

**EDUCATIONAL IMPLICATIONS OF THE SUBTLE  
LATE EFFECTS OF CHILDHOOD LEUKEMIA MEDICAL  
TREATMENT: A CASE STUDY**

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**ABSTRACT**

*This paper presents a four-year longitudinal case study of a nine-year-old student when he was diagnosed with leukemia. Cognitive, neuropsychological, and affective functioning both pre and post chemotherapy treatment were assessed. Full neuropsychological evaluation revealed difficulties with processing speed, concentration, and organization following treatment. Psycho-educational interventions developed through interdisciplinary team collaboration resulted in significant reductions in these problems for the student. Implications and recommendations for all educators and multidisciplinary teammembers are discussed.*

Although rare, leukemia is the most common form of childhood cancer, accounting for 30% of all cancers in children under the age of 15. Medical treatment, consisting of a combination of chemotherapy and radiation, or chemotherapy alone, typically lasts two to three years with a relapse rate of 20% one year post therapy, diminishing up to 3% for the next three to

four years (Margolin, Steuber, & Poplack, 2002). Despite the fact that the survival rate since the mid-1980s has increased from 30 percent to almost 90% (National Institutes of Health, 2002), half of these survivors display long-term learning problems that emerge seven years later or longer following treatment (National Children's Cancer Society, 2006), a phenomenon not actually recognized until the middle 1970s (Bain, 1995). Recent evidence indicates these survivors experience increasing difficulty securing employment (Carmichael, 2008).

While genetic, environmental, and immunodeficiency factors have been the focus of investigation, research suggests that learning deficits appear to be linked to chemotherapy's disruption of normal white matter development in the brain (Reitan & Wolfson, 1993). The effect of white matter dysfunction has been shown to be significantly related to processing speed and higher level cognitive processing deficits (Mahone, Prahme, Ruble, Mostofsky, & Schwartz, 2007). Additionally, there is growing evidence that changes specifically within the white matter cerebellar-frontal connections, which control some fine and gross motor control functions as well as perceptual qualities, are associated with chemotherapy alone (Buizer, DeSonneville, van den Heuvel-Eibrink, Nijikiktjen, & Veerman, 2005). Central Nervous System (CNS) chemotherapy, with or without cranial irradiation, has been associated with learning disabilities, depressed intellectual and academic functioning, and when combined, appear to be additive, but also dependent upon, the aggressiveness of therapy. Other factors, such as age and gender, also play a role, with younger female patients being identified as more vulnerable (Butler, Rizzi, & Bandilla, 1999). Chemotherapy alone has been linked to more subtle sensory, psychomotor deficits, as well as cognitive impairment, including reading, spelling, and comprehension difficulties; attention and concentration problems; limits in filtering; mental shifting; difficulty focusing; distractibility; limited planning and organization skills; and reduced social maturity (Clarke, Gaynon, Hann, Harrison, Masera, Peto, et al., 2003). Additionally, long-term effects of chemotherapy have been linked to hearing and visual deficits as well as pulmonary, cardiac, liver, gastrointestinal, genitourinary and potential reproductive dysfunction including infertility (University of Texas M.D. Anderson Cancer Center, 2008).

## IMPACT ON CLASSROOM PERFORMANCE

Historically, researchers note that early and extensive rehabilitation programs for targeting potential late effects were not implemented because there were few immediately observed effects of neurological impairment in young children shortly after completing a program of chemotherapy. Furthermore, many of the studies were retrospective (Fletcher & Copeland,

1988). More recently, however, Lesnik, Ciesielski, Hart, Benzel, and Sanders (1998) found that children undergoing three years of chemotherapy did in fact exhibit visual-spatial deficits, visuomotor problems, and organizational inefficiency, thus suggesting that as a task requires a higher level of coordinated motor control, significant risk of poorer performance was noted, with younger girls being more vulnerable. It should be noted that, as with other reported studies, no baseline data were available.

Butler and Mulhern (2005) point out that a child's brain functions differently following injury and the effects may persist for years. Of particular concern is their observation that, if untreated, survivors are likely to 'continue to develop into' their difficulties with increasing age rather than out of them if neurological issues are not addressed. More specifically, chemotherapy treatment may negatively impact a student's academic achievement, processing speed, visuospatial skills, and executive functioning (Kazak, Rourke, Alderfer, Ahna, Reilly, & Meadows, 2007). In practical terms, this impact may be manifested by the student having trouble remembering important details and tasks, paying close attention, planning ahead, or even keeping up with his/her friends (Kazak, et al., 2007).

In middle school, the recovering, post-chemotherapy student has several teachers, is given more independence, has more books, notebooks, supplies, a locker, and is expected to deal with increased physical challenges-- at a time of significantly reduced stamina. Assignments might be turned in late- not because they were not completed- but because the student simply forgot to turn them in, perhaps due to illness that morning on the school bus. Feelings of frustration, occasional emotional volatility or depression have been correlated with the changed self-concept and body image that the recovering student is experiencing (Bessell, 2001).

As such, because teachers, school professionals, and parents may not be familiar with late effects, there is the potential for unawareness or even misdiagnosis of subtle learning challenges, especially in otherwise high-achieving, intelligent students. There may be a lack of understanding of subtle signs such as blurred vision or ringing in the ears, and changes in or slowed visual-motor coordination. Teachers and other school staff members may find it difficult to separate the behavior of the typical middle school student and a chemotherapy patient in remission. Academic struggles in the classroom may be falsely attributed to daydreaming, lack of motivation, negative attitude, attention deficit disorder or emotionality. Short-term memory deficits are common; moreover, difficulty with word retrieval, slower processing skills, poor organization, and the inability to multi-task are all common late-effects (Lockwood, Bell, & Colegrove, 1999).

Brown, Madan-Swain, Walco, Cherrick, Ievers, and Conte, et al., (1998)

observed that while survivors of CNS chemotherapy generally display average performance on measures of cognitive and academic ability, they frequently score lower on tests of nonverbal skills, with girls performing even more poorly than boys, aged 5-12. Their findings also indicated that the forty-seven subjects who had undergone CNS chemotherapy were characterized by decreased perceptual and organization skills, lowered freedom from distractibility, and an overall diminished ability to utilize nonverbal perceptual abilities. Although baseline data were not available for the subjects in their study, scores were compared with national norms (50<sup>th</sup> percentile) and revealed a verbal comprehension score (37<sup>th</sup> percentile), full-scale I.Q. (37<sup>th</sup> percentile), yet lower performance I.Q. (30<sup>th</sup> percentile), and even lower perceptual organization skills (25<sup>th</sup> percentile).

Baseline as well as periodic neuropsychological evaluation provides an opportunity to identify and monitor subtle changes and hemispheric differences and to initiate, modify, and implement a collaborative, multidisciplinary treatment plan maximizing the child's learning potential. Neuropsychological testing can aid in understanding how therapeutic treatment has affected thinking, learning, and behavior. Additionally, the assessment can help identify which services and accommodations may be needed in the educational setting, lead to a recommendation of interventions, and identify potential or likely improvements, problems and changes (Espy, Moore, Kaufmann, Kramer, Matthay, & Hunter, 2001). These researchers identified modest declines in arithmetic and visual motor integration four years after the completion of CNS chemotherapy, but because of the lack of baseline data, it was difficult to determine the presence or magnitude of any changes in their scores following treatment. Therefore, the importance of systematic, follow-up neuropsychological assessment is consistent with the recommendations of the Leukemia and Lymphoma Society's emphases on baseline testing, special accommodations, and long-term planning. In this study, it was hypothesized that two years of chemotherapy without radiation would result in subtle, statistically insignificant, but important late-effects, which if identified and addressed, could prevent further loss of neuropsychological functioning.

## **METHODS**

### **SUBJECT AND PROCEDURE**

The case presented describes a nine-year-old third grader diagnosed with leukemia, currently in remission. His parents had requested, and the school system agreed that because of his diagnosis, baseline data would be critical in order to compare pre-chemotherapy with follow-up neuropsychological testing after his treatment was completed and he was in remission.

At baseline, no neurological or neuropsychological deficits were observed prior to two year of prophylactic CNS chemotherapy without irradiation. As part of a full psycho-educational evaluation, tests administered included the Wechsler Intelligence Scale for Children – IV, Quick Neurological Screening Test – Revised, Halstead-Reitan Neuropsychological Battery – Young Child, Stroop Color and Word Test, Projective Drawings, Children’s Apperception Test, and Bender Visual Motor Gestalt Test II. Medical reports indicated that despite the physical discomfort associated with physical examination, blood tests, cytogenesis, bone marrow aspiration, and nausea, he was tolerating CNS prophylaxis very well with complete remission anticipated and later confirmed.

### EVALUATION FINDINGS

Prior to treatment, I. Q. test results placed the subject in the above average range with no discrepancy between verbal and performance measures. His neuropsychological profile and achievement test scores fell at or above average. After two years of chemotherapy, neuropsychological assessment revealed emerging, subtle attention difficulty, slowed processing speed, concentration problems and organization inefficiency when compared with baseline data, and consistent with the previously cited (Brown, et al., 1998) research. While not statistically significant, these discrepancies suggest further clinical analysis. Specifically, a comparison of his baseline, two year post-treatment, and follow-up intellectual scores are found in Table 1.

Analysis of these data indicates that prior to two years of chemotherapy (without radiation), the student’s overall intellectual ability was in the 82%ile-- well above average. After two years of therapeutic intervention, his overall follow-up score placed him in the 73%ile. Each of these overall scores was within the limits of average, but subtle and potentially significant subtest discrepancies were noted. Consistent with previous research following chemotherapy, the student’s verbal and perceptual reasoning abilities appeared to remain intact. With his strong verbal skills, subtle short and long-term working memory deficits (reflected in a drop from the 86%ile to 68%ile) might not be readily observable in the classroom. Furthermore, if not remediated, these areas could continue to decline. Even more striking and notable was a significant reduction in the student’s ability to process incoming information efficiently and effectively, with a measured deficit placing him in the 34<sup>th</sup> percentile when compared to his pre-treatment 79<sup>th</sup> percentile placement. With his excellent vocabulary and logical verbal skills, as well as good verbal comprehension, his working memory deficits, attention/concentration difficulty, and slower processing speed, especially in a timed situation, would be a detriment to his overall academic success. Overall, full-

Table 1. Wechsler Intelligence Scale for Children – IV Results (Percentile Ranks)

	Pre-Treatment	Post-Treatment	One Year Post Treatment
Verbal Comprehension			
Similarities	84	75	75
Vocabulary	63	84	84
Comprehension	63	84	84
Information	84	84	75
Perceptual Reasoning			
Block Design	37	37	84
Picture Concepts	84	84	84
Matrix Reasoning	75	75	75
Picture Completion	95	95	95
Working Memory			
Digit Span	84	75	91
Letter-Number Sequence	84	63	75
Arithmetic	84	63	84
Processing Speed			
Coding	63	63	84
Symbol Search	84	16	37
SCORES SUMMARY			
Verbal Comprehension Index (VCI)	70	82	82
Perceptual Reasoning Index (PRI)	66	70	70
Working Memory Index (WMI)	86	68	86
Processing Speed (PSI)	79	34	66
Full Scale IQ (FSIQ)	82	73	87

scale IQ and working memory dropped to a level which, while not statistically significant, clinically suggested an area which should be monitored, especially in the presence of an ancillary processing speed deficit.

Additionally, it was noted that on the Aphasia Screening Test, his initial word-finding ability was within normal limits, but decreased to mildly impaired; a similar trend was noted in arithmetic computation skills. On the Trail Making Test (A), in which he was required to connect numerically sequenced circles using paper and pencil, no change in scores was noted, but on the more demanding Trails (B), his performance fell into the below average range. On that task he was required to connect alternating numbered and alphabetized circles using paper and pencil. He quickly became confused, lost track of what he was doing, and became increasingly frustrated. Similar discrepancies were observed on the Category Test as well as the Stroop Color and Word Test. As

a task became increasingly complex, he experienced difficulty alternating his attention back and forth between competing elements and became noticeably bothered by his perceived inability to analyze and solve problems rapidly and efficiently.

Performance on the projective measures such as the Children's Apperception Test was characterized by significant external locus of control themes. That is, his responses suggested that he perceived his current situation as something over which he had no control, he was unable to deal with environmental events, and he viewed the world as in control of him. Tension, anxiety, and frustration were also common themes in his projective responses.

On the Quick Neurological Screening Test – Revised, the student's pre – treatment profile fell well within the normal limits range in all categories. However, following treatment, he reported flashing lights in his visual fields, dizziness upon standing, feeling tired during the day and after school, periodic ringing in his ears, and distractibility as well as difficulty concentrating in school. All of these symptoms are consistent with previous research characterizing late effects among children previously treated for acute childhood leukemia receiving chemotherapy as CNS prophylaxis (Brown, et al., 1998).

The subject indicated that sometimes he knew that his answer was not correct, but he could not explain why he gave his answer, felt confused, and became increasingly frustrated with his perceived inability. Furthermore, when reading, he would periodically delete or add words which would alter the meaning of a sentence or paragraph. For example, in reading, "See the black dog. He is a famous winner of dog shows." he would read, "See the black dog. He is a famous winner of a dog show. Frequently, his cognitive performance was characterized by organizational difficulty as well as word finding and naming problems, pronunciation errors, auditory processing difficulty, and at least mild to moderate impulsivity.

## DEVELOPING A TREATMENT PLAN

As the team considered how to address the student's unique needs, provide ongoing monitoring of his progress, and begin to plan for his life in the upper grades and beyond school, it was critical that each member was aware of the types and importance of information generally available from family, school officials, the legal system, and community service agencies, as well as the sources of unique services, networks, and organizations for individuals with disabilities including career, vocational and transitions support. It was important that the team emphasize modes of interaction, goal setting, and collaboration across disciplines with continuous feedback. In addition, the team sought to ensure that the treatment plan developed was consistent with recommendations of

the Leukemia and Lymphoma Society and was designed to address changes in course and testing requirements including state mandated standardized evaluations. Specifically, accommodations to his IEP included:

- Educating the school community regarding the nature of health and raising awareness of the possibility of subtle, late-effects
- One-on-One resource services to address reduced processing speed in reading, speech, writing, and language
- Untimed testing
- Provision of a day-planner to assist with organization of school tasks and leisure activities
- Weekly communication between parents and school
- Monthly team meetings, including the participation of the neuropsychologist
- Access to the school nurse as needed
- Rest breaks as required throughout the school day
- Provision of a duplicate set of school texts to minimize fatigue as well as address memory deficits
- Provision for additional 'snacks' during the school day
- Provision of a clear and predictable schedule of current as well as future assignments for the subject and his parents
- Additional time to examine, organize, and check homework assignments
- Allowance for a shortened school day if necessary
- Modification of school work and homework to reduce cognitive overload
- Provision of anti-bacterial cleansers for work surfaces as well as Recognition of absences or illness as a possible late-effect
- Provision of in-school tutorials if the need is perceived by the subject, teachers, and/or parents
- Access to computer-generated attention and memory stimulation at school and at home
- Instruction in self-management strategies so that could begin to monitor his own progress during learning and social tasks

In addition, the Cognitive Remediation Program (Butler & Copeland, 2002) was incorporated into his treatment plan and emphasized the 50-80 rule in all areas of remediation. If he was not able to obtain a 50 percent level of responding to a task, the activity was substituted with a more basic task. Once 80 percent accuracy was achieved, the next level of task difficulty was reintroduced.



Encouragingly, after one year of intervention, follow-up neuropsychological testing revealed reduction in, or stabilization of, the late effects observed following two years of CNS chemotherapy. As noted in Table 1, three years after initial assessment, including two years of chemotherapy and one year implementation of the collaborative treatment plan, analysis of the student's test scores revealed a verbal comprehension score which remained stable, as did perceptual reasoning. However, overall full-scale I.Q. increased primarily because of significant improvements in short and long-term memory, attention and concentration, and processing speed.

## CONCLUSION AND RECOMMENDATIONS FOR PRACTICE

This study provides a unique view into the comprehensive and collaborative assessment and intervention processes needed by all educators working with children impacted by CNS chemotherapy, particularly if students are potentially evidencing the late effects such treatment often brings. The neuropsychological profile is consistent with those seen in other more extensive research studies published before the impact of late-effects was considered a viable research option.

These findings provide evidence for the importance of a strong, transdisciplinary partnership, including meaningful and sustained communication between general and special educators, parents, as well as medical, counseling, and psychological professionals (Friend & Cook, 2007; Turnbull, Turnbull, Erwin, & Soodak, 2006). The significance of family cohesiveness, and assisting the student in monitoring his own behavior and perceived needs were also determined to be instrumental in the remediation process (Reid, 1999). All members of the multi-disciplinary team were actively engaged in the collaboration process, thereby resulting in a positive educational outcome that addressed the subtle medical, academic, cognitive, psychomotor, physical, emotional and social challenges which might not otherwise have been identified, and for which an appropriate treatment plan could be developed.

Finally, it was recognized by the multi-disciplinary team that late-effects may necessitate reconsidering all aspects of transitioning, not only from elementary school to middle school, but from middle school to high school, high school to post-secondary education, and even post-secondary education to adult employment. Recent data (Carmichael, 2008) indicate that childhood cancer survivors as a group are four times more likely to find no employment opportunities than do healthy individuals.

## IMPLICATIONS AND FUTURE RESEARCH

Since the passage of the No Child Left Behind Act in 2002, educators

have become increasingly aware of accountability and data-driven decisions, including requirements that instruction be based on scientifically researched data. Although the sample size was one, the data analyzed comprised a longitudinal, descriptive, single case study which included quantitative as well as qualitative data collection at multiple time points. In this study, we attempt to address what Guba and Lincoln (1989) and Jason and Rogers (2001) require as appropriate standards for judging the soundness of non-statistical research. That is, the extent to which the findings can be considered credible, transferable, dependable, and confirmable. While the in-depth findings are not generalizable, nor are they necessarily being offered as representative or explanatory of a particular population, they are informative to educators and families working in teams to address the specialized needs of students evidencing late-effects, and for whom a collaborative approach is critical and beneficial. Moreover, the inclusion of multiple sources of data, multiple measures at various intervals prior to and following treatment, as well as the inclusion of multiple voices in treatment planning all lend to the credibility and trustworthiness of the findings.

It was hypothesized that after two to three years of therapeutic chemotherapy for childhood leukemia, the student's subtle late effects that are also noted in the literature could be evaluated by establishing neuropsychological baseline data. An analysis of individual scores as well as normative test results is necessary for evaluating and addressing appropriate intervention strategies. The use of normative data alone limits both the interpretation and generalization of findings. Baseline data provide an opportunity to evaluate the presence or magnitude of any changes in evaluation measures following treatment.

The necessity of using baseline data was emphasized in a study (Berry, Caldwell, Zolten, & Spence, 1992) conducted on monozygotic twins, one of whom was diagnosed with childhood leukemia. No baseline data was gathered, but after chemotherapy, the treated twin subsequently displayed late effect symptoms associated with abstract reasoning skills. The authors argued for a baseline assessment as well as continued monitoring of neuropsychological functioning following treatment. Future investigations should replicate the procedures utilized in this study in order to corroborate the dependability and confirmability of the findings, and additionally should be extended to compare childhood leukemia patients who received chemotherapy alone as well as with irradiation. While it would be improbable to establish neuropsychological baseline data in traumatic brain injury cases, it would be appropriate as a precondition prior to treatment for all cancers, central nervous system tumors, and whole body irradiation prior to bone marrow or stem cell transplantation. Finally, the introduction of another "test" for any of these highly emotional situations requires increased sensitivity on the part of the examiner for the

child as well as his/her family.

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