number of dosage and adjustments were very similar for the three groups with means of 6.2, 6.7, and 7.3 adjustment for Dexedrine, Cylert, and placebo, respectively.

Patients returned for medical evaluation on days 14, 28, 42, and 56 at which time weight, pulse, and blood pressure were recorded. Abbreviated parent and teacher rating forms were obtained at weekly intervals, with some psychological tests repeated at the mid-way period. All psychological tests were repeated at the end of the eight-week period. The schedule of testing and evaluation is shown in Table 3.

Dependent Variables

Symptom Ratings

A 39-item symptom checklist was mailed to teachers at the beginning and end of the drug treatment period. This rating scale had been previously factor-analyzed (Conners, 1969) and yields five factor scores which were separately scored. The five factors are labelled Defiance, Inattentiveness, Anxiety, Hyperactivity, and Sociability. A

93-item Parent Questionnaire was also obtained at the beginning and end of treatment. A previous factor analysis of this instrument (Conners, 1970) yielded eight factors which were separately scored. These factors were labelled Conduct Disorder, Anxiety, Impulsiveness, Immaturity, Psychosomatic, Obsessive, Antisocial, and Hyperactivity. Ten items from the two scales were used as an abbreviated scale and collected at 0, 2, 4, 6, and 8 weeks on the basis of the phone calls to parents and teachers.

Psychological Tests

The following tests were given: Wechsler Intelligence Scale for Children (WISC) (Wechsler, 1949); Harris-Goodenough Draw-A-Man Test (Harris, 1963); the Bender Visual Motor Gestalt Test with scoring by Koppitz (Koppitz, 1964); the Porteus Mazes (Porteus, 1965); the Frostig Test of Developmental Visual Perception (Frostig, 1961); the Wide Range Achievement Test (Jastak & Jastak, 1965).

In addition to these tests, in our laboratory the following tests were obtained: a continous performance test (CPT); the Gates Diagnostic Reading Test (Gates & MacGinitie, 1965); the Gray Oral Reading Test (Gray, 1963); the Illinois Test of Psycholinguistic Abilities (ITPA) (Kirk, McCarthy, & Kirk, 1968); a motor battery consisting of items from the Lincoln-Oseretsky Test of Motor Development (Sloan, 1955); and a measure of hand-arm steadiness.

Results

Global Ratings

A. Clinician. The percent of patients showing improvement at four and eight weeks of treatment is shown in Table 4 for the ratings made by the clinical team. At both four and eight weeks there are

significant treatment effects, with both active drugs better than placebo. At the end of the treatment period approximately 96% of the Dexedrine patients and 77% of the Cylert patients are rated as improved or much improved, while about 30% of the placebo patients are improved, with none being much improved.

B. Teacher. The percent of patients improving at four and eight weeks as rated by the teacher is shown in Table 5. Again, there are highly significant treatment effects for both drugs at four and eight weeks. As with the clinician's ratings it appears that there are more Dexedrine patients showing dramatic improvement, but approximately the same rates of improvement of a moderate degree are occurring. Again, about 30% of the placebo patients show some improvement, but of interest is the fact that 30% also become worse.

Approximately the same results are obtained for the teacher's global ratings of classroom academic work (Table 6). However, there is some indication that the classroom activity is not as impressive at eight weeks as at four weeks.

Factored Ratings

A. Teacher. The five factors of the teacher rating scale were first examined for overall treatment effects by multivariate analysis of variance (Manova). This overall test was significant ($F = 2.36$, $p < .01$). Table 7 gives the mean factor scores and significance levels from the interaction between time and treatments. The results indicate highly significant treatment effects for the Defiance, Inattention, and Hyperactivity factors. When these data are examined for the nature of the changes occurring at each time period (Table 8), a consistent picture emerges. Dexedrine shows a more immediate onset of effect than Cylert, with differences between the treatments being significant at four weeks.

However, by the end of the treatment period at eight weeks, there are no differences between the drugs, with both being superior to placebo. Whereas Cylert shows insignigicant effects at four weeks, by eight weeks its effects on factor scores are indistinguishable from Dexedrine.

Similar results are obtained from the Abbreviated Teacher rating scale, where it may be seen that the effect of Dexedrine is significant as early as two weeks (Table 9 and Figure 1), with Cylert showing clear differences from placebo only at six weeks.

B. Parent. The Manova was significant for parent rating factors ($F = 1.75$, $p < .04$). Table 10 shows that of the eight parent rating factors, four are significantly improved by the drug treatments. Conduct disturbance, impulsivity, immaturity, and antisocial behavior are all improved, as compared with placebo. Table 11 indicates that the same tendency for Cylert to have a more gradual onset of effect occurs in the parent ratings. At week four there are several significant drug-drug differences, all in favor of Dexedrine, but by week eight there are no drug-drug differences. As with the teacher ratings, anxiety-related items are unaffected by either drug. The abbreviated parent symptom rating also shows a drug-drug difference in favor of Dexedrine at two weeks, but just as in the teacher ratings there is no difference on this scale between the two drugs by four weeks, with both drugs continuing to be superior to placebo to about the same extent (Table 12 and Figure 2).

Psychological Tests

The main psychological test scores (exclusive of subtests) were first examined for treatment effects by an overall multivariate analysis of variance. This effect was significant ($F = 2.28$, $p < .004$).

Table 13 and Table 14 give the results for the psychological

tests. Spelling, Reading, Porteus IQs, Frostig Perceptual Quotient, Eye-Motor Coordination and Figure-Ground scores show significant treatment effects. For these measures both drugs show the same degree of improvement, with the exception of the Frostig Figure-Ground scores which do not quite reach significance for the Cylert group.

Laboratory Studies

The results of the blood, chemistiry and urinalysis studies are shown in Tables 15 and 16. One-way analyses of variance indicated no difference among treatments for any of the laboratory values. The incidence of abnormal values was the same for baseline and placebo as for the two active drug groups. In cases where there was an abnormal value at baseline the tests were always repeated, and usually turned out to be laboratory errors or transient effects of unknown origin. No abnormal laboratory values in any of the patients were found which could be related to the drugs. The value of the baseline and placebo measures is shown by the relatively high incidence of spurious abnormal values in these groups.

Systolic, diastolic and pulse-pressure were unchanged for all three groups throughout the study, and ophthalmologic examination were unremarkable. Weight changes were +0.5 kg., +1.1 kg. and +0.9 kg. for Dexedrine, Cylert, and palcebo, respectively. These changes were non-significant between groups.

Side Effects

The major side effects of both drugs were insomnia and anorexia. By the end of the treatment period fewer than 5% of the patients were experiencing moderate or severe insomnia, and all of these were on Dexedrine. Both drugs produced most insomnia between the 17th and 28th day of therapy, and only at day 28 was there a significant drug-placebo

difference (Figure 3). The incidence of severe anorexia ranged from a high of 14% for Dexedrine at day 14, to 4% of patients for both drugs at day 56. Dexedrine produced significantly more sadness and irritability than placebo, but the incidence of these and other side effect complaints were small for both treatments, and in no case did a subject have to be dropped from the study because of persistent side effects after dosage adjustment.

Discussion

Ratings of the efficacy of treatment were made in this study from clinician, parent and teacher using both global ratings and factored symptom lists. All of these ratings give a consistent picture: both active drug treatments significantly reduced symptomatology over placebo controls. All sources of information also are consistent in showing that while Dexedrine acts more quickly, the difference in effect from that of Cylert is relatively small by the end of the eight week treatment period. Further study will be required to determine whether these differences in rate of effect are related to the initial dosages and the rate of dosage adjustment for the two drugs, or are related to intrinsic properties of the absorption, metabolism or central action of the drugs.

Dexedrine appears to produce a more immediate and dramatic effect than Cylert, with more Dexedrine patients being much improved. Nevertheless, Cylert appears to benefit a substantial number of the patients, with fewer complaints of anorexic side effects.

Both active drugs appear to produce no hematologic, liver, kidney or cardiovascular effects of consequence.

Although both active drugs produced significant cognitive,

achievement and perceptual changes, to about the same extent, there were several drug-sensitive tests which surprisingly remained unaltered in this study. For example, in several previous studies the continous performance measure of attention had shown response to Dexedrine or other stimulants, but did not do so to a significant extent in this study. There were a number of trends towards improvement on several of the tests, and further analyses will be done to elucidate the reasons for the lack of group effects. One such possibility is that many subjects may have had ceiling effects with some of the tests, and the data will require examination of those subjects who were more impaired on each test to determine if the trends found are accounted for by those with poorer baseline scores who have room for improvement.

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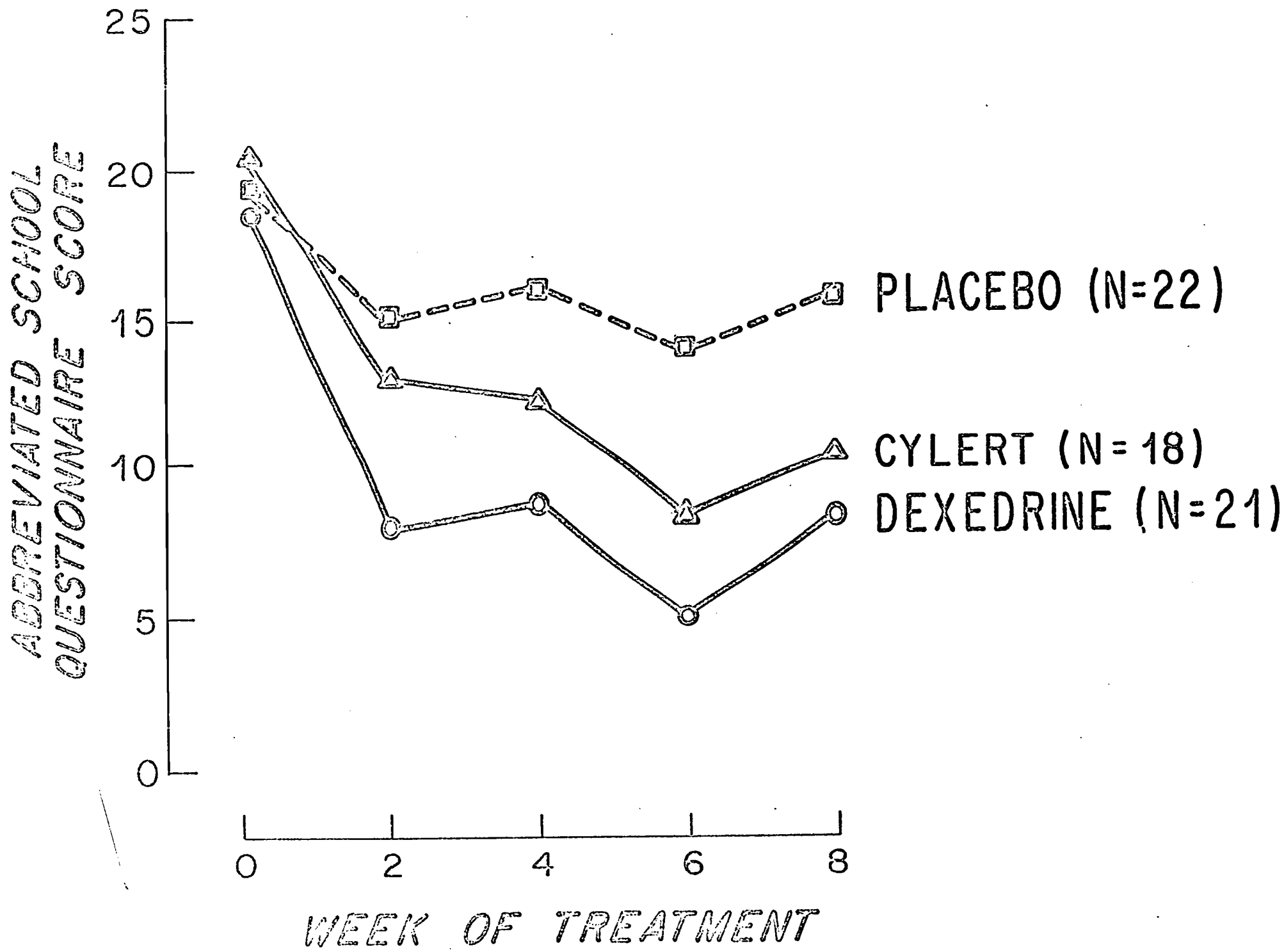
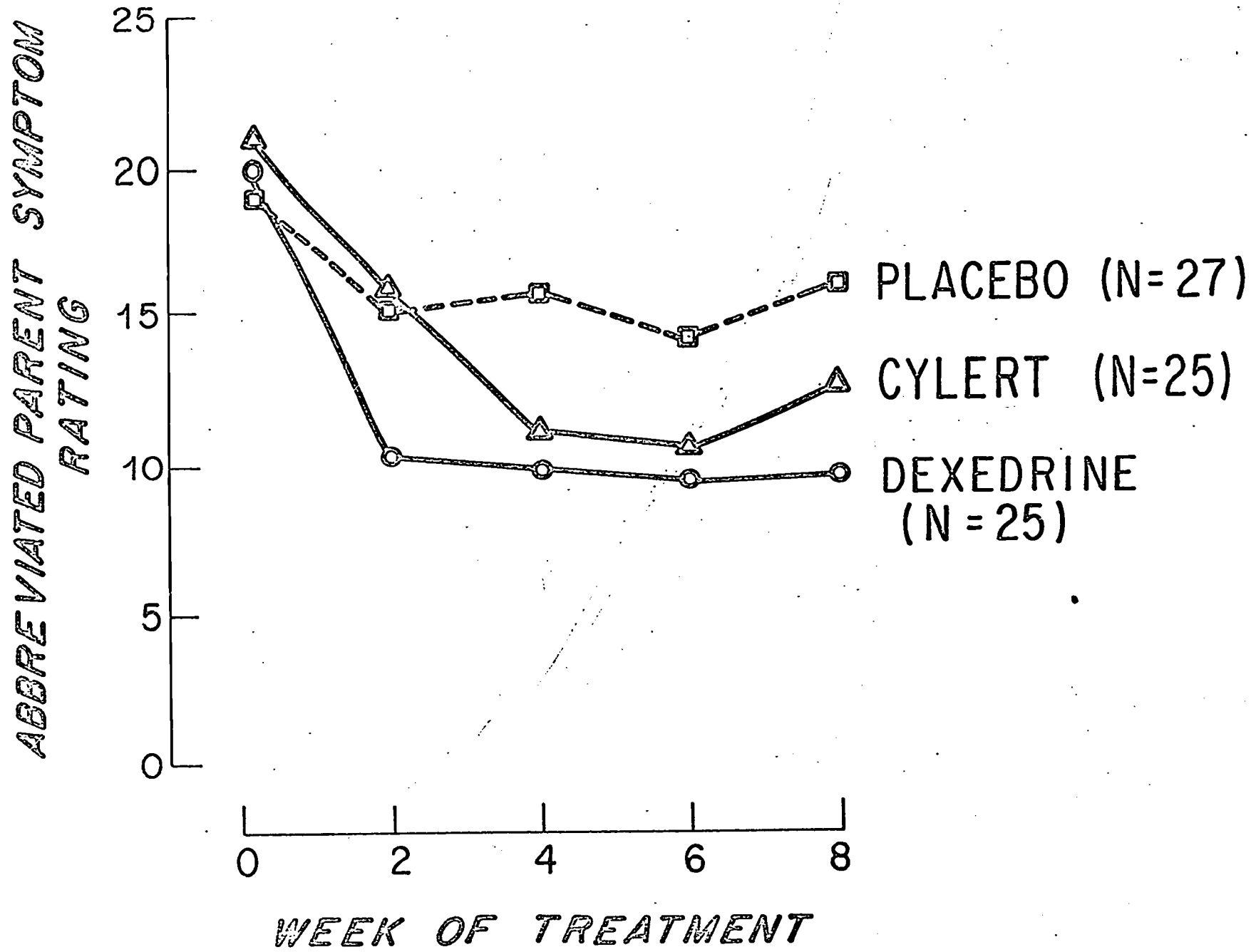
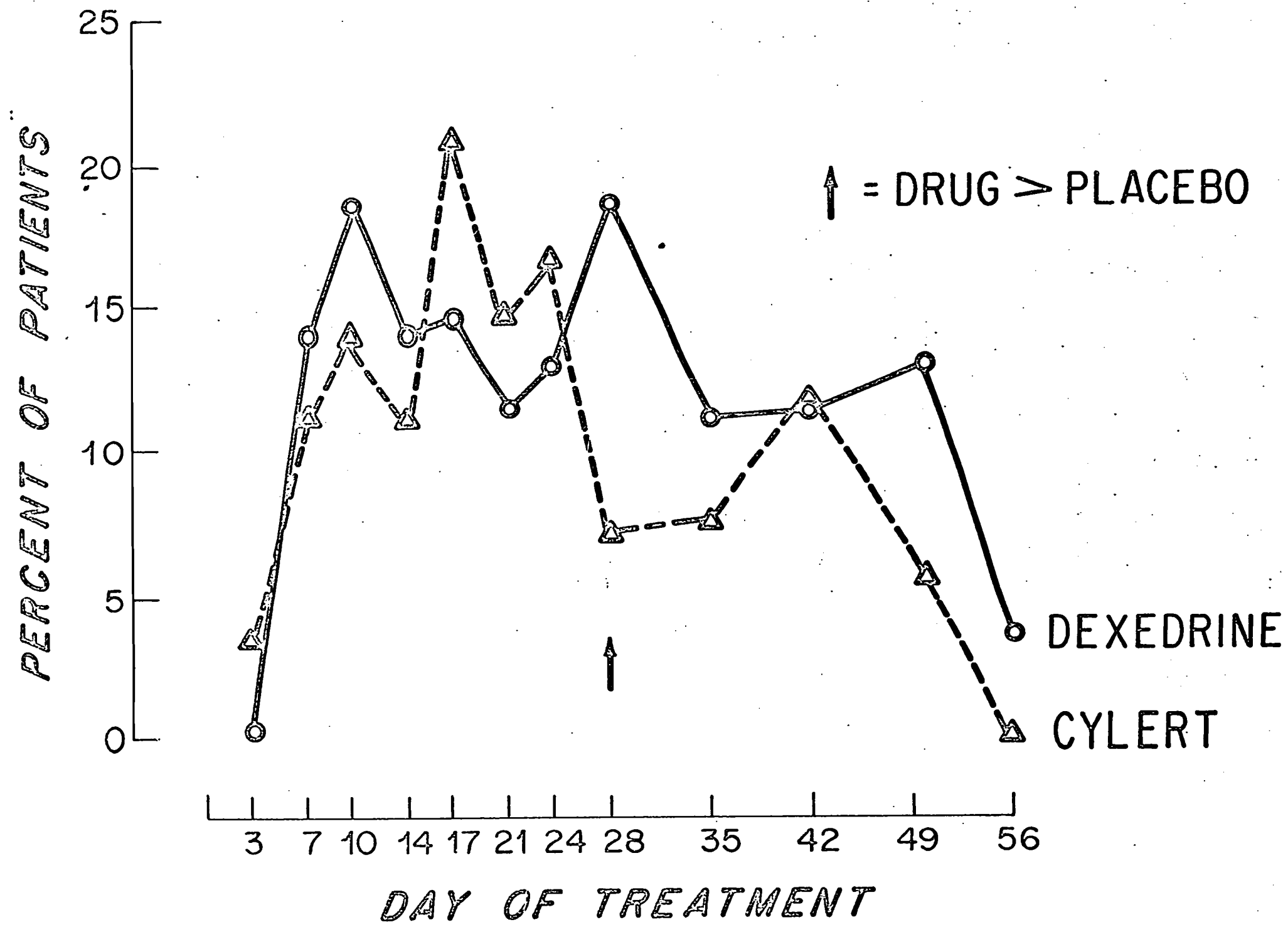
ABBREVIATED TEACHER RATINGS



ABBREVIATED PARENT RATING FORM



MODERATE AND SEVERE INSOMNIA



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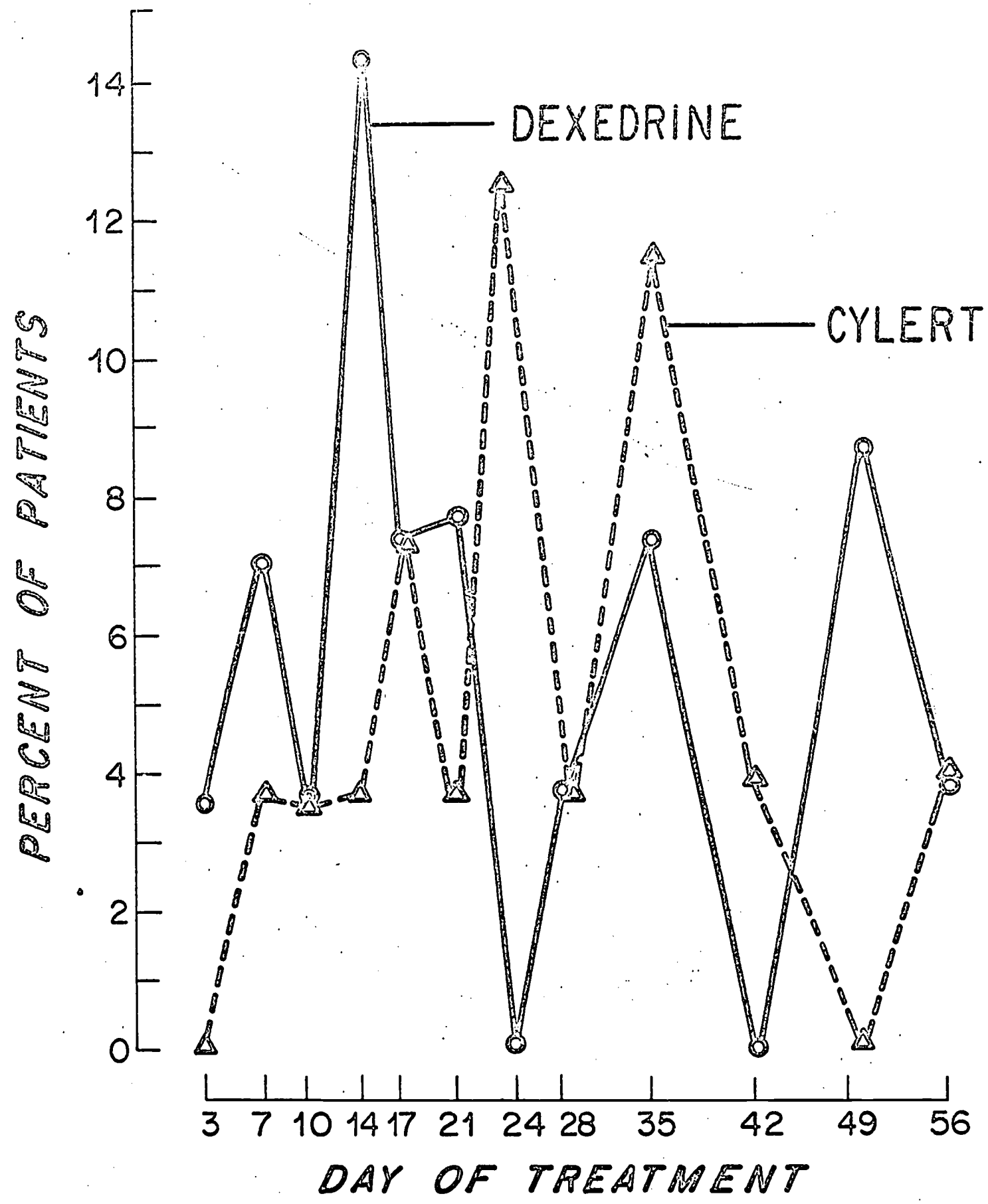

Table 1

Age and Social Class of Sample

Hollingshead Two-Factor Index of Social Position

Class	%	N*
I	7.2	6
II	19.3	16
III	37.3	31
IV	31.3	26
V	4.8	4

*Data not available for one patient

Age Distribution of Sample

Age in Months	%	N
70-72	6.0	5
72-83	20.2	17
84-95	13.1	11
96-108	29.8	25
109-131	26.2	22
131-144	4.8	4

Mean Age = 98.99 months (8.24 years); S.D. = 17.95 months

Table 2

Schedule of Drug Administration

for All Drugs and Placebo

Week of Treatment	Day of Treatment	Number of Pills (Morning Bottle)	Number of Pills (Afternoon Bottle)
1	1	1	0
	4	1	1
2	8	2	1
	11	2	2
3	15	3	2
	18	3	3
4	22	4	3
	25	4	3
5	29	5	3

Table 3

Examination and Testing Schedule

Test	Control	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8
Medical History	*								*
Medical Examination	*				*				*
Laboratory Battery	*				*				*
Wechsler Intell. Scale	*								*
Draw-A-Man	*								*
Bender-Gestalt	*								*
Porteus Maze	*				*				*
ITPA	*								*
Frostig Test	*								*
Wide Range Achievement	*								*
Gray Oral Reading	*								*
School Apperception	*								*
Motor Battery	*								*
Cont. Perf. Test	*				*				*
Teacher Rating	*		*Abb.		*Comp.		*Abb.		*Comp.
Parent Rating	*		*Abb.		*Comp.		*Abb.		*Comp.
Gates Diag. Reading	*								
Standard Physical Exam.	*								
Evoked Response	*								*
EEG	*								
Paired Assoc. Learning	*								*
Psychiatric Examination	*								*

Abb. - Abbreviated parent/teacher rating form

Comp. - Complete parent/teacher rating form

Table 4

Clinical Global Improvement Ratings

at Four and Eight Weeks

Week Four

	Dexedrine (N=27)	Cylert (N=26)	Placebo (N=27)
Much Worse	0.0	0.0	0.0
Worse	0.0	11.5	7.4
Unchanged	11.1	23.1	63.0
Improved	77.8	57.7	29.6
Much Improved	11.1	7.7	0.0

$Chi^2 = 23.7$, $p < .001$

Week Eight

	Dexedrine (N=27)	Cylert (N=27)	Placebo (N=27)
Much Worse	0.0	0.0	0.0
Worse	0.0	7.4	3.7
Unchanged	3.7	14.8	66.7
Improved	63.0	59.3	29.6
Much Improved	33.3	18.5	0.0

$Chi^2 = 35.8$, $p < .001$

NOTE: Cell entries are percent of patients in each treatment group.

Table

Teacher Global Ratings of Overall Behavior at Four and Eight Weeks

Week Four

	Dexedrine (N=26)	Cylert (N=26)	Placebo (N=26)
Much Worse	0.0	0.0	0.0
Worse	0.0	0.0	11.5
Same	11.5	50.0	50.0
Improved	65.4	42.3	34.6
Much Improved	23.1	7.7	3.8

$Chi^2 = 20.4$, $p < .003$

Week Eight

	Dexedrine (N=22)	Cylert (N=22)	Placebo (N=23)
Much Worse	4.5	0.0	13.0
Worse	4.5	4.5	17.4
Same	13.6	31.8	39.1
Improved	40.9	50.0	30.4
Much Improved	36.4	13.6	0.0

$Chi^2 = 19.1$, $p < .015$

NOTE: Cell entries are percent of patients in each treatment group.

Table 6

Teacher Global Ratings of Classroom Performance at Four and Eight Weeks

Week Four

	Dexedrine (N=26)	Cylert (N=26)	Placebo (N=26)
Much Worse	0.0	0.0	3.8
Worse	0.0	11.5	11.5
Same	7.7	38.5	38.5
Improved	73.1	46.2	46.2
Much Improved	19.2	3.8	0.0

$Chi^2 = 20.1$, $p < .01$

Week Eight

	Dexedrine (N=21)	Cylert (N=22)	Placebo (N=23)
Much Worse	4.8	4.5	8.7
Worse	4.8	9.1	17.4
Same	14.3	22.7	39.1
Improved	42.9	50.0	34.8
Much Improved	33.3	13.6	0.0

$Chi^2 = 13.6$, $p < .09$

Table 7

Factor Scores of Teacher Symptom Ratings

at Zero, Four, and Eight Weeks

Factor	Dexedrine (N=23)			Cylert (N=20)			Placebo (N=20)		
Week	0	4	8	0	4	8	0	4	8
Defiance	13.1	4.5	4.9	15.2	11.0	9.7	13.4	8.8	12.2
Inattention	11.1	7.1	6.4	11.5	8.9	7.7	11.1	9.3	9.8
Anxiety	8.4	6.8	6.5	7.0	6.4	5.9	8.9	7.4	6.7
Hyperactive	15.4	6.9	6.2	16.5	11.2	9.8	16.4	12.7	13.3
Sociability	3.8	2.8	2.6	3.9	2.7	2.5	2.7	2.0	2.2

Scores are included only for patients with ratings available at all three periods.

Time By Treatment Interaction Effects

Factor	F	Degrees of Freedom	P
Defiance	3.79	4/120	.007
Inattention	3.64	4/132	.008
Anxiety	0.354	4/126	NS
Hyperactivity	5.52	4/132	.001
Sociability	0.521	4/126	NS

Table 8

Comparison of Effects from Zero to Four Weeks and Zero to Eight Weeks for Teacher Symptom Rating Factor Scores*

Probability Values

Factor	Dex vs Cylert		Dex vs Placebo		Cylert vs Plac.	
	0-4	0-8	0-4	0-8	0-4	0-8
Defiance	.029#	.490	.024	.002	NS	.011
Inattention	.096	.381	.005	.002	.161	.012
Anxiety	.331	.484	NS	NS	NS	NS
Hyperactivity	.014#	.115	.001	.001	.161	.005
Sociability	NS	NS	NS	NS	NS	.090

*Probability values based on two-tail test for drug-drug comparisons and one-tail test for drug-placebo comparisons

#Dexedrine improves more than Cylert

Table 9

Abbreviated School Questionnaire Changes

at Two, Four, Six and Eight Weeks*

Week	Dex vs Cylert		Dex vs Placebo		Cylert vs Placebo	
	t	p	t	p	t	p
0-2	1.95	.057	2.98	.0025	0.67	NS
0-4	2.36	.022	4.26	.001	1.51	.068
0-6	0.50	NS	4.43	.001	3.68	.001
0-8	0.57	NS	3.52	.001	2.74	.004

*Probability values based on two-tail test for drug-drug comparisons and one-tail test for drug-placebo comparisons

Treatment By Time Analysis of Variance for

Abbreviated School Questionnaire Data

Source	Mean Square	df	F-Test	Significance
Treatments	985.53	2	9.65	.001
Subjects	102.115	58		
Time	924.910	4	53.587	.001
Treat X Time	64.539	8	3.739	.001
Time X Subjects	17.26	304		

Table 10

Factor Scores of Parent Symptom Ratings

at Zero, Four, and Eight Weeks

Factor	Dexedrine (N=27)			Cylert (N=25)			Placebo (N=27)		
Week	0	4	8	0	4	8	0	4	8
Conduct	22.8	12.7	12.3	20.9	14.1	12.6	20.2	16.7	16.7
Anxiety	9.4	6.2	6.5	7.8	6.0	5.6	8.9	7.9	7.9
Impulsivity	22.5	11.2	11.0	22.9	15.3	13.2	21.4	18.5	19.1
Immaturity	6.5	3.4	3.0	6.9	5.5	4.3	7.1	5.8	5.9
Psycho-somatic	4.0	3.2	2.6	2.7	3.1	2.8	2.6	2.3	2.1
Obsessional	1.7	1.7	1.9	2.6	2.4	2.4	2.5	2.0	2.3
Antisocial	1.7	0.5	0.9	1.0	0.6	0.5	1.4	1.6	1.7
Hyperactive	17.1	10.4	10.6	15.4	10.6	10.0	16.8	13.4	13.4

Time By Treatment Interaction Effects

Factor	F	Degrees of Freedom	P
Conduct	2.87	4/152	.026
Anxiety	1.35	4/152	.253
Impulsivity	7.65	4/152	.001
Immaturity	2.48	4/152	.047
Psychosomatic	1.50	4/152	.204
Obsessional	.218	4/152	NS
Antisocial	3.85	4/152	.006
Hyperactivity	1.79	4/152	.135

Table 11

Comparison of Effects from Zero to Four Weeks and Zero to Eight Weeks for Parent Rating Factor Scores**

Factor	Probability Values					
	Dex vs Cylert		Dex vs Placebo		Cylert vs Placebo	
	0-4	0-8	0-4	0-8	0-4	0-8
Conduct	.122	.478	.005	.008	.080	.047
Anxiety	.151	.500	.034	.082	.229	.173
Impulsivity	.051*	.438	.001	.001	.019	.003
Immaturity	.033*	.405	.015	.007	.003	.104
Psychosomatic	.073*	.087	.186	.060	.101	.241
Obsessional	over .500	over .500	.212	.250	.238	.250
Antisocial	over .049*	.500	.002	.006	.047	.021
Hyperactivity	over .140	.500	.024	.032	.198	.117

*Dexedrine improves more than Cylert

**Probability values based on two-tail test for drug-drug comparisons and one-tail test for drug-placebo comparisons

Table 12

Abbreviated Parent Questionnaire Changes

at Two, Four, Six and Eight Weeks*

Week	Dex vs Cylert		Dex vs Placebo		Cylert vs Placebo	
	t	p	t	p	t	p
0-2	2.209	.032	2.041	.024	.306	.250
0-4	1.169	.248	3.991	<.001	2.740	.005
0-6	0.373	over .500	3.348	.001	.012	.060
0-8	0.474	over .500	4.142	<.001	2.776	.004

*Probability values based on two-tail test for drug-drug comparisons and one-tail test for drug-placebo comparisons

Treatment by Time Analysis of Variance for

Abbreviated Parent Questionnaire Data

Source	Mean Square	df	F-Test	Significance
Treatments	617.366	2	6.598	.003
Subjects	93.574	74		
Time	899.945	4	43.173	<.001
Treat X Time	80.788	8	3.876	<.001
Time X Subjects	20.845	296		

Table 13

Mean Psychological Test Gains, F-Tests, and

Significance of Group Differences

Test	Dexedrine	Cylert	Placebo	F	P
WISC Full Scale	7.58	4.76	3.52	2.77	.069
Verbal IQ	4.96	2.08	2.52	1.06	.354
Perf. IQ	8.46	6.84	3.96	1.61	.208
Information	0.65	0.16	0.15	0.45	.500
Comprehension	0.58	0.28	0.26	0.12	.500
Arithmetic	0.35	0.12	0.19	0.07	.500
Similarities	1.12	1.00	1.82	0.54	.500
Vocabulary	0.08	0.33	-0.30	0.32	.500
Digit Span	0.96	0.52	0.33	0.70	.500
Picture Completion	1.08	1.36	-0.33	2.79	.068
Picture Arrangement	0.85	0.40	0.00	0.41	.500
Block Design	0.92	0.28	1.59	2.90	.062
Object Assembly	2.15	1.52	0.96	1.23	.300
Coding	1.92	1.36	0.31	2.73	.072
WRAT Reading	0.37	0.39	0.16	2.00	.144
Spelling	0.36	0.25	0.03	3.70	.030
Arithmetic	0.23	0.32	0.16	0.99	.376
Gray Oral Reading	0.51	0.44	-0.01	3.20	.049
Porteus Test Quotient	21.31	14.36	2.15	8.01	.001
Porteus Qualitative	-3.92	1.44	-1.63	0.33	.500
Draw-A-Man IQ	7.58	2.64	3.19	1.49	.233
Bender Gestalt	2.00	0.56	0.96	1.53	.225
Paired Associates	25.21	24.83	17.13	0.48	.500
Frostig Perceptual Qt.	7.35	10.12	0.30	9.96	.001
Eye-Motor	0.77	0.64	-0.78	6.18	.004
Figure-Ground	1.65	0.84	0.22	3.68	.030
Form Constancy	0.27	1.28	0.82	1.48	.234
Position in Space	0.42	1.32	0.15	2.57	.084
Spatial Rel.	0.73	0.40	0.22	0.92	.405
CPT Commissions	-9.96	-9.87	-2.31	1.07	.349
CPT Omissions	-10.4	-7.52	-8.27	0.55	.500
Reading Comprehension	0.41	0.39	0.05	0.55	.500
Reading Speed	0.07	-0.28	0.59	1.17	.322
Reading Accuracy	0.33	0.65	0.09	2.66	.084
ITPA Age Gain	0.58	0.77	0.68	0.73	0.485

Table 14

T-Test Comparisons of Psychological Test Changes Showing Overall Significance by Analysis of Variance

Test	Dex vs Cylert	Dex vs Placebo	Cyl vs Placebo
WRAT Spelling	NS	.006	.035
Gray Oral Reading	NS	.012	.019
Porteus Test Quotient	.149	.001	.006
Frostig Perceptual Qt.	.252	.001	.001
Frostig Eye-Motor	NS	.002	.005
Frostig Figure-Ground	.148	.004	.130

Table 15A

Laboratory Data (Baseline)

	Cylert			Dexedrine			Placebo		
	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.	N
WBC/CU MM	7757.1	1982.0	28	7073.2	2179.0	28	7598.2	2290.8	28
Neutrophils(%)	51.8	10.9	28	52.8	10.4	28	52.0	10.7	28
Stabs/Bands(%)	0.4	1.0	28	0.1	0.4	28	0.6	1.8	27
Lymphocytes(%)	36.8	11.1	28	35.1	8.1	28	35.0	11.7	28
Monocytes(%)	6.0	4.0	28	6.5	4.2	28	6.5	4.4	28
Eosinophils(%)	2.8	2.7	28	2.9	2.4	28	3.7	4.5	28
Basophils(%)	0.2	0.6	28	0.2	0.4	28	0.2	0.6	27
Other(%)	1.3	2.7	27	1.4	2.8	27	0.9	1.7	28
Hematocrit (Vol%)	37.2	2.3	28	37.1	2.2	28	37.8	2.7	28
Hemoglobin (GMS./100ML)	13.0	0.9	25	12.7	2.2	27	13.4	1.1	27
Platelet Est.	1.0	0.0	27	1.0	0.0	28	1.0	0.2	27
BUN(Mg/100ML)	11.8	2.1	28	12.5	2.4	28	12.8	2.1	28
Alkaline Phosphatase Units	9.3	1.7	28	10.0	1.7	28	9.7	2.2	28
SGOT	22.2	7.2	28	19.7	5.9	28	21.5	5.0	28
LDH	121.2	20.9	28	123.3	20.4	26	129.7	21.2	28
Bilirubin Total (MG/100 ML)	.3	.1	28	.3	.2	28	.3	.1	28
Urine-Specific Gravity	1.0	0.0	27	1.0	0.0	25	1.0	0.0	28
Urine-PH	6.1	1.0	28	6.2	.8	28	5.9	.7	28
Urine-Albumin	0.0	.3	28	0.0	0.0	28	0.0	0.0	28
Urine-Glucose	0.0	0.0	28	0.0	0.0	28	0.0	0.0	28
Urine-Acetone	0.0	0.0	28	0.0	0.0	28	0.0	0.0	28
Urine-Microscopic	1.0	0.2	25	1.0	0.3	27	1.0	0.3	26

Table 15B

Laboratory Data (4 Weeks)

	Cylert			Dexedrine			Placebo		
	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.	N
WBC/CU MM	7244.4	1550.1	27	6940.7	1754.7	27	7615.3	3133.2	26
Neutrophils(%)	50.7	12.6	27	50.8	10.4	27	54.2	11.3	27
Stabs/Bands(%)	0.6	1.0	27	0.7	3.1	27	0.4	1.0	27
Lymphocytes(%)	34.2	11.4	27	35.5	11.2	27	35.6	11.3	27
Monocytes(%)	6.6	3.5	27	6.6	2.4	26	5.4	3.0	27
Eosinophils(%)	3.0	3.6	27	3.1	3.0	27	2.9	2.9	27
Basophils(%)	0.1	0.4	27	0.4	0.9	27	0.1	0.4	27
Other(%)	3.8	7.0	27	2.3	2.9	27	1.2	2.1	27
Hematocrit (Vol%)	37.8	2.5	27	39.4	2.4	27	38.2	2.2	27
Hemoglobin (GMS/100ML)	13.2	0.8	26	13.6	1.0	24	13.3	1.0	25
Platelet Est.	1.0	0.0	27	1.0	0.0	25	1.0	0.0	27
BUN(Mg/100ML)	14.0	2.8	2	0.0	0.0	0	0.0	0.0	0
Alkaline Phos-phatase Units	8.2	2.1	2	0.0	0.0	0	0.0	0.0	0
SGOT	20.5	0.7	2	0.0	0.0	0	0.0	0.0	0
LDH	130.0	0.0	2	0.0	0.0	0	0.0	0.0	0
Bilirubin Dtal (MG/100ML)	0.4	0.3	2	0.0	0.0	0	0.2	0.0	1
Urine-Specific Gravity	1.0	0.0	19	1.0	0.0	22	1.0	0.0	23
Urine-PH	6.2	1.0	26	6.4	0.9	27	6.0	0.9	26
Urine-Albumin	0.0	0.2	26	0.0	0.0	27	0.0	0.0	26
Urine-Glucose	0.0	0.0	26	0.0	0.0	27	0.0	0.0	26
Urine-Acetone	0.0	0.0	26	0.0	0.0	27	0.0	0.0	26
Urine-Micro-scopic	1.0	0.0	24	1.1	0.4	26	1.0	0.0	25

Table 15C

Laboratory Data (8 Weeks)

	Cylert			Dexedrine			Placebo		
	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.	N
WBC/CU MM	8790.3	3280.2	26	7709.6	2314.1	26	7865.3	1955.4	26
Neutrophils (%)	54.2	9.9	26	51.4	11.9	26	54.6	10.7	26
Stabs/Bands (%)	0.2	0.7	26	0.1	0.6	26	0.0	0.3	26
Lymphocytes (%)	34.4	8.4	26	37.2	10.7	26	35.7	9.1	26
Monocytes (%)	6.1	2.7	26	6.4	3.4	26	5.8	2.9	26
Eosinophils (%)	3.1	3.3	26	2.7	3.0	26	3.1	3.9	26
Basophils (%)	0.4	0.9	26	0.1	0.3	26	0.0	0.4	26
Other (%)	1.4	2.8	26	0.4	0.7	26	0.5	1.1	26
Hematocrit (Vol%)	37.6	2.4	26	38.0	1.9	26	37.5	2.2	26
Hemoglobin (GMS/100ML)	13.3	0.9	22	13.1	0.7	23	13.5	0.9	21
Platelet Est.	1.0	0.0	26	1.0	0.0	26	1.0	0.0	26
BUN (Mg/100ML)	12.6	2.7	25	12.6	2.6	26	13.2	3.6	27
Alkaline Phosphatase Units	9.0	1.7	24	9.2	2.0	26	9.5	2.3	27
SGOT	22.2	4.6	26	20.0	3.6	26	22.9	4.5	27
LDH	122.0	22.4	26	117.4	15.3	25	129.1	15.2	27
Bilirubin Total (MG/100ML)	0.3	0.1	25	0.3	0.2	26	0.4	0.2	27
Urine-Specific Gravity	1.0	0.0	23	1.0	0.0	21	1.0	0.0	25
Urine-PH	6.0	0.9	24	6.1	0.8	26	5.7	0.6	27
Urine-Albumin	0.0	0.2	23	0.0	0.0	26	0.0	0.2	27
Urine-Glucose	0.0	0.0	24	0.0	0.0	26	0.0	0.0	27
Urine-Acetone	0.0	0.0	24	0.0	0.0	26	0.0	0.0	27
Urine-Microscopic	1.0	0.2	22	1.1	0.3	25	1.0	0.3	25

Table 16A

Range of High and Low Values for Laboratory Data (Baseline)

	Cylert		Dexedrine		Placebo	
	High	Low	High	Low	High	Low
WBC/CU MM	11850.0	4000.0	11950.0	3500.0	15200.0	4650.0
Neutrophils(%)	73.0	30.0	73.0	35.0	69.0	28.0
Stabs/Bands(%)	4.0	0.0	2.0	0.0	7.0	0.0
Lymphocytes(%)	56.0	9.0	50.0	19.0	65.0	14.0
Monocytes(%)	18.0	1.0	16.0	1.0	21.0	0.0
Eosinophils(%)	9.0	0.0	10.0	0.0	24.0	0.0
Basophils(%)	2.0	0.0	1.0	0.0	2.0	0.0
Other(%)	13.0	0.0	13.0	0.0	5.0	0.0
Hematocrit(Vol%)	42.0	32.0	43.0	34.0	44.0	32.0
Hemoglobin (GMS/100ML)	14.9	11.1	14.6	2.7	15.2	11.4
Platelet Estimate	1.0	1.0	1.0	1.0	2.0	1.0
BUN(Mg/100 ML)	15.0	8.0	18.0	9.0	17.0	9.0
Alkaline Phosphatase Units	12.0	3.3	13.3	5.9	15.6	6.6
SGOT	50.0	9.0	30.0	10.0	35.0	15.0
LDH	172.0	85.0	170.0	95.0	190.0	100.0
Bilirubin Total (MG/100ML)	.8	.2	.9	.2	.6	.2
Urine-Specific Gravity	1.0	1.0	1.0	1.0	1.0	1.0
Urine-PH	9.5	5.0	7.5	5.0	7.5	5.0
Urine-Albumin	1.0	0.0	0.0	0.0	0.0	0.0
Urine-Glucose	0.0	0.0	0.0	0.0	0.0	0.0
Urine-Acetone	0.0	0.0	0.0	0.0	0.0	0.0
Urine-Microscopic	2.0	1.0	2.0	1.0	2.0	1.0

Table 16B

Range of High and Low Values for Laboratory Data (4 Weeks)

	Cylert		Dexedrine		Placebo	
	High	Low	High	Low	High	Low
WBC/CU MM	10500.0	4750.0	12000.0	3700.0	20300.0	4450.0
Neutrophils(%)	79.0	25.0	76.0	31.0	75.0	31.0
Stabs/Bands(%)	3.0	0.0	16.0	0.0	5.0	0.0
Lymphocytes(%)	56.0	7.0	54.0	13.0	58.0	16.0
Monocytes(%)	15.0	2.0	12.0	3.0	12.0	1.0
Eosinophils(%)	13.0	0.0	11.0	0.0	12.0	0.0
Basophils(%)	1.0	0.0	4.0	0.0	1.0	0.0
Other(%)	35.0	0.0	10.0	0.0	10.0	0.0
Hematocrit(Vol%)	43.0	32.0	44.0	35.0	42.0	34.0
Hemoglobin (GMS/100ML)	14.6	10.8	15.2	12.1	14.9	10.5
Platelet Estimate	1.0	1.0	1.0	1.0	1.0	1.0
BUN (Mg/100ML)	16.0	12.0	-	-	-	-
Alkaline Phosphatase Units	9.7	6.8	-	-	-	-
SGOT	21.0	20.0	-	-	-	-
LDH	130.0	130.0	-	-	-	-
Bilirubin Total (MG/100 ML)	.6	.2	-	-	.2	.2
Urine-Specific Gravity	1.0	1.0	1.0	1.0	1.2	1.0
Urine-PH	7.5	5.0	8.0	5.0	8.0	5.0
Urine-Albumin	1.0	0.0	0.0	0.0	0.0	0.0
Urine-Glucose	0.0	0.0	0.0	0.0	0.0	0.0
Urine-Acetone	0.0	0.0	0.0	0.0	0.0	0.0
Urine-Microscopic	1.0	1.0	2.0	0.0	1.0	1.0

Table 16C

Range of High and Low Values for Laboratory Data (8 Weeks)

	Cylert		Dexedrine		Placebo	
	High	Low	High	Low	High	Low
WBC/CU MM	19400.0	5000.0	13750.0	4900.0	11750.0	5200.0
Neutrophils(%)	76.0	31.0	78.0	29.0	72.0	27.0
Stabs/Bands(%)	3.0	0.0	2.0	0.0	1.0	0.0
Lymphocytes(%)	55.0	21.0	59.0	15.0	56.0	22.0
Monocytes(%)	12.0	1.0	14.0	1.0	15.0	1.0
Eosinophils(%)	14.0	0.0	13.0	0.0	17.0	0.0
Basophils(%)	4.0	0.0	1.0	0.0	2.0	0.0
Other(%)	12.0	0.0	2.0	0.0	4.0	0.0
Hematocrit(Vol%)	43.0	33.0	41.0	34.0	43.0	34.0
Hemoglobin (GMS/100ML)	14.9	10.7	15.2	12.1	16.5	12.1
Platelet Estimate	1.0	1.0	1.0	1.0	1.0	1.0
BUN(Mg/100ML)	20.0	9.0	17.0	8.0	28.0	9.0
Alkaline Phosphatase Units	11.4	4.1	12.3	4.1	14.4	4.7
SGOT	32.0	15.0	26.0	13.0	31.0	12.0
LDH	170.0	85.0	155.0	85.0	165.0	95.0
Bilirubin Total (MG/100ML)	.7	.2	1.0	.2	1.2	.2
Urine-Specific Gravity	1.0	1.0	1.0	1.0	1.0	1.0
Urine-PH	7.5	5.0	8.0	5.0	7.5	5.0
Urine-Albumin	1.0	0.0	0.0	0.0	1.0	0.0
Urine-Glucose	0.0	0.0	0.0	0.0	0.0	0.0
Urine-Acetone	0.0	0.0	0.0	0.0	0.0	0.0
Urine-Microscopic	2.0	1.0	2.0	1.0	2.0	1.0