THE administration of pharmacologic agents to children with learning impediments or disabilities is not a new method of treatment. Publications of related investigations date back more than 30 years. An accurate assessment of the effectiveness of the chemotherapeutic approach poses numerous difficulties. These stem from factors such as (1) the lack of uniform terminology, (2) marked variability in methodology for evaluation, (3) the absence of standardized requirements for precise diagnosis and classification of the symptomatology constituting learning impediments, and (4) the paucity of long-term, properly controlled studies. As a result, a valid evaluation of response and objective comparison of the effectiveness of drugs administered in an attempt to mitigate or lessen learning impediments becomes impossible.

The clinical manifestations that collectively constitute learning disabilities are grouped as general classifications; or, in attempts to be specific, they are classified into etiologic and/or descriptive terminology. For instance, the symptomatology referred to by the broad term “minimal brain dysfunction syndrome” consists of learning and behavioral impediments “associated with impairment in perception, conception, language, memory and control of attention, impulse or motor function.” A subcategory of this syndrome includes the slightly more specific hyperkinetic syndrome, which is the term most generally used and the behavior impediment most commonly investigated in the studies reviewed. The use of general terms which allude to varied conclusions makes the specificity of diagnosis imperative prior to the administration of any drug, especially in evaluating efficacy.

The more specific vocabulary used in the classification of learning impediments includes cortical brain dysfunctions, lethargy, fluctuations in mood and thought, stuttering, speech-voice disorders, 14–6 cps EEG patterns, and learning deficits which consist of “poor attention span; reading, spelling, audio-verbal receptivity impairment, poor performance in arithmetic and/or English.” Although not as generalized as “minimal brain dysfunctions,” these terms still lack clarity and distinction between the organic and/or psychogenic etiological factors either before or after the administration of the drug under evaluation.

The methods used in evaluating the drugs consisted of varied techniques dependent on the behavioral manifestations under assessment. Standardized objective tests used to determine changes in such areas as intelligence and personality included Bender-Gestalt, Goodenough Draw-A-Person, WISC, Wechsler-Bellevue forms, Hundleby and Cattell (personal function), Rorscharch inkblot, Raven Progressive Matrices, and others. An actometer was used to measure the motor activity of some children. EEG patterns provided another criteria of evaluating changes in the subjects, as well as criteria for participation in some studies. Other methods consisted of investigator-devised and/or standardized tests for coordination and perception; personality and behavioral rating forms; and written or oral personal observations by parents, teachers, physicians, interviewers, and others.

In arriving at conclusions, most investigators appeared to be in agreement about the achievement of some beneficial results from the administration of certain drugs as an aid in alleviating learning impediments. However, discrepancies exist in reference to which drug produces the most beneficial results with a minimum of adverse side-effects. The few (controlled) studies appeared to be limited to two drugs and a placebo. The investigators seemed vague...
and inconclusive in respect to the actual influences of the drug in specific areas which should receive consideration; they often came to feeble but encouraging conclusions on the basis of certain positive results, disregarding or attempting to explain away inconsistencies. Generally, investigators based their promising conclusions on either a broad spectrum of positive and negative results or on an individual and a specific encouraging effect.

Numerous variables affect the validity of the conclusions reached in the articles reviewed and in turn the validity of the evaluation of the drugs employed.

1. Well controlled studies employing a double-blind, cross-over design and/or placebo drug were too few in number. The absolute necessity of using a placebo receives reinforcement from study results, especially since the effects of one of the drugs under evaluation differed only slightly from the placebo.

2. The number of patients involved in a study ranged from 10 to over 100, but they averaged anywhere from 14 to 40, which is too sparse a sampling for definite conclusions.

3. The psychologic effect of being in a study (Hawthorne effect) must receive consideration. The stimulation produced by participation and the general effect of increased personal attention can result in an improvement unrelated to the effects of the drug. This would be accounted for in controlled studies. Position in the treatment schedule has shown its effect, even in controlled studies.

4. Test situations which remove a patient from his general environment provide for a variable often resulting in improvement.

5. Utilization of more sensitive and precise diagnostic criteria would eliminate the possibility of undetected, underlying organic disease unknowingly affecting test results.

6. Discrimination between the organic and/or psychogenic effects produced by the drugs is lacking. The administration of appropriate or effective anti-epileptic agents to patients with abnormal EEG patterns may result in some improvement.

7. Well controlled investigations evaluating the influences of drugs on epileptic children, nonepileptic children, and children with normal and abnormal but not diagnostic EEG patterns need to be implemented.

8. There is need for focus on specific learning problems, with a corresponding identification of the influence of a drug on the specific symptom. As an example, one study detected an improvement reflecting a motivational factor but not a change in intellectual ability. Specifically, does the drug affect personality, behavior, motivation, and/or intelligence, and in what aspects?

9. The potential adverse side-effects of the drugs warrant more attention.

10. The variations in observational methodology and lack of continuity in the observers result in incomparable data.

The drugs evaluated in the publications reviewed are listed in Table I.

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
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<tbody>
<tr>
<td>Central Nervous</td>
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<tr>
<td>System Stimulants</td>
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<tr>
<td>methylphenidate</td>
<td>Ritalin</td>
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<tr>
<td>amphetamines</td>
<td>Dexedrine and Benzedrine</td>
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<tr>
<td>deanol</td>
<td>Deaneer</td>
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<tr>
<td>cyelert</td>
<td></td>
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<tr>
<td>Tranquilizing Agents</td>
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<td>Librium</td>
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<tr>
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<td>Thorazine</td>
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<td>Atarax</td>
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<td>Taractan</td>
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<td>Sparine</td>
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<tr>
<td>antihistaminies</td>
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<td>phenothiazines</td>
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<tr>
<td>Anticonvulsants</td>
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<td>Mysoline</td>
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<tr>
<td>diphenylhydantoin</td>
<td>Dilantin</td>
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<tr>
<td>ethosuximide</td>
<td>Zaronitn</td>
</tr>
</tbody>
</table>

TABLE I

DRUGS USED TO LESSEN LEARNING IMPEDIMENTS
Chemotherapy provides no panacea for the physician confronted with the varied manifestations of learning impediments. In most instances, chemotherapy should support and be compatible with the therapeutic approaches of the parents, the school, and other allied health professionals, and then only after a specific and detailed diagnosis. Ideally, when administered, the drug should produce none or only the minimal adverse side-effects and should reduce the major learning impediment, i.e., reduction of motor hyperactivity and improvement of such factors as memory, attention span, visual and auditory perception, coordination, and general behavior. Until a valid interpretation of the beneficial and adverse effects of the individual drugs is available, physicians should proceed with caution in the use of pharmacologic agents to alleviate learning impediments.

SUMMARY

Studies indicate that certain drugs have a promising effect in the treatment of children with learning impediments. The valid assessment of the true pharmacologic effect necessitates an accumulation of comparable, long-term, properly controlled studies and a careful evaluation of these data compared alone and with adjunctive therapy.

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REFERENCES

AN EVALUATION OF THE PHARMACOLOGIC APPROACHES TO LEARNING IMPEDIMENTS

Charles F. Weiss, Sumner J. Yaffe, Howard M. Cann, Arnold P. Gold, Frederic M. Kenny, Harris D. Riley, Jr., Irwin Schafer, Leo Stern and Harry C. Shirkey

Pediatrics 1970;46;142

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