In 1925, Thomas Cooley and Pearl Lee reported a severe form of anaemia occurring in children of Italian origin, which was characterized by splenomegaly and distinctive bone changes. The disease was later termed "thalassemia", derived from the Greek word thalassa, meaning sea, because all early cases were reported in children of Mediterranean origin.

Today, the β-thalassemias are found throughout the Mediterranean region, Africa, the Middle East, the Indian subcontinent, Southeast Asia, the Malay Peninsula. Within these regions, gene frequencies can range anywhere from 3 to 10 percent. Although the incidence and prevalence of this disorder occurs less frequently in North America, with increasing immigration from the above regions, the rates are expected to rise.

Clinical management of this disorder has improved significantly in recent years. With this advancement came new demands on the adolescent patient for adherence with a more complex treatment regime. Studies have shown that as adolescents mature and strive for independence and a sense of normalcy, desferrioxamine treatment is seen as a significant barrier to these processes and thus, they do not always adhere to the treatment regimen. Similarly, advances in treatments have placed new demands on health care professionals to optimize adolescents’ compliance. The most powerful predictor in compliance of adolescents with chronic illnesses is support from nurses. Nurses are in a unique position to identify and work with adolescents who are struggling to comply with their treatments. Furthermore, compliance is significantly improved when health care professionals work in collaboration with adolescents and encourage them to participate in decisions regarding their treatment regimens in order to improve compliance rates.

The pathophysiology of β-thalassemia

Beta-thalassemia is a genetic disorder in which there is a total absence (βº thalassemia) or decreased synthesis (β+ thalassemia) of the β-globin chain of hemoglobin, resulting in severe anaemia. An individual who is heterozygous for β-thalassemia has very mild anaemia and hypochromic microcytic red cells. Interestingly, there is evidence that heterozygotes of β-thalassemia have a protective advantage against Plasmodium falciparum malaria, thus explaining the high frequency of this genetic disorder in the tropics.

When an individual is homozygous for β-thalassemia (β-thalassemia major), he/she will present with severe anaemia requiring lifelong chronic blood transfusion therapy. A hypochromic anaemia results due to the decreased levels of absence of adult hemoglobin (Hb A). A hemolytic anaemia
develops as a result of the excess alpha chains in the red blood cells that remain unbound from the scant β chains. In response to these hemoglobin alterations, erythropoiesis may be increased by as much as ten-fold; however, more than 95 percent of the hemoglobin may be ineffective. As a result of the ineffective erythropoiesis, erythroid marrow expansion occurs as much as 30 times the normal levels. Marrow hyperplasia eventually leads to increased iron absorption and continual deposition of iron in tissues.

Clinically, β-thalassemia major is recognized during the first year of life. Afflicted infants present with pallor, failure to thrive, hepatosplenomegaly and anaemia. Linear growth and weight gain are delayed.

**TRANSFUSIONAL THERAPY FOR β-THALASSEMIA AND ITS SIDE EFFECTS**

When the diagnosis of β-Thalassemia is made, therapy consists of education, counseling and red blood cell transfusions. Transfusion therapy usually starts during the first year of life when hemoglobin levels are less than 60 g/L. Transfusions are usually given monthly and once begun, the hemoglobin is maintained at 90-100 g/L; one complication of this therapy is iron accumulation. One milliliter of transfused packed red blood cells contains approximately 1 mg of elemental iron. As a result, transfusional therapy can add 2 to 5 grams of iron each year to the body. Normal nutritional absorption of iron in a non-affected individual is 0.5 grams per year. There is no physiologic way of eliminating excess iron, and iron accumulation occurs.

After a year of transfusion therapy, iron begins to be deposited into parenchymal tissues, causing substantial toxicity. As iron loading continues, iron binding and iron storing proteins become saturated. Non-transferrin bound iron (NTBI) or “free iron” begins to accumulate. It is theorized that NTBI participates in the generation of hydroxyl radicals, which then partake in oxygen free radical mediated damage. These free radicals cause lipid peroxidation, cellular damage, and eventual cell death. As a result, “free iron” can initiate widespread tissue damage in numerous organs including the heart, liver, spleen, pancreas and brain. As illustrated, the use of red blood cell transfusions in the treatment of β-thalassemia has brought forth new complications that must be managed.

**THE TREATMENT OF IRON OVERLOAD**

The most significant complication of red blood cell transfusion is increased iron burden. This is a major focus of clinical management. In patients who are not receiving transfusions, abnormally regulated iron absorption results in as much as 2 to 5 grams of iron accumulating within the body every year. Monthly blood transfusions can double this iron burden. Clinical complications as a result of iron deposition include liver failure, arrested sexual development, hypothyroidism, cardiac failure and arrhythmias. It is not until the second decade of life that clinical manifestations of toxicity occur. However, serial liver biopsies in children have shown that iron disposition in vital organs occurs early in life, due to the continual need for transfusions.

In an attempt to reduce these complications, the iron-chelating agent desferrioxamine (Desferal) was introduced in the mid 1970s. This drug is specific for the removal of iron from both the parenchymal and reticuloendothelial cells, and causes the excretion of iron from the body in the urine and bile. Subcutaneous infusion administered with a battery powered syringe pump over a period of 8 to 12 hours at night, 5 to 7 days per week, has become the gold standard of treatment. A patient using subcutaneous Desferal will achieve a negative iron balance within a few years, depending on the severity of iron-overload. The success of this treatment depends upon an individual’s strict compliance. In children who are striving for autonomy from their parents, acceptance from their peers and in the midst of developing their own identity, compliance with chelation therapy is not always optimal.

**COMPLIANCE IN INDIVIDUALS WITH CHRONIC ILLNESS**

The traditional concept of compliance has been criticized due to its connotations of paternalism, coercion and acquiescence. Alternative concepts have been suggested in the literature such as adherence, co-operation, mutuality, and therapeutic alliance. More recently, compliance has been redefined as an active, intentional and responsible process of care, in which the individual works to maintain his or her health in close collaboration with the health care personnel. This definition stresses the individual’s active commitment to care, instead of solely focusing on the individuals’ ability to follow the medical instructions.

Research into adolescent compliance has identified several factors that contribute to and detract from effective compliance. Several of these include the relationship between the adolescent and their families, the characteristic of the disease and the characteristics of the treatment regime. First, compliance has been found to be greater when the adolescent and or the parent have fully understood the susceptibility to and the seriousness of the illness, when the individual is knowledgeable surrounding his/her illness and the benefits of the therapeutic regime. Second, studies have shown that compliance is inversely related to the complexity of the therapeutic regimen, the duration, and the frequency of the therapy itself. Third, the perceived financial, physical and psychological cost of treatment compared to the benefits received weigh on the compliant behaviour of the individual. Fourth, family support is regarded as a central factor in the compliance of adolescents with a chronic disease. Family variables, such as a positive family climate and open relationships between the family members, are related to good compliance. Close relationships help children build their identity and competence. On the other hand, family instability has an unfavourable influence on the adolescent’s adherence to treatment. Finally, close relationships with friends are an important source of support for chronically ill adolescents. During this time, adolescents distance themselves from their parents to align themselves with their peers. Adolescents may have conflicting feelings about their parents because they still rely on their parents for support,
yet seek to distance themselves and gain independence.\textsuperscript{30,31}

**COMPLIANCE WITH CHELATION THERAPY IN INDIVIDUALS WITH β-THALASSEMIA**

Numerous studies have examined compliance in children with mainstream disorders such as diabetes, epilepsy, and asthma.\textsuperscript{22,26,30,32,33} Fewer studies have examined compliance in the child afflicted with β-thalassemia.

Vullo \textit{et al.}\textsuperscript{34} reported that compliance with chelation therapy had a significant positive correlation with participation in group conferences, parents level of education, and high socioeconomic status. This finding supports the notion that health care workers must look beyond the individual when examining non-compliant behaviour and also direct attention to the external factors, such as family dynamics and socio-economic status, as these aspects may be contributing to adolescents’ non-compliant behaviour.

The investigators initiated a program to improve compliance, which included both physician and patient education and the administering of calendars to adolescents to help them keep track of their treatment schedule. This regulated approach revealed a decrease (20% to 3%) in the number of individuals who refused therapy over a period of three years.\textsuperscript{34} One significant drawback to the study was that the investigators only focused on factors at the level of the individual when developing this program (i.e., education and a calendar to remind the adolescent when to administer chelation), rather than implementing a program to facilitate improved family relations or the strengthening of support networks.

A second study of 113 patients with homozygous β-thalassemia examined non-compliance in these individuals and their psychiatric health.\textsuperscript{28} Non-compliance was defined as patients who took less than 60% of the recommended desferrioxamine dose during the study period. The investigator found that 31 (27.5%) of the sample was non-compliant with chelation. Of these, 21 fulfilled the criteria for the presence of one or more personality disorders. The frequency of these psychiatric disorders was 68% for the non-compliant group and 10% for the compliant group. In 17 of the 21 patients with personality disorders, the disorder was present prior to the onset of non-compliance. The most frequent personality disorder associated with non-compliance was oppositional disorder and those affiliated with this disorder demonstrated the most profound deviation from compliance.

In the first years of life oppositional behaviour is an expression of growing autonomy of the child and an attempt to define ego boundaries. In certain children, this process does not evolve smoothly and they continue to use defiance as a way of asserting their boundaries and as a defense against dependency needs, resulting in oppositional behaviour disorder. The investigators speculated that the syringe pump is a constant reminder of a dependency state and a pull toward earlier and more passive levels of development, which the adolescent wants to reject and hence, the reason why non-compliance is greater in these adolescents.\textsuperscript{28}

The presence or absence of symptoms in relation to missing therapy also appears to be related to compliance.\textsuperscript{35} When blood transfusions are missed, there is a drop in hemoglobin levels. This results in the immediate onset of physical symptoms. When chelation therapy is missed, there is not an immediate onset of physical symptoms. This may explain the high compliance to blood transfusions and the lower compliance with chelation therapy.

A study by Ahmad and Atkin\textsuperscript{35} examined the understanding of young people’s experience of living with thalassemia with the broader context of growing up, by conducting semi-structured interviews with 25 young people between the ages of 10 and 19. All those over the age of 13 had failed to comply with chelation therapy at some stage and for those between the ages of 13 and 16, non-compliance was more common than compliance. For those under 12, chelation remained a parental responsibility and they did not reflect on the effects that the treatment regime had on their sense of normalcy. Three-quarters of the adolescents remarked that they hated using the pump and they felt symbolically and physically tied to it, as chelation therapy dominated their life. In the majority of cases, the older children hated chelation therapy because it marked out their difference from their peers. A sense of difference exercises an important influence on their identity and individuals of this age group dislike anything that suggests divergence from acceptable youth culture.\textsuperscript{32} The inability to separate oneself from chelation therapy has contributed to sadness and depression amongst the interviewed subjects as they were unable to be normal like their peers.

As adolescents afflicted with thalassemia struggle to establish their identity, the process can contribute directly to non-compliance as they reject others’ definitions of their problems.\textsuperscript{35} This process acts as a double-edged sword. Young people had to face the dilemma of how to reconcile a wish for independence with the threat of increased illness-related dependence. Those over 13 years of age felt more dependent on their parents than their peers and did not have the ability to make choices that were presented to their peers. This threat-
ened their sense of independence and explained why they disliked constant reminders about the value of their treatment by their parents. This may explain why non-compliance was especially high for those aged 13-17, an age when status transition is occurring and when they begin to take responsibility for their own treatment. Several individuals recounted upsetting comments from their peers on the use of chelation therapy, which made them feel ashamed and undermined their efforts to be normal. These experiences reduced compliance with chelation therapy.

In establishing a balance between well-being and independence, an adolescent’s coping strategies are important. In adolescence, these coping strategies may be vulnerable and at times they may be overwhelmed by the difficulties they face in striking this balance. The greater the sense of being overwhelmed, the more likely they are to reject chelation therapy. As the young person gains his/her independence, they begin to assume more responsibility for their own care. For many, the pump quickly became a chore as well as a symbol marking out their difference. This can lead to a feeling of estrangement and consequently, the recommended dosing schedule is no longer followed by these individuals.

The responses of these young people appear no different from other children who have an equally demanding medical regimen and many of the difficulties leading to non-compliance seem common to other chronic illnesses.

THE ROLE OF NURSES FOR CLIENTS WITH β-TALASSEMIA

Given these challenges to compliance, it is important to look towards health professionals for support in improving compliance. Nurses are in contact with adolescents and their families at various times, including education sessions, adolescent and family counseling sessions, routine follow up visits to hematology clinics and when the adolescent requires transfusional therapy. As a result, nurses are in a key position to provide emotional support to adolescents, facilitate family support, encourage active participation in their own care, provide holistic care and are in a position to develop and facilitate support groups for adolescents. A study by Kyngas found the most powerful predictor in compliance of adolescents with chronic illnesses is support from nurses which included their role of educator, counselor and by providing encouragement and praise. The likelihood of adolescents supported by nurses complying with health regimens was 7.28-fold compared with those who did not receive support from nurses. Clearly the role of nurses is deserving of increased attention.

Adolescents afflicted with β-thalassemia undergo normal developmental crises similar to all adolescents. The severity of these crises may be heightened because of the barriers that are experienced by these adolescents due to their illness. In the context of such struggles, nurses and health care providers are well positioned to provide encouragement, and positive feedback as adolescent’s struggle to manage their chronic illness and normal developmental crises. Several ways in which nurses can contribute to compliance are outlined here.

As family support is also a strong predictor of compliance, nurses should involve the family in care whenever possible. It is also necessary to ensure that the involvement of family members and their role is acceptable to the adolescent. The care of a thalassemic adolescent is negotiated within the context of family relations, obligations and reciprocities. Compliance in adolescents with thalassemia can be a specific source of disagreement between parents and the adolescent. This can be a result of the adolescent’s attempts to assert his/her sense of independence and control over their own health. The nurse can act as facilitator to help determine the family’s role in the care of the adolescent that is acceptable to both the adolescent and the involved family members.

Contingency contracting, whereby subjects and investigators together determined target increases in the number of days subjects would undergo chelation treatment, was found to be successful in 76% of subjects over a 6 month period. Sixty-nine percent of subjects maintained improvement in adherence over a 2 month period after the program. The use of contingency contracting is thought to optimize the perception of self responsibility for behaviour, and feelings of competence. These factors are essential for long term adherence. A collaborative framework is created by the contract whereby realistic goals are set together by the adolescent and healthcare worker.

Nurses are in key position to develop these contingency contracts with adolescents in order to improve compliance rates. It is interesting to note that in this study, the very act of monitoring behaviour may have improved adherence, due to the fact that the majority of adolescents (18 of 23) received no tangible reinforcers during the 6-month study period. This suggests that the focused attention on the desired healthy behaviour and support from the health care worker involved in the study was itself reinforcing of the behaviour. In practice, nurses can develop their own reward systems with adolescents.

As seen in contingency contracting, discussion between adolescents afflicted with β-thalassemia and nurses helps to establish a mutual understanding that aims at the negotiation of a contract of management between caregiver and adolescent. Since adolescents often feel that their illness and chelation therapy impedes their progress into adulthood, it is necessary to negotiate with them and give them some authority to alleviate these feelings. Nurses can encourage adolescents to actively participate in decisions regarding the care and treatment regimens. In doing so, nurses can help the β-thalassemia individual become more committed to treatment decisions and increase their autonomy, thus resulting in the attainment of higher levels of compliance.

As caregivers to adolescents with β-thalassemia, nurses must remember that they also have other needs, personal priorities and social roles (e.g. student, family member, peer member, etc.), which they want to be recognized in their care. Nurses must maintain holistic care and recognize that β-thalassemia and its treatment only constitute one aspect of the individual’s life. Customized treatment plans are necessary to ensure that treatment accommodates all aspects of their life.

Mental health is an important factor that effects compliance.
One study demonstrates that the presence of oppositional disorder and other personality disorders makes it more likely that the thalassemic adolescent will express negative attitudes towards compliance and become non-compliant with the recommended treatment. Nurses need to assess the mental health of those in their care and identify those adolescents who exhibit characteristics of these personality disorders. When mental health problems are identified, psychiatric intervention may be necessary to prevent, decrease or stop non-compliant behaviour.

Additionally, nurses may get involved by helping to organize support groups for adolescents, thus providing an opportunity for them to share the burden of their illness. These support groups would allow them to see how others cope with their parents, their peers, as well as with their fears and how others struggle with compliance and what strategies they employ to overcome non-compliance. Healthcare providers could help adolescents with β-thalassemia to organize support groups.

**CONCLUSION**

The advancement in treatment for children afflicted with β-thalassemia has brought with it an improved quality of life and an increased lifespan for those who follow the recommended treatment regimen. During their adolescent years, young people are striving to develop their own self-identity, their independence, and are attempting to gain a sense of normalcy. The use of chelation therapy to control iron-overload in adolescents is often seen as a hindrance by these individuals for achieving these developmental goals and thus, compliance may be diminished. Nurses are in a unique position to provide support, to analyze factors that are contributing to non-adherence and to work with the adolescent to enable them to follow the recommended treatment regime, while ensuring that the adolescent continues to establish independence and a sense of normalcy. Opportunities exist for nurse researchers to examine the factors that lead to compliance and non-compliance and for the development and evaluation of programs and strategies to increase compliance rates in this population.

**REFERENCES**


**Author Biographies**

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The Peterborough Regional Health Centre (PRHC) is nestled in the picturesque Kawartha Lakes Region. The Kawarthas offer a unique and diverse range of natural wonders, cultural activities, and countless destinations to explore. Within an hour’s drive of the GTA, Peterborough is a family-oriented community where you can enjoy golfing, boating, horseback riding, hiking, and cycling.

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