The Relationship between Methylphenidate (Ritalin) and Growth Patterns in Children Diagnosed as Hyperactive

Teri Mitchel Hibbard
Western Michigan University

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THE RELATIONSHIP BETWEEN METHYLPHENIDATE (RITALIN) AND GROWTH PATTERNS IN CHILDREN DIAGNOSED AS HYPERACTIVE

by

Teri Mitchel Hibbard

A Thesis
Submitted to the Faculty of The Graduate College in partial fulfillment of the requirements for the Degree of Master of Arts Department of Psychology

Western Michigan University Kalamazoo, Michigan August 1983
The relationship between methylphenidate (Ritalin) and growth patterns in children diagnosed as hyperactive

Teri Mitchel Hibbard, M.A.
Western Michigan University, 1983

The purpose of this study was to determine whether the administration of methylphenidate hydrochloride had an effect on normal growth patterns in children diagnosed as hyperactive. Subjects were assigned to one of three methylphenidate treatment groups by the amount of time (in years) they received medication. Length of treatment ranged from up to one year through three years. Using NCHS growth charts, measurement percentiles (height and weight) were compared to pre-treatment percentiles to determine effect of medication. Results indicated that the administration of methylphenidate had a significant growth suppressing effect on children, the effect was proportional across measurements i.e., height and weight, and pre-treatment height percentiles were lower than national averages. Further analysis of the data suggest a transient effect of growth suppression during long term administration of methylphenidate.
ACKNOWLEDGEMENTS

The author would like to acknowledge the cooperation of the Kalamazoo Child Guidance Clinic, Kalamazoo, Michigan and especially thank Ray O. Creager, Brett Lincoln, Laura Combs and Jill Rich for their support and assistance in the study.

I am greatly indebted to Malcolm Robertson for his editorial assistance. I would also like to thank Chris Koronakos for his assistance with the Human Subjects Review Committee. Additional thanks go to R. Wayne Fuqua for his methodological suggestions and assistance.

Finally, I would like to thank Susan Killa for her clerical assistance.

Teri Mitchel Hibbard
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WESTERN MICHIGAN UNIVERSITY M.A. 1983

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## TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td>ii</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>iv</td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
<td>iv</td>
</tr>
<tr>
<td>INTRODUCTION AND REVIEW OF SELECTED LITERATURE</td>
<td>1</td>
</tr>
<tr>
<td>METHOD</td>
<td>7</td>
</tr>
<tr>
<td>Subjects</td>
<td>7</td>
</tr>
<tr>
<td>Experimental Design</td>
<td>7</td>
</tr>
<tr>
<td>Treatment</td>
<td>8</td>
</tr>
<tr>
<td>RESULTS</td>
<td>11</td>
</tr>
<tr>
<td>DISCUSSION</td>
<td>19</td>
</tr>
<tr>
<td>BIBLIOGRAPHY</td>
<td>25</td>
</tr>
</tbody>
</table>
LIST OF TABLES

TABLES

1. Length and Dosage of Methylphenidate Hydrochloride Treatment .................. 9
2. Height and Weight Percentiles Over Time in Hyperactive Children Receiving Methylphenidate ........................................... 12
3. Relationship Between Children's Initial Height and Weight and Change with Methylphenidate Treatment ........................................... 17
4. Percentiles for Height and Weight Prior to and by the End of Methylphenidate Treatment ................................................................. 18

LIST OF FIGURES

FIGURES

1. Mean Height Percentiles Before Treatment and After Each Treatment Year .... 13
2. Mean Weight Percentiles Before Treatment and After Each Treatment Year .... 16
INTRODUCTION AND REVIEW OF SELECTED LITERATURE

A specific and common behavior disorder in children is an attention deficit disorder (previously known as minimal brain damage, minimal cerebral dysfunction and minor cerebral dysfunction). The disorder is characterized by hyperactivity, short attention span and poor concentration, impulsiveness, irritability, emotional lability, explosiveness, variability, and poor school work (Laufer & Denhoff, 1957). For decades children diagnosed as "hyperactive", "hyperkinetic" or the like have been administered amphetamines to help them maintain situationally appropriate behavior. Although the effect of stimulant drugs on the child's nervous system is not yet entirely understood, the use of amphetamines is not viewed as being a paradox. These drugs appear to produce a heightened alertness with correspondingly greater ability to focus attention (Treegoob & Walker, 1976). Various portions of the higher levels of the central nervous system have inhibition as their function, and stimulation of these portions might indeed produce the clinical picture of reduced activity through increased voluntary control (Bradley, 1937; Jasper & Andres, 1936).

The value of amphetamines in the treatment of hyperkinetic behavior was first emphasized by Bradley in 1937. In a study conducted at the Emma Pendelton Bradley Home,
children with a variety of behavior disorders similar to hyperkinetic symptomatology were administered benzedrine (beta aminopropylbenzene; benzyl methyl carbinamine). There was a "spectacular improvement in school performance in half of the children" (Bradley, 1937, p. 578). A large proportion of the patients became emotionally subdued without losing interest in their surroundings. This was seen as a major breakthrough, since prior to this parents were either at the mercy of their out of control child, or in extreme cases were forced to institutionalize their children.

Currently a number of different medications are indicated as adjunctive therapy in the treatment of hyperkinesia. Drugs, such as magnesium pemoline (Cylert), methylphenidate hydrochloride (Ritalin), imipramine (Tofranil), dextroamphetamine (Dexedrine), as well as other forms of amphetamines, have been and are currently used. These drugs yield positive results when incorporated in a total therapeutic treatment package i.e., including psychotherapy, as well as educational and social program.

While such results are outwardly encouraging, numerous side effects have been noted with prolonged use of these medications. Such undesireable effects include: insomnia (Arnold et al., 1976; Claghorn et al., 1971; Conners et al., 1972), decreased appetite (Garkinkel et al., 1975; Hoffman et al., 1974; Knobel, 1962), irritability (Lucas & Weiss, 1971; McConnel et al., 1964; Rapoport et al., 1971),
abdominal pain (Rapoport et al., 1974; Schain & Reynard, 1975; Segar & Hallum, 1974), and headaches (Weiss et al., 1971; Werry & Sprague, 1974).

Another side effect that has been noted is one of growth suppression i.e., less than normal weight and height gain (Downs, 1979; Hechtman et al., 1978; Mattes & Gittleman, 1983; Safer et al., 1972). These studies examined growth patterns in relation to administration of methylphenidate hydrochloride, and so far have yielded inconsistent findings. While the above studies have suggested that the administration of methylphenidate appears to promote growth suppressions, other studies have found the contrary (Beck et al., 1975; Eisenberg, 1972; McNutt et al., 1977; McNutt et al., 1976; Millichap & Millichap, 1975; Millichap, 1977). Furthermore, unpublished data on children with long term regimens of methylphenidate (up to seven years) have shown favorable results, and have failed to show any significant growth suppression with careful monitoring of physical development (Creager, 1983).

Numerous studies have been conducted on the use of methylphenidate, each looking at several variables attempting to answer the question: "Does the administration of methylphenidate affect the normal growth patterns of children diagnosed as hyperactive?" Variables previously examined include the relationship between dosage and the amount of growth suppression, the comparison of methylphenid-
idate with other medications with respect to side effects, and the physiological changes following administration.

Little relationship has been found in the amount of growth suppression and dosage levels of methylphenidate (Werry & Sprague, 1974). Although there appears to be no relationship between growth and dosage levels, researchers warn that current doses may be too high and side effects more common than stated (Safer & Allen, 1975).

In a study comparing methylphenidate to dextroamphetamine in regard to growth suppression, dextroamphetamine inhibition of weight gain was significantly greater than that observed with methylphenidate (Safer & Allen, 1975). Furthermore, Greenberg et al. (1975) found that methylphenidate was slightly more efficacious and produced fewer severe side effects than imipramine with improve social relatedness and coordination.

The effects of chronic methylphenidate treatment has shown to promote a number of physiological changes in laboratory rats (Greeley & Kizer, 1980). These changes include significant decreases in skeletal growth, delayed vaginal patency in females, depressed serum prolactin levels in both males and females, decreased basal serum insulin levels, significantly depressed growth hormone levels in females, but not males, as well as decreased luteinizing hormone and follicle-stimulating hormone levels in males.

The present study examined the effects of methylphenidate
hydrochloride on growth patterns in children diagnosed as hyperkinetic or displaying hyperkinetic symptoms.

Methylphenidate was selected for two reasons. First, it has been found to be one of the most commonly prescribed medications for hyperkinesis (Treegoob & Walker, 1976). Second, it has proved to be more effective therapeutically, with fewer side effects that other medications often prescribed (Conners, 1971). Several studies report that methylphenidate helps improve ratings of behavior, attentiveness, performance I.Q., motor control, and speech productivity in children with minimal brain dysfunction (Conners, 1972; Knights & Hinton, 1969; Knobel, 1962).

It has been shown that children with minimal brain dysfunction show a wide individual variability in their growth patterns (Kaffman et al., 1979). Kaffman et al. hypothesized that children may actually be atypical in size and do not show growth retardation per se, but continue to gain weight and grow in height proportionally, though slightly below the national average.

Using National Center of Health Statistics growth charts (Hamill et al., 1976) this study investigated the following questions: (1) Is there evidence of growth suppression in height and weight, in hyperactive children receiving long term methylphenidate treatment; (2) Is there a consistent pattern of normal height and weight gain in children receiving the medication; (3) Is there variability in
developmental growth patterns of children who are diagnosed as hyperactive, or who display hyperactive symptoms?
METHOD

The current data were drawn from the archives of an unpublished comprehensive longitudinal study of children diagnosed as hyperactive and assigned a regimen of methylphenidate.

Subjects

Subjects were 42 male children, between the ages of 4 years-0 months to 12 years-0 months at the time of evaluation. All children were evaluated at a children oriented outpatient clinic and exhibited various degrees of hyperkinetic behavior. Referrals were made either by the subject's parents or by his school. All children were given a complete neuropsychiatric and comprehensive psychological evaluation before diagnosis was made.

Experimental Design

The research employed a group design wherein individual subjects were grouped by the amount of time (in years) they spent under the medication. Of the total 42 children included in the initial sample, 36 were treated for one year, 23 of the 42 were treated for two years, and 7 were treated for three years. The number of subjects per year steadily decreased due to the amount of time each individual was
under medication (e.g., some of the original 42 children were only on methylphenidate for one year). Children receiving treatment up to three years were included in the statistics for all previous years.

Treatment

Following evaluation and diagnosis, all subjects were assigned a regimen of methylphenidate hydrochloride (but no other stimulant) for up to three years. Clinical guidelines were followed for prescription.

Since the children began treatment at various times during the year, the average amount of time of methylphenidate treatment during year one was 30.4 weeks, during year two 73.6 weeks and during year three 121.1 weeks (Table 1). Many of the children discontinued the medication regimen during the summer; methylphenidate therapy was reinstated in the fall only if behavioral complaints from school were received, or if the child's parents requested it.

The treatment approach was to increase dosage gradually until benefit was clearly maximal both at home and school. Methylphenidate dosage was increased up to a maximum of 60 mg/day. As shown in Table 1, mean methylphenidate dosage was 39.8 mg/day for the first year, and 49.7 and 54.29 mg/day after years two and three, respectively.

Children were measured and weighed (without shoes and outdoor attire) on a professional scale on the average of
Table 1

Length and Dosage of Methylphenidate Hydrochloride Treatment

<table>
<thead>
<tr>
<th>Treatment Period</th>
<th>0-1 year (N=42*)</th>
<th>1-2 years (N=23*)</th>
<th>2-3 years (N=7*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of methylphenidate treatment, wk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>30.4</td>
<td>73.6</td>
<td>121.1</td>
</tr>
<tr>
<td>SD</td>
<td>9.9</td>
<td>16.2</td>
<td>25.4</td>
</tr>
<tr>
<td>Daily dosage while receiving methylphenidate, mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>36.84</td>
<td>49.69</td>
<td>54.29</td>
</tr>
<tr>
<td>SD</td>
<td>12.72</td>
<td>13.10</td>
<td>15.12</td>
</tr>
</tbody>
</table>

* Total N=42; children receiving treatment up to three years were included in the statistics for all previous periods.
every 8 months, ranging from 3 months to 12 months, with at least three measurements for those involved in the three year group. Some children were measured more frequently if deemed necessary (e.g., if appetite suppression was suspected).

If parents or children reported appetite suppression within the first 2 week period of administration, which occurs approximately 40% of the time (L. Combs, personal communication, July 1983), the parents of that particular child were encouraged to monitor eating patterns to see if this condition persisted. If this pattern continued parents were advised to switch children from a basic three average size meals per day to five smaller meals per day. If this change did not prove successful, medication dosage was either lowered, or another medication was used alone or in conjunction with methylphenidate (e.g., magnesium pemoline).

At home, parents of the children were responsible for monitoring medication compliance. While at school, nursing personnel handled and monitored medication compliance. Prescriptions were refilled at least once per month in accordance with legal regulations.
RESULTS

The children's weight and height percentiles obtained at the end of each year were compared with their percentiles before treatment, using paired t tests.

Significant decreases between pretreatment and subsequent weight percentiles were found at each measurement period (ranging from P<.05 to P<.001; Table 2).

As given in Table 2, the pretreatment height percentiles were all slightly below the population median of 50, with very minimal percentile reduction across all three year groups (1.23 percentile points being the most dramatic change at the 1-2 year period). These data suggest that the average child in this treatment group was shorter than the national average. The pretreatment weight percentiles were less than the population median of 50 (49.42 for the 0-1 year period), and were slightly over the median for the next two periods (51.30 and 51.94 for the 1-2 and 2-3 year periods, respectively). On the whole, the average weight within this treatment group was relatively consistent with national averages before medication was introduced.

A slight, though non-progressive decrement in height percentile was found over time (Figure 1). It averaged .94 percentile points after year 1 (P<.01), 1.23 points
Table 2

Height and Weight Percentiles Over Time In Hyperactive Children Receiving Methylphenidate Hydrochloride

<table>
<thead>
<tr>
<th>Year</th>
<th>Pretreatment Mean</th>
<th>Pretreatment SD</th>
<th>End of Year Mean</th>
<th>End of Year SD</th>
<th>N*</th>
<th>t+</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>48.99</td>
<td>1.93</td>
<td>48.05</td>
<td>1.94</td>
<td>36</td>
<td>3.48</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>1-2</td>
<td>49.19</td>
<td>2.36</td>
<td>47.96</td>
<td>2.53</td>
<td>23</td>
<td>4.24</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>2-3</td>
<td>48.80</td>
<td>1.81</td>
<td>48.07</td>
<td>1.51</td>
<td>7</td>
<td>1.22</td>
<td>NS</td>
</tr>
</tbody>
</table>

Weight Percentile

<table>
<thead>
<tr>
<th>Year</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
<th>N*</th>
<th>t+</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>48.42</td>
<td>7.38</td>
<td>45.63</td>
<td>7.61</td>
<td>36</td>
<td>2.27</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>1-2</td>
<td>51.30</td>
<td>10.25</td>
<td>45.91</td>
<td>8.51</td>
<td>23</td>
<td>6.13</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>2-3</td>
<td>51.99</td>
<td>12.88</td>
<td>47.97</td>
<td>12.33</td>
<td>7</td>
<td>4.10</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

* N value for 0-1 year group is lower than in Table 1 because some children failed to come to the clinic when growth measures were taken and because the clinic staff neglected to obtain the measures in some cases.

+ Paired t tests, two tailed. The percentile at the end of each year was compared with the pretreatment percentile.
Figure 1. Mean height percentiles before treatment and after each treatment year.
after year 2 ($P < .001$), and .73 after year 3 (not significant) of methylphenidate treatment.

A somewhat consistent decrement was found in weight percentile over time (Figure 2). It average 2.79 percentile points after year 1 ($P < .05$), 5.39 and 4.02 percentile points, respectively, after 2 and 3 years of methylphenidate treatment ($P < .001$ and $P < .01$).

As given in Table 3, initial height percentile correlated significantly with change in height percentile at the end of years 1 and 2, $r = .65$ and .85, respectively ($P < .001$) and with change in weight percentile at the end of years 1 and 2, $r = .57$ and .66, respectively ($P < .001$). Initial weight percentile also correlated significantly with change in weight percentile for all three years, $r = .52$ to .98, ($P < .01$) for year 1 group, and ($P < .001$) for years 2 and 3, respectively.

Table 4 shows the percentiles for height and weight prior to and at the end of drug therapy. Before drug treatment the distribution of height in the sample shows a homogeneous grouping, with the entire sample falling within the 45-55 percentile range. The distribution of weight in the sample shows a positively skewed distribution with 36 percent in the lower range (3-45 percentile range) and 16 percent in the upper range (55-97 percentile range).

Table 4 also shows that at the end of the treatment there was only a slight change in the average height before
and after medication i.e., 3 children falling into the lower range or 8 percent. There was a considerable change in the average weight before and after medication. The percentage of children falling into the lower range increased from 36 percent before treatment to 66 percent after treatment, and the percentage of children falling into the upper range decreased from 16 percent before treatment to 13 percent after treatment.
Figure 2. Mean weight percentiles before treatment and after each treatment year.
Table 3

Relationships Between Children's Initial Height and Weight and Change With Methylphenidate Treatment

<table>
<thead>
<tr>
<th>Start Percentile</th>
<th>After 1 yr</th>
<th>2 yr</th>
<th>3 yr</th>
<th>After 1 yr</th>
<th>2 yr</th>
<th>3 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Height</strong></td>
<td>.65**</td>
<td>.85**</td>
<td>.56</td>
<td>.57**</td>
<td>.66*</td>
<td>.50</td>
</tr>
<tr>
<td>N</td>
<td>36</td>
<td>23</td>
<td>7</td>
<td>36</td>
<td>23</td>
<td>7</td>
</tr>
<tr>
<td><strong>Weight</strong></td>
<td>.69**</td>
<td>.70**</td>
<td>.69</td>
<td>.52*</td>
<td>.92**</td>
<td>.98**</td>
</tr>
<tr>
<td>N</td>
<td>36</td>
<td>23</td>
<td>7</td>
<td>36</td>
<td>23</td>
<td>7</td>
</tr>
</tbody>
</table>

+Pearson's r

** P .001, two-tailed test
* P .01
Table 4
Percentile for Height and Weight Prior to and by the End of Methylphenidate

<table>
<thead>
<tr>
<th></th>
<th>Height Percentile</th>
<th></th>
<th>Weight Percentile</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3-45</td>
<td>45-55</td>
<td>55-97</td>
<td>3-45</td>
</tr>
<tr>
<td>N % N % N % N % N % N %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before Methylphenidate</td>
<td>0 0 42 100 0 0</td>
<td></td>
<td>15 36 20 48 7 16</td>
<td></td>
</tr>
<tr>
<td>*By the end of Therapy</td>
<td>3 8 33 91 0 0</td>
<td></td>
<td>24 66 7 19 5 13</td>
<td></td>
</tr>
</tbody>
</table>

*End of Therapy N value is lower than pre-treatment N value because some children failed to come to the clinic when growth measures were taken and clinic staff neglected to obtain the measures in some cases.
DISCUSSION

The results indicate that the use of methylphenidate hydrochloride treatment in response to hyperactive behavior does in fact significantly effect growth patterns (both height and weight) in children. Although weight suppression was more pronounced (over a 5 percentile point decrement at highest point), height suppression was also noted (over 1 percentile point decrement at highest point). Although the difference between percentile point decrement appears large i.e., weight over 5 percentile points at highest point, compared to over 1 with height measurement, both are considered equally important due to the fact that height retardation would be much more difficult to amend than weight retardation.

There were also high correlations between initial height and height gain, as well as initial weight and weight gain following treatment. There were also high correlations found between initial height and weight gain during treatment; the same applied to the relationship between initial weight and height gain. These results suggest a proportional relationship across both measurements i.e., there was little fluctuation between height gain and corresponding weight gain, or there was not an extreme increase in one measurement, while the other remain unchanged. This
finding suggests an overall or non-specific growth suppression effect of methylphenidate treatment.

Entry height in comparison with population norms was consistent with Kaffman et al. (1979) in that children were found to be shorter in stature before treatment than the national average. However, findings were not consistent with Kaffman et al. in regard to entry weight; before onset of methylphenidate treatment, children were not lower in weight in comparison to population norms.

The use of naturalistic observations and comparisons with population norms to study treated children over time poses difficult interpretational problems, since it is not possible to ascertain whether, without intervention, the growth pattern of the treated children would have been similar to that of the normative population (Mattes & Gittleman, 1983). In other words, the lack of an untreated control group precludes any conclusion as to whether the response to any kind of intervention is spontaneous or therapeutic. Without a control group, the findings of the present study are open to question. However, a report by Roche et al. (1979) found that untreated hyperactive children do not grow differently than normal subjects; thus reduced growth, when found, is likely to be due to stimulant (e.g., methylphenidate) treatment. Furthermore, many previous studies of growth suppression have compared a drug treated group with an untreated control group, or normative data
Such group comparison studies estimate the average effects of the standard treatment on the modal treated child. If, however, only certain aspects of drug treatment affect growth (e.g., physiological reaction) and if those aspects vary from one child to another (as appears to be the case), group studies will underestimate the effects of treatment (Loney et al., 1981). Therefore, it is reasonable to assume that these findings, even though significant, could underestimate the effects of methylphenidate in respect to degree and magnitude of growth suppression.

Although the present findings and others lend caution to long term treatment with stimulant medication, studies have indicated that growth suppression may be a transient phenomenon. Animal research has shown that the use of methylphenidate during neonatal periods may significantly affect growth and endocrine function of the developing rat, but some of the adverse effects have been found to be transient (Greeley & Kizer, 1980).

According to Gross and Wilson (1974), MBD (minimal brain dysfunction) children who receive methylphenidate show a temporary slowing of expected growth, weight and height, but when followed through adolescence these children exhibit a growth spurt that returns any weight or height reductions to the expected growth pattern. This pattern may have been approached in the current study. After the initial
affect of the drug, mean percentiles for post-treatment progressively approached the norm i.e., 50th percentile (Table 2). A follow-up study is needed to confirm this observation.

Growth suppression has also been linked to the loss of appetite. However, recent studies have shown that weight decreases due to the anorectic effect of medication were regained immediately following cessation of the drug administration (Kaffman et al., 1979). As presented previously, the effects of appetite suppression were accounted for within this study, and the relationship between weight loss and appetite suppression was not considered significant.

Considering that the administration of methylphenidate is likely to cause growth reduction, it is surprising that the medication is prescribed so frequently. Although it has been shown that with methylphenidate children respond immediately and dramatically (with a reduction of overactivity and the integration of activity in a more constructive direction (Bender & Cottington, 1942), other investigators have either not found such a reaction or have obtained better results with other medication (e.g., other stimulants).

After extensive research on inpatient care of hyperactive children receiving methylphenidate, Fish (1971) concluded that even though their symptoms worsen when the medication is stopped, their improvement on the stimulant
is never as complete as it is on subsequent trials with phenothiazines. Fish contends that stimulants are more often than not over-prescribed for hyperactivity, and should be screened more closely to maximize benefit to patients.

Phenothiazines, or specifically in this case "Thorazine", is used for the treatment of severe behavioral problems in children marked by combativeness and/or explosive hyperexcitable behavior. It has also been prescribed in the short term treatment of hyperactive children who show excessive motor activity with accompanying conduct disorders, which consist of one or all of the following symptoms: impulsivity, difficulty sustaining attention, aggressivity, mood lability and poor frustration tolerance.

Although these findings are encouraging, the use of phenothiazines carry their own side effects along with their own accompanying stigma i.e., associated with severe mental disorders.

Studies dealing with test performance have shown that when compared with magnesium pemoline, methylphenidate administration yielded lower WRAT subtest scores in those diagnosed as hyperactive. Moreover, non-hyperactive clinical groups have exhibited more improvement in test performance while receiving methylphenidate than hyperactive groups receiving the same (Dykman et al., 1980).

Unfortunately, the clinician is faced with a dilemma.
For especially disruptive children, medication is needed as a starting point within a treatment program. Without medication, psychotherapy is futile. However, considering the side-effects of medication, many clinicians are hesitant to assign such regimens. For this reason, hyperactive children are a population at risk for psychiatric disability, and yet are less likely to be taken on as treatment cases by most clinics because of their unsuitability for the preferred mode of treatment, namely psychotherapy (Eisenberg, et al., 1961).

In view of the evidence that growth gain is suppressed by long term use of stimulants, the following precautions should be taken when possible: 1) height and weight recordings should be conducted frequently, especially in the initial stages of therapy and with particularly small children, regardless of whether growth reduction is considered transient; 2) stimulants for children should not be administered during the summer months, school vacation periods, and on weekends; 3) other forms of medication should be considered in dealing with this specific population, and combined with a total therapeutic program.


Creager, R. Personal communication, June, 1983.


Dykman, R., Ackerman, P., and McCray, D. Effects of methylphenidate on selective and sustained attention in hyperactive, reading-disabled, and presumably attention-disordered boys. Journal of Nervous and Mental Disease, 1980, 168, 745-752.


